The Japanese Imaging Guideline

2013

Japan Radiological Society (JRS)
Japanese College of Radiology (JCR)
Joint committee for The Japanese Imaging Guideline 2013

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General statements
Diagnostic imaging is undoubtedly important in modern medicine, and final clinical decisions are often made based on it. Fortunately, Japan has the highest numbers of diagnostic imaging instruments such as CT and MRI devices, and boasts easy access to them as well as a high level of diagnostic accuracy. In consequence, a very large number of imaging examinations are performed, but diagnostic instruments are installed in so many medical facilities that expert management of these examinations tends to be insufficient. Particularly, in order to avoid risks, clinicians have recently become indifferent to indications of imaging modalities and tend to rely on CT or MRI resulting in increasing the number of imaging examinations in Japan. This is a serious problem from the viewpoints of avoidance of unnecessary exposure and medical economy.

Under these circumstances, the Japan Radiological Society and Japanese College of Radiology jointly initiated the preparation of new guidelines for diagnostic imaging. However, the field of diagnostic imaging is extremely wide, and it is impossible to cover all diseases. Therefore, in drafting the guidelines, we selected important diseases and focused on “showing evidence and suggestions in the form of clinical questions (CQs)” concerning clinically encountered questions and “describing routine imaging techniques presently considered to be standards to guarantee the quality of imaging examinations”. In so doing, we adhered to the basic principles of assuming the readers to be “radiologist specializing in diagnostic imaging”, “simultaneously respecting the global standards and attending to the situation in Japan”, and “making the guidelines consistent with those of other scientific societies related to imaging.

As a result, the guidelines became the largest ever, consisting of 152 CQs, 9 areas of imaging techniques, and 7 reviews, but no other guidelines in the world summarize problems concerning diagnostic imaging in the form of CQs. In this sense, the guidelines are considered to reflect the abilities of diagnostic radiologists in Japan. The contents of the guidelines are essential knowledge for radiologists, but we believe that they are also of use to general clinicians and clinical radiological technicians. While the number and contents of CQs are still insufficient, and while chapters such as those on imaging in children and emergency imaging need to be supplemented, the guidelines will be serially improved through future revisions.

Lastly, we would like to extend our sincere thanks to the 153 members of the drafting committee who authored the guidelines, 12 committee chairpersons who coordinated their efforts, 6 members of the secretariat, and affiliates of related scientific societies who performed external evaluation.

Yasuyuki Yamashita
Evidence levels and recommendation grades

Introduction

In this chapter, a general appraisal of the level of evidence and grading of recommendations are presented. In addition, the policy of our committee in dealing with problems encountered in the actual process of the guideline development are explained.

Basic principle of evidence ranking schemes and study design of research papers in the field of diagnostic imaging

Generally, the study design is regarded as an important factor in evidence appraisal. Randomized controlled trials (RCT) with blinding are ranked as the best evidence because of their research design least affected by biases. According to the Minds (Medical Information Network Distribution System) Guide for developing Clinical Practice Guidelines 2007 of the Japan Council for Quality Health Care,\(^1\) the evidence level is highest for systematic reviews (including meta-analyses) summarizing the results of multiple RCTs, followed by (1 or more) RCT, non-randomized controlled trials, and analytical or epidemiological studies such as cohort studies and case-control studies.

However, the RCT is a rare research design in the field of diagnostic imaging (except for clinical questions on mammographic screening for breast cancer and a few other topics). Cohort studies are also rare. In diagnostic imaging, cross-sectional studies are common since the diagnostic ability (performance of the examination compared with a reference standard e.g. sensitivity/specificity) of the modality at the time of the study is considered important. Conventional classifications of evidence were designed for clinical studies of treatment, and papers in the field of diagnostic imaging tended to be underreated due to difference in study design described above. The Oxford EMB Centre (OCEBM) proposed a method to evaluate and classify evidence according to clinical questions.\(^2\) In this classification, evidence is evaluated by classifying clinical questions into different categories such as treatment, diagnosis, and screening. There was also an assessment method specific to diagnostic procedures, which may be applied to papers on diagnostic imaging. While the early version was difficult to use, a recent revised version was based on the concept that “the common research design on diagnosis is the cross-sectional study”, and the assessment method finally became a feasible one. Due to the absence of other relevant classification methods, the present guidelines were developed on the basis of the OCEBM Levels of Evidence.

Practical steps for evidence level appraisal

The classification workflow can be summarized as follows (See table for details).

1) Systematic reviews of level 2 studies are classified as level 1.
2) Among cross-sectional studies, those performed with consecutive sampling, consistent reference standard, and blinding are classified as level 2, that is the highest evidence level for individual studies.
3) Among cross-sectional studies, those that cannot be classified as level 2 due to problems in study design (e.g., inconsistency of the reference standard) are classified as level 3.
4) Case-control studies are classified as level 4.

The OCEBM Levels of Evidence were introduced primarily to help busy clinicians to appraise evidence quickly. They are not suited for detailed assessment of evidence and may not be appropriate for the development of guidelines. The particular issues raised during guideline development using the OCEBM Level of Evidence, and our solutions are listed below.

1) Papers not focusing on imaging findings and those without a reference standard, e.g., those on technical improvements, could not be evaluated.

Many papers directly related to clinical questions used some reference standard, but some papers necessary for the understanding of recommendation grades deal with are technical matters. Such papers were included as references but were not assigned an evidence level.

2) There was no mention about the level appropriate for systematic reviews/meta-analyses that collected multiple level 3 or 4 studies (cross-sectional studies that cannot be classified as level 2 due to inconsistency or ambiguity of the reference standard or lack of consecutive selection of research subjects).

The evidence level of systematic reviews/meta-analyses, which are based on multiple pieces of evidence, is considered to be higher than that of individual papers, but it is affected by evidence levels of the original papers reviewed. In principle, the lowest evidence level of the papers included in the review was determined, and the level 1 grade higher than the lowest level was given to the systematic review/meta-analysis paper.

3) Regarding the research quality, consecutive sampling, consistency of the reference standard, and blinding were included in the evidence table, but other criteria (such as ambiguity of the exclusion criteria) are not mentioned in the table. In this guideline development, priority was given to consistency of standards for leveling, and the evidence level was not changed, in principle, on the basis of items not included in the evidence table. However, items that were not
included in the criteria for evidence leveling but were considered to important (such as the difference in the research subjects from those mentioned in the CQ) were taken into consideration in the determination of the recommendation grade.(* the following footnote is added on the original OCEBM evidence level table; levels may be graded down on the basis of study quality, imprecision, indirectness, because of inconsistency between studies, or because the absolute effect size is very small).

(4) There were several reference standards, and their accuracy varied. For example, the accuracy is considered to differ between pathological diagnoses using surgical samples and those using biopsy samples. If the reference standard varies among reports, how the results should be evaluated? Generally, the diagnostic ability of biopsy is lower than that of surgery. However, the possibility of bias is considered to increase with the lack of consistency of the reference standard. Therefore, in our guideline development, priority was given to the consistency of the reference standard, and the evidence level was not lowered due to the use of biopsy as the only reference standard if it was commonly used.

### Determination of recommendation grades

The recommendation grades were determined according to the Minds Guide for developing Clinical Practice Guidelines 2007 mentioned above (Table 2). It considers not only the evidence level but also the number of studies, variation in conclusion, magnitude of clinical efficacy, clinical applicability (ability of physicians, regional characteristics, medical resources, medical insurance system), and harms and cost. Particularly, in diagnostic imaging, availability of diagnostic instruments were also taken into consideration as medical resources. In addition, factors that were not in the evidence level table but were considered to affect the quality of evidence (mentioned in (3) of the previous section) were also evaluated in the determination of the recommendation grade.

There are particular situation requiring special consideration. Some examinations that have been used for ages, diagnostic modalities themselves were used as reference standards for the diagnosis, and there have been no study comparing them with surgical/clinical findings, or, if there are such studies, they were performed before the the concept of EBM became popular and were of low quality. For example, the evidence concerning the usefulness of CT for the staging of kidney cancer is unexpectedly scarce, but the modality is in wide clinical use and is recommended in overseas guidelines. We decided that CT was considered recommendable and graded as A. Some fields with limited number of evidence, grading was made by members of each subcommittee.

Subjective elements could not be completely excluded, but we aimed to determine recommendation grades appropriate for the current clinical setting in Japan while based on evidence as much as possible.

The above is a summary of the policy of this committee in evidence level appraisal and recommendation grades in developing the present guidelines. The methods to evaluate evidence and to develop guidelines concerning diagnostic imaging may change in the future with changes in the study quality. We selected the methods that were considered to be the most feasible and valid at present.

### References


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<th>Level 1</th>
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<th>Level 3</th>
<th>Level 4</th>
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<td>Individual cross sectional studies with consistently applied reference standard and blinding</td>
<td>Non-consecutive studies, or studies without consistently applied reference standards standard</td>
<td>Case-control studies, or poor or non-independent reference</td>
<td>Mechanism-based reasoning</td>
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<tr>
<td>B</td>
<td>There is scientific evidence recommending the procedure</td>
</tr>
<tr>
<td>C1</td>
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</tr>
<tr>
<td>C2</td>
<td>There is no scientific evidence, and the procedure is recommended.</td>
</tr>
<tr>
<td>D</td>
<td>There is scientific evidence suggesting ineffectiveness or harm, and the procedure is recommendated.</td>
</tr>
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</table>
About MINDS

- MINDS (Medical Information Network Distribution Service) is an information service provided by the Japan Council for Quality Health Care (JCQHC), a public interest incorporated foundation.
- The MINDS project has been financially supported by the Ministry of Health, Labor and Welfare of Japan since its inception in 2002 through a Grants-in-Aid for Scientific Research from 2002 to 2010 and as a consignment project since 2011.
- The aim of MINDS project is to help medical practitioners to fully utilize the information related to the evidence-based medicine (EBM) in their practice. MINDS also provides patients and the public with information to help understand the basics of diseases and to share with their practitioners the up-to-date evidence, on which modern medical practices are based.
- MINDS functions as a guideline clearinghouse; clinical practice guidelines developed in Japan are formally evaluated by the guideline evaluation committee, and only those guidelines which meet with the quality standard are disseminated through the MINDS website.
- Some guideline developers have translated their guidelines into English to share with medical professionals abroad, and on this page, MINDS provides these English-translated clinical practice guidelines developed in Japan.
Introduction

CT and MRI play important roles in diagnostic imaging. The development of imaging devices and new imaging technology/methods has continued uninterrupted, but an involvement of physicians specializing in diagnostic imaging is necessary to draw out optimal performance, and make sufficient clinical use, of modalities. In Japan, however, many CT and MR systems are operated in the absence of a radiologist. Moreover, this tendency has shown no improvement for 10 years since the beginning of the survey.\(^3\)

In Japan CT or MR systems are introduced by the judgment of medical organizations, and no political measures have been taken about the arrangement or installment conditions of medical instruments. As a result, the numbers of CT and MR systems per population are markedly higher than in foreign countries, and 60-70% of them are in operation in the absence of a radiologist. The number of CT or MR examinations in Japan is also high on a global basis. Therefore, it is necessary to ensure the appropriateness of the implementation of imaging studies and reduce negative elements of imaging including radiation exposure.

In this chapter, the state of CT and MRI in Japan is compared with that in foreign countries, and its background is presented.

Comparisons between Japan and foreign countries

Some characteristics of medical imaging in Japan are clarified by comparison of the numbers of operating systems and examinations with those in foreign countries. Although data concerning foreign countries are limited, the OECD Health Data are frequently updated and informative. Although the latest edition is OECD Health Data 2011,\(^2\) the values shown in the 2009 edition were used, because the numbers of both systems and examinations were available. Data not found in the OECD 2011 were supplemented from References 3 and 4 concerning Japan, and the latest values shown by the OECD were used concerning foreign countries (4 countries) (Table 1).

1) Number of systems

In Japan, data concerning the number of CT systems are often limited to those about MDCT, but the number per 1 million population is highest among 27 countries (54.9 vs. a mean of 21.1). Actually, a considerable number of SDCT systems are in operation in Japan. According to the latest survey of medical facilities, the number of SDCT systems was 6,360 in 2008, and the sum with 6,060 MDCT systems was 12,420.\(^5\) This means there were 97.4 CT systems per 1 million population, which is about 5 times the mean of various countries. The number of MR systems per population is the highest among 26 OECD countries (46.8 vs. a mean of 12.4\(^\ast\)).

2) Number of examinations

Data for the number of examinations are available for smaller number of countries. The number of CT annual examinations per 1,000 population in Japan was the 6th among 17 countries (146 vs. a mean of 122), and that of MR examinations was the 4th (68 vs. a mean of 45). Japan belongs to the group with a high number of examinations, but the number is not impressive, considering the very high number of systems (Figure 1).

3) Utilization - Number of annual examinations per system

Annual examinations per unit can be considered to be an index of utilization. It could be compared among 15 countries. Contrary to the highest number of units, utilization of CT and MR in Japan was reverse in rank of the number of existing systems. Concerning CT, it was the 3rd from the lowest for MDCT alone (2,662 vs. a mean of 6,730 examinations/system) and by far the lowest when SDCT was included (1,500 examinations/system). Regarding MR, the utilization was the second from the lowest (1,447 vs. a mean of 4,665 examinations/system). For both CT and MR systems, the utilization was about 1/3 of the mean of foreign countries and near the bottom.

Details of the situation of CT and MR imaging in Japan

In part 1, gross data regarding CT and MR, which can be compared easily among countries, were evaluated. Here, the state CT and MR imaging in Japan is analyzed into some more detail.

1) Relationships with specialists in diagnostic imaging

The percentage of facilities equipped with CT or MR system with specialists in diagnostic imaging has shown no overall improvement since 2004, when the survey was initiated. Only about 1/3 of the MDCT systems and 1/3 of all MR systems are managed by specialists in diagnostic imaging, i.e., 2/3 of the MDCT and MR systems were operating without the regular presence of specialists in diagnostic imaging.\(^3\) In addition, there were wide differences in the percentage of facilities with specialist among machine types (Figure 2). Images are read by specialists in diagnostic imaging, but the percentage of CT and MR images read is estimated to be 43% from the number of additions of the reimbursement of medical fees for the management of imaging diagnosis.\(^5\) However, the true figure is considered to be even lower, because while the examinations are included in the DPC, the addition for the management of imaging diagnosis is not.
Table 1 Numbers of CT and MR unit, examinations, and, examinations per unit

<table>
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<th>Population (thousands)</th>
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<th>Exams/year/1,000 population</th>
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[Note 1] The data concerning foreign countries were cited from the OECD Health Data (primarily the 2009 edition), those concerning the number of systems in Japan from New Med Jpn (2009), and those concerning the number of examinations from the Surveys of Medical Care Activities in Public Health Insurance (2009). The values in italics are data supplemented from the OECD Health Data before 2009, because the data were not presented in the 2009 edition: Belgium 2008, Denmark 2007, United Kingdom 2008, United States 2007.

Also, the data for Japan (A) are the number of MDCT systems alone, and those for Japan (B) are the sum of MDCT+SDCT systems (cited from the Survey of Medical Institutions 2008).

[Note 2] The number of CT examinations was also investigated in the Survey of Medical Institutions (static analysis), but the values were 30-40% higher than those shown by the Surveys of Social, Medical, and Clinical Actions of the same years (2008 and 2011).
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2) Number of examinations according to the machine type
The number of scans per system (2010) varied widely.

As for CT:
- MDCT with 16 or more detector rows ............... 2,799 Exams (56%)
- MDCT with less than 16 detector rows ............. 1,120 Exams (28%)
- SDCT ............................................. 675 Exams (17%)

As for MR:
- ≥1.5T .............................................. 1,961 Exams (67%)
- <1.5T ............................................. 1,108 Exams (33%)

Thus, more than half of both CT and MR examinations were performed using high-performance systems. The number of SDCT systems was estimated to be 4,383 from the data in 2008, assuming that they have been gradually replaced by more advanced systems.

3) Annual changes in the number of examinations and medical expenditure
The number of CT and MR examinations continued to increase, and about 19 million CT examinations and 10 million MR examinations were performed annually (2010). Since the frequency of imaging examinations increases with the patient’s age, the number of examinations as a whole is expected to increase at least until 2050 in Japan due to aging of the population structure despite a decrease in the total population.

In the medical fee reimbursement system, CT and MR are categorized together as computed tomography examinations, and the medical expenditure in this category has continued to increase and topped 500 billion yen, accounting for 60% of the total expenditure of all diagnostic imaging modalities, in 2010.

4) Summary
The number of CT and MR systems in Japan is markedly high compared with that in foreign countries, but utilization is low and near the bottom. Domestically, also:
- About 2/3 of the CT (MDCT) and MR systems are operating in the absence of full-time specialist in diagnostic imaging.
- Only about 40% of all images are estimated to be evaluated by a specialist at most.
- More than 50% of examinations are performed using high-performance machines (MDCT with 16 or more detector rows or MR at 1.5T or higher magnetic field strength).
- Due to aging of the population, the number of examinations is expected to increase at least until 2050.
Figure 2: Facilities with the involvement of full-time radiologist by the types of CT (A) and MR (B) systems
The shaded and white areas are the systems in operation at facilities with and without full-time radiologist, respectively. High percentages of high-performance machines are in operation with an involvement of full-time radiologist, but only 35 and 36% of all MDCT and MR systems, respectively, are in operation in the presence of a specialist. A longitudinal survey showed little increase in the involvement of radiologists these 10 years.

References
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4 Improving medical services in Japan starting with radiological practice

Efficiency of medical services in Japan

When the quality of medical services in Japan is measured by international ranking, I am probably not the only one who is embarrassed by the magnitude of variation of the ranking among items. Medical services in Japan have made remarkable achievements in mean life expectancy and infant mortality rate, which are among the highest in the world. However, Japan ranks near the bottom among advanced countries in the number of physicians engaged in medical services per population (Figure 1). The medical expenditure in Japan relative to GDP stays at the lowest level among advanced countries (Figure 2). However, access of people to medical services is generally satisfactory, and, despite some regional differences, patients in urban regions can have access to any department of any medical organization at a low cost. Such superficial achievements are often cited as grounds for justification of the status quo, but favorably evaluating the whole on the basis of selected items with good results permanently denies opportunities to reform weaknesses.

In reality, data that question the efficiency of medical services in Japan are abundant. First, concerning the cost, the number of visits to medical facilities per patient is highest in Japan (Figure 3), number of beds is highest (Figure 4), duration of hospital stay is longest (Figure 5), and percentage of the fee of drug prescriptions in the medical expenditure is in the higher bracket (Figure 6), among the OECD member countries. Japan ranks by far the highest in the number of CT/MRI systems installed per population (See page 6). In fact, the total number of CT examinations is high, but, as a result, the dose of medical radiation exposure is conspicuously high among the OECD member countries (discussed later). On the other hand, the degree of utilization of CT/MRI per unit is near the lowest (See the section, “CT and MR systems and the state of their operation in Japan” (page 5)). If the total medical expenditure per population in Japan is still relatively low despite such inefficiency, it would be natural to think that it is due to low unit prices of medical services. Regarding medical performance, the ranking of Japan varies widely in mortality rate (per 100 thousand people) due to major diseases (malignant neoplasms, cardiac disorders, cerebrovascular disorders) (Figure 7) or disability-adjusted life year (Figure 8), which is a measure of overall disease burden to society, according to the disease, and shows no overall excellence compared with foreign countries.

Problems caused by the present state to Japanese society

As observed above, there seem to be inefficient areas in medical services in Japan that need improvement. Then, what effects do such weaknesses exert on medical services in Japan? Regarding the radiological diagnosis and treatment, this question boils down to an increase in medical radiation exposure, delay of implementation of necessary examinations, and deterioration of the clinical skill of physicians in various clinical departments. Because of the good access to medical services, outpatient clinics of medical organizations (particularly, those of middle-sized or large hospitals) are always crowded above the capacity of physicians assigned to outpatient care, allowing the mocking phrase, “waiting for 2 hours, treated in 5 minutes”. This may be partly due to the patients’ preference for large hospitals, but I would venture to say, taking the risk of misunderstanding, that the low cost of each visit is a cause of the high frequency of patient consultations (i.e., high patient-regulated demand). As a result, in hospital outpatient clinics, each physician must examine 50 or more patients until evening without even taking lunch. An outpatient physician is required to reach some conclusion about the diagnosis and treatment within 10 minutes for each patient on the initial visit. The physician makes a medical interview, performs physical examinations, determines an examination plan, explains the plan to the patient, obtains consent, explains the results to the patient coming back after the examinations, shows possible diagnoses, explains the treatments, obtains consent, and performs them, all within 10 minutes. The fact that medical actions are performed in Japan in such a short time can never be understood by physicians in Western countries. If the situation is explained to them, they would reply that it is impossible to perform the diagnosis and treatment in such a short time (without mistakes). As patients demand increasingly higher quality of medical services, their tolerance to medical errors is diminishing, and physicians inevitably rely on imaging diagnostic modalities such as CT and MRI to quickly reach some conclusion or treatment plan without overlooking problems. The physicians are also prompted to eliminate buds of medical errors, though their possibility may be low, by resorting to roughly targeted treatments such as the prophylactic administration of anti-influenza virus agents or antibiotics even when spontaneous cure is expected.

For patients on revisits, administrations are continued, and follow-up examinations are repeated, without carefully talking to them or reevaluating the prescriptions. Thus, in busy outpatient clinics, radiological examinations, which are originally supportive diagnostic procedures, have been transformed to low-cost automatic diagnostic devices. The medical fee reimbursement system may also be promoting orders by conditional reflex. The fees for outpatient care are paid on a fee-for-service basis, and payments are made even when a physician orders examinations without carefully evaluating their indications, possibly contributing to an increase in examinations that are unlikely to be necessary. However, if such practice becomes routine, waiting time for necessary examinations is prolonged. Also, if the number
Figure 1: Number of physicians (per 1,000 people, 2010 or latest)
The number of physicians is low among the OECD member countries.

Figure 2: Medical expenditure (relative to GDP, 2010 or latest)
The medical expenditure is low among developed countries but near the average among the OECD member countries.
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Figure 3: Number of outpatient visits (per person, 2010 or latest)
The number of outpatient visits in Japan is at the highest level.

Figure 4: Number of beds (relative GDP, 2010 or latest)
The number of beds in Japan is by far the highest.
Figure 5: Mean duration of hospital stay (due to all diseases, 2010 or latest)
The mean duration of hospital stay is long and at the top level among the OECD member countries.

Figure 6: Expenditures for drugs and medical expendables (relative to total medical expenditure, 2010 or latest)
The expense for drugs is in the higher brackets.
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Figure 8: Disease burden according to the disability-adjusted life year (2004)

The disability-adjusted life year, calculated as the sum of the number of years potentially lost due to early death caused by disease and the number of years of healthy life lost due to health damage or disability due to disease, is an index of disease-related loss (burden) of society. It is frequently used to evaluate the order of priority for improvements in public hygiene or medical services in general. Burden to society is larger as the value is higher. The ranking of Japan in developed countries varies among diseases, e.g., respiratory diseases, malignant tumors, and cardiovascular disorders, and shows no striking difference. The superiority of the effects of medical intervention to diseases in Japan is not obvious compared with other countries.
of examinations increases, the number of outpatient visits increases further, because, due to extreme busyness of the laboratory and physicians, the examination results are presented on another day. In addition, for diagnostic devices to be always available, even small medical facilities are required to install them. This results in an increase in the number of installations of CT/MR devices, and installation of devices in unnecessary numbers leads to low level of utilization and poor maintenance. Efforts to increase the degree of utilization under such circumstances result in hospital-induced demand, i.e., the use of devices in patients for whom the examination may be unnecessary and even the general public.

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The trap of cost increase due to uniform control of medical fees and necessity of redistribution of resources for improvements in efficiency

As observed above, the efficiency cannot be improved as expected from attempts to reduce the cost by universal compression of medical fees. We call this paradox the “trap of cost increase due to uniform control of medical fees”. Unquestionably, the national budget allocated to medical services is limited, and the state finance is in a critical state due to long-standing economic stagnation. If such uncontrolled increases in the number of imaging examinations continue, the government would reasonably be tempted to uniformly cut the budget for diagnostic imaging. Indeed, fees for CT and MR examinations have been repeatedly cut at each revision of fees for medical services. However, many studies in Japan and abroad have demonstrated that the policy to universally reduce reimbursement of medical fees is a double-edged sword that ironically invites rises in the medical cost by provoking demands. In Japan, also, such uniform compression of fees for examinations and drugs is accompanied by the risk of promoting excessive use of drugs and diagnostic tools including CT. If apparently wasteful medical expenditures are difficult to eradicate in Japan, the medical administration may be caught in the “trap of cost increase due to uniform control of medical fees”. In taking measures to improve the efficiency of medical services, it is necessary to evaluate the causes of the excessive use of drugs and diagnostic devices as mentioned above and to remove fundamental causes. In advanced countries such as Japan, the days when the efficiency of medical services was measured simply in terms of quantity are gone. We are in the era of quality-oriented assessment of medical services. Regarding radiological services, policies that ensure the highest payment when 1) a roadmap to mildly invasive and accurate diagnoses with minimum radiation exposure is drawn by a specialist in diagnostic imaging, 2) examinations are performed using appropriate and quality-controlled devices and 3) protocols, 4) diagnoses are made properly by qualified specialists in diagnostic imaging, 5) treatments based on such diagnoses are carried out, and 6) patients are rehabilitated through the shortest process are awaited to be implemented. We consider it necessary to redistribute medical resources to apply proper incentives for movements in such a direction.

Excessive examinations and increases in medical radiation exposure

It is very pleasing for specialists in diagnostic imaging that imaging modalities are appropriately used in clinical practice. In fact, the use of radiation including CT is undoubtedly making great contributions to improvements in the people’s hygiene, but the excessive use of radiation for reasons mentioned above is considered to cause adverse effects. The paper by Barrington de Gonzales that appeared in Lancet in 2004 showed that diagnostic radiation is used most frequently in Japan among the OECD member countries and that the associated risk of carcinogenesis is also estimated to be high. As this report was featured in Japanese newspaper, people began to foster anxiety over medical radiation exposure, and, responding to such a public mind, the Japan Radiological Society issued an announcement concerning this problem. In Japan, anxiety of people over health damage due to low-dose radiation exposure is growing further, particularly, after the accident of the nuclear power plants in Fukushima. However, medical radiation exposure plays a greater role than nuclear power plants in low-dose exposure in daily life of all Japanese people, and we are obligated to respond to this anxiety. A symposium on medical radiation exposure was held at the 63rd Annual Meeting of the Japan Radiological Society in 2004, when the paper by Gonzales et al. attracted attention, and the results were summarized by the chairman. The following are excerpts of the parts of the summary related to the goals of future actions by radiologists.

(1) To carry out a large-scale fact-finding investigation about the clinical practice of radiology, evaluate its significance, and transmit the results in Japan and abroad. To call for cooperation in such actions to related scientific societies/organizations and the government.
(2) To urge the medical society to make judgments in consideration of the patients’ radiation exposure without sacrificing appropriate diagnostic information in performing radiological diagnosis.
(3) To make efforts in the QC/QA and improvements/development of imaging procedures and instruments in consideration of reduction of the patients’ radiation exposure.
(4) To initiate the evaluation for appropriate recording of medical radiation exposure in individual patients.
(5) To make the medical staff engaged in radiological diagnosis capable of specifically and appropriately explain medical radiation exposure, its risk, and safety measures to the patients, their families, and medical staff of other departments.
(6) To prompt and promote research on low-dose exposure, which is important to improve the understanding of the risk of low-dose radiation exposure, in cooperation with related scientific societies/organization.

Today, more than 8 years after the proposal, regarding the fact-finding investigation of radiological diagnosis and
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The Japanese imaging guideline 2013 treatment, attempts to understand the true state of clinical practice of radiology including questionnaire surveys are being made by the Japan Radiological Society and Japanese College of Radiology. Also, efforts to reduce the exposure dose including the application of iterative reconstruction to CT are continued through the industry-academia-government cooperation. However, the goals have not been sufficiently achieved. We consider that a large-scale fact-finding survey on radiological practice primarily by the Japan Radiological Society or by an external agency consisting of not only a group of experts including radiologists but also the administration and general people, who are recipients of medical services, is necessary in an early stage. Along with analysis of the present state, the urge for the preparation of an environment of medical services in which indications of radiological examinations are evaluated by specialists in diagnostic imaging, appropriate examination plans using appropriate machines are determined, prompt and appropriate diagnoses are made, and life-long recording of radiation exposure of individual patients is implemented is considered to be growing.

Closing comments

Medical services in Japan, which appear to be making considerable achievements at a low cost, also have inefficient areas and may be improved further by their correction. If radiological practice accounts for a large part of this inefficiency, we are bound to be more serious in improving the situation.

Summary

4) Berrington de Gonzalez A, Darby S: Risk of cancer from diagnostic X-rays: estimates for the UK and 14 other countries. Lancet 31; 363 (9406): 345-351, 2004
5) “3.2% of cancer caused by diagnostic exposure”, Yomiuri Simbun, Feb. 10, 2004, front page
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Brain and nervous system
Background/objective

Non-traumatic subarachnoid hemorrhage is caused primarily by rupture of cerebral aneurysms, which is an important cause of stroke. CT is usually used for diagnosis in the acute phase, but as some subarachnoid hemorrhage is falsely negative on CT (Figure A), a lumbar puncture is necessary for exclusion. There are also reports that MRI, particularly FLAIR imaging, is more sensitive than CT for the detection of subarachnoid hemorrhage (Figure B). In this section, the detection rate of subarachnoid hemorrhage is compared between CT and MRI, and their diagnostic usefulness is evaluated.

Comments

Non-contrast CT is considered to be the principle diagnostic technique for subarachnoid hemorrhage. In a study of evaluating the diagnosis of subarachnoid hemorrhage in 3,132 patients who underwent CT within 6 hours after the onset of symptoms, radiologists diagnosed subarachnoid hemorrhage with both a sensitivity and specificity of 100%. However, the detection rate of hemorrhage is related to both the severity and time-to-imaging after the onset. The sensitivity of CT for the detection of subarachnoid hemorrhage is 98-100% within 12 hours after symptom onset, 93% after 24 hours, 85% after 5 days, 57-85% after 6 days, and 50% after 1 week, showing a decline with time.

The usefulness of MRI (FLAIR, proton density-weighted, and T2*-weighted imaging) for the diagnosis of subarachnoid hemorrhage has also been reported. In an evaluation of 22 patients using a 1.5T system, the sensitivities of FLAIR MRI, T2*-weighted MRI, and CT were 100, 90.9, and 91%, respectively, up to 5 days after symptom onset, while those of FLAIR MIR and CT decreased to 33.3 and 45%, respectively, and subsequently that of T2*-weighted MRI increased to 100%. Similarly, in an evaluation of 41 patients using a 1.5T system, the sensitivities of T2*-weighted and FLAIR imaging were reported to be 94 and 81%, respectively, up to 4 days after the onset and 75%, respectively, 5-14 days after the onset. FLAIR imaging is useful in the acute phase, but as its sensitivity decreases with time, it is necessary to perform T2*-weighted imaging in addition to FLAIR imaging in the subacute phase. However, the judgment of whether subarachnoid hemorrhage is new or old is occasionally difficult by T2*-weighted imaging.

The misdiagnosis rate of subarachnoid hemorrhage in the setting of the emergency outpatient clinic is reported to be 5-12%, and omission of non-contrast CT is a primary cause of misdiagnoses. Additionally, about one-fourth of the patients who develop subarachnoid hemorrhage do not complain of headache and about half show no neurological abnormalities. Therefore, subarachnoid hemorrhage may not be diagnosed even by CT if symptoms at onset are mild and the volume of hemorrhage is small (i.e. the so-called “sentinel bleed” or “warning leak”). In a prospective cohort study of 592 neurologically normal patients with non-traumatic acute headache presenting within 14 days after symptom onset, the sensitivity and specificity of CT for the detection of subarachnoid hemorrhage were 90 and 99%, respectively, and a combination of CT and lumbar puncture was suggested to be sufficient to exclude subarachnoid hemorrhage (sensitivity: 100%, specificity: 67%).

In 12 patients in whom subarachnoid hemorrhage was CT occult but diagnosed by positive lumbar puncture, the FLAIR images obtained using a 1.5T system (within 2 days after CT in 10 and within 1 week in 2) had a false negative result in 10 patients. This suggests that subarachnoid hemorrhage not detected by CT is also difficult to detect by FLAIR and that FLAIR images cannot be substituted for lumbar puncture. Also, in FLAIR images, the cerebral sulci and cisterns may show high intensity signal due to causes unrelated to hemorrhage, including meningitis or meningeal metastasis, acute infarction, moyamoya disease, venous thrombosis, oxygen administration, intravenous anesthesia using propofol, and artifact. Particularly, as ghost artifact is likely to occur in the basal cisterns due to pulsation of cerebrospinal fluid, FLAIR images must be assessed carefully for the diagnosis of subarachnoid hemorrhage.

What imaging modalities are appropriate for the diagnosis of subarachnoid hemorrhage?

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Non-contrast CT is strongly recommended for detection of subarachnoid hemorrhage in the acute phase. MRI may be considered if the diagnosis is difficult by non-contrast CT.
A search of PubMed was performed using “subarachnoid hemorrhage,” “subarachnoid haemorrhage,” “MRI,” “CT,” “fluid attenuated inversion recovery,” and “FLAIR,” as keywords, returning 310 hits. Documents were further restricted to those published in and after 2000 and considered to be related to the diagnosis in question. These documents and documents cited in them were used as references.

References

3) Van der Wee N et al: Detection of subarachnoid haemorrhage on early CT: is lumbar puncture still needed after a negative scan? J Neuro Neurosurg Psychiatry 5: 357-359, 1995 (Level 3)
4) Sames TA et al: Subarachnoid hemorrhage diagnosis: lumbar puncture is still needed when the computed tomography scan is normal. Acad Emerg Med 3: 827-831, 1996 (Level 3)
2. Which examinations are appropriate for screening of unruptured cerebral aneurysms?

**Recommendation grade**

MRA is recommended. If the information obtained by MRA is insufficient and further evaluation is necessary, CTA is recommended.

**Background/objective**

There have been a number of evaluations of the diagnostic utility of cerebral aneurysms by the more invasive digital subtraction angiography (DSA) examination as a gold standard versus using less invasive computed tomographic angiography (CTA) or magnetic resonance angiography (MRA) (Figure). In this section, the accuracy of these examinations for the diagnosis of unruptured aneurysms is reviewed, and examinations recommended for aneurysm screening are evaluated.

**Comments**

Diagnosis of cerebral aneurysms by CTA ranges in sensitivity and specificity from 95.0 and 96.2%, respectively, according to the latest meta-analysis. Moreover, its diagnostic ability has been reported to improve with increases in the number of detector rows: The sensitivity and specificity of 16-detector-row CTA are reported to be 96.9-98.3% and 97.0-98.0%, respectively, and those of 64-detector row CTA to be 97.8-98.2% and 98.7-100%, respectively. Moreover, evaluations using dual-energy CT have recently been carried out, and a similar diagnostic power has been reported. It has also been reported that the likelihood of clinically important cerebral aneurysm is very low if CTA is negative on screening for unruptured cerebral aneurysms. Therefore, CTA is an excellent modality for the diagnosis of cerebral aneurysms.

As for MRA, a systematic review primarily of reports using 0.5-1.5T systems in the 1990s reported that the sensitivity and specificity were 87 and 95%, respectively. The size of cerebral aneurysms is considered a risk factor of rupture, and, according to a subgroup analysis, the sensitivity for detecting cerebral aneurysms exceeding 3 mm in diameter was 94%. With the recent increase in the availability of 3T systems, the effects of differences in the strength of magnetic field on detection power has also been evaluated in a limited number of subjects. A recent study using a 3T system has reported the sensitivity and specificity to be 99.3 and 96.9%, respectively, and the precision of MRA using a stronger magnetic field is considered to be comparable to that of DSA. Therefore, MRA is also an excellent modality for screening of cerebral aneurysms.

Regarding direct comparison between CTA and MRA, it was reported in the early 2000s that there was no significant difference in the sensitivity between 1.5-2T MRA and CTA and alternatively that CTA was more sensitive although there was no significant difference in the specificity. Concerning the comparison between the recent 3T MRA and 64-detector row CTA, the sensitivity and specificity were reported not to differ significantly, and CTA and MRA using the latest equipment perform similarly in the diagnosis of cerebral aneurysms.

While CTA has advantages such as the short scanning time and less artifact, it has disadvantages such as the use of a contrast agent, radiation exposure, and necessity of 3-dimensional reconstruction for distinction from bony structures. Although MRA is free from these problems, it has problems such as the presence of contraindications, long scanning time, signal attenuation due to turbulent flow and in areas with a low flow rate, and poor diagnostic power of low compared with high magnetic field systems. There are pluses and minuses of each examination. However, for screening of unruptured cerebral aneurysms, it is recommended to perform MRA first using a high magnetic field (≥1.5T) MR system because of its low invasiveness and then to perform CTA if further evaluation is necessary. In addition, MRA is considered preferable for the follow-up of unruptured cerebral aneurysms in terms of invasiveness and radiation exposure.

**Index words and secondary materials used as references**

A search of PubMed was performed using “cerebral”, “intracranial”, “aneurysm”, “CT”, and “MRA” as key words, and the Japana Centra Revuo Medicina was searched using cerebral aneurysm, digital subtraction angiography, DSA, CTA, and MRA as key words.

**References**

Neurosurg 112: 563-571, 2010 (Level 2)
8) Li MH et al: Contrast-free MRA at 3.0 T for the detection of intracranial aneurysms. Neurology 77: 667-676, 2011 (Level 2)
Which imaging modalities are appropriate for the diagnosis of acute intracerebral hemorrhage?

**Recommendation grade**
Non-contrast CT is strongly recommended to evaluate the presence or absence of intracerebral hemorrhage.

**Background/objective**
While non-contrast CT has been used widely for the diagnosis of stroke because of its high detection power for brain hemorrhage and its versatility, MRI has also been increasingly used for the diagnosis of stroke as it has become more available in Japan. However, it is unclear whether or not MRI can replace non-contrast CT as a modality for the diagnosis of acute intracerebral hemorrhage. The diagnostic power of non-contrast CT and MRI, imaging modalities used for the diagnosis of acute stage intracerebral hemorrhage, was evaluated.

**Comments**

1) **CT**
Intracerebral hemorrhage accounts for about 20% of stroke, and the presence or absence of such hemorrhage is important for therapeutic decision making in stroke patients. While the sensitivity and specificity for detecting subarachnoid hemorrhage using lumbar puncture as a gold standard have been reported, such data for intracerebral hemorrhage relies only on reports from the 1970s comparing findings using early models of CT scanners with surgery and autopsy findings. Thus, there is no sufficient data regarding the sensitivity or specificity of non-contrast CT for the diagnosis of acute intracerebral hemorrhage. Nevertheless, non-contrast CT has been accepted and used widely as the first line examination for detecting acute intracerebral hemorrhage. However, it must be noted that the ability to detect intracerebral hemorrhage is affected by factors including the time from symptom onset, site and size of hematoma, and hematocrit.

2) **MRI**
There have been few reports comparatively evaluating MRI sequences for detecting intracerebral hemorrhage, and evidence concerning which procedure is preferable is insufficient. With the change from oxyhemoglobin to deoxyhemoglobin after hemorrhage, the appearance of acute hemorrhage changes from an iso-intensity to slightly high-intensity area on T1-weighted imaging but from a high-intensity to low-intensity area on T2*-weighted and diffusion-weighted imaging. Additionally, T2*-weighted imaging (gradient-echo sequence) is considered to be useful for the diagnosis of acute stage hemorrhage, because it depicts oxyhemoglobin as an iso-intense or high-intense signal but deoxyhemoglobin, which is a paramagnetic material, has a markedly hypo-intense signal due to magnetic susceptibility effects.

In a study that retrospectively evaluated 43 patients with hemorrhagic stroke and 43 patients with non-hemorrhagic stroke (41 with arterial cerebral infarction and 2 with transient ischemic attack), the sensitivity and specificity of T2*-weighted imaging were 100 and 95-97.5%, respectively. On T2*-weighted imaging, chronic hemorrhage was judged to be acute hemorrhage in 1 patient. In a report that prospectively evaluated 217 stroke patients, acute intracerebral hemorrhage was observed in 12 patients, and the sensitivity and specificity of T2*-weighted imaging (or diffusion-weighted imaging at b=0 if the quality of T2*-weighted images was poor) for the diagnosis of acute stage intracerebral hemorrhage using non-contrast CT as a reference standard were 83 and 100%, respectively.

According to a study of 200 patients suspected to have stroke within 6 hours after symptom onset, acute hemorrhage was detected by both CT and MRI in 25 patients and by MRI alone in 4, who all showed hemorrhagic changes in ischemic areas. Acute hemorrhage was detected by CT alone and was diagnosed to be chronic hematomas on MRI in 3. In 1 patient, a small volume of subarachnoid hemorrhage was detected by CT but not by MRI. Chronic hemorrhage was noted on MRI alone in 52 patients but was difficult to detect on CT. The agreement rate of the diagnosis of acute hemorrhage among readers was higher on CT.

In 62 patients with acute brain hemorrhage within 6 hours after symptom onset, the sensitivity and specificity of MRI using non-contrast CT as a gold standard were both 100% in physicians experienced in diagnostic imaging of stroke. However, the accuracy of the diagnosis of hemorrhage by MRI is considered to vary with experience, and expertise is necessary for diagnosing acute stage brain hemorrhage by MRI. If the time of onset is unclear, or if MRI findings are inconclusive, confirmation by CT is important.

Presently, there is no evidence that supports the superiority of MRI compared with CT for the evaluation of acute intracerebral hemorrhage, and they are often reported to be comparable. Particularly, in critically-ill patients, these procedures must be performed in consideration of restriction of body movements and changes in the vital signs during

References

9) Kidwell CS et al: Comparison of MRI and CT for detection of acute intracerebral hemorrhage. JAMA 292: 1823-1830, 2004 (Level 2)

Figure: Acute hemorrhage of the thalamus 3 hours after the onset

A  Non-contrast CT     B  MRI T1-weighted image    C  MRI T2-weighted image
Since intravenous injection of a recombinant tissue plasminogen activator (rt-PA, alteplase) became covered by insurance in Japan in 2005, the demand for diagnostic imaging in patients suspected to have acute stage cerebral infarction has increased. However, no consensus about indications of the imaging for thrombolytic therapy has been reached. Recently, transarterial thrombectomy using a catheter has been approved and begun to be performed more frequently. We evaluate the usefulness of imaging modalities, particularly non-contrast CT and MRI, for the pretreatment evaluation for planned thrombolytic therapy using intravenous rt-PA.

**Comments**

Presently in Japan intravenous injection of rt-PA is indicated for acute cerebral infarction within 4.5 hours after the onset at 0.6 mg/kg, a dose smaller than in Western countries. However, the Guidelines for Appropriate Intravenous rt-PA Infusion Therapy issued by the Committee on Medical Improvements and Social Insurance of the Japan Stroke Society showed that this regimen is comparable in efficacy and safety to 0.9 mg/kg in Western populations on the basis of a clinical trial in Japan.

For the prediction of the effectiveness of thrombolytic therapy, it is important to evaluate the potential area that would be salvaged upon reestablishment of the blood flow following treatment (penumbra). In the above mentioned guidelines, there are exclusion criteria and relative contraindications, but concerning diagnostic imaging only exclusion of other disorders and intracranial hemorrhage by non-contrast CT or MRI is required, and no guidelines concerning the penumbra have been established.

Non-contrast CT has excellent sensitivity to acute stage intracranial hemorrhage. However, due to the risk of embolization, it is important to exclude the presence of a dissection or intracranial hemorrhage before thrombolytic therapy. Therefore, non-contrast CT is strongly recommended as a preliminary examination.

Non-contrast CT is useful for excluding hemorrhage and is strongly recommended. The evaluation of early ischemic changes (EIC) by non-contrast CT using the Alberta Stroke Program Early CT Score (ASPECTS) is useful for the evaluation prior to thrombolytic therapy and establishing prognosis and is recommended. Diffusion-weighted MR imaging should be considered because it does not delay treatment and is sensitive for the detection of ischemic lesions compared with CT.

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*Note: Western countries and Australia revised guidelines since 2010 and recommended to widen the indication of rt-PA intravenous infusion therapy to stroke within 3-4.5 hours after the onset. In Japan, also, on the basis of the results of integrated analysis of multiple meta-analyses, the insurance coverage of the administration of this drug was widened to stroke 3-4.5 hours after the onset in September 2012. In association, the Guidelines for Appropriate Intravenous rt-PA (Alteplase) Infusion Therapy was revised, and a new guideline about the administration within 4.5 hours was issued.*
Figure 2: ASPECTS study form (Lancet 355: 1670-1674, 2000)
The region supplied by the unilateral middle cerebral artery is divided into 10 areas, the presence or absence of EIC is evaluated in each area, and the findings are scored by a point-deduction method. The score is 10 if no EIC are observed and 0 if EIC are observed in the entire MCA region. C: Head of the caudate nucleus, L: Lentiform nucleus, IC: Posterior limb of internal capsule, I: Insular cortex, M1-M3: MCA region (basal ganglion level), M4-M6: MCA region (corona radiata level).

MRI early after the onset (for example, within 4.5 hours) is expected to reduce the risk of symptomatic hemorrhage after treatment, no marked difference is observed in outcomes, and the establishment of criteria for indications for MRI including DWI is necessary.

In MRI, the penumbra is often evaluated as the difference in the ischemic area between DWI and perfusion-weighted imaging (PWI) (so-called DWI/PWI mismatch). There have been a number of reports on this DWI/PWI mismatch, but a problem is that the procedure and evaluation criteria of PWI are diverse and lack a standard method. Arterial spin labeling (ASL) performed without a contrast agent and dynamic susceptibility contrast (DSC) imaging performed by rapid intravenous injection of a contrast agent are known as PWI procedures, but the spread of ASL is hampered by the scarcity of facilities that can perform it. In 2 recent large-scale studies using DSC imaging in which the therapeutic effect of rt-PA was compared in patients with cerebral infarction within 3-6 hours after the onset, the mismatch was defined as a decrease in the cerebral blood volume of ≥10 ml (delay of Tmax ≥8 s) on PWI and a high signal area on DWI of 120% or larger than the low blood flow area on PWI. When early reperfusion was achieved, the outcome was more favorable in patients with than without mismatch (odds ratio: 5.4, p=0.039), the spread of the infarct area was smaller, and reperfusion was observed more frequently, after 90 days in the rt-PA group compared with the placebo group. However, PWI is not generally performed at many Japanese facilities, and standardization of the procedure and evaluation method is necessary for the evaluation of indications according to mismatch. As for methods to evaluate the hemorrhage and is very useful for the exclusion of intracranial hemorrhage. Diagnosing the extent of EIC (Figure 1) is important for establishing indication for thrombolytic therapy. The guidelines recommend to evaluate the presence or absence of EIC because a favorable prognosis is expected if the extent of EIC is 1/3 or less of the area supplied by the middle cerebral artery (MCA) (the 1/3 MCA rule), However, there is no clear definition of what constitutes EIC or vascular territories, and the interpretations vary among examiners. Therefore the American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend ASPECTS. ASPECTS (Figure 2) divides the MCA territory into 10 areas, evaluates EIC in each area, and scores them with the maximum score being 10. It is a relatively simple method and shows a higher inter-rater agreement rate than the 1/3 MCA rule. The PROACT-II and NINDS trials reported that the functional outcome 90 days after the rt-PA administration was more favorable than in the control group if the ASPECTS on the initial CT was >7 and that the mortality rate was reduced by the rt-PA administration. However, both evaluation methods were limited to the MCA region, and the appropriateness of the scoring design (e.g., the scores are distributed evenly regardless of whether the area is functional or non-functional) has not been sufficiently validated. The evaluation method for regions other than the MCA has not been established.

There are also reports that the evaluation methods themselves are not useful for the selection of treatments, and the assessment of the penumbra for the pretreatment evaluation prior to thrombolytic therapy by non-contrast CT alone has limitations.

An advantage of performing MRI for the diagnosis of acute stage cerebrovascular disorders is that diffusion-weighted imaging (DWI) can be performed. Mildly high intensity areas observed on DWI may be reversible, and their significance has not been established, but infarct areas can be clearly diagnosed from an early stage with small inter-rater variability. Also, as DWI has excellent sensitivity to small lesions in the brainstem, cerebellum, cortex, and subcortical areas, its diagnostic ability for acute cerebral infarction is considered high. It has been reported that, when high intensity areas observed on DWI were rated using the ASPECTS (DWI-ASPECTS), the DWI-ASPECTS was about 1 point lower than CT-ASPECTS and that, while both scores were useful for the prediction of symptomatic brain hemorrhage after treatment and functional outcome after 3 months, the prediction using the DWI-ASPECTS was more accurate.

Presently, indication for thrombolysis are evaluated by DWI using the same criteria as CT. While the evaluation by MRI early after the onset (for example, within 4.5 hours) is expected to reduce the risk of symptomatic hemorrhage after treatment, no marked difference is observed in outcomes, and the establishment of criteria for indications for MRI including DWI is necessary.
penumbra other than PWI, the estimation of the penumbra has been attempted using DWI-MRA mismatch, DWI-clinical mismatch, and DWI-FLAIR mismatch, but no clear evidence has been established. Regarding DWI-FLAIR mismatch, whether or not the time of onset can be estimated from the presence or absence of high signals on FLAIR and DWI findings was evaluated, and it was reported that mismatch was not sensitive for identifying ischemia within 4.5 hours after the onset but showed high specificity and positive predictive value.\(^{15}\) Therefore, the penumbra may potentially be evaluated by modalities other than PWI in the future.

MRI also shows a high detection power for acute stage intracranial hemorrhage (see the chapter on brain hemorrhage for details). It is particularly effective for detecting microbleeds (MBs), but the evaluation of the relationship between the presence of MBs and hemorrhagic complications after thrombolytic therapy remains insufficient. In a small-scale study, the relationships among the number of MBs before treatment, presence or absence of symptomatic hemorrhage 1-3 days after treatment, and hemorrhagic changes were evaluated retrospectively in patients with acute stage brain ischemia who underwent intravenous rt-PA infusion or intra-arterial urokinase infusion within 6 hours after the onset, and no correlation was reported between the number of MBs and symptomatic hemorrhage after treatment or between the presence or absence of MBs and hemorrhagic changes.\(^{16}\)

The penumbra evaluated by MRI is expected to be useful as an index for evaluation of need for thrombolytic therapy in patients in whom the time after the onset is within 4.5 hours or unknown. However, if the initiation of treatment may be delayed by performing MRI, the evaluation using CT is recommended.

**Index words and secondary materials used as references**

A search of PubMed was performed using “acute ischemia”, “thrombolysis”, “brain”, “CT”, and “MRI” as keywords. Also, the Guidelines for Appropriate Intravenous rt-PA (Alteplase) Infusion Therapy edited by the Intravenous rt-PA (Alteplase) Therapy Guidelines Subcommittee, Committee on Medical Improvements and Social Insurance of the Japan Stroke Society, Japanese Guidelines for the Management of Stroke 2009 edited by the Joint Stroke Guidelines Committee, AHA/ASA guidelines for the early management of patients with ischemic stroke, and the Cochrane Collaboration were used as references.

**References**

1) Intravenous rt-PA (Alteplase) Therapy Guidelines Subcommittee, Committee on Medical Improvements and Social Insurance of the Japan Stroke Society: Guidelines for Appropriate Intravenous rt-PA (Alteplase) Infusion Therapy (October 2005), Stroke 27: 327-354, 2005 (Level 5)
2) Yamaguchi et al: Japan Alteplase Clinical Trial (J-ACT) Group. Alteplase at 0.6 mg/kg for acute ischemic stroke within 3 hours of onset: Japan Alteplase Clinical Trial (J-ACT). Stroke 37: 1810-1815, 2006 (Level 2)
7) Barber PA et al: Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before throm-
9) Hill MD et al: Selection of acute ischemic stroke patients for intra-arterial thrombolyis with pro-urokinase by using ASPECTS. Stroke 34: 1925-1931, 2003 (Level 2)
12) Nezu T et al: Early ischemic change on CT versus diffusion-weighted imaging for patients with stroke receiving intravenous recombinant tissue-type plasminogen activator therapy; stroke acute management with urgent risk-factor assessment and improvement (SAMURAI) rt-PA registry. Stroke 42: 2196-2200, 2011 (Level 2)
18) Intravenous r-tPA (Alteplase) Therapy Guidelines Subcommittee, Committee on Medical Improvements and Social Insurance of the Japan Stroke Society: Guidelines for Appropriate Intravenous r-tPA (Alteplase) Infusion Therapy, Second Edition (October 2012). (Level 5)
Is CT appropriate for children with minor head trauma?

**Background/objective**

Head injuries in children are often encountered at the emergency outpatient clinic, and most are mild and can be managed by observation alone. Abnormalities are observed in few patients on CT, and those that require surgery are even fewer. Whether or not CT is necessary for children with minor head trauma and what patients need CT are evaluated.

**Comments**

Studies to evaluate the risk of intracranial injury in patients with minor head trauma and to define indications for CT have been performed over many years, but the results have varied. No consensus has been reached regarding what patients should undergo CT. Recently, a few large-scale studies have been carried out, and criteria with a high evidence level have been presented.

Dunning et al. performed a cohort study in 22,772 patients with head injuries aged 2-16 years and prepared the Children’s head injury algorithm for the prediction of important clinical events (CHALICE) rule(9,12) (Table). According to this rule, the risk of intracranial injury is considered to be high and requiring CT when any of the following conditions is met: Loss of consciousness (LOC) of >5 min duration, history of amnesia of >5 min duration, abnormal drowsiness, ≥3 vomits, suspicion of abuse, seizure in a patient with no history of epilepsy, GCS <14, GCS <15 in those aged <1 year, suspicion of penetrating or depressed skull injury or tense fontanelle, signs of basal skull fracture (ear bleeding, panda eyes, CSF leakage, Battle’s sign), neurological abnormalities, subcutaneous hematoma or bruise ≥5 cm in diameter in those aged <1 year, and severe mechanism of injury. The CHALICE rule shows high sensitivity (98%) and specificity (87%), its use for the diagnosis of head trauma in children is recommended by guidelines for diagnostic imaging in the United States. In the United Kingdom, it provided the basis for the national diagnostic and therapeutic guidelines and is in wide clinical use.

In addition, the Pediatric Emergency Care Applied Research Network (PECARN) rule recently reported by Kupperman et al. and Canadian Assessment of Tomography for Childhood Head Injury (CATCH) rule proposed by Osmoid et al. are regarded as highly sensitive criteria based on a large-scale multi-center cohort study.10,11) The PECARN rule shows criteria of low-risk intracranial injury separately for those aged <2 years and ≥2 years and suggests CT to be unnecessary if the risk is low.

Those aged <2 years: Normal level of consciousness, no scalp hematoma other than those in the frontal region, no loss of consciousness or loss of consciousness of <5 seconds duration, non-severe mechanism of injury, no palpable skull fracture, and acting normally as interpreted by parents.

Those aged ≥2 years: Normal level of consciousness, no loss of consciousness, no vomiting, non-severe mechanism of injury, no signs of basilar skull fracture, no headache.

The CATCH rule shows criteria for high- and moderate-risk intracranial injuries and recommends CT as necessary when the following conditions are met.

High risk: GCS <15 at 2 hours after injury, suspected open or depressed skull fracture, history of worsening headache, irritability on examination.

Moderate risk: Any sign of basal skull fracture, large hematoma of the scalp, dangerous mechanism of injury.

In children with minor head trauma, the risk of intracranial injury should be evaluated using the above criteria, and CT should be performed only in high-risk patients. CT should not be performed otherwise from the viewpoints of exposure and medical cost.

**Index words and secondary materials used as references**

A search of PubMed was performed using “children”, “minor head injury”, “trauma”, and “CT” as keywords. Also, Evidence-based imaging, Springer, 2011 and Evidence-based imaging in Pediatrics 2010 were used as references.

**References**

1) Greenes DS et al: Clinical Indicators of Intracranial Injury in Head-injured Infants. Pediatrics 104: 861-867, 1999 (Level 2)
The Japanese imaging guideline 2013

Table: CHALICE rule

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of consciousness of &gt;5 min duration</td>
<td></td>
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<tr>
<td>History of amnesia of &gt;5 min duration</td>
<td></td>
</tr>
<tr>
<td>Abnormal drowsiness</td>
<td></td>
</tr>
<tr>
<td>≥3 vomits</td>
<td></td>
</tr>
<tr>
<td>Suspicion of abuse</td>
<td></td>
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<tr>
<td>Seizure in a patient with no history of epilepsy</td>
<td></td>
</tr>
<tr>
<td>GCS &lt;14, GCS &lt;15 in those aged &lt;1 year</td>
<td></td>
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<tr>
<td>Suspicion of penetrating or depressed skull injury or tense fontanelle</td>
<td></td>
</tr>
<tr>
<td>Signs of basal skull fracture (bleeding from the ear, panda eyes, CSF leakage, Battle’s sign)</td>
<td></td>
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<tr>
<td>Neurological abnormalities</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous hematoma or bruise &gt;5 cm in diameter in those aged &lt;1 year</td>
<td></td>
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<tr>
<td>Dangerous mechanism of injury such as high-energy trauma</td>
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</tbody>
</table>

*Close examination using CT is necessary if any of the above items is positive.

CT findings after head trauma are occasionally negative despite persistence of disturbance of consciousness. If there is such dissociation between neurological symptoms and CT findings, MRI is often performed for further examination. Various MRI sequences have been reported to be useful for such evaluation. How sensitive MRI is for detecting lesions of head trauma, and how useful it is for the prediction of the neurological prognosis, are evaluated.

Comments

1) CT and MRI
For the diagnosis of brain hemorrhage, brain contusion, and diffuse axonal injury (DAI) in head trauma, MRI shows higher contrast resolution and detectability than CT. However, DAI often escapes detection by regular MRI sequences such as T1- and T2-weighted imaging and needs to be interpreted cautiously. Dionei et al. compared CT and MRI in 55 patients with head trauma and reported that T2-weighted, T2*-weighted, and FLAIR MRI sequences were significantly more sensitive for detecting acute subdural hematoma, traumatic subarachnoid hemorrhage, brain contusion, and DAI.

2) FLAIR and diffusion-weighted imaging
Among common MRI sequences, FLAIR and diffusion-weighted imaging are sensitive for detecting lesions such as non-hemorrhagic DAI. Ashikaga et al. retrospectively evaluated FLAIR and T2-weighted images in 56 patients and reported that the sensitivity of FLAIR imaging was comparable to, or higher than, that of T2-weighted imaging for detecting DAI, brain contusion, and subdural hematoma in all patients. Also, Kinoshita et al. retrospectively compared the sensitivity of FLAIR and diffusion-weighted imaging for DAI in 36 patients and reported that they were comparable, suggesting the usefulness of both sequences.

3) T2*- and magnetic susceptibility-weighted imaging
DAI is often manifest as small hemorrhagic lesions, and T2*- or magnetic susceptibility-weighted imaging, which strongly reflects differences in the magnetic susceptibility, may be performed for its detection. T2*-weighted imaging has a higher detectability for DAI than other sequences and shows excellent sensitivity for small lesions. Scheid et al. detected DAI at a total of 233 lesions in 66 patients with head trauma by T2-weighted imaging but at 608 lesions by T2*-weighted imaging and reported that the latter sequence was significantly more sensitive. Moreover, Tong et al. compared the number of DAI lesions detected by T2*- and magnetic susceptibility-weighted imaging in 7 patients with severe head trauma and reported that the detectability of the latter sequence was significantly higher with a mean number of DAI lesions detected per patient being 28±8 and 134±27, respectively (Figure). Also, small petechial hemorrhages are occasionally detected by magnetic susceptibility-weighted imaging in the brain parenchyma of individuals who repeatedly sustain minor head traumas such as boxers, suggesting that small lesions of DAI can also be detected by magnetic susceptibility-weighted imaging in head trauma patients.

4) Neurological prognosis
Regarding the neurological prognosis according to DAI and the Glasgow Coma Scale, there are reports that the number of lesions detected by T2*-weighted imaging was not correlated with outcome but the findings of magnetic susceptibility-weighted imaging were correlated with the outcome as, for example, disturbance of consciousness persisted with increases in the number of detected lesions. It is recommended to perform magnetic susceptibility-weighted imaging, if possible.

Index words and secondary materials used as references
A search of PubMed was performed using “brain contusion”, “diffuse axonal injury”, “hemorrhage”, and “MRI” as key words.
The Japanese imaging guideline 2013

References
4) Paterakis K et al: Outcome of patients with diffuse axonal injury: The significance and prognostic value of MRI in the acute phase. J Trauma 49: 1071-1075, 2000 (Level 2)
8) Scheid R et al: Comparative magnetic resonance imaging at 1.5 and 3 tesla for the evaluation of traumatic microbleeds. J Neurotrauma 24: 1811-1816, 2007 (Level 2)

Figure: Persistent disturbance of consciousness after injury due to a traffic accident
On magnetic susceptibility-weighted imaging, a large number of petechial low signal areas were observed in the splenium of corpus callosum, and a diagnosis of diffuse axonal injury was made.
Is neurodiagnostic imaging appropriate in patients suspected to have febrile seizure?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>C1 For atypical or frequent seizures and seizures accompanied by neurological deficits</th>
<th>C2 For typical seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>For atypical or frequent seizures and seizures accompanied by neurological deficits, head MRI may be considered for evaluation. Head CT is useful as a test before lumbar puncture and may be considered. For typical seizures, diagnostic imaging (CT, MRI) is not recommended.</td>
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</tbody>
</table>

Background/objective

According to guidelines concerning febrile seizures, a febrile seizure is a paroxysmal disorder (including convulsive and non-convulsive seizures) usually associated with a fever of 38°C or higher occurring in early childhood without a clear causative disorder such as infection of the central nervous system or metabolic disease.

A majority of patients with a febrile seizure are reported to have only 1 attack in their lifetime, and it is basically considered to be a transient benign disorder. However, it is important to differentiate it from conditions that require prompt and aggressive treatments such as encephalopathy and encephalitis and, if seizure is recurrent, to exclude organic disorders. Whether or not diagnostic imaging should be performed when febrile seizure is suspected and important diseases to be differentiated are evaluated.

Comments

Febrile seizure is considered to be the most frequently encountered type among convulsive disorders of children. In Japan, its prevalence is reportedly 7-8%, which is slightly higher than that in Western countries (2-5%). Convulsive attacks associated with febrile seizure are typically generalized attacks of convulsion such as generalized tonic-clonic seizures. Partial seizures, seizure sustained for a prolonged period (10-15 minutes or longer), and seizures recurring within 24 hours are considered to be atypical seizures and risk factors of epilepsy. In addition, clear neurological abnormalities before the onset of febrile seizure, developmental retardation, and a familial history of epilepsy in parents and siblings are factors related to the occurrence of epilepsy and recurrence of febrile seizure.

There are no reports with a high evidence level recommending diagnostic imaging (CT, MRI) for children with febrile seizure showing typical attacks. While the definition of atypical attacks differs slightly, the American Academy of Pediatrics (AAP) issued a statement recommending against CT or MRI for febrile seizure with typical attacks. However, there may be positive imaging findings in atypical attacks.

Diseases from which febrile seizure needs to be differentiated include bacterial/viral encephalitis/meningitis, tuberculous encephalitis/meningitis, subdural/epidural abscess, brain abscess, and acute encephalopathy. In children, clinical findings are often difficult to obtain, and diagnostic imaging plays a considerable role. A delay of the diagnosis and treatment of these diseases, while they are observed less frequently than febrile seizure, decrease the life expectancy/functional outcome prognosis, so early diagnosis and treatment are important.

Also, the above guidelines recommend aggressive lumbar puncture if encephalitis/meningitis is suspected, and diagnostic imaging has significance in excluding intracranial space-occupying lesions that are contraindications of lumbar puncture.

Acute viral encephalopathy is a disease exhibiting seizure and sudden disturbance of consciousness in the acute stage of highly febrile viral infection. However, pathogenic viruses and clinicopathological classification do not show one-to-one correspondence. Thus, a particular virus may cause diverse clinicopathological features, and various viruses may cause the same clinicopathological features. Moreover, acute encephalopathy is often triggered by viral infection, but it may also be caused by congenital metabolic abnormalities, non-viral infections such as bacterial infection, cat scratch disease, and Q fever, and diseases other than infection such as autoimmune disorders.

Acute encephalopathy is caused by various mechanisms. Particularly, in the first episode of acute encephalopathy with biphasic seizures showing no disturbance of consciousness, the differential diagnosis from simple febrile seizure is difficult, and it is important to detect high intensity signals in the subcortical white matter (bright tree appearance) by diffusion-weighted imaging before the occurrence of recurrent partial seizures 4-5 days after the onset.

Splenial lesions appear in various diseases and situations including after drug administration, and lesions distributed within the splenium and white matter to Rolando’s area are known to be reversible in acute encephalitis/encephalopathy patients.

In the chronic stage, MRI reportedly disclosed hippocampal atrophy in 6 of the 15 patients with febrile seizures...
showing atypical attacks, while the evidence level is not high.\(^1\) Febrile seizure patients are also reported to be at a higher risk of developing epilepsy, and diagnostic imaging is considered to play a role in close evaluation in the chronic stage if, for example, attacks are recurrent.\(^2\)

**Index words and secondary materials used as references**

A search of PubMed was performed using “febrile seizure”, “CT”, and “MRI” as key words. The guidelines listed as References 1) and 2) and the recommendation listed as Reference 3) below were also used as references.

### References

What imaging modalities are appropriate for the diagnosis of temporal lobe epilepsy?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Imaging modalities</th>
</tr>
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<tbody>
<tr>
<td>B</td>
<td>MRI, SPECT</td>
</tr>
<tr>
<td>C1</td>
<td>CT</td>
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</table>

MRI is the first choice imaging modality for temporal lobe epilepsy and is recommended. Ictal SPECT is recommended for the identification of epileptic foci. While CT is less sensitive for detecting responsible lesions than MRI, it is useful for detecting calcification and may be considered.

Background/objective

Epileptogenic lesions in temporal lobe epilepsy are classified into sclerosing lesions (neuronal loss and gliosis), tumors, vascular anomalies, cortical dysplasia/brain anomalies, posttraumatic gliosis, and inflammatory lesions. The significance of diagnostic imaging lies in the localization and qualitative diagnoses of these epileptogenic lesions. There have been various reports concerning the usefulness of CT, MRI, and SPECT/PET for the diagnosis of temporal lobe epilepsy. Their effectiveness is evaluated.

Comments

1) CT
Reports evaluating the usefulness of CT for detecting epileptogenic lesions have been few. According to a retrospective report on CT including its comparison with MRI in children, the sensitivity of CT for the detection of responsible lesions (31%) was lower than that of MRI (64%). However, the addition of CT is considered useful if lesions accompanied by tissue calcification such as tumors and cavernous hemangiomas are suspected. CT is also selected if MRI cannot be performed due to patient factors or the presence of a cardiac pacemaker and if there are signs of an elevation of the intracranial pressure, suggesting conditions such as intracranial hemorrhage and the possible necessity of emergency surgical treatment.

2) MRI
The most important disease related to temporal lobe epilepsy is hippocampal sclerosis (mesial temporal sclerosis). As findings suggestive of hippocampal sclerosis, (1) atrophy and signal abnormality of the hippocampus, (2) reduced delineability of the internal structure (striation) of the hippocampus, (3) loss of digitations in the hippocampal head, and (4) rotational abnormalities of the body of hippocampus have been reported using MRI at various magnetic intensities (Figure). Of these findings, rotational abnormalities of the body of hippocampus is frequently observed also in healthy individuals and needs caution.

Hippocampal atrophy is basically evaluated visually by comparison with the opposite hippocampus. However, caution is necessary because there are cases of bilateral hippocampal sclerosis. There are also reports that atrophy cannot be detected in about 15-30% of the patients with temporal lobe epilepsy. Concerning quantitative evaluation of the hippocampal region, there have been a number of reports including those on the method to determine the hippocampal volume by manually setting the region of interest and whole-brain analysis using voxel-based morphometry. However, there is also a report that visual qualitative evaluation is more useful for the diagnosis, and, presently, quantitative analysis is not used for the diagnosis on an individual basis.

The sensitivity and specificity for the diagnosis of temporal lobe epilepsy reach about 80-90% by combining findings of hippocampal atrophy with abnormal signals in T2-weighted and FLAIR images. Regarding reduced delineability of the internal structure (striation) of the hippocampus, temporal lobe epilepsy can be diagnosed with a sensitivity of 76% and a specificity of 80% by T2-weighted imaging using 3T MRI, and its sensitivity is reported to be higher than that of hippocampal atrophy (44%) or abnormal signals on T2-weighted imaging (48%). The sensitivity and specificity of loss of digitations in the hippocampal head using a 1.5T system have been reported to be 92 and 100%, respectively, and the finding was reported to be observed frequently in atrophied hippocampi but has recently been reported using a 7T system to be unrelated to the presence or absence of atrophy.

Hippocampal sclerosis is often complicated by disorder of neuroblast migration, and local lesions are often observed at sites other than the hippocampus. Therefore, it is necessary to scan the whole brain. The addition of contrast-enhanced MRI is unnecessary for the diagnosis of atrophic lesions of the brain including hippocampal sclerosis or brain anomalies. However, contrast-enhanced MRI is necessary if brain tumor, cerebrovascular anomalies, or inflammation are suspected for their qualitative diagnosis.
In surgical treatment, functional MRI (fMRI) may be considered to identify the localization of verbal and memory functions. There have been many reports supporting the superiority of fMRI compared with the conventional Wada test (Amytal test) from the viewpoints of invasiveness and reliability of the test itself, and the Wada test may be replaced by fMRI in the future.

3) SPECT/PET

SPECT or PET is used to identify the sites showing changes in the blood flow or metabolism in epileptogenic foci. Iomazenil SPECT, by which benzodiazepine receptors are visualized, is also performed. Presently, the most widely employed modality is interictal brain perfusion SPECT. Its sensitivity is only 40-60%, and the interpretation of images is not necessarily in agreement among readers. The sensitivity of interictal PET has been reported to reach 84%, but it is lower than that of ictal SPECT (≥90%). However, as ictal SPECT images are modified by various factors including the seizure type, duration of seizure, radionuclide, and timing of its injection, it is often difficult to identify epileptogenic foci by SPECT alone. Presently, these functional brain imaging techniques are performed supplementarily with morphological evaluation using MRI or in preparation for surgery.

Index words and secondary materials used as references

A search of PubMed was performed using “CT”, “MRI”, and “temporal lobe epilepsy” as key words.

References

9. Are CT and MRI appropriate for patients with an apparent first unprovoked seizure?

**Background/objective**

Seizure is the name of a symptom characterized by involuntary and paroxysmal contraction of muscles of the whole or part of the body, and epilepsy is the name of a disease in which symptoms including seizure are caused by excessive neuronal excitation. In this article, an apparent first seizure is defined as a seizure without a history of epilepsy or an acute pathological condition such as head trauma, stroke, drug poisoning, and electrolyte abnormality and with normalization of neurological functions after the episode. Unprovoked seizures are classified as epilepsy in 40-50% of the patients by subsequent close examinations.

**Comments**

In evaluating imaging examinations, the detection rate of lesions and effects on the therapeutic strategy must be considered. In a cohort study by Shinnar et al., imaging examinations were performed in 218 (CT in 159, MRI in 59) of the 411 children who exhibited an apparent first unprovoked seizure, and abnormalities were noted in 45 (21%). The lesion detection rate was higher on MRI (34%) than on CT (22%), but the treatment in the acute stage was changed in only 4 (1.8%).

In an evidence-based review of children with a first nonfebrile seizure (many of them examined by CT alone) carried out by the American Academy of Neurology, abnormalities that caused changes in the treatment were detected by CT in 0-7% of the children. On CT, abnormalities were noted more frequently in adults (18-34%), and the therapeutic effectiveness of imaging studies was lower in children than in adults. This review included a case series study of adults and children by King et al., in which imaging examination was performed in 277 (92%) of 300 patients with a first episode of seizure (MRI in 263, CT alone in 14), resulting in the detection of lesions in 38 (by MRI in 36 (14%) and by CT in 2 (14%)). Of these patients, 17 had tumors, and the treatment was changed. Of the 38 patients with a lesion, CT was performed in 28, and lesions in agreement with the MRI findings were observed in only 12 patients. The American Academy of Neurology also reported an evidence-based review of adults with an apparent first unprovoked seizure, according to which abnormalities were detected in 1-57% (mean: 15%) by CT, and the results affected the therapeutic strategy in 1-47% (mean: 10%). In older individuals, in particular, the possibility of detecting abnormalities was higher than in children, and imaging studies were considered to be sufficiently worth evaluating.

Concerning comparison between CT and MRI, there is a retrospective study by Kollar et al. Of the 84 patients with an apparent first unprovoked seizure, 21 underwent CT alone, and 6 underwent MRI alone, and abnormalities were detected in 16 (76%) and 4 (67%), respectively. In 57 patients, both CT and MRI were performed, and abnormalities were detected by MRI but not by CT in 12 (21%) and by both CT and MRI in 17 (30%); MRI had a significantly high diagnostic value than CT (p<0.0001).

Thus, while more lesions are detected by MRI than by CT, the detection of lesions does not necessarily lead to changes in treatment, so the evidence supporting routine neuroimaging is considered insufficient. However, the possibility of detection of abnormalities by imaging studies increases if there are focal seizures or focal neurological deficits. Imaging examination by CT or MRI should be performed in patients who show focal neurological deficits after a seizure persisting for a prolonged time or clouded consciousness lingering over several hours after a seizure. MRI is preferable if possible. Moreover, although there is no urgency, evaluation using MRI should be considered in patients with unexplained cognitive or motor dysfunctions, partial seizures, EEG findings contradicting benign childhood epilepsy, or primary generalized epilepsy, and children aged less than 1 year.
Index words and secondary materials used as references
A search of PubMed was performed using “CT”, “MRI”, and “first unprovoked seizure” as key words.

References

14) Hui ACF et al: Recurrence after a first untreated seizure in the Hong Kong Chinese population. Epilepsia 42: 94-97, 2001 (Level 4)
What imaging modalities are appropriate for patients presenting with subacute/chronic symptoms and suspected to have an intracranial space-occupying lesion?

**Background/objective**

Generally, CT and MRI are used widely for imaging studies of intracranial space-occupying lesions, but there are no clear guidelines concerning which examination should be performed first. The usefulness of CT and MRI was evaluated in intracranial space-occupying lesions in patients with a subacute/chronic presentation, excluding stroke and traumatic lesions. While clinical symptoms suggestive of an intracranial space-occupying lesion vary widely, they include generalized symptoms, which are typically headache, seizure, and impairment of cognitive function, and local neurological symptoms, which are typically local hyposthenia, sensory disturbance, and impairment of vision or visual field.

**Comments**

For most intracranial abnormalities, the sensitivity of MRI is comparable to, or higher than, that of CT.\(^1\) MRI is superior in contrast resolution and delineation of details compared with CT and can scan cross-sections of arbitrary planes. It is also excellent in detecting asymptomatic lesions.\(^{1-3,5,6}\) Moreover, MRI excels in delineating areas surrounded by bones and permits more accurate evaluation of lesions in the posterior cranial fossa, brainstem, and middle cranial fossa (Figure).\(^{2,6-11}\) Regarding sellar and suprasellar lesions, MRI is superior to CT in evaluating the state of surrounding structures such as the optic nerve, optic chiasm, and internal carotid artery.\(^{7,8}\) However, CT is more useful for detecting calcification in lesions and evaluating associated bony changes.\(^{1,10,12}\)

Kent et al. reviewed the literature comparing MRI with other modalities including CT and reported that some studies showed that MRI affected the therapeutic approaches but exerted no major effect on the quality of life.\(^2\) The hardware of both CT and MRI has been markedly improved during the past 20 years, but CT can still be performed more quickly than MRI in most cases. Also, MRI is more expensive than CT and may not be performed promptly depending on the facility. CT suffices for detecting a large intracranial mass or hemorrhage that requires immediately intervention.\(^1\) It must also be noted that some implanted metal devices such as a cardiac pacemaker are contraindications for MRI. CT, however, involves X-ray exposure, and unnecessarily performing it must be avoided.

The use of an iodine-based contrast agent in CT and a gadolinium-based contrast agent in MRI are both useful for improving the delineability for intracranial tumors and evaluating the entire picture of lesions.\(^{1,13-16}\) Generally, contrast-enhanced MRI has higher lesion detectability and delineability than contrast-enhanced CT. Contrast enhancement is clearer by contrast-enhanced MRI than by contrast-enhanced CT in primary intracerebral tumors, typically, glioma and many intracranial tumors such as metastatic tumors, meningioma, and schwannoma, and MRI is more useful for the evaluation of the area of involvement of lesions (Figure).\(^{12,16-20}\) According to many reports, the detection rates, particularly, of brain and meningeal metastases are higher by contrast-enhanced MRI than by contrast-enhanced CT.\(^{3,16-18,20}\) Therefore, in close evaluation of intracranial masses using a contrast agent, contrast-enhanced MRI is recommended.

The evaluation of large meningioma and schwannoma is often possible also by non-contrast MRI.\(^{13}\) It must, however, be remembered that contrast-enhancement is not observed in all intracranial tumors.

**Index words and secondary materials used as references**

A search of PubMed was performed using “brain”, “intracranial”, “central nervous system”, “tumor or neoplasm or mass or occupying”, “CT”, “MR”, and “sensitivity or specificity”, as keywords and the literature with a large number of cases and a high evidence level were preferentially selected. Evidence-Based Imaging: Optimizing Imaging in Patient Care. Medina LS and Blackmore C (eds), Springer, 2011 was also used as a reference.

**References**

Figure: Left acoustic schwannoma
A  Non-contrast CT  B  Non-contrast bone-window CT  C  MRI  T2-weighted image
D  MRI  Contrast-enhanced T1-weighted image
The diagnosis of the presence of the mass is possible by both CT and MRI, but the entire contour of the lesion is delineated most clearly by contrast-enhanced MRI. Dilation of the internal auditory meatus is clearly observed by bone-window CT.

7) Lee BC et al: Sellar and juxtasellar lesion detection with MR. Radiology 157: 143-147, 1985 (Level 4)
17) Sze G et al. MR imaging of the cranial meninges with emphasis on contrast enhancement and meningeal carcinomatosis. AJR 153: 1039-1049, 1989 (Level 3)
Is CT or MRI appropriate in adults with primary headaches?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>For atypical headaches, headaches otherwise unclassifiable, and trigeminal autonomic cephalalgia</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>For atypical headaches, headaches otherwise unclassifiable, and trigeminal autonomic cephalalgia, CT or MRI is occasionally useful and may be considered.</td>
</tr>
<tr>
<td>C2</td>
<td>For primary headaches not accompanied by neurological deficits, CT or MRI is only marginally useful and is not recommended.</td>
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</table>

Background/objective

The International Classification of Headache Disorders; 2nd Edition (ICHD-II) issued by the International Headache Society (IHS) classifies headaches into primary and secondary headaches and cranial neuralgias, central or primary facial pain, and other headaches. Primary headaches are classified into migraine, tension-type headache, cluster headache and other trigeminal autonomic cephalalgias, and other primary headaches. Secondary headaches include headaches attributed to various conditions such as trauma, vascular disorders, non-vascular intracranial disorders, infection, and psychiatric disorder. Generally, primary headaches are considered to be synonymous with chronic headaches, but their diagnosis relies primarily on the history and close evaluation of findings on neurological examinations, and the role of imaging modalities is considered to be small. In actual clinical settings, however, CT or MRI is often performed before classification of headaches, and the assessment of primary headaches has not become a common practice. In this section, the effectiveness of neuroimaging for the diagnosis of primary headaches is evaluated.

Comments

Since the reports evaluating the usefulness of neuroimaging for the diagnosis of primary headaches are limited to observational studies such as cohort and case-control studies, its usefulness is estimated from their results. In 1985, Joseph et al.\(^1\) evaluated 48 patients who underwent CT or MRI for headache and reported brain tumors in 5 and arteriovenous malformation in 1. Of these patients who exhibited abnormalities on imaging, 5 showed neurological abnormalities, and 1 presented with headache on exertion, an unclassifiable headache. Also, Weingarten et al.\(^2\) reviewed 100,800 adults with migraine and reported that the detection rate of patients who complained of chronic headache but showed no neurological deficits and were found to need surgical treatment by CT was about 0.01%.

In 1994, the American Academy of Neurology issued guidelines for the neuroimaging diagnosis of headaches without neurological deficits.\(^3\) Their proposal was based on the evaluation by Fishberg et al.\(^4\) reported in the same year. They reviewed 17 reports published in 1974-1991 and evaluated the findings of 897 times of CT or MRI performed in migraine patients. As a result, only 4 patients (0.4%) showed abnormalities requiring treatment, i.e., 3 with brain tumors and 1 with arteriovenous fistula. On the basis of these results, the guideline commented, “The necessity of neuroimaging for patients with typical migraine is low.” However, admitting that there are organic disorders that require treatment, it stated, “Atypical headaches, a history of seizure, and neurological deficits can be indications for CT or MRI.”

In 2004, Sandrini et al.\(^5\) presented guidelines concerning the usefulness of neurological and neuroimaging examinations in patients with non-acute headaches on the basis of a review of the literature. The guidelines were revised in 2010, and a second edition is now available.\(^6\) In this revised edition, a prospective study in 1,876 headache patients with a non-acute onset by Sempere et al.\(^7\) is cited. While all patients underwent CT or MRI, only 1.2% of them exhibited important organic disorders, and only 0.9% of the patients with headache not accompanied by neurological deficits were found to have intracranial disorders. In this report, the authors concluded that headache patients infrequently have intracranial lesions and that factors that suggest such lesions are neurological findings, clinical course, and history of present illness.

In 2005, Tsushima et al.\(^8\) evaluated MR images of 306 patients with chronic headache not accompanied by neurological deficits and reported that no abnormality was noted in 169, mild abnormalities were noted in 135, and important organic disorders were detected in only 2 (0.7%), namely, 1 with pituitary adenoma and 1 with chronic subdural hematoma.

Thus, all reports were negative about the usefulness of imaging examinations for chronic headaches without neurological deficits but admitted some necessity for atypical headaches and headaches otherwise unclassifiable.

Recently, group-based studies in migraine patients have reported that migraine in women is a risk factor of deep white matter lesions and that migraines with predictive signs increase the risk of asymptomatic ischemic lesions of the brain.\(^9,10\) However, no relationship between the detected lesions and headache has not been established, and further evaluation is necessary.
Willbrink et al.\textsuperscript{11} reviewed 56 case reports of trigeminal autonomic cephalalgias characterized by frequent attacks of headache of a short duration accompanied by unilateral autonomic symptoms of the face and noted secondary causes associated with organic lesions such as brain tumor and vascular lesions in many patients. On the basis of these findings, they reported that neuroimaging is indicated if trigeminal autonomic cephalalgia is suspected by appropriate assessment. Also, it is recommended to perform modalities appropriate for the evaluation of cervical vessels and parasellar or paranasal sinus regions, if necessary, in addition to routine head MRI.

**Index words and secondary materials used as references**

A search of PubMed was performed using “chronic headache”, “diagnostic imaging”, “guideline”, “migraine”, and “cephalalgia” as key words. Also, the Headache Classification Committee, International Headache Society: The International Classification of Headache Disorders; 2nd Edition (ICHD-II) was used as a reference.

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What imaging modalities are appropriate for detecting metastatic brain tumors?

**Recommendation**
If metastatic brain tumors are suspected, contrast-enhanced MRI is recommended.

**Background/objective**
In cancer patients, the presence or absence of brain metastasis is important for the determination of the therapeutic strategy, and the exact number, size, and site of brain metastatic foci are necessary for the selection of treatments. CT and MRI are used frequently for their evaluation, but the modality performed first may differ among facilities. In this section, the modality that should be performed as the first choice for the evaluation of brain metastases in cancer patients suspected to have metastatic brain tumors is evaluated.

**Comments**
Since the reports evaluating the usefulness of imaging modalities for metastatic brain tumors are limited to those of observational studies such as cohort and case-control studies, it is estimated on the basis of their results. Since the late 1980s, there have been a number of comparative studies of CT and MRI for the detection of metastatic brain tumors.\(^\text{1-6}\) According to a report in which contrast-enhanced CT and contrast-enhanced MRI were compared in 50 consecutive patients suspected to have parenchymal brain metastases, more metastatic foci were detected by contrast-enhanced MRI than by contrast-enhanced CT in 8 of the 27 patients found to have metastases, but no metastatic foci were identified in 6 by contrast-enhanced MRI.\(^\text{3}\) Also, contrast-enhanced MRI was excellent in detecting metastatic foci in the posterior cranial fossa and cortex. In a report that compared the detectability for brain metastases of CT using a contrast agent at 2-fold the usual dose, T2-weighted MRI, and contrast-enhanced T1-weighted MRI using a contrast agent at a normal dose in 23 patients suspected to have brain metastases, 37, 40, and 67 metastatic foci could be identified, respectively.\(^\text{4}\) In a study comparing the detectability for brain metastases of contrast-enhanced CT, T1-weighted MRI, T2-weighted MRI, and contrast-enhanced T1-weighted MRI using a contrast agent at a usual and 3-fold doses, decreasing numbers of metastatic foci were detected by contrast-enhanced T1-weighted MRI at a 3-fold dose, contrast-enhanced T1-weighted MRI at a usual dose, contrast-enhanced CT, T2-weighted MRI, and non-enhanced T1-weighted imaging in this order. The detectability was significantly higher in contrast-enhanced T1-weighted MRI at a 3-fold dose compared with the other imagings, and the difference was particularly notable in the detection of metastatic lesions 5 mm or less in diameter.\(^\text{5}\) In a report prospectively evaluating contrast-enhanced CT and contrast-enhanced T1-weighted MRI using a contrast agent at 2-fold the usual dose and a 1.5T system in 134 consecutive patients who underwent the examination for staging of lung cancer, metastases were identified in 19 by contrast-enhanced MRI and in 12 by contrast-enhanced CT, with a significant difference.\(^\text{6}\) Since these reports consistently indicated the superiority of contrast-enhanced MRI, it should be recommended as the first choice imaging modality for the evaluation of metastatic brain tumors.

The dose of the contrast agent, scan timing, size of the metastatic focus, magnetic field strength, and scanning sequence have been evaluated as factors that affect the detectability of lesions on contrast-enhanced MRI. There have been a few reports that the sensitivity for brain metastases was increased by administering the contrast agent at 3-fold a usual dose compared with usual dose.\(^\text{5,7-10}\) According to a report evaluating the effects of the dose of the contrast agent, interval between the administration of the contrast agent and scanning, and size of the metastatic focus on the delineability of lesions at 1.5T in 45 patients with metastatic brain tumors, all metastatic foci larger than 10 mm in diameter could be identified regardless of the dose of the contrast agent or the interval between the administration and scanning, but the detectability of lesions 10 mm or less was affected by the dose of the contrast agent and the interval between the administration and scanning.\(^\text{8}\) About twice as many metastatic foci less than 5 mm in diameter were detected by scans 20 minutes compared with immediately after the administration of the contrast agent, about 3 times more metastatic foci could be delineated at 3-fold the usual dose in scans immediately after the administration, and more metastatic lesions were delineated in scans immediately after the administration of the contrast agent at 3-fold the usual dose than in scans 20 minutes after the administration at the usual dose. From these results, the report concluded that the dose of the contrast agent exerts the greatest effect on the detectability of small lesions.\(^\text{8}\) In a report comparing the delineability of brain metastases between 3-fold the usual dose and usual dose and between magnetic field strengths of 1.5 and 3T, the detectability was highest by scanning at 3T and 3-fold the usual dose.\(^\text{9}\) For metastatic foci less than 5 mm in diameter, the detectability was significantly higher with 3-fold the usual dose than usual dose at both magnetic field strengths.

On the other hand, in a report prospectively evaluating 136 consecutive patients suspected to have brain metastasis...
at 1.5T, tripling the dose was not useful in all patients, because false positives increased, and tripling the dose was recommended only for lesions that are unclear at a usual dose and solitary metastases. In Japan, the administration of an MR contrast agent is permitted at a maximum of 2-fold the usual dose for patients suspected to have brain metastases. Therefore, administering a contrast agent at 2-fold the usual dose in patients showing unclear results at the usual dose or solitary metastases is recommended.

Concerning the MRI procedure at 3.0T for imaging of brain metastases, 3-dimensional sequences such as 3-D gradient echo and 3-D fast spin echo sequences have been reported to be useful. Nephrogenic systemic fibrosis (NSF) has been widely recognized recently as a serious adverse effect of gadolinium-based contrast agents. Therefore, contrast agents should be administered carefully with evaluation of renal function.

Index words and secondary materials used as references

A search of PubMed was performed using “brain metastasis”, “CT”, and “MRI” as key words. Evidence-Based Imaging: Improving the Quality of Imaging in Patient Care, Springer, 2011 was also used as a reference.

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## What MRI techniques are appropriate for patients suspected to have primary parenchymal tumor of the brain?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Technique</th>
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<tr>
<td>A</td>
<td>Contrast-enhanced MRI</td>
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<tr>
<td>B</td>
<td>Diffusion-weighted imaging</td>
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<tr>
<td>C1</td>
<td>Perfusion imaging, MR spectroscopy</td>
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**Contrast-enhanced MRI is strongly recommended because it provides information useful for the evaluation of the site, properties, and degree of malignancy and differential diagnosis of primary parenchymal tumors of the brain.**

Diffusion-weighted imaging is recommended, because it is useful for the evaluation of the properties and degree of malignancy and differential diagnosis of primary parenchymal tumors of the brain.

Since useful information not obtained by conventional MRI sequences may be acquired by the use of advanced imaging techniques such as perfusion imaging and MR spectroscopy, they may be worth considering.

### Background/objective

In addition to regular MR sequences including T1-weighted, T2-weighted, and FLAIR imaging, techniques such as contrast-enhanced MRI, diffusion-weighted imaging, perfusion imaging, and MR spectroscopy (MRS) are available for the examination of primary parenchymal tumors of the brain such as glioma (Figure). There have been various reports concerning the usefulness of these methods. In this section, the significance of the addition of contrast-enhanced MRI, diffusion-weighted imaging, and advanced imaging techniques to conventional MR sequences is evaluated.

### Comments

When primary brain tumors are suspected by CT or non-contrast MRI, contrast-enhanced MRI using a gadolinium-based contrast agent is important for the evaluation of the site, properties, degree of malignancy and differential diagnosis of the lesions. Specifically, in glioma, the presence of a contrast-enhanced area and inclusion of an area of ring-like enhancement are useful as findings suggestive of a highly malignant lesion. Also, contrast-enhanced MRI is necessary for the determination of the biopsy site and extent of surgical resection and planning of radiation therapy. Multiple contrast-enhanced lesions observed on contrast-enhanced MRI suggest metastatic brain tumors, brain abscesses, multiple sclerosis, etc. rather than primary parenchymal tumors of the brain. If the ring of ring-like enhancement is interrupted in the gray mater, a demyelinated lesion rather than a tumor is suspected.

Although the incidence of adverse events due to a gadolinium-based contrast agent is very low at 0.4-0.76%, nephrogenic systemic fibrosis (NSF) has been reported as a serious adverse event in nephropathy patients and has also been observed in Japan. Terminal nephropathy on long-term hemodialysis, an estimated glomerular filtration rate (eGFR) of less than 30 mL/min/1.73 m², and acute renal failure are contraindications for the use of a gadolinium-based contrast agent, and its unnecessary administration in other conditions must also be avoided.

Diffusion-weighted imaging, which can be performed in a scanning time of about 1 minute and readily permits quantitative evaluation, has been accepted widely and is also useful for the examination of brain tumors. The apparent diffusion coefficient (ADC) calculated from diffusion-weighted images is useful for the differentiation between brain abscesses and tumoral lesions with necrosis, estimation of the degree of malignancy in glial tumors, differential diagnosis of primary brain tumors, differential diagnosis of 3 brain tumors, i.e., highly malignant glioma, malignant lymphoma, and metastatic brain tumors, and prognosis of malignant lymphoma and astrocytoma.

In perfusion imaging, the relative cerebral blood volume (rCBV) is often used for the evaluation of brain tumors. In perfusion analysis, a semi-quantitatively standardized tumor blood flow (normalized CBV) is often used by calculating the ratio of the rCBV in the tumor area relative to that in the contralateral normal brain. In glioma, the rCBV in the tumor is positively correlated with the tumor vascular bed and is useful for the evaluation of the degree of malignancy. It is also reportedly useful for the differential diagnosis of glioma from other brain tumors and tumor-like lesions and the evaluation of the therapeutic effect and outcome after treatment of glioma.

On MRS, proton is usually used as the target, and N-acetyl aspartic acid (NAA), choline (Cho), creatine (Cr), and lactate (Lac) are primarily examined in brain tumors. NAA, a metabolite present exclusively in neurons, decreases in various diseases. Cho is a metabolite and a material of phospholipids necessary for cell membrane metabolism. It is considered to be correlated with disruption and enhancement of cell membrane metabolism and, in glioma, increases with the degree of malignancy. MRS is useful for the estimation of the degree of malignancy of glioma and differentiation between glioblastoma and brain abscess. Also, an increase in the Cho/Cr ratio in the periphery of a tumor showing no contrast enhancement suggests invasive malignant tumor and is useful for its differentiation from metastatic
Index words and secondary materials used as references


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brain tumors.27)
1. Brain and nervous system

What imaging modalities are appropriate for diagnosing Alzheimer’s disease?

**Recommendation grade**

**B MRI, SPECT**

MRI is recommended, because it can detect atrophy of the medial temporal lobe characteristic of Alzheimer’s disease and is also useful for diagnosing diseases that cause cognitive impairment other than Alzheimer’s disease. Brain perfusion SPECT is recommended, because it can delineate reduced blood flow in the bilateral temporal and parietal lobes and posterior cingulate gyrus, characteristic of Alzheimer’s disease.

**Background/objective**

The prevalence of dementia is increasing worldwide, and the increase in mild dementia, particularly Alzheimer disease (AD), associated with aging of the population is also a social issue in Japan. In this section, the usefulness of MRI, brain perfusion SPECT, and PET for diagnosing AD is evaluated.

**Comments**

With the development of diagnostic imaging techniques, it has become possible to detect mild brain atrophy and decreases in the blood flow or metabolism associated with dementia, and the role of imaging techniques in the diagnosis of AD has changed from a supplementary tool to exclude of dementing disorders other than AD to an important means for early diagnosis. Moreover, statistical image analysis concerning the brain volume, cerebral blood flow, and sugar metabolism and amyloid PET are reported to have high predictive precision regarding the conversion of mild cognitive impairment (MCI) to AD and are expected to make clinical contributions in the future.

1) **MRI**

A decrease in neurons is observed in the medial temporal lobe, resulting in atrophy of the brain parenchyma, from an early stage of AD (Figure 1). In a meta-analysis of 12 papers evaluating atrophy of the medial temporal region using MRI, AD patients could be discriminated from normal subjects at a sensitivity of 85% and a specificity of 88%. By statistical image analysis using voxel-based morphometry (VBM), atrophy has been demonstrated in the posterior cingulate gyrus, parietal lobe (precuneus), fusiform gyrus, and on the medial side of, and below, the frontal lobe as well as the medial temporal lobe (hippocampus, entorhinal area). Conventionally, special software was necessary for VBM analysis, but voxel-based specific regional analysis system for Alzheimer’s disease (VSRAD) for simple data analysis has become available in Japan since 2006. The accuracy of the diagnoses by this technique with the hippocampus and entorhinal area as a region of interest was 87.8%. As for MR techniques other than those for the morphological diagnosis, the usefulness of 1H-MR spectroscopy and diffusion tensor imaging, which reflect changes in brain tissue in AD, has been reported. By the former technique using the myo-inositol/N-acetyl aspartate (MI/NAA) ratio, AD could be differentially diagnosed from healthy individuals at a sensitivity of 83% and a specificity of 98%. By the latter method, a decrease in the diffusion anisotropy in the limbic system and uncinated fasciculus is reported to be a characteristic finding.

2) **Brain perfusion SPECT**

In AD patients, the blood flow is reduced in the temporal and parietal lobes and from the precuneus to the posterior cingulate gyrus compared with age-matched healthy individuals, and this can be detected by brain perfusion SPECT (Figure 2). In a large-scale prospective study, AD patients and normal subjects could be differentiated by brain perfusion SPECT with a sensitivity of 89% and a specificity of 80%. Compared with standard clinical examinations, brain perfusion SPECT is inferior in sensitivity (74% vs. 81%) but superior in specificity (91% vs. 70%). In addition, brain perfusion SPECT, which can discriminate AD from dementing disorders other than AD (frontotemporal dementia, vascular dementia) with sensitivity and specificity of 70-79%, is also useful for discriminating AD from other dementing disorders.

3) **PET** ($^{18}$F-FDG PET/amyloid PET)

In Japan, the application of these procedures to AD patients is not covered by medical insurance. However, these modalities are mentioned as they are reportedly useful for the diagnosis of AD. PET can detect decreases in glucose metabolism in the posterior cingulate gyrus, precuneus, and parietal-temporal association area in AD patients. The sensitivity and specificity of PET for discrimination of AD from normal individuals are 86-96 and 80-90%, respectively, and its diagnostic performance is higher than that of brain perfusion SPECT. The diagnostic accuracy can be...
Improved further (sensitivity: 95-97%, specificity: 100%) if it is combined with a statistical image analysis technique such as three-dimensional stereotactic surface projection (3D-SSP).\textsuperscript{11} Amyloid PET is a technique to visually represent accumulation of amyloid β protein in the brain of AD patients, and there have been a number of reports using 11C-PIB. While its diagnostic sensitivity is high at 89%,\textsuperscript{12} accumulation of 11C-PIB may also be observed in some (10-30%) of healthy elderly people, degenerative dementias other than AD such as dementia with Lewy bodies, and amyloid angiopathy, and the specificity of amyloid PET is slightly lower than those of SPECT, MRI, and PET.\textsuperscript{13} Since the half-life of 11C is extremely short (20 minutes), the facilities that can perform amyloid PET using 11C-PIB are presently limited. For the future, the routine clinical use of diagnostic preparations labeled with \textsuperscript{18}F, which has a longer half-life, is anticipated.\textsuperscript{14}
References

What imaging modalities are appropriate for normal pressure hydrocephalus?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Imaging Modality</th>
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<tr>
<td>B</td>
<td>CT, MRI</td>
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<tr>
<td>C1</td>
<td>Brain perfusion SPECT</td>
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CT and, particularly, MRI, which are morphological imaging techniques, are recommended, because they can delineate morphological abnormalities characteristic of idiopathic normal pressure hydrocephalus (iNPH) and are useful for its discrimination from other disorders that cause cognitive impairment including Alzheimer’s disease. Brain perfusion SPECT is also useful for discrimination of iNPH from other disorders and may be worth considering.

**Background/objective**

While iNPH is “a treatable dementia”, the symptoms of which can be alleviated by CSF shunt surgery, its differentiation from other disorders that cause similar symptoms is a prerequisite for evaluating indications for this treatment. Various reports are observed concerning neuroimaging of iNPH. In this section, the usefulness of neuroimaging techniques for the diagnosis of iNPH is evaluated.

**Comments**

1) **Basic morphological changes in iNPH**

   In iNPH, characteristic findings described as “disproportionately enlarged subarachnoid-space hydrocephalus: DESH” are observed, and they are useful for discrimination from other diseases presenting as ventricular dilation associated with brain atrophy. In addition to ventricular dilation with an Evans index (maximum width between the frontal horns of the lateral ventricles/maximum transverse internal diameter of the skull at the same level) exceeding 0.3, the findings indicate uneven distribution of the subarachnoid space, i.e., narrowing at the high convexity and longitudinal fissure of the cerebrum and widening at the sylvian fissure and basilar cistern (Figure). According to a prospective cohort study performed in Japan to clarify the clinical significance of these findings (study of idiopathic normal pressure hydrocephalus on neurological improvement: SINPHONI), their validity was confirmed by an 80% response rate to VP shunt. In addition, an epidemiological study in Japan has demonstrated the presence of elderly people who show morphological changes similar to those in DESH, though they are asymptomatic (asymptomatic ventriculomegaly with features of iNPH on MRI: AVIM), and caution is necessary in the diagnosis.

2) **CT**

   Generally, CT exceeds MRI in few respects. However, it is possible to evaluate morphological abnormalities in DESH and other disorders such as local dilation of cerebral sulci, narrowing of the posterior half of the cingulate sulcus, and sharpened callosal angle by preparing coronal and sagittal images using multi-planar reconstitution technique due to improvements in special resolution associated with increases in detector rows.

3) **MRI**

   Changes around the ventricles and in deep white matter are not essential for the diagnosis of iNPH and are also observed in other disorders. While the flow void phenomenon of the cerebral aqueduct is frequently observed in iNPH, it is a non-specific finding also noted in other diseases causing cognitive dysfunction. The measurement of the CSF flow rate by phase contrast MRI has been reported to be sensitive for the diagnosis of iNPH, but its diagnostic value has not been established. Although changes in the diffusion anisotropy ratio and diffusion coefficient in the cerebral white matter observed on diffusion tensor and diffusion-weighted imaging and a decrease in the N-acetyl aspartate/creatine (NAA/Cr) ratio detected by 1H-MRS are useful for discrimination of iNPH patients from normal individuals, they are also observed in other dementing disorders, and their diagnostic value remains unsettled. It is possible to objectively evaluate findings reflecting DESH, i.e., dilation of the lateral ventricles and sylvian fissures and narrowing of the high-convexity subarachnoid space, by statistical image analysis.

4) **Brain perfusion SPECT**

   On brain perfusion SPECT, decreases in the blood flow are observed not only around the corpus callosum and sylvian fissure but also in the cerebral cortex in various patterns, i.e., anterior-dominant, posterior-dominant, and diffuse. Statistical image analysis suggests relative increases in the blood flow in the high-convexity and median regions in addition to decreases in the blood flow, presumably reflecting a decrease in the subarachnoid space and an increase in the density of the gray matter due to DESH. Such findings have been reported to be useful for discrimination of iNPH.
The Japanese imaging guideline 2013

Index words and secondary materials used as references

A search of PubMed was performed using “idiopathic normal pressure hydrocephalus”, “CT”, “MRI”, “SPECT”, “scintigraphy”, “cisternography”, “cerebral blood flow”, “MR spectroscopy”, and “imaging” as key words. The Japanese Society of NPH iNPH Treatment Guidelines Preparation Committee eds: iNPH Treatment Guidelines, 2nd edition was also used as a reference.

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from other dementing disorders including Alzheimer’s disease.\textsuperscript{13,14)}
Head and neck
Is MRI appropriate for the evaluation of the cause of sensorineural hearing loss?

Since MRI has a high detection power for vestibular schwannoma and is excellent in delineating other inner ear/brain pathologies, it is recommended for the evaluation of the cause of sensorineural hearing loss. It is also useful and recommended for the evaluation of indications for the cochlear implant.

Background/objective

Sensorineural hearing loss is caused by various inner ear/brain pathologies including vestibular schwannoma. The cochlear implant has become popular as a treatment for sensorineural hearing loss, and opportunities to perform imaging examinations for the evaluation of its indications are increasing.

CT and MRI are often performed as diagnostic imaging techniques for sensorineural hearing loss. In this section, whether or not these examinations are necessary in all patients presenting with sensorineural hearing loss, what are examination procedures useful for initiating treatment, whether or not they are medico-economically efficient, and the usefulness of MRI are evaluated.

Comments

In examination of unilateral progressive sensorineural hearing loss, MRI is often performed after otorhinological examinations such as audiography and the auditory brainstem response (ABR) test. It is difficult to detect vestibular schwannoma 1 cm or less in diameter by the ABR test alone, and about 10% of the patients have been reported to be overlooked by an audiographic protocol aimed at vestibular schwannoma screening, indicating limitations in the detectability of the disease by an otorhinological study alone. Regarding the cost of examination, a combination of the ABR test and MRI is more expensive than contrast-enhanced MRI alone, and contrast-enhanced MRI is more expensive than non-contrast MRI.

However, the frequency of MRI examination may be reduced by performing audiography or the ABR test, and the clinical significance of otorhinological examinations before MRI is not small.

Contrast-enhanced MRI is presently a standard MRI procedure for the evaluation of vestibular schwannoma. However, in consideration of the recent improvements in MRI devices and imaging techniques, it may be possible to perform initial screening by non-contrast MRI using high-resolution 3D heavily T2-weighted images. By comparison with contrast-enhanced T1-weighted imaging, the sensitivity and specificity of non-contrast-enhanced 3D heavily T2-weighted imaging for vestibular schwannoma have been reported to be 89-100% and 94-99.7%, respectively. However, the detectability of vestibular schwannoma by this procedure depends markedly on the image quality and image reading ability of the radiologist.

Schwannoma also occurs, though rarely, in the labyrinth such as the cochlea, but false negatives are rare on 3D heavily T2-weighted imaging. On contrast-enhanced MRI, however, false positives may occur in disorders including labyrinthitis (Figure).

Since an onset pattern similar to that of sudden sensorineural hearing loss (SSHL) is observed in 10-20% of the patients with vestibular schwannoma, it is necessary to evaluate and exclude vestibular schwannoma by MRI in patients with SSHL. Sensorineural hearing loss is caused by labyrinthisis, trauma, brain tumor, cerebrovascular disorders, multiple sclerosis, and superficial siderosis as well as vestibular schwannoma. MRI is superior to CT in the evaluation of these disorders except for the diagnosis of temporal bone fracture.

For diagnostic imaging of unilateral or asymmetric sensorineural hearing loss in children, the modality must be selected by understanding the characteristics of CT and MRI. CT is effective for delineating calcification, ossification, decalcification, and abnormalities of the vestibular aqueduct, and MRI is superior in the evaluation of the cranial nerves and membranous labyrinth. Also, CT is less expensive than MRI and can be performed in a shorter period, but it involves X-ray exposure. MRI requires a long imaging time and may require sedation. In imaging examination before cochlear implant surgery, the identification of the cochlear nerve, presence or absence of calcification or fibrosis of the cochlea, presence or absence of inner ear anomalies, and their severity are information important for the evaluation of indications and selection of candidates, and MRI is more effective than CT for the evaluation of the nerves and early cochlear obstruction after meningitis.

Index words and secondary materials used as references

A search of PubMed was performed using “sensorineural hearing loss”, “hearing loss”, “vestibular schwannoma”, “acoustic neurinoma”, “acoustic neuroma”, and “MRI” as key words, further limited to results with a date greater than year 1990. The Japan Radiological Society and Japanese College of Radiology eds.: Guidelines for Diagnostic Imaging 2003 was also used as a reference.
The Japanese imaging guideline 2013

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Figure Vestibular Schwannoma 3D heavily T2-weighted image
A mass (→) is observed in the left internal auditory meatus.
Background/objective

Regarding orbital/ocular disorders, CT is often performed in patients with orbital trauma and those who cannot be sedated. Before the 1990s, CT was used frequently for the examination of orbital/ocular disorders, but MRI has become widely available today, and the frequency of CT examinations for intraocular tumors has decreased due to X-ray exposure and the lack of tissue contrast. In this section, CT and MRI are compared to evaluate what imaging modalities should be selected for typical intraocular tumors (retinoblastoma frequently affecting children and malignant melanoma frequently affecting adults).

Comments

1) Retinoblastoma

Of the retinoblastomas, 95% are diagnosed by the age of 5 years, and 56-72% are detected due to leukocoria. Since the prognosis of retinoblastoma is markedly affected by the early diagnosis and treatment, diagnostic imaging is important. Retinoblastoma is characteristically accompanied by calcification (≥ 90%), and CT, which has a higher detection power for calcification than MRI or ultrasonography, is useful for its diagnosis. However, some question about the use of CT as the first choice in consideration of X-ray exposure in the neonatal period/early childhood. As there is a report that the detectability of calcification of retinoblastoma is about 96% by CT, 95% by ultrasonography, and 89% even by MRI if sequences sensitive for calcification such as T2 star-weighted imaging are added, CT may not be indispensable for the diagnosis of retinoblastoma. Also, there are retinoblastomas that show no clear mass formation or calcification, and such lesions are difficult to diagnose without MRI or ultrasonography. At the very least, frequent CT examination for the follow-up after treatment for retinoblastoma or the use of CT for screening of children for retinoblastoma is not recommended.

Retinoblastoma presents a hyperdense image on CT, and contrast enhancement is observed in 27.5% of the patients, but it is a non-specific finding. Also, the prognosis of retinoblastoma is affected by the presence or absence of choroidal invasion, optic nerve invasion, intracranial infiltration, and dissemination. While choroidal and optic nerve invasion can also be evaluated by CT, it can better be evaluated by MRI with high tissue contrast, and ultrasonography is superior for the evaluation of minute extraocular infiltration. If a tumor infiltrates the vitreous body and subretinal space, it may cause retinal detachment, and the differentiation between the tumor and subretinal effusion becomes necessary. MRI is more effective than CT for this purpose. The administration of an iodine-based contrast medium is necessary for the CT evaluation of tumor invasion, and MRI should be considered first line also from the viewpoint of X-ray exposure. Bilateral retinoblastoma occurs in 25%, and trilateral retinoblastoma (retinoblastoma involving the bilateral retinae and the pineal body or suprasellar region) occurs in 5-15%, of the patients with hereditary retinoblastoma. MRI is superior to CT for the evaluation of intracranial infiltration of the tumor, presence or absence of suprasellar or pineal lesions, and dissemination.

 Diseases that exhibit white pupil and need discrimination from retinoblastoma include persistent hyperplastic primary vitreous (PHPV) and Coats’ disease. This differentiation can be made by MRI with high tissue contrast.

2) Malignant choroidal melanoma

Choroidal melanoma tends to be hyperdense on CT and shows mild-moderate contrast enhancement on contrast-enhanced CT. While the tumor can also be delineated by CT, MRI with high tissue contrast is superior. Melanoma in particular often emits characteristic signals on MRI and ultrasonography surpasses CT in the evaluation of extraocular infiltration of tumors. They are also more effective than CT for the separation and discrimination of associated retinal detachment from tumor. Although melanomas 2 mm or less in diameter are reportedly difficult to delineate by CT or MRI, they may be visualized by MRI due to the recent development of MRI techniques and coils and the increased availability of MRI with a static magnetic field of 1.5T or above. There is no
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Index words and secondary materials used as references

A search of PubMed was performed using “retinoblastoma”, “uveal melanoma”, “ocular tumor”, “CT”, and “MRI” as key words. The Japan Radiological Society and Japanese College of Radiology eds.: Guidelines for Diagnostic Imaging 2003 was also used as a reference.

References

8) Mafee MF et al: Malignant uveal melanoma and similar lesions studied by computed tomography. Radiology156: 403-408, 1985 (Level 4)

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Figure: Ocular tumor (malignant melanoma)
T2-weighted image

A mass, which is hypointense compared with the surrounding vitreous body, is observed in the medial region of the right eye ball (→). It was a malignant melanoma of the choroid.
2. Head and neck

Is MRI appropriate for pretreatment staging (T-stage) of hypopharyngeal cancer?

**Recommendation Grade**

**C1**

MRI is recommended for the evaluation of invasion to cartilage, cervical esophagus, and carotid artery associated with anterior/inferior infiltration of hypopharyngeal cancer. However, its usefulness relative to CT has not been defined, and its complementary use with other examinations is necessary.

**Background/objective**

Concerning the T stage of hypopharyngeal cancer, TNM Classification of Malignant Tumours, Sixth Edition classifies invasion to the thyroid cartilage, cricoid cartilage, and median structures and soft tissues of the neck such as the hyoid bone, thyroid gland, and esophagus as T4a, and invasion to the prevertebral fascia and mediastinum or invasion circumferentially surrounding the carotid artery as T4b, and accurate evaluation by imaging techniques is important. In this section, whether or not MRI is recommended for imaging examination for pretreatment T staging is evaluated by comparing MRI with CT and PET.

**Comments**

For the preoperative imaging examination of hypopharyngeal cancer, CT is the first choice because of its superior cost effectiveness, simplicity, and evaluation of cartilage invasion.\(^1,2\) Regarding pretreatment staging (T-staging), there have been few studies with a high evidence level exclusively on hypopharyngeal cancer, but many studies including laryngeal cancer, which is anatomically similar, and the prognosis of which largely depends on the presence or absence of cartilage invasion, have been reported.

In studies comparing preoperative CT and MRI for the evaluation of cartilage invasion in laryngeal cancer, MRI was more sensitive but less specific than CT because of overestimation of inflammatory changes.\(^3,4\) Also, the addition of erosion and lysis of cartilage to the diagnostic criteria of CT improves the sensitivity but decreases the specificity.\(^5\) In a report using MD-CT, also, no significant improvement in the diagnostic accuracy was noted.\(^6\)

The area from the posterior cricoid cartilage to the cervical esophagus is more clearly delineated by MRI than CT due to greater tissue contrast.\(^1\) Also, the specificity was reported to have improved markedly by discriminating inflammatory changes as hyperintensity on T2-weighted imaging and higher contrast than tumor on T1-weighted imaging from tumor invasion as equal contrast.\(^7\) Therefore, MRI is suggested to become a modality comparable to CT for accurate evaluation of cartilage invasion.

Regarding invasion to the larynx and cervical esophageal region, the tumor volume tends to be overestimated on CT and MRI due to modification of findings by inflammatory changes.\(^8\) Also, FDG-PET tends to underestimate the tumor volume than CT or MRI,\(^9\) and MRI is inferior to CT in the evaluation of invasion to the lateral or posterior pharyngeal wall but is advantageous in the evaluation of longitudinal invasion\(^10\) (Figure).

Thus, it is considered important to comprehensively evaluate the extent of involvement and distant metastasis of tumor by using CT, MRI and PET findings complementarily in addition to physical and endoscopic findings on otorhinological examination.

**Index words and secondary materials used as references**

A search of PubMed was performed using “larynx”, “hypopharynx”, “head and neck”, “carcinoma”, “MRI”, and “CT” as key words and further limited to studies since 1982. The Japan Society for Head and Neck Cancer eds: Guidelines for the Management of Head and Neck Cancer 2009 was also used as a reference.

**References**

6) Li B et al: Overstaging of cartilage invasion by multidetector CT scan for laryngeal cancer and its potential effect on the use of organ preserva-
Figure: Hypopharyngeal cancer (T4a N2b M0)
A MRI  T2-weighted image  B MRI Coronal STIR image  C Contrast-enhanced CT: On T2-weighted imaging, a tumor slightly more hyperintense than muscle considered to have developed from the left piriform recess is observed (→). On the coronal image, infiltration from the mesopharynx to the supraglottal cavity is obvious. Enlarged lymph node aggregate at the left internal jugular level. No invasion of the thyroid cartilage was noted on CT.

Background/objective

Since head and neck squamous cell carcinoma may be cured completely by chemoradiotherapy, it is an important treatment along with surgery, but the methods for the evaluation of its effects and follow-up vary among facilities, and a variety of imaging techniques are selected. In this section, imaging modalities efficient and preferable for follow-up examinations are evaluated.

Comments

Usually clinical examinations such as gross examination, endoscopy, and palpation are performed first to evaluate the response to the chemotherapy regimen or to confirm the radiosensitivity of the lesion during chemoradiotherapy. Ultrasonography, CT, or MRI is used to examine deep areas not approached by clinical examinations or objectively measure the tumor size. While there is no evidence concerning indications for these modalities, guidelines for the evaluation of therapeutic effects in solid tumors (RECIST Guidelines) recommend CT. However, if the lesion has been delineated more accurately by MRI before treatment, the evaluation using MRI is acceptable. However, it is necessary to perform CT or MRI using the same protocols as before treatment.

Images after chemoradiotherapy often differ considerably compared with pretreatment images due to the effects of inflammation. Therefore, images that serve as a baseline are necessary for long-term observation following chemoradiotherapy, and CT is recommended for this purpose. CT images about 6-8 weeks after the end of treatment are appropriate as baseline images. MRI is recommended to obtain baseline images for the follow-up of cancers occurring near the skull base. Baseline MR imaging should be obtained about 12-16 weeks after the end of treatment. PET shows high sensitivity and negative predictive value in the diagnosis of recurrence and is recommended. The time appropriate for PET examination is 6-8 weeks after the end of treatment, because the sensitivity and positive predictive value are low early following the end of treatment (within 4 weeks).

A recommended interval of follow-up imaging is 3-4 months during the first 2 years, when recurrence is considered likely, and 4-6 months during the next 3-5 years for both CT and MRI.

Index words and secondary materials used as references

A search of PubMed was performed using “head and neck squamous cell carcinoma”, “evaluation after treatment”,
“diagnostic imaging”, “MRI”, and “CT” as key words.

References

2) van den Broek GB et al: Response measurement after intraarterial chemoradiation in advanced head and neck carcinoma: magnetic resonance imaging and evaluation under general anesthesia? Cancer 106: 1722-1729, 2006 (Level 3)
7) Martin RC et al: Accuracy of positron emission tomography in the evaluation of patients treated with chemoradiotherapy for mucosal head and neck cancer. Head Neck 31: 244-250, 2009 (Level 3)
2. Head and neck

20 Is MRI appropriate for pretreatment staging (T-staging) of oral cancer?

Although MRI is useful for the evaluation of the extent of invasion, no significant difference compared with CT has been demonstrated. Also, while CT is considered useful for the evaluation of bone cortex invasion, superficial invasion is not a criterion for T4 stage in gingival cancer.

Background/objective

For the pretreatment staging of oral cancer, clinical interview, inspection, and palpation are performed first, and diagnostic imaging is employed to objectively evaluate and record infiltration into deep areas and surrounding tissues. CT evaluation is hampered by metal artifacts due to dental filling materials, and artifacts due to movements such as respiration and swallowing pose problems in MRI. This section compares the recommendation levels of CT and MRI as imaging modalities for the pretreatment T staging.

Comments

In comparative studies with CT regarding T staging, MRI has been reported to have excellent sensitivity and accuracy, but no statistical significance has been shown. Generally, MRI is excellent in soft tissue delineation and is recommended for imaging evaluation of the extent of invasion. Also, in comparative studies with the addition of FDG-PET, MRI has been shown to be useful for the preoperative evaluation of oral cancers, and FDG-PET has been reported to provide little additional information contributing to T staging.

As for site-specific evaluations, in tongue cancer, it is necessary to study invasion into the tongue and surrounding tissues. In the evaluation of the depth of early tongue cancer, a correlation between MRI measurements and histological findings has been demonstrated using the thickness and depth of tumor from the mucosal surface as indices. A correlation between the depth determined by MRI and cervical lymph node metastasis has also been reported.

Floor of mouth cancer and mandibular gingival cancer infiltrate into the mandible from an early stage. In maxillary gingival cancer and hard palate cancer, invasion to the maxilla, maxillary sinus, and nasal cavity must be evaluated. In the TNM classification of gingival cancer, superficial invasion to the bone cortex or alveolar region is not a criterion to stage a lesion as T4 (Figure). Concerning the depth of mandibular gingival cancer, the Guidelines for the Management of Oral Cancers 2009 proposed a classification by the mandibular canal. According to comparative studies of CT and MRI for the evaluation of mandibular invasion, the sensitivity was 42-79% and 58-100%, specificity was 82-100% and 73-97%, and accuracy was 74-92% and 86-94%, respectively, and the results varied among patients and with the imaging equipment and method. However, there are many reports that MRI has high sensitivity but low specificity. There is also a report that, with the addition of reconstructed images, the sensitivity, specificity, and accuracy of CT for mandibular invasion are higher than those of MRI. Generally, CT and MRI are considered useful for the evaluation of bone cortex and bone marrow invasion, respectively, and MRI is recommended for the T staging.

Regarding deep oral invasion, coronal images are occasionally useful for examining soft tissues and the mandible. Contrast agents are used to more clearly delineate the extent of invasion of oral cancers, but precontrast T1-weighted imaging is recommended in early floor of mouth cancer, which is visualized as a soft tissue mass replacing the sublingual glands, to obtain contrast between the tumor and sublingual glands. Precontrast T1-weighted images are also recommended for the evaluation of bone marrow invasion.

Index words and secondary materials used as references

A search of PubMed was performed using “oral”, “tongue”, “gingival”, “mandibular”, “squamous cell carcinoma”, “MRT”, and “CT” as key words. The Japan Society for Oral Tumors/Japanese Society of Oral and Maxillofacial Surgeons eds: Guidelines for the Management of Oral Cancers 2009 was also used as a reference.

References

2) Sigal R et al: CT and MR imaging of squamous cell carcinoma of the tongue and floor of the mouth. Radiographics 16: 787-810, 1996 (Level 5)
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Figure: Stage T3 mandibular gingival cancer (T1-weighted image)

In the TNM classification of gingival cancers, superficial invasion to the bone cortex or alveolar region is not a criterion for stage T4. In this case, invasion to the alveolar region (→) is suggested, but the lesion was staged as T3 due to its maximum diameter on the mucosal surface, which was >4 cm.

118, 2006 (Level 4)
8) Preda L et al: Relationship between histologic thickness of tongue carcinoma and thickness estimated from preoperative MRI. Eur Radiol 16: 2242-2248, 2006 (Level 3)
13) Vidiri A et al: Multi-detector row computed tomography (MDCT) and magnetic resonance imaging (MRI) in the evaluation of the mandibular invasion by squamous cell carcinomas (SCC) of the oral cavity. Correlation with pathological data. J Exp Clin Cancer Res 29: 73, 2010 (Level 3)
2. Head and neck

Is MRI appropriate for the pretreatment staging (T staging) of laryngeal cancer?

**Recommendation grade**
While MRI is considered useful for the evaluation of deep invasion, no significant difference compared with CT has been shown.

**Background/objective**
The pretreatment staging of laryngeal cancer has been made conventionally by medical interview, inspection, and palpation plus endoscopy, but images provided by CT or MRI are necessary for objectively evaluating the tumor size and deep invasion. Moreover, as the sixth edition of the UICC TNM staging system began to classify not only conditions with vocal cord fixation but also those showing invasion to the paraglottic space and/or slight erosion of the thyroid cartilage as T3 (Figure), imaging evaluation has become more important. The usefulness of CT and MRI for pretreatment T staging is compared.

**Comments**
According to studies in the 1990s comparing the effectiveness of preoperative CT and MRI for the evaluation of cartilage invasion,\(^2,3\) the sensitivity was 66-67% and 89-94%, and the specificity was 87-94% and 74-84%, respectively. MRI was superior in sensitivity but inferior in specificity due to overestimation of tumor due to inflammatory changes compared with CT. There has recently been no comparative studies, and the usefulness of CT and MRI is evaluated separately. In the reevaluation of cartilage invasion using CT,\(^4\) diagnostic criteria including erosion and lysis increased the sensitivity but reduced the specificity. In a study using MDCT reported in 2011, no clear improvement was observed in the diagnostic accuracy.\(^5\) There is also a report that arynotenoid cartilage sclerosis, which is a CT diagnostic criterion, is also observed in normal individuals or as a secondary change and is a non-specific finding.\(^6\) On the other hand, in a study reevaluating MRI findings reported in 2008,\(^7\) the specificity was increased without reducing the sensitivity by judging a condition in which cartilage shows a higher signal intensity than tumor on T2-weighted and postcontrast T1-weighted imaging as inflammatory changes but a condition in which it is isointense as tumor invasion. In MRI evaluation of cartilage invasion, it is necessary not only to note abnormal signals but also to use diagnostic criteria in consideration of differentiation from inflammatory changes.

Submucosal pre-epiglottic and paraglottic invasion is delineated as a soft tissue image replacing fat tissue, and this finding on CT and MRI has been reported to be highly sensitive and specific.\(^8\) Concerning the evaluation of the paraglottic space by MRI, overestimation due to inflammatory changes has been reported.\(^9\)

The primary treatment for pharyngeal cancer is radiotherapy for early cases and surgery for advanced cases. The usefulness of pretreatment imaging examinations is evaluated according to pathological findings in surgical cases but therapeutic efficacy in radiotherapy (±chemotherapy) cases. Concerning pre-radiotherapy MRI findings, invasion of glottic cancer to the paraglottic space,\(^1,10\) and invasion of supraglottic carcinoma to the pre-epiglottic space,\(^13\) which are findings corresponding to stage T3, have been confirmed as prognostic factors related to local control. Also, abnormal signals of the thyroid cartilage corresponding to stages T3 (slight erosion) and T4 (transmural invasion) are predictive factors of the therapeutic efficacy.\(^11,12\) Moreover, the MRI diagnostic criteria for the discrimination between cartilage invasion and inflammatory changes are also considered to be prognostic factors.\(^10\) Changes in the therapeutic strategy should be evaluated in patients in whom the local control by radiotherapy is expected to be difficult, i.e., advanced cases, but attention to the risk of losing the possibility of larynx preservation due to overestimation of MRI findings is necessary.\(^5\)

**Index words and secondary materials used as references**
A search of PubMed was performed using “laryngeal”, “glottis”, “squamous cell carcinoma”, “MRI”, and “CT” as key words and further limited to studies since 1990. The Japan Society for Head and Neck Cancer eds: The Guidelines for the Management of Head and Neck Cancers 2009 was also used as a reference.

**References**
Figure: Stage T3 glottic cancer (contrast-enhanced T1-weighted image)

A lesion is diagnosed as stage T3 if there is paraglottic space invasion (→) even without vocal cord fixation. Also, the stage of glottic cancer is T3 if there is only superficial invasion to the thyroid cartilage and T4 if it ruptures the thyroid cartilage.


2. Head and neck

Is the use of a contrast agent appropriate in CT for paranasal sinus disease?

### Background/objective

While the necessity of CT as an imaging modality for paranasal sinus disease should be evaluated first by comparing it with other examinations including MRI and endoscopy, CT is used frequently today for screening of chronic sinusitis. The usefulness of coronal CT as an examination before endoscopic surgery for chronic sinusitis has been established with the recent development of endoscopic sinus surgery (ESS). Under these circumstances, the use of a contrast agent has no benefit and contrast use is unnecessary.

The objective of the use of CT for screening of chronic sinusitis is diagnosing complications such as mucocele/pyocele, abscess, fungal infection, and tumors as well as preoperative roadmapping. CT is also performed in postoperative follow-up to evaluate the persistence or recurrence of the tumor or inflammation. Whether or not the use of a contrast agent in addition to non-contrast CT improves the diagnosability of these conditions is evaluated.

### Comments

Concerning the necessity or usefulness of the use of a contrast agent in CT for paranasal sinus disease, there is no study comparing the diagnostic power between contrast-enhanced and non-contrast CT, and the evidence is insufficient.

In diagnostic imaging of paranasal sinus disease, CT surpasses plain X-ray study or MRI in the evaluation of details of anatomical bony structures and their changes due to space-occupying lesions. Particularly in ESS, coronal CT is reported to be useful and is recommended. However, there is no report indicating the advantage of the use of a contrast agent in ESS, and it is considered unnecessary (Figure). In the differential diagnosis of paranasal sinus disease, also, the usefulness of CT depends entirely on its excellence in the evaluation of bone morphology such as the presence or absence of destruction of anatomical bony structures and detection of calcification associated with fungal sinusitis, and, for this purpose, also, there is no sufficient evidence supporting the use of a contrast agent.

Regarding individual diseases, also, there are a number of reports discussing the characteristics of CT images, but none has suggested the benefit of the use of a contrast agent. As for the differential diagnosis of paranasal sinus disease, however, there is a report suggesting the usefulness of contrast-enhanced MRI, and the use of a contrast agent is considered appropriate if CT is performed for the differential diagnosis when MRI examination is impossible. There is also a report that contrast-enhanced CT was useful for the differential diagnosis of inverted papilloma.

### Recommendation grade

- **B** For the diagnosis of paranasal sinus disease suspected to be tumor, the use of a contrast agent on CT is recommended if the diagnosis cannot be made by MRI or if MRI is unavailable.
- **C2** The evidence that the use of a contrast agent on CT as the initial imaging examination contributes to the diagnosis of paranasal sinus disease is insufficient, and it is not recommended.
- **D** When CT is performed before functional endoscopic sinus surgery for chronic sinusitis, the use of a contrast agent is unnecessary and is not recommended.

### Index words and secondary materials used as references

A search of PubMed was performed using “paranasal sinus”, “maxillary sinus”, “CT”, “contrast media”, and “contrast enhanced CT” as key words. The Japan Radiological Society and Japanese College of Radiology eds: Guidelines for Diagnostic Imaging 2007 was also used as a reference.

### References

Figure: Chronic maxillary sinusitis

In patients who have mild clinical symptoms and are suspected to have simple chronic sinusitis as this case, contrast-enhanced CT is unnecessary. If CT is performed before ESS for chronic sinusitis, reconstructed coronal images are also necessary.

7) Han MH et al: Cystic expansile masses of the maxilla: Differential diagnosis with CT and MR. AJNR 16: 333-338, 1995 (Level 4)
Is MRI appropriate in paranasal sinus diseases other than tumor?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Details</th>
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<tbody>
<tr>
<td>B</td>
<td>MRI is recommended for patients suspected to have intraorbital extension of inflammation or intracranial complications, immunodeficient patients, and patients with fungal or unilateral sinusitis (excluding those clearly diagnosed to have odontogenic maxillary sinusitis by CT).</td>
</tr>
<tr>
<td>C2</td>
<td>In usual sinusitis, there is no clear evidence indicating the usefulness of MRI compared with CT, and MRI is not recommended.</td>
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</table>

**Background/objective**

CT has conventionally played a central role in diagnostic imaging of paranasal sinus diseases. Recently, MRI with higher tissue contrast resolution has been increasingly used for its evaluation, and MRI findings in various paranasal sinus diseases have been reported, but its indications are unclear. In this section, indications for MRI in paranasal sinus diseases, particularly, sinusitis, are evaluated.

**Comments**

There have been few studies that evaluated the indications for MRI concerning all paranasal sinus diseases. This is probably because paranasal sinus diseases include various pathological entities such as inflammatory and tumoral lesions, each of which has multiple important evaluation items, and comprehensive evaluation of indications for MRI is difficult. Presently, when paranasal sinus disease is suspected, clinical symptomatic and rhinoscopic examinations are performed first, and conservative treatments are carried out. If the disease resists conservative treatments, or complications are suspected, and if surgery is considered necessary, CT is the first choice imaging examination. CT is superior to MRI in imaging of minute bony structures and anatomical changes and as an examination before functional endoscopic sinus surgery. There is a report suggesting the usefulness of MRI compared with CT in unilateral sinusitis, which is considered to be of clinical importance, for the diagnosis of its complication by tumor and discrimination between tumor matrix and the area of secondary obstructive inflammation. Therefore, MRI may be indicated if tumor cannot be excluded by the clinical course or findings including images obtained to that point. It has also been reported that the accuracy of the diagnoses of chronic sinusitis and mucocele (pyocele) by preoperative CT was 75 and 85%, respectively, but that all lesions that were difficult to diagnose by CT were nevertheless diagnosed by MRI. Concerning the diagnosis of intracranial complications of sinusitis, the accuracy was reportedly 92% by CT and 100% by MRI, also indicating the superiority of MRI. MRI is also considered to be indicated when symptoms suggest intracranial complications.

In acute sinusitis, an approach based on the clinical history and physical findings is necessary. While there is no report presenting evidence concerning the usefulness of diagnostic imaging, coronal CT has been recommended in patients with persisting symptoms and for preoperative examination. However, the usefulness of MRI is unclear.

In fungal sinusitis, hyperdensity in CT and marked hypointensity in T2-weighted imaging of MRI are important for the diagnosis, but the latter is considered more specific, and MRI has been reported to be useful for the imaging diagnosis of fungal sinusitis (Figure).

**Index words and secondary materials used as references**

A search of PubMed was performed using “paranasal sinusitis”, “non-neoplastic disease”, “complication”, and “MRI” as key words.

**References**

1) Fatterpekar GM et al: Imaging the paranasal sinuses: where we are and where we are going. Anat Rec (Hoboken) 291: 1564-1572, 2008 (Level 5)
5) Ikeda K et al: Unilateral sinonasal disease without bone destruction. Differential diagnosis using diagnostic imaging and endonasal endoscopic
Figure: Non-invasive fungal sinusitis
A  Plain CT  B  T2-weighted image: Non-contrast CT (A) shows a hypo- to isodense area in the right maxillary sinus. Although calcification is unclear, a hypointense area is noted in the sinus in the T2-weighted image, and fungal sinusitis is suggested. MRI is also useful in such cases.

6) Younis RT et al: The role of computed tomography and magnetic resonance imaging in patients with sinusitis with complications. Laryngoscope 112: 224-229, 2002 (Level 3)
2. Head and neck

Is CT appropriate for the follow-up of benign paranasal sinus disease? (If CT is performed, what are the appropriate followup length/intervals?)

CT may be considered for the follow-up of sinusitis and polyps. No clear conclusion has been reached at the present as to the length and intervals of follow-up imaging examinations. Note) MRI rather than CT is recommended for the follow-up of papilloma.

Background/objective

Many paranasal sinus diseases are benign, and, if surgery is necessary, a satisfactory outcome can be obtained by endoscopic surgery. However, these diseases often recur. Sinusitis and polyps are the most frequent benign diseases that require follow-up. Papilloma (including inverted papilloma) is a benign tumor that is likely to recur. Following the established guidelines, the usefulness of imaging examinations for these diseases was evaluated, and which of CT and MRI is more useful and when it should be performed were evaluated by a review of the literature.1-4)

Comments

1) Sinusitis/polyps

In patients who underwent CT of the paranasal sinuses, no correlation was observed between the patient complaint score and CT score or between pathological findings of chronic sinusitis and the severity of CT findings.5-7) However, in chronic sinusitis patients, the Lund Mackay system for CT has high sensitivity, and CT, along with the history of present illness and physical findings, contributes to the accurate diagnosis of chronic sinusitis.5,9) In the follow-up after endoscopic surgery, no difference compared with preoperative findings is observed on CT, but this does not deny its usefulness. CT is also performed postoperatively. CT is particularly significant in evaluating whether or not the ostiomeatal unit is obstructed in patients with persistent symptoms and for comparison with the preoperative condition. The CT score as an objective index showed no marked improvement after compared with before surgery, but improvements were observed in the total score of all sinuses, each maxillary sinus, and ethmoid sinus.10)

If repeat endoscopic surgery (modification surgery) is performed, the Lund Mackay system for CT is also applied as a supplementary diagnostic tool.7 There was a report that, for follow-up, both endoscopy and CT were performed 1 month after endoscopic surgery, but no clear reason for this interval was mentioned.10)

Follow-up is generally performed according to changes in symptoms, and endoscopy or CT is often considered depending on the findings.10-12)

2) Papilloma

For the follow-up of sinonasal papilloma, examination of symptomatic changes and endoscopy are essential, and CT is added as a supplementary diagnostic procedure.13-17) CT is performed first both before and after surgery, and MRI is also performed before and after surgery in patients with expansive lesions.18)

Concerning recurrent papilloma, since there are reports that the recurrent mass could be identified, and the area of involvement could be determined, more accurately by MRI than by CT, MRI is recommended more strongly.18,19)

Index words and secondary materials used as references

A search of PubMed was performed using “paranasal sinus”, “inflammation”, “benign tumor”, “follow up”, and “MRI” as key words. The Japan Radiological Society and Japanese College of Radiology eds: Guidelines for Diagnostic Imaging 2007 was also used as a reference.

References

2) Bhattacharyya N: Radiographic stage fails to predict symptom outcomes after endoscopic sinus surgery for chronic rhinosinusitis. Laryngoscope 116: 18-22, 2006 (Level 2)
7) Bhattacharyya N: Test-retest reliability of computed tomography in the assessment of chronic rhinosinusitis. Laryngoscope 109: 1055-1058,
Is plain radiography useful for the diagnosis of adult paranasal sinus disease?

Plain radiography may be performed, but there is little evidence that it is of diagnostic value.

Background/objective

The present guidelines were prepared using the same clinical questions as those used in the evidence-based Guidelines for Diagnostic Imaging edited by the Japan Radiological Society and Japanese College of Radiology Joint Guidelines Committee (JRS/JCR Joint Guidelines Committee) published in 2007. Compared with those days, plain radiography of the paranasal sinuses appears to have nearly ceased to be performed as the first examination of patients with paranasal sinus-related complaints at the outpatient clinic (primarily the ENT clinic) at least in the university hospital level. However, in local facilities, plain radiography (a combination of Waters view, Coldwell view or its modification, and lateral view or Waters view alone) is still frequently performed as the first imaging study. Depending on the findings by plain radiography, CT, or MRI, or both are performed. However, the diagnostic power of plain radiography is limited, and CT as well as plain radiography is performed in many of (1) patients with relatively severe symptoms, (2) those who resist conservative treatments, and (3) those with recurrence after remission. MRI may also be performed depending on the findings by CT. Such an examination procedure is inefficient in both time and cost and increases the radiation exposure. Therefore, the usefulness of plain radiography in paranasal sinus disease was reevaluated by an additional review of the literature.

Comments

Uncomplicated acute paranasal sinusitis is usually diagnosed on the basis of symptoms, the course, and clinical findings including those by anterior rhinoscopy, and conservative treatments such as the administration of antibiotics and decongestion are performed. Usually, diagnostic imaging is unnecessary. If the symptoms are severe, plain radiography may be indicated. However, the possibility of overlooking lesions in the ethmoid sinus should be considered.

Outpatient examinations including plain radiography are screening tests and are required to have high sensitivity. For this reason, plain radiography, which is not sensitive, should not be performed on a routine basis if acute paranasal sinusitis is suspected.

In chronic sinusitis, the role of imaging modalities differs according to the severity of symptoms and the presence or absence of complications. There is a report that clinical findings, anterior rhinoscopy, endoscopy, and plain radiography suffice for the diagnosis alone. However, CT (direct coronal images or reconstructed coronal images obtained by multiplanar reconstruction (MPR)) should be considered first by omitting plain radiography if the condition exhibits severe symptoms, is complicated by diabetes, etc., or resists conservative treatments and may be an indication of functional endoscopic sinus surgery.

However, in such situations, it may be impossible to immediately perform CT, or the facility may not be equipped with CT. Some papers have also suggested problems with the costs (NHI points) of CT and plain radiography. There was no clear evidence concerning the usefulness of, and radiation exposure involved in, coronal reconstruction by multislice CT. At some facilities, nasal/paranasal sinus endoscopy has been replaced by plain radiography for screening of patients for chronic or recurrent sinusitis.

There was no evidence that plain radiography is useful for the diagnosis of tumoral lesions.

If CT is performed by omitting plain radiography, radiation exposure due to CT should be considered. There is a report that the total exposure dose varies with the protocol and equipment and depends on the tube voltage and mAs (the mean exposure dose of the lens in direct coronal imaging is 70.3 mGy at 475 mAs, 17.6 mGy at 210 mAs, and 4.7 mGy at 30 mAs). The exposure dose of the lens in direct coronal imaging was reported by Stammburger et al. to be 12-90 mGy but by Rowe-Jones et al. to be a mean of 9.81 mGy (SD: ±5.62). It is necessary to examine in each CT system whether or not a diagnostic power (resolution) sufficient for endoscopic surgery can be maintained even when the tube voltage and mAs are reduced.

Index words and secondary materials used as references

A search of PubMed was performed using “plain radiography” and “paranasal sinus” as key words. The Japan Radiological Society and Japanese College of Radiology eds: Guidelines for Diagnostic Imaging 2007 was also used as a reference.
References

1) Fatterpekar GM et al: Imaging the paranasal sinuses: where we are and where we are going. Anat Rec (Hoboken) 291: 1564-1572, 2008 (Level 5)


2. Head and neck

Is CT appropriate for the preoperative diagnosis of parotid gland tumor?

**Background/objective**

Ultrasonography, CT, and MRI are typical imaging modalities used to examine the parotid gland. Recently, as the number of detector rows has been increased, scanning at a thinner slice thickness and in a shorter period and observation of multiple planes by image reconstruction has been facilitated. However, there are problems with CT of the parotid glands such as that artifacts due to dental prostheses are likely to occur, that delineation of tumor is difficult due to poor contrast, that the discrimination of benign and malignant tumors is difficult, and that the procedure involves exposure. In consideration of these factors, the usefulness of CT for the preoperative evaluation of parotid gland tumors was evaluated.

**Comments**

Inspection, palpation, cytological examination, and biopsy can be performed relatively easily in the parotid gland region. If a tumoral lesion is suspected by inspection and palpation, ultrasonography, which can be performed readily without radiation exposure, is considered appropriate as the first choice imaging modality. For the subsequent detailed evaluation using CT or MRI, the modality that is superior in the delineation ability of tumor properties and differential imaging of the tumor and surrounding tissues and more appropriate for local evaluation should be selected.

Since the 1980s, there have been reports that MRI is superior to CT in imaging of parotid gland tumors, and the high tissue resolution of MRI has been mentioned as its reason. Due to high tissue resolution, MRI can visualize parotid gland tumor, parotid gland parenchyma around the tumor, and surrounding structures. MRI has been reported to have delineated the margins of tumors that appeared poorly marginated on CT (Figure), and Barsotti reported a case of pleomorphic adenoma the morphology of which was unclear on preoperative contrast-enhanced CT. The poor delineation of the tumor was ascribed to the closeness of the X-ray absorption coefficient between the tumor and surrounding parotid gland tissue. Pleomorphic adenoma is difficult to detect because of weak contrast enhancement in the early phase of contrast-enhanced CT and the closeness of the absorption coefficient compared with the surrounding parotid gland parenchyma. This tendency is stronger in younger individuals, in whom fat replacement of the parotid gland parenchyma is not advanced. Thus, MRI has been considered useful for the evaluation of parotid gland tumors since 1990 to the present, and Chiriste et al. recently reported that the usefulness of CT for the evaluation of salivary gland tumors is limited.

Pleomorphic adenoma, which accounts for a high percentage of parotid gland tumors, frequently appears as a lobulated mass with a circumferential capsule on MRI, and the capsules of malignant lesions, if they have capsules, are reportedly non-circumferential. Also, by MRI, Warthin’s tumor is considered to be discriminated from other tumors using the time-signal intensity curve of contrast-enhanced dynamic study, and pleomorphic adenoma and malignant lymphoma to be differentiated from other tumors using the ADC value. Thus, MRI allows estimation of the nature of tumor tissue to some extent and is also considered superior to CT in this respect.

Ginsberg et al. reported that MRI excels CT in the detection of perineural spread of tumors. Particularly, if malignant tumor is suspected, MRI should be performed preferentially. If artifacts due to the denture or dental prosthetics appear in CT, they reach the parotid gland, unavoidably deteriorating the image. In MRI, however, the area affected by artifacts is narrower than in CT, being limited to the alveolar processes and intraoral structures, and the evaluation of the parotid gland is less likely to be hindered.

However, MRI is poorer in delineation of bone lesions and calcification than CT. MRI can detect bone destruction if it is evident but is not appropriate for the imaging of localized bone destruction or microcalcifications in the interior of tumor observed in pleomorphic adenoma. These should be evaluated by CT.

Thus, MRI is considered to be more useful than CT for close examination of parotid tumors themselves with exception of the evaluation of calcification and bone invasion.

**Index words and secondary materials used as references**

The Japan Centra Revuo Medicina was searched using “parotid gland tumor”, “preoperative”, and “CT” as key words, and PubMed was searched using “superior”, “MRI”, “CT”, and “parotid” as key words. The Japan Radiological Society and Japanese College of Radiology eds: Guidelines for Diagnostic Imaging 2003 was also used as a reference.
Figure: Pleomorphic adenoma of the deep lobe of the parotid gland
The tumor is clearly delineated in the T1-weighted image (A), but its properties are unclear due to artifacts of dental prostheses on contrast-enhanced CT (B).

References

7) Kei PL et al: CT “invisible” lesion of the major salivary glands a diagnostic pitfall of contrast-enhanced CT. Clin Radiol 64: 744-746, 2009 (Level 3 or 4)
What imaging modalities are appropriate for the postoperative follow-up of squamous cell carcinoma of the head and neck region? (Which of CT, MRI, and PET are useful for the follow-up and at what interval should they be performed?)

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>B</td>
<td>PET is recommended. It should be performed 6-8 weeks or more after surgery, because the sensitivity and positive predictive value are low early after surgery (within 4 weeks) due to postoperative changes. Baseline images are necessary for long-term follow-up, and CT or MRI is recommended for this purpose. CT images obtained about 6-8 weeks post treatment are desirable as baseline images. Also, MR images about 12-16 weeks post treatment are recommended as baseline images.</td>
</tr>
<tr>
<td>C1</td>
<td>While the evidence about the timing of follow-up imaging is insufficient, a recommended interval for both CT and MRI is every 3-4 months during the first 2 years, when recurrence is likely, and every 4-6 months during the next 3-5 years. While evidence about long-term follow-up using PET is insufficient, it is recommended from clinical and economic viewpoints to perform it about 12, 21, and 33 months after surgery.</td>
</tr>
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</table>

**Background/objective**

Squamous cell carcinoma of the head and neck region may be curatively treated by chemoradiotherapy, but radical surgery is performed in patients with advanced cancer or those who respond poorly to chemoradiotherapy. The early detection of postoperative recurrence is an important prognostic factor, but the follow-up method varies among facilities, and many imaging modalities are selected. Imaging modalities efficient and suitable for the follow-up are evaluated.

**Comments**

Postoperative imaging findings differ considerably from preoperative ones due to the effects of organ reconstruction, changes in the hemodynamics, and postoperative inflammation. Therefore, baseline images are necessary for the long-term follow-up. CT images about 6-8 weeks post treatment are considered desirable as baseline images, but MR images are useful as baseline images for the follow-up of cancer near the skull base. However, as the effects of postoperative changes on MRI persist over a long period, it is desirable to obtain baseline images about 12-16 weeks post treatment.

For the postoperative follow-up, it is recommended to perform both CT and MRI every 3-4 month during the first 2 years, when the recurrence is likely, and every 4-6 months during the next 3-5 years.

PET is the best modality to diagnose the recurrence after treatment. However, its sensitivity and positive predictive value have been invariably reported to be low early after treatment (within 4 weeks). Despite some differences among reports, it is recommended to perform PET 6-8 weeks or more after the treatment. The recommended timing of PET for long-term follow-up is 12, 21, and 33 months after treatment.

**Index words and secondary materials used as references**

A search of PubMed was performed using “head and neck squamous cell carcinoma”, “post-surgical operation”, “follow up”, “diagnostic imaging”, “CT”, “MRI”, and “PET” as key words.

**References**

Figure: Images after surgery for hypopharyngeal cancer

Neck status post resection of the hypopharynx, larynx, and cervical esophagus and reconstruction by free flap transfer for hypopharyngeal cancer. The figure shows contrast-enhanced CT images about 5 weeks after surgery (A, B: transverse images, C: coronal reconstructed image). They serve as baseline images for the subsequent follow-up.
28 Is PET appropriate for staging of head and neck cancers?

**Background/objective**

For the pretreatment staging of head and neck cancers, PET has been introduced clinically at increasing facilities since the late 1990s to 2000, and it is nearly established today as a modality indispensable for high-precision staging. In this section, the usefulness of PET (referring here to 18F-FDG PET or PET/CT, which are widely performed) is compared with that of other modalities including CT and MRI.

**Comments**

According to a meta-analysis of studies that evaluated the diagnostic ability of 18F-FDG PET in patients with head and neck squamous cell carcinoma in a period of 1994-2007, the sensitivity was 79%, specificity was 86%, positive likelihood ratio was 5.84, and negative likelihood ratio was 0.24. On comparison between PET and CT, the sensitivity was 80 vs. 75%, and specificity was 86 vs. 79% on comparison between PET and CT/MRI, the lesion detection rate was 0.973 vs. 0.928 (P=0.026), and the lymph node detection rate was 0.974 vs. 0.717 (P=0.02).

PET has generally higher diagnostic ability than conventional diagnostic methods. Particularly, for staging of lymph nodes (N staging), the diagnostic precision of PET is higher than CT or MRI, and its diagnostic ability for lesions considered borderline lesions on CT or MRI is excellent. In addition, PET-CT fusion imaging and PET/CT are significantly more sensitive and specific than PET alone and contributes to reducing the false positive rate.

On the other hand, for staging of primary lesions (T staging), PET tends to show high sensitivity but low specificity, and the detection rate in patients in whom lymph node metastasis cannot be identified clinically (clinical N0) is reportedly about 50%. There have been few studies comparing PET with other modalities by the site of head and neck cancer, and no evidence that PET has absolute advantage over CT or MRI at particular sites has been obtained, but it plays an important role in pretreatment staging concerning the determination of the N and M staging, which contribute to the sensitivity and precision.

Concerning the evaluations using the SUV value obtained by PET, there have been reports that the disease-free survival period differed significantly between SUVmax of ≥6.5 and ≤6.5 that the SUV value was significantly higher in patients with extracapsular lymph node invasion (P=0.0007) and those with distant metastasis (P=0.05) and an SUVmax of 1.0 or higher in the primary lesion was an exacerbating factor of the total survival rate, and that the diagnostic precision was significantly improved (sensitivity: 79%, specificity: 99%) by the addition of a cutoff value of SUVmax based on the lymph node size on PET (Figure).

Thus, while PET may not be advantageous for staging of head and neck cancers depending on the site and size of the lesion, it is recommended as it provides more high-precision information compared with conventional examinations.

**Index words and secondary materials used as references**

A search of PubMed was performed using “head and neck cancer”, “PET”, “MRI”, and “CT” as key words and further limited to studies since 2000.

**References**

5) Ishikita K et al: Additional value of integrated PET-CT over PET alone in the initial staging and follow up of head and neck malignancy. Ann Nucl Med 24: 77-82, 2010 (Level 4)

Figure: Hypopharyngeal cancer (cancer of the right piriform sinus)  T4a  N2c
CT (A) shows metastatic lymph nodes only on the right side, which is the affected side, and the diagnosis was N2b. On PET (B), however, bilateral lymph node metastasis was suspected. Surgery revealed bilateral metastases, and the stage was N2c.
2. Head and neck

Is MRI appropriate for the evaluation of cervical lymph node metastasis?

**Recommendation grade**

MRI is recommended when the differential diagnosis of benign and malignant cervical lymph node lesions is difficult by CT or ultrasonography.

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**Background/objective**

Imaging examination of cervical lymph node metastasis is often performed by CT or ultrasonography. Contrast-enhanced CT is used at many facilities to detect lymph node metastasis using diagnostic criteria based on the size and internal morphologies of lymph nodes. Ultrasonography is used frequently as a screening test because of the convenience and lack of radiation exposure. The wide use of these examinations may be ascribed to the short scanning time and the availability of the equipment at many facilities. As for their problems, CT involves X-ray exposure, and ultrasonography is dependent on the skill of the examiner and can scan only a narrow area at a time.

MRI is selected less frequently than CT or ultrasonography as the first choice imaging examination for cervical lymph node metastasis. However, due to the recent improvements in MRI, increased clinical availability of machines with 1.5T or a high magnetic field strength, improvements in various imaging sequences including fat-suppressed imaging, thinning of the available slice thickness, and realization of multiplanar image reconstruction, MRI has become a more usable diagnostic tool than before. In consideration of these points, whether MRI, which has excellent tissue resolution, is useful for the diagnosis of cervical lymph node metastasis is evaluated.

**Comments**

According to a report by Curtin et al., contrast-enhanced CT was superior to MRI in the evaluation of cervical lymph node metastasis of head and neck squamous cell carcinoma using diagnostic criteria based on both the lymph node size and a combination of the size and internal morphologies. Later, King et al. reported that MRI was comparable to contrast-enhanced CT in detecting necrotic changes in lymph node metastasis of head and neck squamous cell carcinoma. More recently, Sumi et al. reported that, in evaluating the presence or absence of cervical lymph node metastasis of head and neck squamous cell carcinoma according to internal morphologies observed in metastatic nodes such as cancer nests, necrosis, and keratinization, MRI showed a significantly higher detection power than contrast-enhanced CT for lymph node metastasis 10 mm or less in short diameter. As a reason for these results, they suggested that focal defects caused by lymph node metastasis have become more detectable due to the improvements in the performance of recent MRI systems, which provide high-resolution images in a short period.

The hilum of lymph node, which contains fat, often presents as fat density on CT. However, as it contains not only fat but also blood vessels, it is occasionally visualized at water density, making its discrimination from local defects reflecting necrosis or tumor invasion difficult. This tendency is particularly notable in small lymph nodes 10 mm or less in short diameter. On MRI, however, the hilum of lymph node is hyperintense in pre- and postcontrast T1-weighted imaging regardless of the lymph node size, and this hyperintensity disappears if there are local defects. Therefore, MRI is considered to be superior for the judgment of the presence or absence of focal defects.

For the presence diagnosis of, and screening for, lymph node metastasis by MRI, fast spin echo T2-weighted imaging using fat suppression is appropriate, because many cervical lymph nodes are surrounded by adipose tissue, and lymph nodes can be delineated clearly by fat suppression. Fat-suppressed T2-weighted imaging is also excellent for the evaluation of interior properties of lymph nodes. Cancer nests in metastatic lymph nodes consist of cancer cells, necrosis, and keratinization, and liquefactive necrosis is visualized as a hyperintense area in fat-suppressed T2-weighted images. Coagulative necrosis and keratinization may present hypo- to medium intensity signals on fat-suppressed T2-weighted imaging. Thus, fat-suppressed T2-weighted images show signals reflecting histological features in the interior of metastatic lymph nodes.

Coronal fast short T1 inversion recovery (STIR) imaging is also appropriate for screening of cervical lymph node metastasis because of the relatively short imaging time (about 2 minutes) compared with fast spin echo fat-suppressed T2-weighted imaging and resistance to susceptibility artifacts. In STIR images, signals emitted by lesions are not specific to their malignancy or benignancy. Therefore, STIR imaging is not suited for the evaluation of internal morphologies associated with the diagnosis of lymph node metastasis but is excellent in the size evaluation. It has also been reported that the hyperintense area extending around lymph nodes (“flare” sign) in STIR and fat-suppressed T2-weighted images and shaggy margin in contrast-enhanced T1-weighted images are useful for the diagnosis of extranodal or extracapsular spread of lymph node metastasis.

A diagnostic method for lymph node metastasis being evaluated at present uses the ADC map obtained from diffusion-
weighted imaging. However, the variation with the magnetic field strength of the MRI system is large, and further development of the study is anticipated.\(^{(9,10)}\)

The figure provides a flow chart for the diagnosis of cervical lymph node metastasis.

**Index words and secondary materials used as references**

The Japana Centra Revuo Medicina was searched using “cervical lymph node metastasis” and “MRI” as key words, and PubMed was searched using “neck”, “nodes”, “metastasis”, and “MRI” as key words.

**References**

03

Thoracic region
Is CT appropriate for the discrimination between adult community-acquired pneumonia and non-infectious diseases?

**Recommendation grade**

| C1 | While scientific evidence of the usefulness of CT is insufficient, there are HRCT findings characteristic of infectious and non-infectious diseases, and their discrimination is possible to an extent. |

**Background/objective**

There are various lung diseases that require differentiation from community-acquired pneumonia. In immunocompetent individuals, they include pulmonary edema, eosinophilic pneumonia, hypersensitivity pneumonia, idiopathic interstitial pneumonia, and drug-induced lung disorders. In immunodeficient individuals, in addition to these disorders, many pathological conditions such as opportunistic infection and changes due to malignant neoplasm are considered. The role of HRCT for the differential diagnosis of community-acquired pneumonia from these non-infectious disorders, particularly acute respiratory disease exhibiting diffuse opacifications, was evaluated.

**Comments**

Many plain chest X-ray findings in community-acquired pneumonia overlap with those in diffuse lung diseases, and there are no disease-specific findings. However, CT, particularly high-resolution CT (HRCT), has been reported to provide additional information. According to a report of patients with community-acquired pneumonia who required hospitalization and underwent CT, CT was useful for the detection of cavities and masses in the lesion undetected by plain chest radiography and exclusion of masses suspected to be present by plain chest radiography, and the modality was suggested to be useful for the exclusion of some diseases and collection of important information though it may fall short of differentially diagnosing community-acquired pneumonia from infectious pneumonia. There was a questionnaire survey in pulmonologists to clarify the state of the use and usefulness of HRCT in diffuse lung diseases. Of the valid answers obtained from 230 pulmonologists, 67-89% affirmed the usefulness of HRCT for the diagnosis of diseases including idiopathic interstitial pneumonia, eosinophilic pneumonia, Langerhans cell histiocytosis, lymphangioleiomyomatosis, and bronchiectasis.

There are reports of 4 case series studies evaluating the discrimination between infectious and non-infectious diseases by HRCT. These reports suggest common differential points in images. In an evaluation of acute pulmonary parenchymal lesions that developed in immunocompetent patients, centrilobular nodules were the most important finding for the differentiation between infectious and non-infectious diseases, and they were usually not observed in non-infectious diseases. In addition, segmental distribution and the presence of wedge-shaped consolidations primarily in the segmental bronchi were findings characteristic of infections. Also, in an evaluation of patients showing multiple consolidations on plain chest radiography, HRCT findings important for the differentiation of infections from non-infectious diseases were centrilobular nodules and branched structures (i.e. tree-in-bud) due to mucus plugs in the airway. Centrilobular branched structures are not observed in non-infectious lung diseases such as hypersensitivity pneumonitis, pulmonary emphysema, obstructive bronchiolitis, and idiopathic organizing pneumonia. In a report of patients with immunodeficiency not due to acquired immunodeficiency syndrome who developed acute lung disorders including infection, the sensitivity and positive predictive value of CT for various diseases were 0.27-1.0 and 0.25-1.0, respectively, showing variation among diseases. Centrilobular lesions and lesions of the secondary lobule level were frequent HRCT findings in bacterial pneumonia, and CT halo sign and cavities were observed frequently in fungal infection and tuberculosis. Malignant tumors included leukemia, malignant lymphoma, and carcinomatous lymphangiosis, and thickening of the bronchovascular bundles, nodes, and lymph node enlargement were observed frequently in these disorders. Also, in immunocompromised patients who developed acute lung disorders, inflammatory disorders (infections, in particular) were reported to be suspected when nodes were the primary finding.

In addition to the differential diagnosis, CT has been reported to be useful for collection of alveolar lavage fluid, transbronchial lung biopsy, and determination and confirmation of the site of surgical biopsy and, thus, may contribute to the discrimination between pneumonia and non-infectious disorders.

**Index words and secondary materials used as references**

A search of PubMed was performed using “pneumonia” and “computed tomography” as key words. Also, the Japan Radiological Society and Japanese College of Radiology eds.: Guidelines for Diagnostic Imaging 2005 was used as a reference.
Figure 1: Bacterial pneumonia
(*Pseudomonas aeruginosa*)
Homogeneous infiltrative shadow showing segmental distribution is observed on the ventral side of the right lower lobe. Thickening of the bronchial wall in the neighborhood (→) and centrilobular granular opacities (▲) are also noted.

Figure 2: Mycoplasma pneumonia
Centrilobular branched/granular opacity (→) and acinar to lobular ground-glass opacity/infiltrative opacity (▲) are noted in the right upper lobe and part of the lower lobe. Thickening of the bronchovascular bundles is also notable.

References

3. Thoracic region

Is CT appropriate for the discrimination between bacterial and atypical pneumonia?

CT is useful and may be considered for the discrimination between pneumococcal pneumonia and *Mycoplasma pneumoniae* pneumonia, but the evidence of its usefulness for the diagnosis of diseases caused by other microorganisms is limited.

### Background/objective

The guidelines by the Japanese Respiratory Society recommend to treat pneumonia following discrimination of atypical pneumonia from community-acquired pneumonia. Whether or not CT is useful for the discrimination between bacterial and atypical pneumonia in adults was evaluated.

### Comments

Primarily, CT findings were compared between pneumococcal pneumonia, which is the most frequent bacterial pneumonia (Figure 1), and common atypical pneumonia (*Mycoplasma pneumoniae*, *Chlamydia* sp, and influenza virus pneumonia) (Figure 2). Characteristics of pneumococcal pneumonia, *Mycoplasma pneumoniae* pneumonia, and influenza virus pneumonia have been relatively established. Concerning the discrimination between bacterial and atypical pneumonia using CT, 7 reports on retrospective comparative studies were found.

Tanaka et al. compared CT findings in 18 patients with bacterial pneumonia and 14 with atypical pneumonia. In atypical pneumonia, centrilobular shadow, consolidation and ground-glass attenuation with lobular distribution were observed more frequently than in bacterial pneumonia.

According to the report by Nambu et al. (24 patients with *Chlamydia pneumoniae* pneumonia, 30 with *Mycoplasma pneumoniae* pneumonia, and 41 with pneumococcal pneumonia), thickening of bronchovascular bundles was noted more frequently in *Mycoplasma pneumoniae* pneumonia and *Chlamydia pneumoniae* pneumonia than in pneumococcal pneumonia.

In the evaluation of CT findings in a total of 114 patients including 35 with bacterial pneumonia, 28 with *Mycoplasma pneumoniae* pneumonia, and 41 with pneumococcal pneumonia, centrilobular nodules were observed more frequently in *Mycoplasma pneumoniae* pneumonia and viral pneumonia than in bacterial pneumonia, and no consolidation was noted in viral pneumonia.

Ito et al. compared CT findings in 94 patients with bacterial pneumonia (including 65 with pneumococcal pneumonia) and 31 patients with atypical pneumonia (including 20 with *Mycoplasma pneumoniae* pneumonia and 7 with *Chlamydia pneumoniae* pneumonia). Centrilobular nodules, thickening of bronchovascular bundles, and lobular opacity were observed significantly more frequently in atypical pneumonia, and these findings were useful for its discrimination from bacterial pneumonia. However, *Chlamydia pneumoniae* pneumonia and bacterial pneumonia were difficult to differentiate.

Miller et al. evaluated CT findings in 93 patients with viral pneumonia and 22 with bacterial pneumonia and frequently noted ground-glass opacity and diffuse air space consolidation in bacterial pneumonia.

According to the reports by Miyashita et al. (64 patients with *Mycoplasma pneumoniae* pneumonia and 68 with pneumococcal pneumonia) and Nei et al. (36 patients with *Mycoplasma pneumoniae* pneumonia and 52 patients with community-acquired pneumonia including 20 with pneumococcal pneumonia), bronchial wall thickening and centrilobular nodules were also observed significantly more frequently in *Mycoplasma pneumoniae* pneumonia.

There are other reports concerning CT findings in pneumococcal pneumonia and *Mycoplasma pneumoniae* pneumonia, and bronchial wall thickening and centrilobular nodules are considered to be useful for their discrimination.

Major reports on CT findings in *Chlamydia pneumoniae* pneumonia have been few. Compared with *Mycoplasma pneumoniae* pneumonia, bronchial wall thickening and centrilobular nodules are observed less frequently, and lobular ground-glass opacity and lobular consolidation are observed more frequently. However, its discrimination from pneumococcal pneumonia is difficult.

As for influenza virus pneumonia, there are major reports concerning seasonal influenza virus and novel influenza virus pneumonia that intralobular reticular opacity is observed frequently. Fujita et al. reported CT findings in 12 patients with virus-associated pneumonia. In patients with mixed infection with bacteria pneumonia, segmental consolidation was noted, and the consolidation could be discriminated from pure virus pneumonia. There have also been a number of reports of similar finding (intralobular reticular opacity) in pneumonia due to other viruses such as adenovirus. CT may be useful for the discrimination of virus and bacterial pneumonia.

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3.1 Is CT appropriate for the discrimination between bacterial and atypical pneumonia?

CT is useful and may be considered for the discrimination between pneumococcal pneumonia and *Mycoplasma pneumoniae* pneumonia, but the evidence of its usefulness for the diagnosis of diseases caused by other microorganisms is limited.

### Recommendation

- **Grade C1**

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3.1 Is CT appropriate for the discrimination between bacterial and atypical pneumonia?

CT is useful and may be considered for the discrimination between pneumococcal pneumonia and *Mycoplasma pneumoniae* pneumonia, but the evidence of its usefulness for the diagnosis of diseases caused by other microorganisms is limited.
Index words and secondary materials used as references

A search of PubMed was performed using “pneumonia” and “computed tomography” as key words. The Japan Radiological Society and Japanese College of Radiology eds: Guidelines for Diagnostic Imaging of Adult Community-Acquired Pneumonia 2007; the Japanese Respiratory Society eds: Guidelines for the Management of Adult Community-Acquired Pneumonia 2007; and the following documents were also used as references.


References

2) Nambu A et al: Chlamydia pneumoniae: comparison with findings of Mycoplasma pneumoniae and Streptococcus pneumoniae at thin-section CT. Radiology 238: 330-338, 2006 (Level 3)
10) Agarwal PP et al: Chest radiographic and CT findings in novel swine-origin influenza A (H1N1) virus (S-OIV) infection. AJR 193: 1488-1493, 2009 (Level 3)
3. Thoracic region

Is CT appropriate for the diagnosis of pneumoconiosis?

CT is useful for the diagnosing the presence, distribution, and severity of pneumoconiosis lesions and complications and is recommended.

**Background/objective**

According to the Pneumoconiosis Law, plain chest radiography plays the central role in the diagnosis of pneumoconiosis, and the severity of the disease is defined by the PR classification based on plain chest radiograms. Clinically, however, CT findings are used complementarily for the diagnosis.

**Comments**

In silicosis, there are reports that CT has excellent detection power for healing tendency and large opacities.\(^1\,^2\) CT has also been reported to improve the inter-reader agreement rate.\(^3\) In patients exhibiting small round opacities classified as “type p” on plain chest radiography, the addition of HRCT not only improves the detection rate of granular opacities themselves\(^4\) but also allows the differentiation between the actual presence of small round opacities and the presence of only fibrosis around respiratory bronchioles,\(^5\) making more accurate PR classification possible.

Regarding lung asbestosis, as the diagnosis of lung lesions in general is difficult by plain chest radiography alone if pleural plaques are notable, the concomitant use of CT is desirable.\(^6\) A characteristic CT finding in lung asbestosis is subpleural curvilinear opacity, which is observed frequently (Figure).\(^7\) Such mild fibrosis is impossible to visualize without CT including HRCT.

In both silicosis and asbestosis, the diagnosis of complications such as lung cancer, mesothelioma, and tuberculosis is also of clinical importance.\(^8\) In diagnosing complications, the diagnostic ability of plain radiography may be reduced by the presence of pneumoconiosis-related small round opacities, irregular opacities, and pleural plaques.\(^9\) Earlier diagnosis of these complications becomes possible by the use of CT.

**Index words and secondary materials used as references**

A search of PubMed was performed using “pneumoconiosis”, “silicosis”, “asbestosis”, and “CT” as key words.

**References**


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**Figure: Lung asbestosis**

A linear opacity along the pleura is observed immediately below the upper dorsal pleura, and some granular opacities appear to be aggregated. This is a typical image of subpleural curvilinear shadow (SCLS) observed in lung asbestosis.
Is CT appropriate for the evaluation of the severity of COPD?

Since various quantitative evaluations are possible even by low-dose CT, and since CT findings correlate well with the severity of COPD, CT may be considered.

Background/objective

COPD is a disease defined as a forced expiratory volume in 1 second as percent of FVC (FEV1.0%) of 70% or less, and its severity is evaluated comprehensively on the basis of not only respiratory function but also symptoms such as dyspnea and the presence or absence of complications. In the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease (GOLD), CT is given a supplementary diagnostic role. However, the guidelines by the Japanese Respiratory Society consider the classification of the disease into emphysematous and non-emphysematous types according to CT findings to be useful.

Comments

When COPD is viewed from pathological aspects of the lung, 3 factors, i.e., destruction of the lung parenchyma due to pulmonary emphysema, narrowing of the peripheral airways, and decrease in the pulmonary vascular bed, are involved in a complex manner. Therefore, the separate evaluation of each factor by CT does not necessarily lead to an accurate diagnosis of COPD. For example, in a report evaluating whether or not COPD can be diagnosed according to the LAA% (percent of the low attenuation area/total lung area) alone in 1,140 patients, the sensitivity and specificity of the LAA% were 63 and 88%, respectively.

However, quantitative evaluation of each factor using CT is useful. Concerning pulmonary emphysema in particular, there are multiple reports that the low attenuation area of CT corresponds to pathologically confirmed pulmonary emphysema, and CT is recommended for the evaluation of the severity of emphysema.

Pulmonary emphysema is evaluated by CT, using indices such as a macroscopic score (Goddard classification), LAA%, and mean CT value of the entire lung. The macroscopic evaluation has been shown in a study of 9,000 patients to correlate with the GOLD classification despite some inter-rater variation.

The LAA% is the most widely used qualitative index of pulmonary emphysema, and commercial software for its calculation is available. The LAA% shows a high correlation with the forced expiratory volume in 1 second (FEV1), by which COPD is staged, with an r of -0.63 to -0.659. In its actual determination, it must be noted that the CT value varies with the imaging device and imaging conditions (slice thickness, reconstruction algorithm, etc.) and that the threshold of the LAA% is presently not established although it is set at -950 HU in many reports.

The airway wall is evaluated by CT grossly or using parameters such as the percent of the airway wall area/total airway area (WA%). The WA%, which can be calculated using commercial software, is correlated with the FEV1 as well as findings in surgical specimens.

Finally, regarding vascular lesions, a method using the total cross-sectional area of small pulmonary vessels (%CSA<5) is proposed.

Index words and secondary materials used as references

A search of PubMed was performed using “CT”, “lung”, and “COPD and CT”, and “emphysema” as key words. The GOLD COPD guidelines (http://www.goldcopd.org/) and the Japanese Respiratory Society Guidelines Committee eds: Guidelines for the Diagnosis and Treatment of COPD 4th edition, 2013 were also used as references.

References


9) Nakano Y et al: The prediction of small airway dimensions using computed tomography. Am J Respir Crit Care Med 171: 142-146, 2005 (Level 2)

Is lung cancer screening by plain chest radiography appropriate?

Although scientific evidence is insufficient, screening for lung cancer using plain chest radiography is currently performed widely in Japan, and its implementation under sufficient systematic supervision may be considered.

Background/objective

In Japan, the mortality rate due to lung cancer is increasing, and lung cancer has been the leading cause of death in males since the late 1990s. With males and females combined, the number of deaths due to lung cancer exceeded 63,000 in 2006 and is reportedly increasing further.

Comments

One of the well-known studies regarding the usefulness of mass screening for lung cancer is the Mayo Lung Project, which concluded that the screening scheme using plain chest radiography combined with sputum cytology does not cause a decrease in the mortality rate. A subsequent investigation of the long-term prognosis reported that some patients in the screened group had favorable outcomes but that the mortality rate was not reduced.

In contrast, there have been reports of case-control studies from Japan that, as a result of the application of screening for tuberculosis using plain chest radiography to lung cancer, deaths due to lung cancer were reduced by 20-60%.

The above studies have been subjected to various criticisms. For example, in the Mayo Lung Project, the intervention group underwent plain chest radiography and sputum cytology every 4 months but the no-intervention group underwent these examinations annually, and there have been controversy about the control group and research design. Since the reports from Japan were case-control studies, they were excluded from the evaluation due to emphasis on analysis based on randomized controlled trials, and the reported decreases in the mortality rate were rejected.

Under these circumstances, a study of the effects of screening for 4 cancers including lung cancer on the mortality rate, in which an intervention group underwent plain chest radiography annually 4 times and a no-intervention group underwent no radiographic examination, reported no difference in the mortality rate between the two groups after a 13-year follow-up. Various views have been presented regarding these results: Screening was found to be effective on re-analysis of the screening methods and conclusions, new cancers arose during a long-term follow-up after screening over a limited period, and the evaluation of an appropriate observation period has been suggested to be necessary.

Index words and secondary materials used as references

A search of PubMed was performed using “lung cancer”, “screening”, and “chest radiograph” as key words. The Japan Lung Cancer Society eds: Guidelines for the Diagnosis and Treatment of Lung Cancer by Techniques of EBM 2003, 2005 were also used as references.

References

4) Nishi K et al: A case-control study of lung cancer screening in Okayama prefecture, Japan. Lung Cancer 34: 325-332, 2001 (Level 2)
Are CT and PET appropriate for the differential diagnosis of benign and malignant lung nodules?

**Recommendation grade**

- **A** High-resolution CT (thin-section CT), which allows micromorphological evaluation, is strongly recommended for the differential diagnosis of benign and malignant lung nodules.
- **C1** Contrast-enhanced CT, PET

**Recommendation**

At facilities capable of performing PET, its implementation may be considered.

**Background/objective**

Concerning the handling of lung nodules detected by plain chest radiography or CT on screening for lung cancer or during follow-up of other diseases, it is the present protocol to first perform high-resolution CT and to make the judgment of whether or not invasive examinations such as bronchoscopy or percutaneous biopsy should be performed is made by comprehensively evaluating the nodule size, marginal characteristics, degree of enhancement, internal structure, and state of the surrounding lung parenchyma. However, there are no objective criteria for the interpretation of morphological findings, and inter-reader variability cannot be excluded. Also, if invasive examinations are not performed, serial examinations are performed to evaluate time-associated changes. Recently, the clinical application of the judgment of the degree of malignancy of lung nodules based on the measurement of the doubling time has been initiated.

For the differential diagnosis by contrast-enhanced CT or MRI, analysis of the degree of contrast enhancement by comparison between pre-and post-contrast images and pattern of signal intensification by dynamic study is also performed. Moreover, since PET/CT, which has become available at many facilities, provides information concerning metabolism of nodules by the use of the standardized uptake value (SUV) in addition to morphological information by CT, the precision of the discrimination between benign and malignant nodules is expected to be improved by the use of such additional information.

**Comments**

1) **High-resolution CT**

There have been a large number of studies comparing high-resolution CT and pathological findings, and the understanding of the histological background of the margins and internal properties of lung nodules in high-resolution CT images has been advanced. However, as high-resolution CT images are interpreted by subjective criteria of image readers, and as no objective criteria for the discrimination of benign and malignant nodules have been established, differences in the evaluation criteria among studies are problematic. This has led to marked variation in the sensitivity and specificity depending on histological types and properties of nodules included in the study and the state of the surrounding lung tissue. According to the present protocol, the differential diagnosis of solitary lung nodules is first performed non-invasively by high-resolution CT in consideration of the size. Nodules less than 5 mm in diameter are followed up after 1 year, and those 5 mm or greater and less than 10 mm are followed up after 3 months, and, if enlargement is observed, invasive examinations are utilized. Nodules 10 mm or greater in diameter are examined by PET, and more invasive examinations may be recommended depending on the results.

If a lung nodule is detected incidentally in asymptomatic patients, it has become possible to measure its volume by helical scanning of high-resolution CT. This has made the calculation of its doubling time from the interval of 2 serial scans possible. The doubling time is calculated by such a quantitative method even on a short-term follow-up, during which no visual change can be perceived, and tentative classification of nodules with a short doubling time of less than 400 days as malignant has been introduced.

2) **Contrast-enhanced CT/MRI**

Since contrast enhancement is considered to be stronger in malignant than benign nodules, the discrimination of non-calcified benign and malignant nodules using a cutoff value of the difference in the CT value between before and after the administration of an iodine-based contrast agent was also evaluated in a multi-center study. When nodules showing 15 HU or higher contrast enhancement were regarded as malignant and those showing less contrast enhancement as benign, the sensitivity and specificity were 98 and 58%, respectively. These results suggest that nodules showing contrast enhancement of less than 15 HU are very likely to be benign but that those showing contrast enhancement of 15 HU or higher may also be benign diseases including organizing pneumonia. Also, according to meta-analysis of studies concerning the differential diagnosis of benign and malignant lung nodules by contrast-enhanced dynamic CT,
the sensitivity and specificity were 98-89% and 88-43%, respectively, and no improvement in the diagnostic ability compared with contrast-enhanced CT can be expected. The sensitivity and specificity of contrast-enhanced dynamic MRI were 99-95% and 79-64%, respectively, being comparable to those of contrast-enhanced CT.\textsuperscript{11)}

3) PET

PET, by which benign and malignant lung nodules can be differentially diagnosed according to the degree of glucose metabolism, has been shown by a number of studies to have higher diagnostic power than CT (\textit{Figure 2}).\textsuperscript{11-14} Moreover, since the SUV, which is used as a semi-quantitative index, is affected by factors including the model of PET equipment, imaging method, patient’s glucose level, and site of the lesion (apex or base), there is limitation in the use of a fixed cutoff value for the discrimination of benign and malignant nodules. Therefore, it is not recommended to attempt the differential diagnosis of benign and malignant lesions by the SUV alone in daily clinical practice. In addition, there is a marked volume effect in relatively small tumors, and the diagnostic ability is known to be markedly reduced in nodules less than 10 mm in diameter. Therefore, PET is recommended to be used for the discrimination of benign and
malignant nodules 10 mm or greater in diameter. Also, regarding histological characteristics, tumors of intermediate malignancy, those showing lepidic growth, mucin-producing tumors, and tumors with marked central scar and known to show false negative images even when they are 10 mm or greater in diameter. On the other hand, some granulomatous inflammatory nodules such as tuberculosis and cryptococcosis are known to give false positive results.\textsuperscript{5,16} Therefore, it is recommended to consistently diagnose lung nodules comprehensively by morphological examination using high-resolution CT and in consideration of information concerning glucose metabolism obtained by PET.

### Index words and secondary materials used as references

A search of PubMed was performed using “lung nodule” and “differential diagnosis” as key words. The Japan Lung Cancer Society eds: Guidelines for the Diagnosis and Treatment of Lung Cancer 2005 was also used as a reference.

### References

1. Aoki T et al: Evolution of peripheral lung adenocarcinomas: CT findings correlated with histology and tumor doubling time. AJR 174: 763-768, 2000 (Level 2)
2. Furuya K et al: New classification of small pulmonary nodules by margin characteristics on high-resolution CT. Acta Radiol 40: 496-504, 1999 (Level 2)
4. Seemann MD et al: Usefulness of morphological characteristics for the differentiation of benign from malignant solitary pulmonary lesions using HRCT. Eur Radiol 9: 409-417, 1999 (Level 2)
16. Nomori H et al: Evaluation of 18F fluorodeoxyglucose (FDG) PET scanning for pulmonary nodules less than 3 cm in diameter, with special reference to the CT images. Lung Cancer 45: 19-27, 2004 (Level 2)
Is high-resolution CT (HRCT) appropriate for the diagnosis of drug-induced lung injuries?

While scientific evidence is insufficient, its implementation may be considered.

Background/objective

There is no reliable non-invasive diagnostic method for drug-induced lung injuries. Clinical diagnostic criteria include the presence of reports of lung disorders caused by the suspected drug, occurrence of lung disorder after its administration, improvement after its cessation and recurrence of lung disorder on its readministration, but it is essential to exclude similar diseases such as the progression of primary disease and infection.

Comments

Imaging findings of drug-induced lung injuries are non-specific, and a definitive diagnosis is impossible by imaging studies alone, but they have some benefits. Imaging findings in drug-induced lung injuries are extremely diverse, and clinical findings including the disease history and course should be evaluated comprehensively with imaging, laboratory, and pathological findings for the diagnosis. Existing chronic fibrosing interstitial pneumonitis is a risk factor of drug-induced lung injury and of poor life prognosis after its occurrence.

An imaging finding at the onset is a bilateral extensive ground-glass opacity or infiltrative opacity accompanied by interlobular septal thickening and intralobular reticular pattern. While there is no characteristic finding, if only one lung is affected, the intact lung is likely to show more distinct opacities. Images are classified into patterns based on resemblance to those of idiopathic diseases such as hypersensitivity, eosinophilic, and organizing pneumonia, but the validity or reproducibility of this classification of image patterns or precise image-pathology correlation has not been sufficiently evaluated, thus the image pattern classification should be used with knowledge of its limitations. The severest lung disorder is the diffuse alveolar damage (DAD) type, which purports a poor prognosis. Findings of structural remodeling observed on CT such as traction bronchiectasis mean DAD type lung disorder and suggest a poor prognosis. However, no structural remodeling such as traction bronchiectasis is noted in the exudative phase, an early stage of DAD, and it is important to note limitations of imaging modalities.

The roles of imaging modalities in the diagnosis and treatment of drug-induced lung injuries include: (1) Evaluation of the presence or absence and severity of existing chronic interstitial pneumonia, (2) determination of the time of the onset of lung disease, (3) helping with the differential diagnosis at the onset, (4) prognosis, and (5) evaluation of the severity.
therapeutic effects. Images are objective evidence of the occurrence of lung injuries and are important for analysis of the temporal relationship of the onset with the history of drug administration.

### Index words and secondary materials used as references

PubMed was searched using “drug”, “lung injury”, and “CT or imaging” as key words. The Japanese Respiratory Society eds: Guidelines for the Diagnosis and Treatment of Drug-Induced Lung Disease, 2nd edition was also used as a reference.

### References

Is expiratory CT appropriate for the diagnosis of obstructive lung diseases?

**Recommendation grade**

| C1 | While scientific evidence is insufficient, its implementation may be considered. |

**Background/objective**

Expiratory CT is a technique for functional respiratory imaging used basically for research purposes such as the evaluation of air trapping as a result of obstruction of narrowed peripheral airways and tracheal and bronchial collapse during expiration in bronchial asthma and chronic obstructive pulmonary disease (COPD). Whether or not expiratory CT is useful for the diagnosis of obstructive lung diseases was evaluated.

**Comments**

CT examination is not considered essential for the diagnosis of obstructive lung disease as observed in the GOLD and COPD guidelines of the Japanese Respiratory Society. The basic principle of the diagnosis of obstructive lung disease is examination of the respiratory function. Therefore, CT is unnecessary for the diagnosis of various obstructive lung diseases per se. However, these guidelines also mention that CT is useful when they must be morphologically discriminated from other diseases or for detecting mild pulmonary emphysema. Expiratory CT has also not been reported to be necessary for the diagnosis of various obstructive lung diseases itself. However, it may be used clinically for planning treatments and evaluating therapeutic effects as a method for functional respiratory imaging targeted to air trapping and tracheal/bronchial collapse in obstructive lung diseases. Therefore, expiratory CT may be needed depending on the objective.

In obstructive lung diseases, expiratory CT is used typically for 1) the evaluation of air trapping, 2) evaluation of airway collapse, 3) quantitative evaluation of pulmonary emphysema, and 4) diagnosis of obstructive diseases with normal inspiratory CT but abnormal expiratory CT findings (Figure).

Evaluation of air trapping and pulmonary function by expiratory CT: By expiratory CT, air trapping is evaluated by methods using the lung densitometry threshold or mean lung density, and the degree of air trapping in various obstructive lung diseases evaluated by all methods have been reported to be correlated with the severity of obstructive ventilatory defect indicated by respiratory function tests. However, as air trapping is also observed in healthy individuals, it must be interpreted carefully.

Evaluation of tracheal/bronchial collapse and lung function by expiratory CT: Bronchial collapse is evaluated by comparing changes in the luminal areas of the segmental, subsegmental, and subsubsegmental bronchi compared with those on inspiratory CT. It has been reported that the inspiratory/expiratory luminal area ratio in COPD patients was correlated with obstructive ventilator defect and that this tendency was most notable in the peripheral subsubsegmental bronchi.

Evaluation of pulmonary emphysema by expiratory CT: By expiratory CT, a tendency to underestimate pulmonary emphysema has been suggested, and inspiratory CT has been reported to be superior to expiratory CT in the quantitative evaluation of pulmonary emphysema.

Obstructive diseases with normal inspiratory CT and abnormal expiratory CT findings: Bronchiolitis obliterans and bronchial asthma are typical examples of obstructive diseases with normal inspiratory CT and abnormal expiratory CT findings. In these diseases, the possibility of early detection of mild abnormalities by expiratory CT has been suggested. Particularly, it has been reported to be useful for the diagnosis of bronchiolitis obliterans syndrome occurring after lung transplantation with sensitivity and specificity of 83 and 89%, respectively.

There are several methods for expiratory CT including 1) end-expiratory scan, 2) continuous expiratory scan, and 3) dynamic scan. End-expiratory scan performed during breath-holding at the residual volume level is most widely employed. While dynamic scan has been reported to have excellent ability to detect airway collapse in tracheobronchomalacia, merits of its use in clinical settings are few except for special purposes from the viewpoint of X-ray exposure. It is also necessary to reduce the exposure in the scanning protocols of expiratory CT. Although the inter-reader agreement rate and confidence level of image evaluation decrease with the tube current, decreases to 20 mAs have been reported not to cause problems.
Index words and secondary materials used as references

A search of PubMed was performed using “CT” and “expiratory OR expiration” as key words. The Global Strategy for Diagnosis, Management, and Prevention of COPD (Updated December 2011) and Japanese Respiratory Society eds: Guidelines for the Diagnosis and Treatment of COPD (chronic obstructive pulmonary disease), 3rd edition, 2009 were also used as references.

References

2) Arakawa H et al: Air trapping on expiratory high-resolution CT scans in the absence of inspiratory scan abnormalities: correlation with pulmonary function tests and differential diagnosis. AJR 170: 1349-1353, 1998 (Level 4)
Is high-resolution CT appropriate for the diagnosis of idiopathic pulmonary fibrosis (IPF)?

While IPF is not always diagnosable by high-resolution CT, the modality shows a high positive predictive value for usual interstitial pneumonia (UIP) and is strongly recommended.

Background/objective
While about half the patients with IPF show atypical images on high-resolution CT (HRCT), the ATS/ERS diagnostic criteria for idiopathic interstitial pneumonias attach importance to HRCT findings because of high diagnostic accuracy for UIP with typical HRCT findings. How HRCT should be used for the diagnosis of IPF is discussed.

Comments
According to the ATS/ERS guidelines, the following 7 diseases are included in idiopathic interstitial pneumonias as clinicopathological entities: idiopathic pulmonary fibrosis (IPF), cryptogenic organizing pneumonia (COP), acute interstitial pneumonia (AIP), non-specific interstitial pneumonia (NSIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), desquamative interstitial pneumonia (DIP), and lymphocytic interstitial pneumonia (LIP). Histological findings of IPF are those of UIP. Each of these diseases shows characteristic HRCT features (Figure).

In IPF, it is impossible to judge whether the condition is idiopathic or not by pathological examination or HRCT. All causative interstitial pneumonias must be excluded clinically to determine that the disease is idiopathic. However, HRCT occupies the most important place in non-invasive examinations for the diagnosis of IPF. The 2002 edition of the ATS/ERS guidelines concerning idiopathic interstitial pneumonias mentions that HRCT is indispensable for the evaluation of idiopathic interstitial pneumonias and that clinical imaging and pathological findings must be integrated for the diagnosis. Moreover, the guidelines recommend to first judge whether a pattern typical of UIP is present or not in reading HRCT images, because the diagnostic accuracy is 90% or higher when there is an HRCT pattern typical of UIP. Within UIP, the prognosis of UIP is poorer than those of other interstitial pneumonias, and they require different treatments. If there is an HRCT pattern typical of UIP, surgical lung biopsy is unnecessary.

In the literature evaluating the accuracy of HRCT diagnoses of chronic idiopathic interstitial pneumonias, the diagnoses were correct in 79%, and the percentage of correct diagnoses was 62% for UIP, 86% for NSIP, 83% for RB-ILD or DIP, and 79% for LIP. In a study of patients suspected to have IPF, UIP was diagnosed accurately in about 60% by chest radiology experts, and the positive predictive value was 96%. The accuracy of the diagnosis of idiopathic interstitial pneumonias by HRCT varies widely among subjects and according to diagnostic criteria. If the condition is complicated by pulmonary emphysema, the diagnostic accuracy decreases significantly. In an evaluation of HRCT findings in 98 patients with IPF, the diagnosis was definite UIP in 34% and NSIP in 30%. Also, the HRCT diagnoses are correlated with the degree of confidence of image readers, and 84.4% of the diagnoses as probable UIP and 91.7% of the diagnoses as definite UIP were correct. According to the 2011 edition of the ATS/ERS guidelines concerning IPF, the diagnosis is IPF if HRCT findings suggest UIP even when pathological findings indicate possible or non-classifiable fibrosis but, in contrast, is possible IPF if the HRCT findings are inconsistent with UIP even when pathological findings indicate UIP. A diagnosis of definite UIP requires the presence of honeycomb lung, dominant basilar subpleural distribution, and absence of findings inconsistent with UIP (upper/middle lung field dominant, peribronchovascular dominant, or extensive ground-glass opacities, granulomatous changes, cysts, mosaic pattern/air trapping, and consolidation).

In interstitial pneumonias, a retrospective study showed that HRCT findings changed 50% or more of the initial diagnoses by internists. According to another report, the degree of agreement (kappa coefficient) of diagnoses by multiple clinicians was 0.41 when the diagnosis was made by HRCT alone, increased to 0.51 when the diagnosis was made by HRCT and clinical information, increased to 0.67 when a radiologist participated in the diagnosis, became 0.75 when pathological findings were added, and increased to 0.85 by consensus diagnoses involving a clinician, radiologist, and pathologist. HRCT is used for the prognosis as well as diagnosis. In IPF, the degree of traction bronchiectasis has been reported to affect the prognosis. Also, it has been reported that, similarly to pathological diagnoses, a significant difference was observed in the survival rate between those diagnosed as UIP and those diagnosed as NSIP by HRCT and that the prognosis differed between typical cases of UIP with a pathological diagnosis of UIP and showing honeycomb lung on HRCT and atypical cases.

Index words and secondary materials used as references
A search of PubMed was performed using “HRCT”, “interstitial pneumonias”, “sensitivity”, and “specificity” as key
words. The ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis eds: ATS/ERS Guidelines, 2002 and 2011, and related materials were also used as references.

References

1) Souza CA et al: Idiopathic pulmonary fibrosis: spectrum of high-resolution CT findings. AJR 185: 1531-1539, 2005 (Level 4)
Is CT appropriate for the diagnosis of ALI/ARDS?

While CT is not essential for the diagnosis of ALI/ARDS, it is useful for the evaluation of disease activity, and its implementation may be considered.

Background/objective
Acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) are conditions in which imaging findings play important roles in the diagnosis. The usefulness of plain chest radiography and CT in the diagnosis of each condition is evaluated.

Comments
ARDS was first reported in 1967 by Ashbaugh et al., with description of diffuse infiltrative opacities in the bilateral lungs on plain chest radiography from the onset (Figure 1). Subsequently, Petty et al. proposed the concept of adult respiratory distress syndrome, and, through a joint consensus conference by the American Thoracic Society (ATS) and European Society of Intensive Care Medicine in 1992, its definition and diagnostic criteria were eventually compiled in 1994. As shown in the table, hypoxemia with an acute onset, infiltrative bilateral lung opacities on plain chest radiographs, and a PaO2/FiO2 (ratio of partial pressure of arterial oxygen and fraction of inspired oxygen) of ≤300 mmHg or 200 mmHg is defined as ARDS if cardiogenic pulmonary edema can be excluded. Thus, the diagnostic criteria for ALI/ARDS include plain chest X-ray findings, and radiography is essential for their diagnosis. Also, plain chest radiography can be performed frequently at the bedside, and plain chest radiography performed routinely in the ICU or on changes in the patient’s condition has been reported to markedly affect the subsequent therapeutic strategy. Plain chest radiography is also considered important for monitoring of patients in a critical condition who may develop ALI/ARDS and those who have developed ALI/ARDS.

CT, on the other hand, is not an essential diagnostic criterion. It also involves the risk of moving patients in a critical condition and cannot be performed as frequently as plain chest radiography. However, CT has advantages that plain radiography lacks. First, HRCT findings have been reported to closely reflect pathological findings in ALI/ARDS. Pathologically, ALI/ARDS is diffuse alveolar damage (DAD), but, in a study comparing pathological findings and CT images in 14 DAD patients, ground-glass opacities and infiltrative opacities without traction bronchiectasis corresponded to pathological features of the exudative or early proliferation phase (Figure 2), and ground-glass opacities and infiltrative opacities accompanied by traction bronchiectasis corresponded to pathological features of the proliferative or fibrotic phase (Figure 3). Also, CT has been reported to be useful for the differentiation between direct (pneumonitis, aspiration, lung injury) and indirect (sepsis, trauma other than thoracic injuries) causes of ALI/ARDS. In a study of 29 ARDS patients, the extent of abnormalities on CT was broader, and the duration of the stay in the ICU was longer (median: 21 vs. 12 days), in direct than indirect lung injuries. In addition, HRCT findings have been reported to reflect the prognosis of ALI/ARDS. A study using a scoring system of HRCT findings reported that features resembling those of traction bronchiectasis showing fibrotic proliferation were a factor of a poor prognosis. According to another study, abnormal opacities occupying 80% or more of the lung field on CT, a ratio of right/left atrial diameters of 1 or higher, and varicose bronchiectasis were factors of a poor prognosis. Thus, CT is considered to be clinically useful, though not essential for the diagnosis of ALI/ARDS.

Index words and secondary materials used as references
A search of PubMed was performed using “acute respiratory syndrome” and “computed tomography” as key words. The Japanese Respiratory Society, Guidelines for the Diagnosis and Treatment of ALI/ARDS, 2nd edition was also used as a reference.

References
Figure 1: Plain chest radiographic image of ARDS
Infiltrative opacities/ground-glass opacities are noted in the bilateral lung.

Figure 2: Chest CT image 6 days after the onset of ARDS
Infiltrative opacities/ground-glass opacities are distributed as patches in the bilateral lung. No bronchial dilation is noted.

Figure 3: 1 month after the onset of ARDS
Ground-glass opacities/infiltrative opacities are observed in the bilateral lungs and are accompanied by features of traction bronchiectasis.

Table: Diagnostic criteria

<table>
<thead>
<tr>
<th>ALI</th>
<th>Acute</th>
<th>PaO₂/FiO₂ ≤300 mmHg (regardless of the PEEP)</th>
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<td></td>
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<td>Infiltrative opacities of the bilateral lungs</td>
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<td>PAWP ≤18 mmHg on the measurement or no</td>
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<td></td>
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<td>clinical signs of left atrial pressure elevation</td>
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<table>
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<th>ARDS</th>
<th>Acute</th>
<th>PaO₂/FiO₂ ≤200 mmHg (regardless of the PEEP)</th>
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<td></td>
<td>Infiltrative opacities of the bilateral lungs</td>
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<tr>
<td></td>
<td></td>
<td>PAWP ≤18 mmHg on the measurement or no clinical signs of left atrial pressure elevation</td>
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</table>

Is lung cancer screening by low-dose CT appropriate?

**Recommendation grade**

- C1 High-risk group (aged ≥50 years with a Brinkman index ≥600)
- C2 Non-high-risk group

| C1 | For the high-risk group, while scientific evidence is insufficient, low-dose CT may be considered as a measure for population-based screening. For the non-high-risk group, low-dose CT is not recommended as a means for population-based screening because of the lack of scientific evidence. For individual screening, it may be performed after appropriate explanation about its unclear effects and disadvantages such as overdiagnosis and exposure. |
| C2 |

**Background/objective**

Lung cancer screening using low-dose CT has been performed on a limited basis for individual rather than population-based screening because of the lack of sufficient evidence that it reduces the mortality rate (Figure), but reports affirming its effectiveness have appeared recently.

**Comments**

1) **Indirect evidence (detection rate, 5-year survival rate)**

   The detection rate of stage I lung cancer by screening using low-dose CT is high, being 75-100% on the initial screening and 79-100% on repeated screening, according to the reports from Japan by Sobue et al., Sone et al., Nawa et al., and Yoshimura et al. and the report of the International Early Lung Cancer Action Program (I-ELCAP). The 5-year survival rate of patients found to have lung cancer by screening was reported by Sobue et al. to be 76.2% in those detected on the initial screening and 64.9% in those detected on repeated screening. Nawa et al. reported that they were 91 and 84%, respectively, and suggested the female gender, non-smoker, small tumor diameter, and non-solid morphology as factors of a high survival rate.

2) **Direct evidence**

   In 2011, the National Lung Screening Trial (NLST), which was a randomized controlled trial, reported that the mortality rate due to lung cancer in the high-risk group was reduced by 2.47/1,000 person-years by low-dose CT screening with a decrease of 20.0% (95% CI: 6.8-26.7, P=0.004) compared with 3.09/1,000 person-years by screening using plain chest radiography. Regarding the validation of the effectiveness in the non-high-risk group, reports are still awaited.

3) **Notes**

   Non-low-dose CT (tube current >50 mAs) should not be performed for screening of healthy people. There are also problems to be solved such as overdiagnosis, radiation exposure, accuracy control, and cost.

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**Figure: Well-differentiated adenocarcinoma pT1N0M0, Stage IA**

A Low-dose CT image    B High-resolution CT image
Index words and secondary materials used as references

A search of PubMed and MEDLINE were performed using “lung cancer”, “screening”, “low-dose”, “CT”, “sensitivity”, “specificity”, and “mortality” as key words. The Group for “Research on the Establishment of Methods for Appropriate Cancer Screening and its Assessment” funded by a Ministry of Health, Labour and Welfare Cancer Research Grant 2006 eds: Guidelines for Lung Cancer Screening Based on Efficacy Assessment, 2006 (http://canscreen.ncc.go.jp/pdf/guideline/guide_lung070111.pdf) and Joint Committee on the Concept of Lung Cancer Screening by Low-Dose CT eds: Manual for Lung Cancer Screening by Low-Dose CT, 2005 were also used as references.

References

4) Yoshimura A et al: A Pilot Study of Lung Cancer Screening with Low-Dose Spiral CT. Jpn J Lung Cancer 40: 99-105, 2000 (Level 4)
Background/objective

The therapeutic approaches and prognosis of lung lesions of collagen disease vary with the type of collagen disease. Also, collagen diseases preceded by lung lesions are observed at a relatively high frequency, and the identification of collagen diseases may be difficult in an early stage. Whether or not the types of collagen disease can be diagnosed according to HRCT images of lung lesions was evaluated.

Comments

There is no report that evaluated differences in HRCT findings in various collagen diseases (rheumatoid arthritis (RA), systemic sclerosis (SSc), polymyositis/dermatomyositis (PM/DM), mixed connective tissue disease (MCTD), primary Sjögren’s syndrome (pSjS), and systemic lupus erythematosus (SLE)) in a single paper. There is a paper that evaluated whether or not the collagen disease type can be diagnosed from HRCT findings of lung lesions in 49 patients diagnosed with NSIP by surgical biopsy. According to this paper, the collagen disease could be accurately diagnosed in 22 (45%) of 49 patients. The accuracy of the diagnosis varied among collagen disease types: 47% for RA, 38% for SSc, 61% for PM/DM, 25% for pSjS, and 0% for MCTD. The authors concluded that the diagnosis is possible to some extent if typical findings such as intralobular reticular opacities in SSc and immediately subpleural linear opacities in PM/DM are present.

Concerning the characteristics of CT findings in various collagen diseases, the following information can be obtained by analysis of reports on CT findings in various collagen diseases.

In RA, airway lesions are observed frequently, and bronchiectasis, bronchiolitis obliterans, and follicular bronchiolitis are observed relatively frequently. Reflecting these disorders, mosaic perfusion, centrilobular shadows, and air trapping are noted. In interstitial pneumonia, the UIP and NSIP patterns appear at similar frequencies, and the OP pattern is also occasionally observed. Reflecting these changes, HRCT presents ground-glass attenuation (GGA), reticular opacities, and consolidations, and honeycombing is more distinct than in other collagen diseases.

SSc is characterized by overlapping of microreticular opacities in GGA on the dorsal side and immediately below the pleura, reflecting the fact that the NSIP pattern is pathologically the most frequent, and is accompanied by traction bronchiectasis. The findings are closer to those in idiopathic NSIP than to those in IPF/UIP.

In PM/DM, reflecting the NSIP and OP patterns, which are frequent pathological findings, fused GGA and consolidation are superimposed over immediately subpleural linear or band-like opacities predominantly in the lower lung field. Compared with other collagen diseases, high frequency of consolidations and low frequency of honeycombing are characteristics. Also, rapidly progressing interstitial pneumonia may occur in DM without muscle symptoms (amyopathic DM: ADM), and clinical attention to the presence of ADM is necessary if the above findings are noted.

In MCTD, the UIP or NSIP pattern has been reported pathologically, and findings including GGA, consolidations, honeycombing, and centrilobular nodular opacities have been reported.

In pSjS, airway lesions such as follicular bronchiolitis (FB) are observed frequently as in RA, and centrilobular opacities and tree-in-bud are noted. Concerning interstitial pneumonia, there have been reports about LIP, NSIP, and UIP, and LIP is characterized by centrilobular opacities and cyst formation.

In SLE, acute lupus pneumonia and diffuse alveolar hemorrhage are important complications, and both show diffuse or mottled GGA or consolidations.

Lung lesions of collagen disease are diverse. Also, since the NSIP pattern is observed most frequently, GGA is a frequent HRCT finding, and differences among collagen diseases are difficult to find. However, RA or pSjS is suggested by airway lesions, RA is suggested by conspicuous honeycombing, SSc is suggested by GGA with internal reticular opacities, and PM/DM is suggested if consolidations in peripheral areas or along the bronchi are noted, possibly allowing the estimation of collagen disease types.

Index words and secondary materials used as references

PubMed and Japana Centra Revuo Medicina were searched using “collagen disease”, “connective tissue disease”,

High-resolution CT findings of lung lesions in various collagen diseases markedly overlap, and clear differences are difficult to find, but discrimination is possible to a degree if characteristic features are observed.

Recommendation grade

No relevant grade

Is high-resolution CT appropriate to differentiate among collagen vascular disease types?

3. Thoracic region
individual collagen diseases ("rheumatoid arthritis", "systemic sclerosis", "dermatomyositis", "polymyositis", "lupus erythematosus", "systemic", "mixed connective tissue disease", "Sjögren’s syndrome"), "CT", and "lung" as key words.

References

Is MRI appropriate for the diagnosis of mediastinal tumors?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>B</td>
<td>MRI is useful for the diagnosis of cystic lesions of the mediastinum and may also provide additional information concerning solid tumors of the mediastinum. It is also very useful for the diagnosis of posterior mediastinal tumors and is recommended.</td>
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</table>

**Background/objective**

Usually, CT is used first for the imaging diagnosis of mediastinal tumors. MRI (Figure) may be performed after CT, but its necessity or usefulness has not been sufficiently evaluated. The effectiveness of MRI for the diagnosis of mediastinal tumors was evaluated.

**Comments**

Mediastinal tumors are classified into anterior, middle, and posterior mediastinal lesions. They are also classified into cystic and solid lesions according to the internal properties. The site of origin and internal properties must be taken into consideration in discussing the usefulness of MRI.

There have been few reports directly comparing the usefulness of CT and MRI in mediastinal tumors. According to comparison of the diagnostic ability of CT and MRI for anterior mediastinal tumors,\(^1\) the diagnostic accuracy was 84 and 81% for thymoma, 45 and 15% for thymic cancer, 67 and 33% for teratoma, 36 and 27% for malignant germ cell tumor, and 55 and 40%, respectively, for malignant lymphoma. In these anterior mediastinal solid tumors, CT shows equal or higher diagnostic ability compared with MRI. Particularly, for the diagnosis of teratoma, CT is significantly superior to MRI. Cystic masses of the mediastinum such as thymic, bronchial, and esophageal cysts are known to show a wide variety of densities and signals on plain CT and T1-weighted MRI due to bleeding or protein content,\(^2,3\) making the diagnosis difficult, but, according to the above report, the diagnostic accuracy for thymic cysts was 46% by CT and 71% by MRI, being significantly higher for MRI.\(^4\) In a report comparing the delineability of various findings of thymic epithelial tumors by CT and MRI,\(^5\) the visualization rate was 18 and 75% for the peritumoral capsule, 13 and 43% for intratumoral septa, and 5 and 17%, respectively, for intratumoral hemorrhage, indicating higher delineation power of MRI. Fibrotic septa that separate the tumor or a capsule around the tumor visualized by MRI have been reported to suggest low-malignancy thymoma. There is also a report that stage III thymoma could be differentiated by dynamic MRI.\(^6\) By a study evaluating the correlation between MRI findings and the WHO histological classification of thymic epithelial tumors,\(^7\) encapsulated, distinctly-bordered, round tumors were reported to suggest type A thymoma, and tumors with intratumoral hypointense areas on T2-weighted image or mediastinal lymph node enlargement to suggest thymic cancer. It is difficult to diagnose the WHO histological classification from MRI findings in other tumor types. Chemical shift imaging has been reported to be useful for the discrimination between thymoma and thymic hyperplasia.\(^8\)

Since CT and MRI are equally useful for the evaluation of great vessel invasion of thymic epithelial tumors,\(^4\) the invasiveness of the tumor may be evaluated by MRI if contrast-enhanced CT is impossible due to iodine allergy.

Most masses arising in the posterior mediastinum are neurogenic tumors such as schwannoma, neurofibroma, gangliocytoma, paraganglioma, and neuroblastoma, and MRI is useful for the evaluation of the relationships of the tumor with the nerves and intervertebral foramen (Figure).\(^9\) Recently, it has become possible to readily prepare MPR images using volume data of CT and to reconstruct images other than transverse views. While the superiority of MRI is diminishing, there is no report comparing the usefulness of CT and MRI concerning posterior mediastinal tumors.

**Index words and secondary materials used as references**

A search of PubMed was performed using “MRI”, “thymoma”, “thymic epithelial tumor”, “lymphoma”, “mediastinum”, and “mediastinal tumor” as key words.

**References**

4. Sadohara J et al: Thymic epithelial tumors: comparison of CT and MR imaging findings of low-risk thymomas, high-risk thymomas, and thymic...
The Japanese imaging guideline 2013


carcinomas. Eur J Radiol 60: 70-79, 2006 (Level 4)

**Figure: Gangliocytoma**

A  Contrast-enhanced CT: A mass is observed in the posterior mediastinum (right paravertebral region). Contrast enhancement is moderate, and the interior is nearly homogeneous.  
B  Coronal T1-weighted MRI: The vertical extent of the tumor is easy to evaluate by MRI. The lesion is a long and thin tumor showing wide-based spread involving multiple vertebral bodies.
43 Is CT appropriate for the discrimination of benign and malignant pleural lesions?

CT is useful for the discrimination of benign and malignant pleural lesions and is recommended.

Background/objective

Pleural lesions are often asymptomatic, and their detection by imaging examinations is important, but the diagnostic ability of plain chest radiography is limited. The usefulness of CT findings for the differential diagnosis of benign and malignant pleural lesions was evaluated.

Comments

The discrimination of pleural and intrapulmonary lesions by plain chest radiography is not necessarily easy, and CT is performed for diagnosing pleural lesions. By CT the extent and morphology of pleural lesions, degree of their intrathoracic growth, presence or absence of bone destruction, presence or absence of thoracic wall invasion, etc. can be evaluated.

The differentiation of benign and malignant pleural lesions is considered possible in most cases. In a retrospective study performed in 1989 examining 74 patients with diffuse pleural diseases (39 with malignant and 35 with benign diseases) by CT (a contrast agent was used except in those exposed to asbestos), the specificity and sensitivity using (1) circumferential pleural involvement/pleural rind, (2) nodular pleural thickening, (3) ≥1 cm thickening of the parietal pleura, and (4) mediastinal pleural lesions were 100, 94, 94, and 88% and 41, 51, 36, and 56%, respectively, and 28 of the 39 malignant tumors could be diagnosed by fulfilling 1 or more of these 4 criteria.1

In a prospective study reported in 2001, in which 40 patients with pleural effusion were examined by thoracic contrast-enhanced CT using similar diagnostic criteria, malignant diseases could be diagnosed in 28 of the 32 patients, and benign diseases could be diagnosed in all 8 patients (specificity: 84%, sensitivity: 100%), according to pleural surface findings (nodular change or irregularity). This study indicated that circumferential pleural involvement/pleural rind was a poorly reliable finding observed at similar frequencies in benign and malignant lesions.2

According to a retrospective study in which 215 patients with pleural diseases (99 with malignant mesothelioma, 39 with pleural metastatic tumor, and 77 with benign pleural diseases) were examined using contrast-enhanced CT, circumferential pleural involvement/pleural rind was noted in 70% of the patients with malignant mesothelioma but...
in 15% of those with metastatic pleural tumor, 9% of those with tuberculous pleuritis, 5% of those with progressive benign pleural disease, and none of those with pyothorax. Nodular pleural thickening was observed in 48% of those with malignant mesothelioma and 13% of those with metastatic pleural tumors, but none of those with tuberculous pleuritis or pyothorax, and nodule-like thickening was noted in 16% of those with progressive benign pleural disease. Thickening of the parietal pleura of ≥1 cm was noted in 59% of the patients with malignant mesothelioma, 17% of those with metastatic pleural tumors, 75% of those with tuberculous pleuritis, 61% of those with pyothorax, and 53% of those with progressive benign pleural disease and is considered unreliable. Mediastinal pleural lesions were reported in 85% of those with malignant mesothelioma, 33% of those with metastatic pleural tumors, 22% of those with tuberculous pleuritis, 12% of those with pyothorax, and 16% of those with progressive benign pleural disease (Figures 1, 2)³

Changes in the pleural surface (nodular change or irregularity) and the presence of a mediastinal pleural lesion were particularly reliable findings, and circumferential pleural involvement/pleural rind and thickening of the parietal pleura of ≥1 cm are considered to be usable as reference findings depending on the situation. A contrast agent should be used.

Index words and secondary materials used as references

A search of PubMed was performed using “pleural tumor” and “CT” as key words. The Japan Lung Cancer Society eds: Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma, 2007 was also used as a reference.

References

Are CT and MRI appropriate for the diagnosis of T stage in lung cancer?

<table>
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<tr>
<th>Recommendation grade</th>
<th>CT</th>
<th>MRI</th>
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CT has strong scientific evidence and strongly recommended.

If involvement of the chest wall, vertebral bodies, brachial plexus, or diaphragm is uncertain by CT, the implementation of MRI may be considered.

**Background/objective**

The usefulness of CT and MRI for the pre-treatment diagnosis of T stage of lung cancer was evaluated.

**Comments**

Concerning T stage, CT is essential for the accurate measurement of the tumor diameter. Particularly, if the tumor is long in the craniocaudal direction, reconstructed coronary and sagittal images are useful (Figure 1). CT is also useful for the diagnosis of the presence or absence of atelectasis and obstructive pneumonia, presence or absence of invasion to adjacent structures, and extent of involvement of the proximal bronchi.1,3 There is no significant difference in the sensitivity or specificity between CT and MRI for the differentiation between T0-2 and T3-4 (CT: 63 and 84%, MRI: 56 and 80%), but MRI is reportedly superior regarding mediastinal invasion.1,5 MRI has been reported to exceed CT in diagnosing the presence or absence and extent of involvement of the chest wall, vertebral bodies, brachial plexus, subclavian artery and vein, diaphragm, and mediastinum,1,4,5 and many reports suggested its usefulness, particularly for the diagnosis of apical tumors (Pancoast tumor).4,5 MRI is recommended if CT shows no clear mass in the chest wall or bone destruction in the ribs, and the diagnosis is uncertain (Figure 2).

However, no prospective study comparing reconstructed sagittal or coronal CT images based on isotropic volume data obtained by MDCT and MRI has been conducted. The diagnostic accuracy using 1.25mm thick reconstructed sagittal images was significantly higher than that using 5mm thick images for invasion of the interlobar pleura, chest wall, and mediastinum,6 but there has been no comparison with MRI, and the superiority of MRI has not been confirmed. Also, cine-MRI using respiratory motion has been reported to be useful for the diagnosis of chest wall and mediastinal involvement, and chest wall invasion can be excluded if separate movements of the tumor and chest wall can be visualized.7 It is indicated when the tumor appears to have wide contact with the chest wall or mediastinal structures such as the great vessels on CT, and invasion is suspected.

**Index words and secondary materials used as references**

A search of PubMed was performed using “lung cancer”, “T-stage”, “invasion”, and “CT” as key words. The NCCN (ver.2.2012) and ACCP (2nd ed) guidelines and the official ATS/ERS statements were also used as references.

**References**

**Figure 1: Primary lung cancer (pT2aN0M0, stage IB)**

A  In the transverse HRCT image: The maximum diameter is 28 mm (2 cm<, ≤ 3 cm, cT1b).

B  Reconstructed coronal image: The tumor is vertically elongated with a maximum diameter of 48 mm (3 cm<, ≤ 5 cm) and is judged to be cT2a.

**Figure 2: Lung cancer (cT3N2M0, stage IIIA)  Rib invasion**

A  Contrast-enhanced CT: An irregularly-shaped mass is observed on the ventral side of the right upper lobe. While it is in contact with the right first rib, no clear bone destruction or chest wall mass is noted.

B  Postcontrast T1-weighted image: An area of contrast enhancement (→) is noted in the right first rib and surrounding soft tissue, suggesting chest wall invasion.
**Background/objective**

CT is an essential examination for not only the T-stage diagnosis but also anatomical localization of lymph nodes (lymph node mapping) in the N-stage diagnosis. However, concerning the presence or absence of metastasis (N0 or N1/2/3), PET has a higher diagnostic ability than CT and is widely used. With improvements in the imaging techniques, MRI has also been reported to be useful for the N-stage diagnosis. The diagnostic abilities of CT, MRI, and PET/CT for lymph node metastasis were compared.

**Comments**

In CT, a short diameter of ≥1 cm is often used as a criterion for lymph node enlargement, but its sensitivity and specificity (52-75% and 66-88%, respectively) are inferior to those of PET (83-91% and 86-92%, respectively). On comparison between CT and MRI using the same criterion (short diameter: ≥1 cm), the diagnostic ability is comparable and showed no significant difference. Regarding the diagnostic ability of PET/CT for intrathoracic lymph node metastasis, it has been reported that the sensitivity, specificity, and accuracy were 54.2, 91.9, and 80.5%, respectively, and that the accuracy of the diagnosis of N2N3 was 84.9%. Therefore, PET/CT is recommended for the N-stage diagnosis (Figure 1).

Recently, STIR turbo spin-echo (SE) and diffusion-weighted sequences of MRI have been applied to the N-factor diagnosis, resulting a report that the diagnostic ability of STIR was higher than that of PET/CT or diffusion-weighted imaging and that the diagnostic abilities of PET/CT and diffusion-weighted imaging were comparable. To use these techniques as standard examinations, the standardization of the imaging methods and cut-off values is necessary, and research at multiple facilities is awaited (Figure 2).

**Index words and secondary materials used as references**

A search of PubMed was performed using “lung cancer”, “lymph node”, “metastasis”, “CT”, “MR”, and “PET” as key words. The NCCN (ver.2. 2012) and ACCP (2nd ed) guidelines and the official ATS/ERS statements were also used as references.

**References**


Figure 1: Lung cancer (cT1bN2M1b, stage IV)
A  Two lymph nodes with a short diameter of <1 cm are observed in the right lower paratracheal region (#4R).
B  PET/CT: Marked accumulation of FDG is noted in the #4R lymph nodes.

Figure 2: Lung cancer (cT2aN3M1b, stage IV)
A  Contrast-enhanced CT: An enlarged lymph node with a short diameter of >1 cm (thick →) is noted in the right lower paratracheal region (#4R) along with lymph nodes with a short diameter of <1 cm (thin →) in the left lower paratracheal region (#4L).
B  Diffusion-weighted MRI (b=1,000 s/mm²): The primary lesion in the right upper lobe (▲) and #4R (thick →) and #4L (thin →) lymph nodes are all hyperintense.
Is brain contrast-enhanced MRI more appropriate than contrast-enhanced CT for the diagnosis of brain metastasis of lung cancer?

**Recommendation grade**

Head contrast-enhanced MRI has scientific evidence and is strongly recommended to be performed.

### Background/objective

The brain is the most frequent site of distant metastasis of lung cancer, and the diagnosis of its brain metastasis is important. The diagnostic ability of contrast-enhanced MRI for brain metastasis was compared with that of contrast-enhanced CT.

### Comments

Contrast-enhanced MRI has been reported to show higher sensitivity for detecting brain lesions than non-contrast MRI, contrast-enhanced CT, or non-contrast CT and to be able to detect more and smaller metastatic lesions. This is considered to be due to higher density resolution, higher contrast-enhancing effect of the contrast agent, and less bone artifacts in contrast-enhanced MRI compared with CT (Figure). However, there is also a report that, while the detection rate was higher and smaller metastases could be detected by contrast-enhanced MRI than contrast-enhanced CT, no significant difference was noted in the mean survival period or 2-year survival rate.

According to meta-analysis of 18 papers comparing clinical and CT findings concerning brain metastasis in 1,830 patients with non-small cell lung cancer, the median prevalence of brain metastasis was 3%, and the median negative predictive value was 97%, in 9 reports exclusively evaluating clinically asymptomatic patients, but the median prevalence of brain metastasis was 14%, sensitivity was 76%, and specificity was 82%, in 9 reports evaluating both clinically symptomatic and asymptomatic patients. However, in a study of brain metastasis in patients with small cell lung cancer, the detection rate by MRI (24%) was higher than that by CT (10%), and while patients with CT-detected brain metastasis were all symptomatic, 11% of those with MRI-detected brain metastasis were asymptomatic.

The ACCP guidelines recommend brain MRI, also from the viewpoint of cost-effectiveness, for patients with non-small cell lung cancer when there are clinical central nervous system symptoms/signs, because the brain metastasis-positive rate is low at 3%, and the negative predictive value is very high in patients negative on clinical examinations. However, as there is a report that the prognosis is more favorable in asymptomatic than symptomatic brain metastasis, the NCCN guidelines (ver.2. 2012) recommend head MRI for stage IB or more advanced non-small cell lung cancer regardless of symptoms for the detection and early treatment of asymptomatic brain metastasis. For small cell lung cancer, the guidelines recommend brain MRI to all patients regardless of whether the disease is of the limited or extensive type in consideration of the high prevalence of brain metastasis in asymptomatic patients. However, as the histological diagnosis is often unavailable at preoperative staging of the disease, contrast-enhanced brain MRI is recommended for staging of all lung cancers.

In a study of bronchioloalveolar carcinoma 3 cm or less in diameter, all 25 cases were reported to be T1N0M0, and further evaluation is necessary concerning patients showing pure ground-glass opacity (GGO) on CT. Contrast-enhanced CT is also considered appropriate when contrast-enhanced MRI is impossible due to reduced renal function, implanted electronic devices, or implanted metals.

### Index words and secondary materials used as references

A search of PubMed was performed using “lung cancer”, “brain metastasis”, “MR”, and “CT” as key words. The NCCN (ver.2. 2012) and ACCP (2nd Edition) guidelines and official ATS/ERS statements were also used as references.

### References

Figure: Multiple brain metastases of lung cancer (cT2aN2M1b, stage IV)
A  Contrast-enhanced MRI: Hyperintense nodules (→) are observed at 2 sites in the left frontal and left parietal lobes. B  Contrast-enhanced CT: A hyperdense area is visualized in the left temporal lobe (→), but the lesion in the left frontal lobe is difficult to detect.

Is bone scintigraphy useful for the diagnosis of bone metastasis of lung cancer?

While scientific evidence is insufficient, bone scintigraphy is worth considering. It should be considered particularly when PET cannot be performed in patients clinically suspected to have bone metastasis.

**Background/objective**

At the initial examination, bone metastasis is observed in 10-30% of the patients with primary lung cancer, and the diagnosis of bone metastasis is important for the prognosis and selection of treatments. Search for bone metastasis used to be made by bone scintigraphy, but recently it is often replaced by PET. This is because PET is comparable in sensitivity but superior in specificity compared with bone scintigraphy as the enhancement of tracer uptake also in trauma, infection, and arthritis reduces the specificity of bone scintigraphy. In contrast, advantages of bone scintigraphy are the short scanning time and a lower false negative rate for osteoblastic bone metastasis compared with PET. The diagnostic power for the diagnosis of bone metastasis of primary lung cancer was compared between bone scintigraphy and PET.

**Comments**

According to meta-analysis of 8 papers (723 patients), the sensitivity and specificity of bone scintigraphy for bone metastasis were 82 and 62%, respectively, in primary lung cancer patients with a mean prevalence of 20%, with a relatively low sensitivity. However, according to meta-analysis of 17 papers consisting of 9 on PET/CT, 6 on PET, 6 on MRI, and 16 on bone scintigraphy (2,940 patients), the sensitivity and specificity of PET/CT, PET, MRI, and bone scintigraphy were 92, 87, 77, and 86% and 98, 94, 92, and 88%, respectively, and the odds ratio was significantly higher by PET/CT (449.17) and PET (118.25) than by MRI (38.27) and bone scintigraphy (63.37) (Figure). Papers not included in these meta-analyses also reported a higher diagnostic ability for PET than for bone scintigraphy.

The ACCP guidelines and official ATS/ERS statements recommend bone scintigraphy only for patients with clinical symptoms. However, according to a study by Schirrmeister et al., bone metastasis was detected in 27% of asymptomatic patients, the sensitivity of bone scintigraphy was 87%, and bone metastasis was overlooked in 14-22% of the patients without bone scanning, resulting in unnecessary surgery or preoperative chemotherapy.

The latest NCCN guidelines recommend PET in all stages and disrecommend the implementation of bone scintigraphy in all patients to exclude asymptomatic bone metastasis. PET, which is performed to detect both mediastinal lymph node metastasis and distant metastasis, is regarded as the first choice, and bone scintigraphy is considered to be recommended only to symptomatic patients at facilities incapable of performing PET.

**Index words and secondary materials used as references**

A search of PubMed was performed using “lung cancer”, “bone metastasis”, and “bone scintigraphy” as key words. The NCCN (ver. 2. 2012) and ACCP (2nd ed) guidelines and official ATS/ERS statements were also used as references.

**References**

Figure: Lung cancer (cT1bN2M1b, stage IV)
A  Bone scintigraphy  Anterior view  Marked accumulation is noted in the lower lumbar vertebrae, suggesting metastasis, but no clear abnormal accumulation is observed at other sites.  B  PET  Many high-uptake areas (→) are observed in the thoracic and lumbar vertebrae and left ilium. All lesions enlarged on follow-up CT examinations, and a diagnosis of multiple bone metastases was made.
3. Thoracic region

48 Is PET appropriate for the N-/M-stage staging of lung cancer?

**Recommendation grade**

| PET is effective for the N-/M-factor staging of lung cancer and is recommended. | B |

**Background/objective**

PET is a modality carried out by administering a radioisotope that emits positrons and visualizing its distribution in the body to make diagnoses according to the distribution and kinetics of the tracer. Characteristics of PET include (1) high resolution and (2) the possibility to correct uptake values in the body, and the procedure has been used along with CT for staging lung cancer (Figures 1, 2).

**Comments**

1) N-stage diagnosis

Mediastinal lymph node (N2) metastasis is the most important factor for staging, particularly preoperative staging, of lung cancer. PET is known to have advantages such as (1) high sensitivity, (2) high resolution, and (3) the possibility to correct uptake values in the body, but it has four major pitfalls in diagnosing mediastinal lymph node (N2) metastasis: (1) Lack of diagnostic cutoff values based on semi-quantitative analysis, (2) a poor resolution limit of 7-10 mm, (3) weak uptake by well-differentiated, low-grade tumors, and (4) false positive results in inflammation. There have been a number of reports on (N2) stage analysis using PET. Silvestri et al. reviewed 44 studies related to mediastinal lymph node (N2) factor diagnosis published in 1994-2006. As a result of sROC analysis of data from 2,865 lung cancer patients, the sensitivity was 74% (95% CI: 69-79%), and the specificity was 85% (95% CI: 82-88%). The results indicated that the mediastinal lymph node (N2) diagnosis by PET is more accurate than that by CT but is not perfect. Particularly, mediastinal lymph node (N2) diagnosis using PET is significant in patients suspected to be in stage IB-IIIB, and close preoperative examination of lymph nodes by measures including EBUS, thoracoscopy, and mediastinoscopy is recommended if abnormal findings are obtained by PET.

Gould et al. performed meta-analysis by restricting the targets to lymph node lesions 10 mm or greater in diameter in consideration of the resolution limit of PET, which is 7-10 mm. The sensitivity and specificity of PET was 100 and 78%, respectively. However, similar analysis targeted to lymph nodes less than 10 mm in diameter showed sensitivity of 82% and specificity of 93%, respectively, indicating that the results of PET are false negative in about 20% of the patients. Regarding the results of multicenter randomized controlled trials using PET/CT, Fischer et al. reported sensitivity of 95% and specificity of 85%, showing improvements compared with the data of PET.

2) M-stage diagnosis

For the M-stage diagnosis of lung cancer using PET, unexpected metastases are known to be found in 10-20% of the patients. While this information has a strong clinical impact, much of the data were obtained by single-facility, small-scale, prospective studies. Problems with PET in the M-stage diagnosis include (1) unstandardized evaluation method, (2) definition of brain metastasis, (3) method to validate negative PET findings, and (4) contribution to the patient’s prognosis. Depending on the organ, the sensitivity of PET for brain metastasis is only 60%, and MRI shows the highest accuracy regarding the extent of small lesions and tumors. While the diagnostic accuracy in liver metastasis is 92-100%, data are considered insufficient. Concerning bone metastasis, the sensitivity and specificity of PET are both 90% or higher, but it is known to cause false negative results in osteoblastic bone metastases characteristic of breast and prostate cancers. Although the diagnostic accuracy of adrenal metastasis is 100%, data are insufficient. Concerning lung and pleural metastasis, since the uptake of small nodular lesions several mm in diameter is underestimated, confirmation by diagnostic chest CT is necessary.

**Index words and secondary materials used as references**

PubMed, the Cochrane Library, and National Guideline Clearing House were searched for important papers with high diagnostic and therapeutic evidence levels using “lung cancer”, “bronchogenic carcinoma”, “staging”, “PET”, “PET/CT”, and “FDG” as key words.
Figure 1: The diagnosis of mediastinal lymph nodes according to the General Rules for Clinical and Pathological Recording of Lung Cancer (reproduced with permission)

Figure 2: Transverse PET/CT image

References

04 Cardiovascular region
What imaging modalities are appropriate for the diagnosis of acute pulmonary thromboembolism?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Imaging modality</th>
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<tr>
<td>A</td>
<td>Contrast-enhanced CT of the chest</td>
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<td>B</td>
<td>Pulmonary perfusion scintigraphy, lower extremity venous ultrasound, lower extremity venous CT</td>
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CT is recommended as there is strong evidence supporting its usefulness. Pulmonary perfusion scintigraphy is also useful and recommended. These examinations may be performed alone or in combination. Lower extremity venous ultrasound or CT is useful and recommended for the diagnosis of deep venous thrombosis.

Background/objective

To efficiently diagnose pulmonary thromboembolism, appropriate selection of examinations and evaluation of the results are necessary. In Western countries, the diagnostic utility has been established on the basis of the results of a number of studies, and the selection of examinations based on the clinical probability is recommended, but this method has not been widely accepted in Japan. Here, the value of contrast-enhanced CT (of the chest, lower extremity), pulmonary perfusion scintigraphy, and lower extremity venous ultrasound in the diagnostic procedure are evaluated.

Comments

Pulmonary thromboembolism requires prompt and accurate diagnosis because a delay of treatment may result in aggravation of the condition and even death, but the selection of examinations and evaluation of the results differ according to the patient’s condition (Figure 1).

If a patient suspected to have pulmonary thromboembolism exhibits a state of circulatory collapse, emergent CT should be performed and treatment started after a definitive diagnosis. Other thoracic disorders that need to be differentiated including aortic dissection and pericardial effusion can also be diagnosed. If emergent CT cannot be performed, right heart strain is assessed by transthoracic echocardiography, and, if acute pulmonary thromboembolism is clinically suspected, anticoagulant therapy is evaluated. In such situations, CT should be performed as early as possible to confirm the diagnosis (Figure 2).

If the hemodynamic status is stable, the clinical probability should be evaluated according to the patient’s clinical information. This evaluation is made by clinicians, but radiologists must also be informed of the results. The Wells score is the best known evaluation method.

If the clinical probability is moderate or low, D dimers are assayed first. If the D dimer level is normal, pulmonary thromboembolism can be excluded, and no further examination or treatment is necessary. If the D dimer level is higher than the normal range, CT or, depending on the situation, pulmonary perfusion scintigraphy should be performed. If both examinations are negative, no treatment is required.

If, on the other hand, the clinical probability is high, the D dimer level, associated with a low negative predictive value, is not useful, so CT should be performed first, with pulmonary perfusion scintigraphy depending on the situation. According to a multicenter progressive study reported in 2006 (prospective investigation of pulmonary embolism diagnosis II: PIOPED II), the negative predictive value in this group was low at 60%, and additional examinations (pulmonary perfusion scintigraphy, lower extremity venous ultrasound) should be considered, if the thrombus cannot be confirmed by CT.

Which of CT and pulmonary perfusion scintigraphy should be used is controversial, but the greatest advantage of CT is its high availability. Emergency pulmonary perfusion scintigraphy can be performed at few facilities. Also, CT has many advantages such as that it can delineate the thrombus itself and that aortic, pulmonary, and thoracic lesions can be diagnosed, so it is usually the first choice. However, while the exposure has been reduced in recent CT devices, presently the exposure is lower by pulmonary perfusion scintigraphy. Therefore, pulmonary perfusion scintigraphy should be considered in examination of young patients and for repeated follow-up examinations. Pulmonary perfusion scintigraphy is recommended in patients with a history of adverse reactions to the contrast agent and those with renal dysfunction. Also, as pulmonary perfusion scintigraphy shows a high negative predictive value, this less invasive modality is recommended for patients with a low clinical probability and normal chest plain radiographs.

More than 90% of the thrombi that cause pulmonary thromboembolism are lower extremity venous thrombi, and the evaluation of the lower extremity veins is necessary for the determination of the therapeutic approach including the necessity of an inferior vena cava filter. Lower extremity venous ultrasound and CT venography, in which the pelvic region and lower extremities are imaged in the delayed phase of pulmonary artery CT, are diagnostic methods for lower
extremity venous thrombosis. In the PIOPED II,\(^6\) the sensitivity for the diagnosis of pulmonary thromboembolism was reported to have improved from 82 to 90% by the inclusion of CT venography in the diagnostic procedure. However, it must be remembered that the inclusion of CT venography significantly increases the exposure. Caution is needed, particularly in young women. Since the diagnostic accuracy is considered comparable between lower extremity venous ultrasound and CT venography, the former is more desirable if possible.\(^1\)

**Index words and secondary materials used as references**

A search of PubMed was performed using “pulmonary embolism”, “diagnosis”, and “guideline” as key words. The JCS Joint Working Group: Guidelines for the diagnosis, treatment and prevention of pulmonary thromboembolism and deep vein thrombosis 4) were also used as a reference.

**References**

1) Torbicki A et al: Guidelines on the diagnosis and management of acute pulmonary embolism: the task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Heart J 29: 2276-2315, 2008 (Level 5)
3) American college of emergency physicians clinical policies subcommittee on critical issues in the evaluation and management of adult patients presenting to the emergency department with suspected pulmonary embolism: critical issues in the evaluation and management of adult patients presenting to the emergency department with suspected pulmonary embolism. Ann Emerg Med 57: 628-652, 2011 (Level 5)
Background/objective

With the advent of multislice CT, non-invasive imaging of the coronary artery has become possible. Coronary CTA using a 16-slice CT device has been clinically applied, and 64-slice CT scan is rapidly propagating as a routine clinical examination. Coronary artery CT can provide information useful for the evaluation of the anatomical arrangement of the coronary artery, diagnosis of coronary artery stenosis, and examination of the coronary artery wall. Particularly, concerning its diagnostic accuracy of 64-slice CT for coronary artery stenosis, the sensitivity has been reported to exceed 95% (Figure), and the negative predictive value to be high at about 97-99%. There is a report that the negative predictive value is relatively low when the prevalence is high, but the modality is generally considered useful for the exclusion of stenosis. However, coronary arteriography is the gold standard for the evaluation of coronary artery lesions. Therefore, it is necessary to clarify situations in which coronary CTA is effective.

Comments

Recommendation grade  B

1) When ischemic heart disease is suspected from clinical features (intermediate-risk group on exercise ECG or when exercise ECG cannot be performed)

Patients suspected to have ischemic heart disease are stratified according to age, gender, symptoms, and risk factors (systolic blood pressure, smoking habit, total cholesterol level, presence or absence of diabetes mellitus), and exercise ECG is recommended for those considered to be at intermediate risk. If the risk is estimated to be intermediate on exercise ECG, or if exercise ECG cannot be performed, coronary CTA is recommended (Grade B). If the risk is judged to be high on exercise ECG, coronary arteriography is recommended.

2) Unstable angina/non-ST-elevation myocardial infarction (intermediate- and low-risk groups)

The risk of ACS is stratified according to clinical information such as age and gender, clinical history, new changes on ECG, findings on blood chemistry tests (myocardial injury markers such as troponin), etc. For the intermediate- or low-risk group, coronary CTA, which is useful for the early diagnosis or exclusion diagnosis, is recommended.

3) Evaluation of coronary artery anomalies

In congenital coronary artery anomalies, information concerning the presence or absence and location of abnormal vessels and their spatial relationships with the aorta or pulmonary artery is important, and they can be assessed accurately by coronary CT as well as coronary arteriography. Therefore, CT is strongly recommended for the evaluation of coronary artery anomalies. However, efforts to reduce the radiation exposure are necessary for pediatric and young patients, and coronary MRA should be considered as an alternative if motion artifacts due to high heart rate/breathing at rest are expected.

4) Evaluation after coronary artery bypass surgery

In the evaluation after coronary artery bypass surgery, the use of a non-invasive examination such as coronary CTA for the assessment of the graft and its anastomotic regions and search for new coronary artery lesions is considered greatly beneficial to patients and is recommended.

5) Kawasaki disease

In Kawasaki disease, echocardiography is performed as the first imaging modality, but coronary CTA is excellent
in delineating the total picture of coronary artery lesions including aneurysms, stenotic lesions, wall calcification, and collaterals. In children, who are sensitive to exposure, coronary MRI is more desirable if they are examined repeatedly.14,15)

**Recommendation grade C1**

1) **Follow-up after PCI**

   Evaluation is often possible if the stent diameter is 3 mm or greater. However, stents with a diameter of less than 3 mm are not indications of contrast-enhanced CT because of a low diagnostic accuracy. Therefore, the use of CT for the evaluation of stent patency is considerably limited at present.16,17) Particularly, if the condition is symptomatic, the significance of CT is not high. However, CT is recommended for asymptomatic patients with stents 3 mm or greater in diameter placed in the main left coronary artery (Grade B).

2) **Search for coronary artery lesions causing heart failure**

   While reports on the effectiveness of coronary CTA in heart failure patients are scarce, the significance of non-invasive examination of coronary artery lesions is large, and the clinical usefulness of the modality is considered high. However, since the delineability of the coronary artery is often reduced in heart failure patients, and since the administration of a contrast agent at a large dose causes a volume load, sufficient caution is necessary.

**Recommendation grade C2**

**Asymptomatic high-risk patients**

   Presently, there is no evidence supporting the effectiveness of contrast-enhanced CTA in asymptomatic high-risk patients such as those with diabetes mellitus. Usefulness exceeding the risk of radiation exposure and contrast nephropathy has not been demonstrated. Moreover, the evaluation of the coronary artery is difficult in patients with marked calcification. However, the calcification score is a simple examination and is reportedly effective in asymptomatic high-risk patients aged 40 years and above. In Japan, however, there have been few studies using the calcification score, and the evaluation of whether or not databases in Western countries can be directly applied to Japanese also remains insufficient.

**Recommendation grade D**

1) **Unstable angina/non-ST-elevation myocardial infarction**

   If the possibility of acute myocardial infarction is considered high, the patient is admitted to the ICU, and priority is given to prompt revascularization surgery by coronary arteriography.

2) **ST-elevation acute myocardial infarction**

   As invasive reperfusion therapy has been established as a treatment in the acute stage of ST-elevation acute myocardial infarction, more prompt diagnosis is necessary. Since the diagnosis is confirmed by ECG and echocardiography, and coronary arteriography is performed, there is no indication for coronary CTA in general.

3) **General health screening**

   The effectiveness of the use of coronary CTA for general health screening has not been demonstrated. Coronary CT should not be performed at random in low-risk patients despite the risk of radiation exposure and the use of a contrast agent. In consideration of the balance between the benefit and cost of the examination, there is no ground for its introduction to general health screening.

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**Figure: Coronary artery stenosis**

Coronary CT (A) shows stenoses in the left anterior descending and diagonal branches. The findings are in close agreement with angiographic findings (B).
Index words and secondary materials used as references


References

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Background/objective

In cardiac imaging diagnosis, multislice CT and MRI have made remarkable improvements. With increasing diversification of modalities, the role and usefulness of radionuclide scanning of the heart are evaluated.

Comments

Evaluation was made by dividing ischemic heart disease into acute coronary syndrome and chronic coronary artery disease.

Regarding acute coronary syndrome, myocardial perfusion imaging at rest using 99mTc-labeled perfusion agent, which can be prepared in the hospital, has been reported to be useful for the determination of whether or not a patient who has visited with a primary symptom of chest pain should be admitted to the CCU. In patients clinically diagnosed with acute myocardial infarction based on findings including elevations of cardiac enzyme levels, the infarct size can be estimated from the degree and extent of blood flow decreases by acute-phase myocardial perfusion imaging. The modality is also used for the assessment of the effectiveness of various treatments for acute myocardial infarction, and the estimation of the left ventricular end-diastolic volume in the chronic phase has been reported to be possible from acute-phase SPECT findings. Also, on long-term follow-up of patients after acute myocardial infarction, the incidence of cardiac events and life outcome are related to rest perfusion SPECT findings in the acute phase, and the modality is suggested to be useful for the prognosis. In Japan, I-BMIPP imaging, which reflects myocardial fatty acid metabolism, is clinically applied. The diagnostic accuracy of I-BMIPP SPECT is comparable to that of myocardial perfusion imaging for ST-elevation myocardial infarction but is superior for non-ST-elevation myocardial infarction and unstable angina pectoris (Figure 1). In addition, the diagnostic value of BMIPP imaging for stunned myocardium showing transient hypokinesis is high. In stunned myocardium, the myocardium is viable, but fatty acid metabolism is impaired, so the condition is detected by dissociation between the blood flow and metabolism. Since fatty acid accumulation is resolved with recovery of wall motion in a course of several weeks to a few months, improvements in the cardiac function can also be predicted.

The assessment of the severity and risk of chronic coronary artery disease is indispensable for the selection of treatments, as the basis for the selection of invasive treatments, and for the prognosis. Patients with moderate possibility of coronary artery disease or risk of cardiac events are the best candidates for radionuclide scanning. If the risk is known to be high or low from other clinical findings and non-invasive examinations, the value of radionuclide scanning performed for risk stratification is low. However, in high-risk patients, radionuclide scanning of the heart is recommended as a means for selective application of coronary arteriography from the cost-performance viewpoint. Stress myocardial perfusion SPECT is performed basically for functional imaging to evaluate impairment of the coronary perfusion reserve including the endothelial function during stressing and associated abnormalities of blood flow distribution on the myocardial cell level (Figure 2). Therefore, the findings do not necessarily reflect the anatomical severity of coronary artery stenosis or predict collapse of an unstable plaque that may occur in the near future. Rest myocardial perfusion scan is performed to evaluate the presence or absence of complicating infarction and volume of infarcted myocardium, and stress myocardial perfusion scan is performed to evaluate the myocardial volume with, and severity of, reversible ischemia. Many clinical studies have demonstrated that these parameters are excellent predictive factors of cardiac events (myocardial infarction, cardiac death) and the necessity of coronary revascularization procedures (CABG, PCI).

Index words and secondary materials used as references

PubMed was searched using ischemic heart disease, myocardial SPECT, humans, and English as key words. Klocke FJ et al. ed: AHA/ACC/ASNC guidelines for the clinical use of cardiac radionuclide imaging (ACC 2004) and the Japanese Circulation Society et al. eds: Guidelines for Clinical Use of Cardiac Nuclear Medicine, 2010 edition (JCS 2010) were also used as references.
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References


Figure 1: \(^{123}\text{I}}\text{BMIPP myocardial SPECT of non-ST-elevation myocardial infarction}

In this patient with non-ST-elevation myocardial infarction of the anterior wall, no clear decrease in accumulation is noted on myocardial perfusion SPECT using \(^{99m}\text{Tc-sestamibi}\), but reduced fatty acid metabolism extending from the anterior wall to the apex (\(\rightarrow\)) is clearly visualized by \(^{123}\text{I}}\text{BMIPP myocardial SPECT.}\n
Figure 2: Evaluation of myocardial ischemia using fused images of stress myocardial perfusion SPECT and coronary CT

Coronary CT shows marked stenosis in many branches, but fusion with stress myocardial perfusion SPECT images allows the identification of the vessel responsible for ischemia with the intermediate branch.
Is MRI appropriate for the diagnosis of ischemic heart disease?

### Background/objective

For the diagnosis of ischemic heart disease by cardiac MRI, myocardial ischemia is evaluated by stress myocardial perfusion MRI, myocardial infarction is evaluated by delayed contrast-enhanced MRI, and coronary artery stenosis is evaluated by coronary MRA. Since cardiac MRI is rarely used today as an emergency examination for the diagnosis of acute coronary syndrome, the usefulness of cardiac MRI for the diagnosis of stable angina pectoris and old myocardial infarction among ischemic heart diseases is evaluated in this section.

### Comments

Delayed contrast-enhanced MRI is used for diagnosing myocardial infarction by MRI. The modality has higher resolution than radionuclide imaging and can explicitly diagnose subendocardial infarction and right ventricular infarction, which cannot be detected by SPECT imaging (Figure). The modality is also useful for the assessment of the myocardial viability in patients after myocardial infarction and allows the estimation of the possibility of functional recovery from the extent of infarcted myocardium from the endocardial to epicardial side. Also, in a study following up the outcomes of patients suspected to have ischemic heart disease by delayed contrast-enhanced MRI, the presence or absence of delayed contrast enhancement has been shown to be highly useful for the prediction of cardiac death or major cardiac accidents, and the significance of risk assessment by delayed contrast-enhanced MRI is high, particularly, in groups with a high prevalence of coronary artery disease such as diabetic patients.

In patients with angina pectoris, the objective of coronary artery stenting and bypass grafting is to resolve myocardial ischemia caused by stenosis, but the degree of morphological narrowing determined by coronary arteriography or coronary CT is not necessarily in agreement with the degree of mechanical narrowing, and the evaluation of the presence or absence and extent of myocardial ischemia is important to improve the outcome. There have already been a number of single institutional studies on the diagnostic performance of stress myocardial perfusion MRI in patients with coronary stenosis, and meta-analysis of 1,516 patients reported a high diagnostic performance with a sensitivity of 91% and a specificity of 81%. Also, according to a meta-analysis concerning the diagnostic abilities of myocardial perfusion SPECT, MRI, and PET, their sensitivities were 88, 89, and 84%, and specificities were 61, 76, and 81%, respectively, indicating that the diagnostic power of MRI without exposure is close to that of PET. Whether or not functionally significant coronary stenosis causing ischemia is an indication of coronary artery stenting can be judged by measuring the fractional flow reserve. The diagnostic sensitivity and specificity of stress myocardial perfusion MRI for functionally significant stenotic lesions with an FFR of <0.75 are reported to be 82-91% and 91-94%, respectively, and the modality also contributes to the evaluation of treatment indications.

While coronary MRA has characteristics such as no radiation exposure, no need for the administration of a contrast agent, and no effect by marked coronary artery calcification, it has weaknesses such as lower spatial resolution compared with CT, long imaging time requiring 5-10 minutes, and limitation of facilities equipped with the modality. The sensitivity and specificity of coronary MRA were 88 and 72% in multicenter study using a 5-channel coil and 87 and 86%, respectively, in a single-facility study single institutional research using a 32-channel coil, and the modality is considered to be effective for the diagnosis of coronary stenosis in patients with renal failure and those with marked coronary artery calcification.

As cardiac MRI, cine MRI, stress myocardial perfusion MRI, delayed contrast-enhanced MRI, and coronary MRA are performed as a series of examinations, by which the cardiac function, ischemia, infarction, and coronary artery stenosis can be comprehensively evaluated. The results of a recent randomized controlled trial have indicated that the diagnostic ability of such comprehensive cardiac MRI is significantly higher than that of SPECT.
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Index words and secondary materials used as references

A search of PubMed was performed using “coronary artery disease”, “magnetic resonance”, “sensitivity”, and “specificity” as key words. The Joint Working Group on Guidelines for Diagnosis and Treatment of Cardiovascular Diseases ed: Guidelines for Noninvasive Diagnosis of Coronary Artery Lesions (JCS2009) was also used as a reference.

References

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8) Lockie T: High-resolution magnetic resonance myocardial perfusion imaging at 3.0-Tesla to detect hemodynamically significant coronary stenoses as determined by fractional flow reserve. J Am Coll Cardiol 57: 70-75, 2011 (Level 2)
Nonischemic cardiomyopathy is a general term for myocardial disorders that exhibit abnormal thickening or thinning of the cardiac wall and cause mechanical or electric functional impairment. It includes hypertrophic cardiomyopathy, dilated cardiomyopathy, amyloidosis, and sarcoidosis. Nonischemic cardiomyopathy is known to cause serious cardiac events such as arrhythmia and sudden death. Whether or not MRI and CT are effective for its diagnosis is evaluated.

Comments
Nonischemic cardiomyopathy accounts for about 1/3 of the causes of heart failure, is associated with the risk of sudden death, and has a poor prognosis. While implantable cardioverter defibrillators have been shown to be effective for preventing sudden death, the cost and risk of complications must also be considered. Therefore, the diagnosis of nonischemic cardiomyopathy and risk stratification are important to implement early therapeutic intervention and improve the prognosis and QOL.

In nonischemic heart disease, fibrosis of the myocardium occurs, causing a decrease in compliance, diastolic dysfunction, and atrial overload. Also, myocardial fibrosis causes conduction disorders, and consequent severe arrhythmia or tachycardia induces heart failure. Therefore, non-invasive evaluation of the cardiac function and myocardial fibrosis is considered important.

Cardiac MRI is not only a standard tool for the assessment of the ventricular volume and function but also visualizes fibrosis of the cardiac wall with high contrast resolution due to late gadolinium enhancement (LGE). Nonischemic and ischemic cardiomyopathies can be discriminated on the basis of difference in the distribution of fibrosis, which has also been reported to vary among nonischemic cardiomyopathies (Figures 1, 2). The Consensus Panel report approved by the Society of Cardiovascular Magnetic Resonance and the Cardiovascular Magnetic Resonance Working Group of the European Society of Cardiology also regarded cardiac MRI as appropriate and useful for the evaluation of nonischemic cardiomyopathy. Wu et al. performed a prospective cohort study in patients with nonischemic cardiomyopathy with a left ventricular ejection fraction of <35% and reported that LGE was observed in 42% of the patients and that the risk of cardiac events was about 8-fold higher in those with than without LGE. According to a cross-sectional study by Adabag et al., the risk of ventricular tachycardia was about 7-fold higher in those showing LGE among patients with hypertrophic cardiomyopathy, which is a typical nonischemic cardiomyopathy. Thus, cardiac MRI, which provides information important for the diagnosis and risk assessment of nonischemic cardiomyopathy, is recommended for its diagnosis.

Cardiac CT has a high diagnostic ability for coronary artery disease, and retrospective ECG gating makes accurate evaluation of the cardiac function possible. However, the use of the modality for the assessment of myocardial fibrosis has been limited primarily to case reports, and its usefulness has not been established.

Index words and secondary materials used as references
A search of PubMed was performed using “nonischemic cardiomyopathy” and “computed tomography” as key words for CT and “nonischemic cardiomyopathy”, “magnetic resonance imaging”, and “fibrosis” as key words for MRI. The Consensus Panel report approved by the SCMR/ESC-CMR Working Group and the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography were also used as references.
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**Figure 1: Hypertrophic cardiomyopathy**

In this patient with hypertrophic cardiomyopathy, LGE is noted at the junction of the anterior septum, showing asymmetric thickening, with the right ventricle (→).

**Figure 2: Dilated cardiomyopathy**

In dilated cardiomyopathy, the cardiac wall is thinned, and linear LGE is noted primarily in the intermediate layer from the anterior wall to the septum (→).

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**References**

4) Wu KC et al: Late gadolinium enhancement by cardiovascular magnetic resonance heralds an adverse prognosis in nonischemic cardiomyopathy. J Am Coll Cardiol 51: 2414-2421, 2008 (Level 2)
Background/objective

Ten years have passed since the clinical introduction of MDCT, and CTA has established a firm position as the first choice for imaging study of the aorta. However, MRA has also shown unique development while it is inferior to CTA in resolution and simplicity. Particularly, by unenhanced MRA, blood vessels can be evaluated without using a contrast agent. In this section, indications of CT/MRI for the diagnosis of aortic aneurysms, selection between the two modalities, and evaluation items for their diagnosis are discussed.

Comments

1) Roles of CT/MRI in the evaluation of aortic aneurysms

An aortic aneurysm is “a circumferential or local dilation of part of the aortic wall”, and a dilation of the aorta (fusiform dilation) to more than 1.5 times its normal diameter (4.5 cm in the thoracic region, 3 cm in the abdominal region) is called an “aneurysm”. There are 3 major tasks for vascular imaging of aortic aneurysms. The first task is to diagnose acute aortic disorders. The differentiation of aortic aneurysm from other acute aortic disorders (aortic dissection with patent/closed false lumen, acute aortic syndrome such as penetrating atherosclerotic ulcer) and exclusion of non-aortic disorders such as pulmonary thromboembolism are very significant for the determination of the therapeutic approach.3

After a diagnosis of aortic aneurysm has been made, the second important task is to estimate the risk of rupture by follow-up. Follow-up monitoring of the aortic diameter is made by measuring the short diameter at the widest part of the aneurysm (maximum short diameter). In thoracic aortic aneurysms, the risk of rupture is high when the aneurysmal diameter (external diameter) exceeds 55 mm, and surgical treatment must be considered.2 In female patients, there is the risk of rupture even in smaller aneurysms, and surgery should be evaluated for lesions 45-50 mm in diameter.3 Also, even if the diameter is 55 mm or less, the risk of rupture is high when the annual enlargement rate is greater than 5 mm/year.4 5 On the follow-up of thoracic aortic aneurysms, lesions 50 mm or greater in diameter are examined every 6 months, but those less than 50 mm in diameter are initially examined after 6 months and at 1-year intervals thereafter.1 6 Concerning abdominal aortic aneurysms, the annual risk of rupture is correlated with the diameter, being 0.3% for those less than 40 mm, 1.5% for those 40-49 mm, 6.5% for those 50-59 mm, and increasing rapidly as the diameter exceeds 60 mm.6 Abdominal aortic aneurysms 40 mm or less in diameter are followed up initially after 6 months and at 1-year intervals thereafter if there is no change, but those 40-50 mm in diameter are followed up every 6 months.1 5 Screening of a healthy population for asymptomatic aortic aneurysm using an imaging modality is not recommended as there is no report indicating its effectiveness.5 7

Recently, with the addition of stent grafting as a new therapeutic option to conventional surgical treatment, early treatment for smaller lesions has begun to be considered, and pre-treatment quantitative measurement planning has been given to CTA/MRA as a third new task.3 9

2) Selection of CTA/MRA

The selection between CTA and MRA is related to patient factors including the general condition, renal function, and allergy to the contrast agent and the facility factor, i.e., the accessibility to the modalities at each facility.

Ten years after the clinical introduction of MDCT, the modality has been firmly established as the first choice examination due to its high diagnostic power, short imaging time, wide scanning field, and versatility (Figures 1, 2).1 7 8 Recently, ECG-gated CTA, which is in wide clinical use in the cardiac region, has also been applied to the thoracic region, and it has been suggested to be useful, particularly, for the examination of lesions in the ascending aorta.11 In patients with renal dysfunction, the risk of contrast-induced nephropathy poses a problem, but unnecessary reserve of
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an essential examination due to excessive anxiety should be avoided. The occurrence of contrast-induced nephropathy can be anticipated to an extent from the presence or absence of underlying diseases, presence or absence of the use of a nephrotoxic preparation, and the value of eGFR. The judgment of whether or not contrast enhancement can be tolerated should be made, and, if it is judged to be tolerated, contrast-enhanced imaging should be performed with appropriate preventive measures such as temporary suspension of fluid or drug administration and a decrease in the dose of the contrast agent.\(^{12}\) For the follow-up of aortic aneurysms using CT, contrast-enhanced imaging is preferable, but monitoring of the arterial diameter by non-contrast-enhanced CT occasionally suffices.

MRA is slightly inferior to CTA in resolution and simplicity but has made unique development toward high-speed and high-resolution imaging with improvements in the equipment. MRA of the aorta has been developed primarily as a contrast-enhanced modality using a gadolinium-based contrast agent particularly for visualization of blood vessels and is regarded as an important option for imaging study of aneurysms.\(^{1,5}\) MRA is performed as an alternative modality for patients with allergy to iodine-based contrast agent\(^ {13}\) and has been preferred in children and young patients in consideration of exposure.\(^ {13}\) In addition, the possibility of nephrogenic systemic fibrosis (NSF) has recently discouraged gadolinium-contrasted imaging in patients with renal dysfunction.\(^ {14,15}\) In patients with chronic renal insufficiently requiring dialysis, contrast-enhanced MRA is a contraindication due to the risk of NSF, but the administration of an iodine-based contrast agent for CTA is not contraindicated if dialysis is performed promptly after the examination.\(^ {14,15}\) For patients at high risk of contrast-induced nephropathy, in whom contrast-enhanced CT/MRI cannot be performed, non-contrast-enhanced MRA, the clinical application of which has been increasingly attempted recently, may have a great advantage.\(^ {16}\)

Index words and secondary materials used as references

A search of PubMed was performed using “aortic aneurysm”, “diagnosis”, and “computed tomography” and/or “magnetic resonance imaging” as key words. The Joint Working Group on Guidelines for Diagnosis and Treatment of Cardiovascular Diseases eds: Guidelines for the Diagnosis and Treatment of Aortic Aneurysms/Aortic Dissection, 2011 edition was also used as a reference.\(^ {17}\)

References

Are CT and MRI appropriate for the diagnosis of aortic dissection?

Contrast-enhanced CT (CTA) is recommended for the initial diagnosis and follow-up of aortic dissection as there is strong evidence of its usefulness as the first choice imaging modality. Contrast-enhanced MRA is useful if the patient is allergic to iodinated contrast agents. For the follow-up of chronic phase aortic dissection in patients with renal dysfunction, spin-echo sequences, cine MRI, and unenhanced MRA, which do not involve radiation exposure or require the use of a contrast agent, are useful and recommendable as alternatives for CT.

Background/objective

Since the Guidelines for Diagnosis and Treatment of Aortic Dissection, 2000 were published jointly by 7 major scientific societies including the Japanese Circulation Society, they have been revised to the Guidelines for Diagnosis and Treatment of Aortic Aneurysm and Aortic Dissection (revised in 2006) and to the current 2011 revised edition. Whether or not CT and MRI are useful for the diagnosis of aortic dissection was evaluated by referring to these guidelines.

Comments

In the 2000 guidelines, the following definition began to be used: “Aortic dissection is a state in which two lumens with a considerable length exist along the course of the aorta due to dissection of the aortic wall at the medial level and is a dynamic pathological condition in which a blood flow or hematoma is present in the aortic wall.” The basic feature of the condition is “aortic dissection”, and the term “dissecting aneurysm of the aorta” is used only when part of the lesion is dilated as an aneurysm in the chronic phase.

1) Diagnosis of aortic dissection by CT

According to the 2006 revised edition, aortic dissection is classified clinically from 3 viewpoints: (1) The extent of dissection, (2) disease phase, and (3) state of blood flow in the false lumen. To understand the disease state and determine the therapeutic approach, it is necessary to describe disease types by incorporating these 3 elements.

The Stanford and DeBakey classifications are based on the extent of dissection. The former, which classifies dissections into types A and B depending on whether the dissection reaches the ascending aorta regardless of the location of the entry site (intimal tear), is in wide clinical use. The latter classifies dissections into types I, II, and III (a, b) according to the extent of dissection and location of the entry site.

By the disease phase, aortic dissections are classified into acute and chronic when they are within 2 weeks and 2 weeks or more, respectively, after the onset. Lesions within 48 hours after the onset may be referred to as hyper-acute.

On the basis of the state of blood flow in the false lumen, there are the communicating (Figure 1) and non-communicating (Figure 2) and ulcer-like projection (ULP) types. According to the morphology, aortic dissections are classified into communicating type with blood flow observed in the false lumen and non-communicating type with no blood flow observed in the false lumen (synonymous to the conventional thrombosed type: mentioned later). The former is also called classic aortic dissection (double barrel type) if the tear and flaps are clearly observed.

In communicating aortic dissections, blood flow is visualized in the false lumen by contrast-enhanced CT. In the non-communicating type, a crescent-shaped hyperdensity may be noted in the false lumen on unenhanced CT, and contrast enhancement may be observed in the false lumen in the late phase of contrast-enhanced CT. Since these findings have been suggested to reflect unstable/fluid blood, blood clots, hematoma, etc. before organization of the false lumen, sufficient follow-up is needed.

While some so-called intramural hematomas disappear spontaneously, others may develop into classical aortic dissections or aortic aneurysms. Some Western reports define intramural hematoma (IMH) as a condition in which no intimal tear is identified, and the false lumen is filled with thrombus, but small intimal tears (ULP) may not be identified by imaging studies. Whether or not there are any essential differences between intramural hematoma and non-communicating dissection must be still evaluated, but, in the 2011 revised edition, the description changed to “Since intramural hematoma is properly diagnosed by pathological examination, the clinical use of this term should be avoided.” Also, as the risk of rupture has been reported, it is appropriate to regard intramural hematoma as a variant or subtype of aortic dissection.

Penetrating atherosclerotic ulcer (PAU) reported by Stanson et al., i.e., an ulcerated atherosclerotic lesion of the aorta reaching layers below the media, is confused with ULP in many papers, and as problems remain, utmost caution is necessary in using this term.
2) Diagnosis of aortic dissection by MRI

In patients with a poor general condition, MRI, which requires a long imaging time and has limitations in patient monitoring, is not recommended for the diagnosis of acute aortic dissection. However, the modality is useful for imaging evaluation in the chronic phase. The examination is performed basically by the spin-echo or fast spin-echo sequences (Figure 3) and additionally by cine MRI capable of evaluating the blood flow kinetics, unenhanced time-of-flight (TOF) sequences, phase-contrast (PC) sequences, black blood imaging, and contrast-enhanced MR angiography.\(^{18}\)

Generally, the points of diagnosis of aortic dissection are the presence diagnosis, disease typing, and diagnosis of complications, but the evaluation of morphological changes and diagnosis of complications are important in the chronic phase.

While contrast-enhanced MRA is usually performed, non-contrast-enhanced MRA is used as an alternative for the follow-up of chronic phase aortic dissection in patients with allergy to iodinated contrast agents or renal dysfunction. It should also be noted that the use of a gadolinium-based contrast agent in patients with marked renal dysfunction may induce nephrogenic systemic fibrosis (NSF) and that checking of the renal function is necessary.

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Index words and secondary materials used as references

A search of PubMed was performed using “aortic dissection”, “diagnosis”, “guideline”, “human”, and “practice guideline” as key words. The Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases\(^1-3\) were also used as references.

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References


Are CT and MRI appropriate for the diagnosis of Takayasu’s arteritis?

**Recommendation grade**

Contrast-enhanced CT is useful and recommended. If contrast-enhanced CT is difficult to perform, MRI, which is considered to have nearly equal diagnostic power, is recommended. MRI, which involves no exposure, is desirable for long-term follow-up.

### Background/objective

The definitive diagnosis of Takayasu’s arteritis is rarely performed by pathological examination, and the condition is usually diagnosed by comprehensively evaluating the imaging findings, clinical course, and laboratory findings. Particularly, imaging studies play an important role in the diagnosis of this disease, and their appropriate implementation is considered to permit the early diagnosis and initiation of proper treatments.

### Comments

Takayasu’s arteritis is a non-specific vasculitis of unknown etiology that affects elastic vessels such as the aorta, its major branches, and pulmonary artery. The disease is prevalent in Asian countries including Japan and preferentially affects young to middle-aged women. Since patients with this disease are often included in those with fever of unknown origin, young women visiting with fever or malaise should be examined with this disease in mind as a possible differential diagnosis.

#### 1) Points of diagnosis

The diagnostic criteria in Japan (Certification Criteria for Takayasu’s Arteritis, Website of the Japan Intractable Diseases Information Center http://www.nanbyou.or.jp/pdf/065_s.pdf) clearly state that the definitive diagnosis be made by imaging examinations (DSA, CT, MRA). If imaging findings characteristic of this disease (multiple obstructive or dilated lesions of the aorta and its primary branches) are noted in young individuals, this disease should be initially suspected even when inflammatory reaction is negative and can be definitively diagnosed when it is positive. However, the definitive diagnosis must be made after exclusion of (1) arteriosclerosis, (2) inflammatory abdominal aortic aneurysm, (3) vascular Behçet’s disease, (4) syphilitic mesoaortitis, (5) giant cell arteritis, (6) congenital vascular anomalies, and (7) bacterial (infected) aneurysm.

#### 2) Usefulness of CT/MRI in the acute phase

DSA used to be the gold standard for the imaging diagnosis of this disease. However, while DSA is excellent for the evaluation of changes in the vascular lumen such as stenosis and dilatation, it is difficult by this modality to evaluate wall thickening without luminal changes, which is observed in the acute phase. Presently, therefore, the initial diagnosis of this condition is mostly made using CT or MRI. In the acute phase, circumferential thickening of the aortic wall is a characteristic feature, and a thickened aortic wall is occasionally observed as a hyperdensity on unenhanced CT. In the late phase of contrast-enhanced CT, nearly homogeneous contrast enhancement is noted in the thickened wall, but double ring-shaped layer may be observed on careful examination. Such double layer is called the double ring-like sign, and the contrast-enhanced outer layer and mildly enhancing inner layer are considered to correspond, respectively, to inflammatory change accompanied by medial and adventitial vascularization and mucinous/gelatinous edema of the intima. Pulmonary artery lesions are observed relatively frequently in this disease, i.e., 70-80% of the patients, and the presence or absence of pulmonary artery lesions may be a decisive point for the diagnosis of this disease if its discrimination from other diseases is difficult. Therefore, attention to thickening and contrast enhancement of the pulmonary artery is also necessary in the acute phase. Thinning and contrast enhancement of the wall in the acute phase are also noted on contrast-enhanced MRI, and the modality, not involving radiation exposure, is useful for the evaluation of the therapeutic effects and long-term follow-up. If the disease is diagnosed, and steroid therapy is initiated, in this phase, resolution of arterial wall thickening is expected, but non-specific signs of inflammation such as fever of unknown origin are often the only clinical findings, and many patients are not properly diagnosed. Recently, there have been sporadic reports that 18F-FDG PET is useful for the evaluation of the activity of inflammation and extent of the lesion in aortitis such as Takayasu’s arteritis, but this examination is not covered by insurance in Japan.

#### 3) Usefulness of CT/MRI in the chronic phase

Vascular lesions observed in the chronic phase are often stenosis/obstruction due to reactive intimal hypertrophy, but dilated lesions and aneurysms may occur if necrosis of medial smooth muscle cells or destruction of elastic fiber layer is severe while scarring is mild. Stenotic lesions are frequently observed in the left subclavian artery, left common carotid artery, descending thoracic aorta, and abdominal aorta. In contrast, dilated lesions often arise in the ascending aorta, aortic arch, and brachiocephalic artery. Dilated or stenotic/obstructive lesions of the aorta or its branches can
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Figure 1: Takayasu’s arteritis (acute stage: female in her 30s)
Contrast-enhanced CT in the late phase shows wall thickening and contrast enhancement of the aortic arch and right brachiocephalic artery. While the contrast of the outer layer of the thickened wall is enhanced, contrast enhancement of the inner layer is weak, showing the double ring-like sign.

Figure 2: Takayasu’s arteritis (chronic stage: female in her 50s)
The left subclavian artery is obstructed at its origin, and marked stenosis is noted in a distal part of the thoracic descending aorta. Mild dilation is observed in the ascending aorta.

be clearly delineated by CTA or MRA and, presently, are infrequently evaluated by DSA.\(^2,^{11-13}\) Using DSA as the gold standard, the sensitivity and specificity of MRA have been reported to be both 100%, and those of CT to be 95 and 100%, respectively.\(^5,^{13}\) Also, stenosis and obstruction of the pulmonary artery have also been reported to be assessable by CTA and MRA, and the possibility of replacement of pulmonary perfusion scintigraphy by these modalities has been suggested.\(^14\) Disorders that affect the prognosis of Takayasu’s arteritis include (1) hypertension due to renal artery stenosis or atypical coarctation of the aorta, (2) congestive heart failure due to aortic insufficiency, (3) ischemic heart disease due to coronary artery lesions, and (4) rupture of aneurysm. Therefore, to improve the life prognosis of patients, it is necessary to perform appropriate internal treatment for these lesions from an early stage and appropriate surgical treatment for severe ones. Recently, there have been reports that CT is also useful for the evaluation of coronary lesions of Takayasu’s arteritis.\(^15\)

Index words and secondary materials used as references
A search of PubMed was performed using “Takayasu arteritis”, “CT”, and “MRI” as key words. The Joint Working Group on Guidelines for Diagnosis and Treatment of Cardiovascular Diseases ed: Guidelines for Management of Vasculitis Syndrome (2006-2007) were also used as a reference

References
2) Park JH: Conventional and CT angiographic diagnosis of Takayasu arteritis. Int J Cardiol 54 (suppl): S165-S171, 1996 (Level 4)
4. Cardiovascular region

Is contrast-enhanced CT appropriate for the imaging evaluation after stent graft placement for aortic disorders?

### Background/objective

Presently, the therapeutic approach to thoracic/abdominal aneurysms is determined mostly by contrast-enhanced CT. This is not only because the technique allows dynamic evaluation of the hemodynamics using a contrast agent but also because volume data of thin-slice CT are indispensable for the preparation of detailed treatment plans using the image analysis work station, which has been recently developed. For objective recording of the relationship between aortic aneurysm and major vascular branches, CT is the optimal modality. MRI is also used, but the image quality varies widely according to the equipment, so the modality cannot be universally recommended. In this article, whether or not CT is useful for the imaging evaluation after stent graft placement (T/EVAR) for thoracic/abdominal aortic aneurysm is evaluated with a review of the literature.

### Comments

Modalities used for the imaging evaluation after T/EVAR include angiography, contrast-enhanced CT, contrast-enhanced MRI, color Doppler ultrasound (CDU), and contrast-enhanced ultrasound. Of these modalities, angiography is highly invasive and is usually avoided. MRI has never been selected as a method for the imaging evaluation in major clinical trials for the reason mentioned earlier in Chapter 2.

In contrast, contrast-enhanced CT has been used for preoperative and postoperative evaluations in all large-scale clinical studies conducted to date (EVAR in the UK, DREAM in the Netherlands, and OVER in the United States). On the basis of this fact, the 2011 ACCF/AHA Focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline) clearly states, “Patients who have undergone T/EVAR must be evaluated 1 and 6 months after surgery and annually thereafter by CT (or MRI) regarding graft migration, endoleak, and enlargement of the aneurysm diameter.” Therefore, the present article also concludes that CT is useful for the imaging evaluation after stent graft placement for aortic disorders (Figure).

The following points are worth mentioning as reference information. Recently, CDU and contrast-enhanced ultrasound, which have shown marked development, have been applied to the assessment of endoleak after T/EVAR, and excellent results have been reported. However, by comparison with CT, Pittsburgh University concluded that they cannot replace CT as a modality for follow-up studies. In contrast, Chaer RA et al. recommended CDU, which is less expensive than CT and uses no contrast agent or radiation, for patients who show decreases in the aneurysm diameter and are judged to be in a stable period and have no problem such as a physique interfering with the measurement of the aneurysm diameter and imaging of endoleak.

### Index words and secondary materials used as references

A search of PubMed was performed using “aortic aneurysm”, “MeSH”, “x ray computed tomography”, “endovascular procedures”, “clinical trial”, “meta-analysis”, “practice guideline”, and “randomized controlled trial” as key words. The 2011 ACCF/AHA Focused update of the guideline for the management of patients with peripheral artery diseases (updating the 2005 guideline) was also used as a reference.
4. Cardiovascular region

Figure: After stent graft placement for aortic aneurysm
Contrast-enhanced CT

In the image 8 months after stent graft placement (A), type II endoleak from the inferior mesenteric artery is observed. After embolization using NBCA (B), endoleak disappeared, and residue of NBCA is observed. Compared with the image before embolization (C), the aneurysm diameter is reduced after 1 year (D).

References

Are CT and MRI appropriate for the diagnosis of arteriosclerosis obliterans?

**Background/objective**

Trans-arterial digital subtraction angiography (DSA) was used as a standard imaging modality for the diagnosis of arteriosclerosis obliterans (ASO), but CT angiography (CTA) and MR angiography (MRA) have become prevalent due to the development of MDCT and improvements in the performance of MRI devices. The usefulness of CTA and MRA for the diagnosis of ASO is evaluated.

**Comments**

ASO is suspected clinically due to symptoms and an abnormal ankle-brachial index (ABI) and is diagnosed on the basis of anatomical abnormalities detected by imaging examination. ASO has been recently called peripheral arterial disease (PAD).

According to meta-analysis evaluating the diagnostic performance of CTA for 50% or severer stenosis/obstruction in ASO by DSA, the sensitivity and specificity were 96 and 98% in the aortoiliac region, 97 and 94% in the femoropopliteal region, and 95 and 91%, respectively, in the lower leg. The sensitivity and specificity of MDCT were 92 and 93% with 4 or less detector rows but 97 and 98%, respectively, with 16/64 detector rows, being significantly superior for the latter. According to a recent report using 64-row MDCT, the sensitivity and specificity were 100 and 99% in the aortoiliac and femoropopliteal regions and 97 and 99%, respectively, in the lower leg region, and the modality was also useful for the determination of the therapeutic approach in endovascular and surgical treatments. By CTA, the imaging evaluation is performed using axial views, multiplanar reformation (MPR), curved multi-planar reformation (CPR), maximum intensity projection (MIP), and volume rendering (VR) (Figures 1, 2).

Sparing of multidirectional imaging may also cause false negatives (underestimating) on DSA. Symptoms of ASO are divided into intermittent claudication and critical limb ischemia causing rest pain and ulcer. While the subjects of many reports using CTA were patients with intermittent claudication, there are reports that CTA also contributed to the determination of the therapeutic approach in patients with critical limb ischemia. The absorbed dose on CTA has been reported to be 3.0 mSv in males and 2.3 mSv in females using 16-row MDCT and 7.0 and 4.7 mSv, respectively, using 64-row MDCT.

According to a meta-analysis evaluating the diagnostic performance of contrast-enhanced MRA for 50% or greater stenosis/obstruction on DSA, the sensitivity and specificity are reported to be 93.5 and 96.3% in the aortoiliac region, 95.3 and 95.6% in the femoropopliteal region, and 92.2 and 93.3%, respectively, in the lower leg region. By imaging of specific regions with injections of a contrast agent, the sensitivity was 97.2%, being significantly higher than 93.3% by the bolus-chase method with a single injection. The degree of stenosis is evaluated using original images, MIP, and MPR. Reports using unenhanced MRA rather than the conventional time of flight method have appeared recently, and the sensitivity and specificity of unenhanced MRA for 70% or greater stenosis/obstruction on DSA have been reported to be 95.6 and 97.4% in the femoral region and 95.2 and 87.5%, respectively, in the lower leg region.

According to the results of meta-analyses concerning the diagnostic performance of CTA and MRA, their sensitivity and specificity are comparable. By CT and MRI, the differentiation of ASO from extravascular lesions (e.g., adventitial cystic disease, popliteal artery entrapment syndrome) and diagnosis of thrombotic occlusion of aneurysm are possible using original images or MPR.

**Index words and secondary materials used as references**

A search of PubMed was performed using “peripheral arterial disease”, “CT”, and “MR” as key words. The Inter-
4. Cardiovascular region

Society Consensus for the Management of Peripheral Arterial Disease (TASC II) was also used as a reference.

References

4) Sarwar A et al: Calcified plaque: measurement of area at thin-section flat-panel CT and 64-section Multidetector CT and comparison with histopathologic findings. Radiology 249: 301-306, 2008 (Level 3)
5) Schernthaner R et al: Value of MDCT angiography in developing treatment strategies for critical limb ischemia. AJR 192: 1416-1142, 2009 (Level 4)
9) Huber A et al: dynamic contrast-enhanced MR angiography from the distal aorta to the ankle joint with a step-by-step technique. AJR 175: 1291-1298, 2000 (Level 2)
Are CT and MRI appropriate for the evaluation after stent graft placement for arteriosclerosis obliterans?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>CT, contrast-enhanced MRI</th>
<th>Unenhanced MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
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<tr>
<td>C1</td>
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</table>

In both CT and MRI, artifacts appear at the sites of stent graft placement, making the evaluation of lumens difficult. However, the modalities are recommended as there is evidence for their usefulness. Which of CT and MRI should be selected depends on the stent type, but CT is preferable except for tantalum stents. While there is no sufficient evidence, Unenhanced MRI may be considered when contrast-enhanced CT or MRI cannot be performed.

**Background/objective**

Stent graft placement is often selected as an endovascular treatment for revascularization. However, implanted stents are known to cause artifacts on both CT and MRI. The usefulness of CT and MRI for the assessment of patients with arteriosclerosis obliterans after stent graft placement is evaluated.

**Comments**

With the advancing age of the population and Westernization of lifestyle, patients with arteriosclerosis obliterans are also increasing in Japan.

Treatments for arteriosclerosis obliterans include internal treatments such as drug and exercise therapies, endovascular treatments such as stent graft placement and balloon dilatation, and surgical treatments such as endarterectomy and bypass grafting, and the selection of treatments according to the distribution and severity of lesions is recommended.

Ultrasonography, CT, and MRI are non-invasive imaging diagnostic modalities for arteriosclerosis obliterans. Compared with MRI, CT can be performed in a relatively short time and simultaneously provides information concerning bone and calcification. However, it involves radiation exposure and requires the use of an iodine-based contrast agent, and the evaluation of lumens is occasionally difficult in severely calcified lesions. MRI, on the other hand, causes no radiation exposure and is capable of diagnosing even severely calcified lesions, but it cannot be applied to patients with an implanted pacemaker or defibrillator. Also, due to the risk of nephrogenic systemic fibrosis, a gadolinium-based contrast agent is a contraindication in patients with severe renal disorder.

CT or MRI is selected in consideration of their characteristics as above and circumstances of each facility, but selection criteria appropriate for stent materials are also necessary for the assessment of the sites of stent graft placement.

1) **CT**

CT angiography is used for the diagnosis of arteriosclerosis obliterans. At the sites of stent graft placement, lumens show apparent narrowing and decreases in the CT value due to beam-hardening artifacts. Beam-hardening is affected by the stent material and thickness of the skeleton. Also, stenosis is overestimated in stents with a small diameter.

According to evaluations using phantoms, tantalum stents cause marked artifacts, and their lumens are difficult to evaluate. The evaluation of the lumen is possible in nitinol or stainless steel stents (Figure 1). Markers at the ends of a stent may also cause marked artifacts. While the long axis of the stent is often placed in parallel with the X axis in experiments using phantoms, it is placed diagonally to the Z axis in most clinical situations, resulting in severer artifacts due to beam-hardening. There are also artifacts due to calcification of the arterial wall, making the evaluation of lumens even more difficult.

A high-resolution reconstruction algorithm may be selected to reduce beam-hardening artifacts and visualize the stent lumen. Such a high-resolution reconstruction algorithm improves the spatial resolution but increases noise.

2) **MRI**

MR angiography using a contrast agent is performed for the evaluation of arteriosclerosis obliterans. At the sites of stent graft placement, the lumens appear narrower due to susceptibility artifacts. Susceptibility artifacts vary with the stent material. Tantalum stents cause less artifacts. In many nitinol stents, the patency of the stent can, but the degree of stenosis cannot, be evaluated (Figure 2). Signals of the lumen disappear in stainless steel stents (Figure 1C) and some nitinol stents, preventing the evaluation (Figure 1C).

**Index words and secondary materials used as references**

A search of PubMed was performed using “PAOD (peripheral arterial occlusive disease)”, “stent”, “CT (computed tomography, CTA, CT angiography)”, and “MRI (MRA, MR angiography)” as key words. The guidelines of the J Vasc
4. Cardiovascular region

The Japanese imaging guideline 2013

Surg (Norgren L et al., the TASC II Working Group ed: Inter-Society Consensus for the Management of Peripheral arterial Diseases (TASC II), 2007) were also used as a reference.

References

1) Norgren L et al: Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg 45 (suppl S): S5-S67, 2007 (Level 5)
05
Gastrointestinal tract
Which are appropriate and cost-effective imaging modalities in screening patients with chronic liver disease for hepatocellular carcinoma?

**Recommendation grade**

<table>
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**The cost-effectiveness is highest in Sonazoid contrast-enhanced ultrasonography.** It is followed by dynamic CT and EOB·Primovist contrast-enhanced MRI, with no marked difference between these two modalities. The cost-effectiveness is lowest in angiography (including CT).

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**Background/objective**

Controlling the medical expenditure is a social demand and is also a matter of keen interest to some patients. However, suppression of medical expenditure may cause a decline in the quality of medical service. With these circumstances in mind, it is desirable to conduct the diagnosis and treatment with the cost-effectiveness in mind. The cost-effectiveness was compared among contrast-enhanced imaging modalities used for screening of hepatocellular carcinoma.

**Comments**

There have been few studies that directly evaluated the cost-effectiveness of imaging modalities for the diagnosis of hepatocellular carcinoma. Medical expenditures vary among countries and regions, and the results of analyses based on the medical system of a foreign country cannot be directly applied to the practice in Japan. In addition, as the system of remuneration for medical services is frequently revised, research results providing evidence for the evaluation of the cost-effectiveness of various examinations under the current system are deficient. There is a study on the cost-effectiveness of ultrasound hepatocellular carcinoma surveillance in Japan but no such study regarding other imaging modalities.

It must also be noted that, in evaluating the cost-effectiveness, the “cost” and “effect” may vary depending on the viewpoint. The cost-effectiveness differs for society (government or medical insurance system), patients, and the management of a medical facility. Moreover, how the cost or effect itself should be evaluated is unclear in some respects. For example, “the expense for an examination” may be simply regarded as “the cost”, but if which examination is performed makes differences in the subsequent examinations or treatments, it may be necessary to take the total cost that arises thereafter into consideration. Similarly, while the ability to detect hepatocellular carcinoma may be considered the “effect”, it is more reasonable to regard the improvement in the outcome due to a particular examination as its “effect” in view of the significance of the medical action. Thus, the definition of cost-effectiveness itself contains complex problems. In this article, “the ratio between the ability of an examination to detect hepatocellular carcinoma and its cost” is defined as the cost-effectiveness. This simplifies the idea of cost-effectiveness, but it must be noted that, in reality, situations are diverse as mentioned above.

The costs of examinations are evaluated on the basis of the April 2012 version of the Table of Medical Remuneration Points. The medical remuneration points of Sonazoid contrast-enhanced ultrasonography, dynamic CT, and EOB·Primovist contrast-enhanced MRI performed alone on an outpatient basis and angiography (including CT) performed by hospitalizing the patient for 3 days and 2 nights are about 2,000, 3,000, 4,300, and 18,000, respectively (Note: The exact remuneration varies with the facility, equipment, and contrast agent used). Therefore, if the cost of Sonazoid contrast-enhanced ultrasonography is regarded as 1, the relative costs of the other modalities are 1.5 for dynamic CT, 2.2 for EOB·Primovist contrast-enhanced MRI, and 9 for angiography (including CT).

A systematic review reported that the sensitivity and specificity were 60 (95% CI: 44-76%) and 97% (95-98%) by ultrasonography, 68 (55-80) and 93 (89-96)% by CT, and 81 (70-91) and 85 (77-93)%, respectively, by MRI, and concluded that ultrasonography is more specific but less sensitive than the other modalities. This report did not include Sonazoid contrast-enhanced ultrasonography or EOB·Primovist contrast-enhanced MRI. Concerning contrast-enhanced ultrasonography, there is a report that the sensitivity of Sonazoid contrast-enhanced ultrasonography (73-83%) was similar or slightly lower compared with that of non-contrast-enhanced ultrasonography (83-84%) but that its specificity was higher (97-98 vs. 90-94%). Also, the diagnostic performance of Sonazoid contrast-enhanced ultrasonography was reported to be higher than that of dynamic CT. From these reports, since the relative cost of dynamic CT is 1.5, Sonazoid contrast-enhanced ultrasonography is considered to be more cost-effective than contrast-enhanced CT. There have been a number of reports that EOB·Primovist contrast-enhanced MRI showed higher diagnostic performance than dynamic CT. However, as the cost of EOB·Primovist contrast-enhanced MRI is 1.4 times that of contrast-enhanced CT, which modality is superior is unclear (they appear comparable in cost-effectiveness). While studies that directly compared EOB·Primovist contrast-enhanced MRI and Sonazoid contrast-enhanced ultrasonography are few, there is a report that MRI is slightly superior (no significant difference). To summarize the above observations, the cost-effectiveness is considered to be highest in Sonazoid contrast-enhanced ultrasonography, followed by dynamic CT and
EOB-Primovist contrast-enhanced MRI.

CT during angiography (such as CTAP and CTHA) has been reported to be more sensitive than dynamic CT or EOB-Primovist contrast-enhanced MRI, but there is also a report that EOB-Primovist contrast-enhanced MRI showed higher diagnostic performance than CT during angiography. The improvement in the detection rate or diagnostic accuracy by angiography (including CT) is not considered to match its relative cost, and it appears less cost-effective than the other 3 modalities.

Index words and secondary materials used as references

A search of PubMed was performed using “CT”, “MRI”, “sonography”, “US”, “liver”, “hepatocellular carcinoma”, “HCC”, “sensitivity”, and “accuracy” as key words. The Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 update was also used as a reference.

References

6) Hatanaka K et al: Sonazoid-enhanced ultrasonography for diagnosis of hepatic malignancies: comparison with contrast-enhanced CT. Oncology 75 suppl 1: 42-47, 2008 (Level 4)
8) Mita K et al: Diagnostic sensitivity of imaging modalities for hepatocellular carcinoma smaller than 2 cm. World J Gastroenterol 16: 4187-4192, 2010 (Level 4)
What examination is appropriate when a lesion is suspected on ultrasound screening in patients with chronic liver disease?

**Recommendation grade**

**B**

Dynamic CT, EOB, or Sonazoid contrast-enhanced ultrasonography is recommended.

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**Background/objective**

Ultrasoundography is widely used for purposes including screening of high-risk patients for hepatocellular carcinoma such as those with chronic hepatitis and liver cirrhosis due to its simplicity, low invasiveness, and low cost. However, if a liver tumor is detected or suspected by ultrasoundography, a definitive diagnosis cannot be obtained by ultrasoundography alone, and other examinations with higher diagnostic ability become necessary. Such examinations include Sonazoid contrast-enhanced ultrasonography, dynamic CT, EOB, or Primovist contrast-enhanced MRI using a gadolinium-based extracellular contrast agent, which are not highly invasive, and MRI using EOB. If a hepatic lesion has been detected in a high-risk patient for hepatocellular carcinoma, the discrimination of hepatocellular carcinoma from hepatic angioma, dysplastic nodule, or intrahepatic bile duct carcinoma, which requires a different therapeutic approach, is important. If it is a hepatocellular carcinoma, the determination of its location and extent including vascular invasion is necessary.

**Comments**

1) **Scientific statement**

There have been few studies in which the diagnostic ability of contrast-enhanced ultrasonography using Sonazoid (perfluorbutane microbubbles), an ultrasound contrast-agent presently used in Japan, was compared with that of other modalities. Concerning the qualitative diagnosis of hepatic lesions in 196 patients, Moriyasu et al. reported that, when they are divided into hepatocellular carcinoma, liver metastasis, hemangioma, other benign lesions, and other malignant lesions, the diagnostic accuracy using Sonazoid contrast-enhanced ultrasonography (88.9%) was significantly higher than that of non-contrast-enhanced ultrasonography (68.4%) or dynamic CT (80.5%) (p<0.001 and p=0.008, respectively) and that more hepatic lesions were detected by Sonazoid contrast-enhanced than non-contrast-enhanced ultrasonography or dynamic CT (p<0.001 and p=0.008, respectively). However, they also reported that adverse effects of Sonazoid were observed relatively frequently, i.e., 10.4% of the patients. Hatanaka et al. compared the diagnostic abilities of Sonazoid contrast-enhanced ultrasonography and dynamic CT in 74 patients with 108 lesions of hepatocellular carcinoma and liver metastasis or intrahepatic bile duct cancer and 5 lesions of benign dysplastic nodule and reported that the sensitivities of the modalities for malignant diseases were 95.4 and 85.2% (p=0.037), that the diagnostic accuracy was 94.7 and 82.3% (p=0.032), respectively, and that both parameters were significantly higher in Sonazoid contrast-enhanced ultrasonography. On the other hand, Mita et al. reported that the sensitivity of Sonazoid contrast-enhanced ultrasonography, dynamic CT, and EOB contrast-enhanced MRI for diagnosing hepatocellular carcinoma based on characteristic contrast enhancement patterns in 34 lesions 2 cm or less in diameter detected in 29 patients by ultrasonography was 67.6, 52.9, and 76.5%, respectively, showing no significant difference. Also, according to Goto et al., in a hepatic segment-based evaluation concerning 138 lesions of hepatocellular carcinoma in 100 patients using dynamic CT as a reference, the sensitivity and specificity of the post-vascular phase (Kupffer imaging) of Sonazoid contrast-enhanced ultrasonography were 73-83 and 97-98%, but those of B-mode ultrasonography were 83-84 and 90-94%, respectively; the former was more specific but not more sensitive than the latter.

Regarding the diagnosis of hepatocellular carcinoma, in a comparative study of dynamic CT and extracellular gadolinium-enhanced dynamic MRI for the diagnosis of hypervascular hepatocellular carcinoma, the sensitivity and positive predictive value were reported to be 66 and 97% by dynamic CT and 63 and 96%, respectively, by dynamic MRI, showing no difference. Recently, there have been a number of studies comparing EOB contrast-enhanced MRI and dynamic CT. According to some reports, the sensitivity for detecting hepatocellular carcinoma was 67-97% by EOB contrast-enhanced MRI and 44-92.8% by dynamic CT, and the Az value on ROC analysis, sensitivity, and specificity did not differ, or the Az value did not differ between the two modalities. However, more reports indicated that the sensitivity of EOB contrast-enhanced MRI was higher or significantly higher.

2) **Comments**

Generally, when an intrahepatic lesion is suggested by ultrasonography, contrast-enhanced ultrasonography, dynamic CT, or EOB contrast-enhanced MRI is presently the examination performed next. Since EOB contrast-enhanced MRI became available, the use of SPIO contrast-enhanced MRI has become rare. Also, the frequency of the use of extracellular gadolinium contrast-enhanced MRI for liver tumors has decreased, probably because its diagnostic...
performance is comparable to that of dynamic CT using an extracellular contrast agent. In diagnosing liver hemangioma, which is a clinically most frequently encountered benign liver lesion, extracellular gadolinium contrast-enhanced MRI, which presents delayed contrast enhancement characteristic of hemangioma, is considered to be more advantageous than EOB·Primovist contrast-enhanced MRI, but there is no report comparing the two modalities.

According to reports to the present, Sonazoid contrast-enhanced ultrasonography is considered to be comparable or superior to dynamic CT, and EOB·Primovist contrast-enhanced MRI is more often indicated to be comparable or superior to dynamic CT, in diagnosing hepatocellular carcinoma. Sonazoid contrast-enhanced ultrasonography is not in wide clinical use, presumably because skilled technicians are deficient, and because the procedure has complicated originally simple ultrasonography, but this modality is also recommendable from the viewpoint of diagnostic performance.

In patients suspected to have an intrahepatic lesion, dynamic CT is most widely selected as the next examination due to the high processability of the data despite the radiation exposure and high incidence of adverse reactions to the contrast agent. From the viewpoint of diagnostic ability, also, dynamic CT is recommended as the next examination of ultrasonography, but the addition of modalities such as EOB·Primovist contrast-enhanced MRI is necessary when, for example, surgery is anticipated.

EOB·Primovist contrast-enhanced MRI is recommended because of the highest diagnostic power, but there is no report evaluating its diagnostic ability in patients with liver dysfunction or obstructive jaundice, in which contrast enhancement of the liver with EOB·Primovist is reduced, and the possibility of a decline in the diagnostic performance must be considered in such patients. Also, while equipment with 16 or more detector rows that can perform scanning at a sufficient speed has become widely available for MDCT, MRI is still often performed using old or low-field-strength systems, which may provide images unsatisfactory in quality. Therefore, which of CT and MRI should be used needs to be evaluated at each facility.

For the above reasons, if a hepatic lesion is suspected by ultrasound screening for hepatocellular carcinoma, it is recommended to perform dynamic CT, EOB·Primovist contrast-enhanced MRI, or Sonazoid contrast-enhanced ultrasonography as the next examination in consideration of the skill of the technician and performance of the imaging system at each facility.

Index words and secondary materials used as references

A search of PubMed was performed using “CT”, “MRI”, “sonography”, “US”, “liver”, “hepatocellular carcinoma”, “HCC”, “sensitivity”, and “accuracy” as key words. The Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 update was also used as a reference.

References

1) Moriyasu F et al: Efficacy of perflubutane microbubble-enhanced ultrasound in the characterization and detection of focal liver lesions: phase 3 multicenter clinical trial. AJR 193: 86-95, 2009 (Level 4)
2) Hatanaka K et al: Sonazoid-enhanced ultrasonography for diagnosis of hepatic malignancies: comparison with contrast-enhanced CT. Oncology 75 (suppl 1): 42-47, 2008 (Level 4)
3) Mita K et al: Diagnostic sensitivity of imaging modalities for hepatocellular carcinoma smaller than 2 cm. World J Gastroenterol 16: 4187-4192, 2010 (Level 4)
Which modalities are appropriate for detecting early hepatocellular carcinoma in patients with chronic liver disease?

Gd-EOB-MRI has a high diagnostic ability for early hepatocellular carcinoma. There have been few reports on the diagnostic ability of Sonazoid contrast-enhanced ultrasonography for early hepatocellular carcinoma.

Background/objective

Recently, with the development of imaging diagnostic devices and new contrast agents, the evaluation of targets other than the blood flow has become possible, and small lesions have begun to be detected frequently in patients with chronic liver disease. Early hepatocellular carcinoma, which is an unclear nodule 20 mm or less in diameter representing a hypovascular well-differentiated hepatocellular carcinoma, exhibits diverse features on imaging studies due to changes in the portal and arterial blood flows in the nodule in the course of its multistage development. Generally, the disease is often treated in the stage of hypovascular well-differentiated hepatocellular carcinoma, which is an early hepatocellular carcinoma dedifferentiated from a dysplastic nodule (DN), and further dedifferentiated and hypervasculated well-differentiated hepatocellular carcinoma. It is important to have knowledge of findings on contrast-enhanced ultrasonography, dynamic MDCT, and Gd-EOB-MRI and their diagnostic performance in early hepatocellular carcinoma.

Comments

1) Scientific statement

In 30 nodules of early hepatocellular carcinoma diagnosed by hepatectomy, ROC analysis of the diagnostic abilities of dynamic MDCT and Gd-EOB-MRI showed that the Az value, sensitivity, and NPV were significantly higher by Gd-EOB-MRI (0.98-0.99, 94-97%, and 96.8-98.1%) than by dynamic MDCT (0.87, 58-68%, and 80.7-84.4%, respectively), that the specificity and PPV showed no significant difference, but that the diagnostic performance of Gd-EOB-MRI for early hepatocellular carcinoma was significantly higher than that of dynamic MDCT (Table). In a multicenter joint research participated in by 15 facilities regarding the diagnostic ability for hepatocellular carcinoma 2 cm or less in diameter, nodule-by-nodule ROC analysis of 279 hepatocellular carcinomas showed that the sensitivity of Gd-EOB-MRI (38-55.4% for lesions 10 mm or less in diameter, 71.1-87.3% for those 10-20 mm in diameter) was higher than that of dynamic MDCT (26.1-47.3% and 65.7-78.4%, respectively). According to another report on the diagnostic performance for hepatocellular carcinomas 2 cm or less in diameter, the sensitivities of Sonazoid contrast-enhanced ultrasonography (67.6%) and Gd-EOB-MRI (76.5%) were higher than that of MDCT (52.9%), but the differences were not significant (Table). However, in the above 2 reports, the evaluation was not restricted to well-differentiated hepatocellular carcinoma.

From these observations, Gd-EOB-MRI is considered to have higher diagnostic ability than MDCT for early hepatocellular carcinoma. Presently, there is no report providing evidence sufficient for the evaluation of the diagnostic ability of Sonazoid contrast-enhanced ultrasonography or its comparison with that of MDCT or Gd-EOB-MRI.

2) Comments

Early hepatocellular carcinoma is a well-differentiated hepatocellular carcinoma presenting as an unclear nodule 20 mm or less in diameter. It shows poor tumor angiogenesis and is hypovascular. Its biological malignancy is low, it rarely shows intrahepatic metastasis or vascular invasion, and its prognosis is favorable. In hepatocellular carcinoma, the portal and arterial blood flows in the nodule change in the process of multistage tumorigenesis. In early hepatocellular
carcinoma, the arterial blood flow is deficient but becomes richer with decreases in the portal blood flow through the process of dedifferentiation. A tumor in which hypervascular areas develop in the nodule (nodule-in-nodule) is biologically a small advanced hepatocellular carcinoma even if it is histologically well-differentiated hepatocellular carcinoma. Some such lesions cause local intrahepatic metastasis or vascular invasion and may have a poor prognosis. Therefore, diagnosing the disease in the stage of hypovascular early hepatocellular carcinoma is considered to contribute to a better prognosis.

For hyperarterialized moderately or more differentiated hepatocellular carcinoma, various imaging modalities show similar diagnostic performance, but it tends to be higher in Gd-EOB-MRI than in dynamic MDCT. The degree of malignancy of nodules evaluated by CT with intra-arterial contrast injection and signal intensity in the hepatocyte phase of Gd-EOB-MRI are correlated with the degree of malignancy of borderline lesions, and the early liver cancer type was more markedly hypointense and detected more frequently than the DN type. Hepatocyte phase Gd-EOB-MRI very sensitively delineates changes in an early stage of multistage carcinogenesis of lesions from DN to early hepatocellular carcinoma compared with conventional diagnostic methods and has an excellent diagnostic ability for early hepatocellular carcinoma.

In early hepatocellular carcinoma, portal venous and arterial blood in the tumor decreases (Nakajima O: Morphogenesis and progression of liver cancer\(^9\)). Therefore, the tumor is hypovascular and is expected to be hypoechoic compared with non-tumoral areas on perfusion imaging of Sonazoid contrast-enhanced ultrasonography, but no consistent results have been obtained concerning the findings or diagnostic ability of the modality due to the slightness of blood flow changes. Also, in early hepatocellular carcinoma, the contrast of Kupffer cells is reduced equally or more mildly compared with non-tumoral areas,\(^11\) and not many lesions are visualized as defects in the Kupffer phase of Sonazoid contrast-enhanced ultrasonography. Therefore, there is presently no report of a high evidence level concerning the diagnostic ability of Sonazoid contrast-enhanced ultrasonography for early hepatocellular carcinoma.

### Table: Abilities of imaging modalities to detect early hepatocellular carcinoma in chronic liver disease patients

<table>
<thead>
<tr>
<th>Imaging findings</th>
<th>Non-contrast phase</th>
<th>Contrast-enhanced Early phase</th>
<th>Contrast-enhanced Late phase</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sonazoid contrast-enhanced ultrasonography</td>
<td>Shows various echo patterns due to slight changes in the blood flow.(^2,10)</td>
<td>Hypoecho in Kupffer phase: 54-67%(^1,17)</td>
<td>• Simple and mildly invasive&lt;br&gt;• Applicable also to kidney dysfunction patients&lt;br&gt;• No exposure&lt;br&gt;• Real-time evaluation of hepatic blood flow possible</td>
<td>• Presence of dead angles&lt;br&gt;• Detection power affected by the patient’s physique and technician’s skill</td>
<td>Detection power for blood flow of hepatic nodules is significantly higher than dynamic CT or MRI with relatively fixed imaging timing(^7,11)</td>
<td></td>
</tr>
<tr>
<td>Dynamic MDCT</td>
<td>Hypoattenuation nodule: 43-47%(^1,2,14)</td>
<td>Early-phase contrast enhancement: 0-60%(^1,4,5,9)</td>
<td>Hypoattenuation nodule: 40-73%(^2,1,4,14)</td>
<td>• Wide availability of MDCT with 16 or more detector rows&lt;br&gt;• Essential for qualitative diagnosis and determination of therapeutic approach, plays primary role in imaging diagnosis</td>
<td>• Exposure&lt;br&gt;• The use of a contrast agent is difficult in some patients with kidney dysfunction</td>
<td></td>
</tr>
<tr>
<td>EOB Primovist MRI</td>
<td>Hyper intensity T2-signals: 10-32%&lt;br&gt;Fat-containing nodules: 26-53%(^1,4,14,15)</td>
<td>Arterial-phase contrast enhancement: 0-57%(^1,4,5,10)</td>
<td>Hypo intensity in delayed phase: 47-68%&lt;br&gt;Low signal intensity in hepatocyte phase: 79-92%(^1,2,4,5,14,15)</td>
<td>Capable of collecting blood flow information and evaluating hepatocyte function, has high diagnostic power</td>
<td>• Insufficient availability of MRI systems with sufficient diagnostic power of 1.5T or higher&lt;br&gt;• Difficult to perform in some patients with implanted metallic devices or kidney dysfunction</td>
<td>Hepatocyte phase is significantly useful for detecting small HCC(^1), EOB uptake ratio is useful for discrimination between well-differentiated HCC and DN(^1)</td>
</tr>
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carcinoma or comparison of its diagnostic performance with other modalities. However, ultrasonography including that using Sonazoid contrast enhancement is occasionally performed periodically in patients with chronic liver disorders, and early hepatocellular carcinoma is often delineated as a hypoechoic nodule by reflecting fatty change of cancer cells. The frequency of detection of such hypoechoic nodules has been reported to be 40% in small hepatocellular carcinomas 10-15 mm in diameter,\(^\text{16}\) and the detection of such lesions often lead to the diagnosis of early hepatocellular carcinoma. MDCT and Gd-contrast-enhanced dynamic MRI themselves have high detection sensitivity for arterial blood flow, but the evaluation of hypovascular early hepatocellular carcinoma requires precise judgment and is often difficult. Reports of their diagnostic performance also vary widely.

In the papers cited in this CQ, no consensus has been reached regarding the diagnostic ability of Sonazoid contrast-enhanced ultrasonography. While the sensitivity of Gd-EOB-MRI for early hepatocellular carcinoma tends to be higher than that of MDCT, it must be noted that MRI systems capable of high-quality dynamic study were used in the studies cited in this article and that MRI systems with a low magnetic field strength or deficient in diagnostic ability are inappropriate for diagnosing early hepatocellular carcinoma. Such MRI systems capable of high-quality dynamic study are not as widely available as ultrasonographs or MDCT devices, and, in practice, dependence on ultrasonography or dynamic MDCT is unavoidable in follow-up imaging studies.

### Index words and secondary materials used as references

A search of PubMed was performed using “early hepatocellular carcinoma”, “CT”, “EOB MRI”, and “sonazoid ultrasonography” as key words. The Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 update was also used as a reference.

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10. Kobayashi K ed.: Gastrointestinal diseases up to date, Consensus & Controversies. p22-26, 1996 (No applicable level)
What is appropriate management for nodules in patients with chronic liver disease that show no early contrast enhancement?

**Recommendation grade**

**C1**

Biopsy may be considered for nodules 10-15 mm in diameter. Nodules less than 10 mm in diameter should be followed up every 3-6 months by contrast-enhanced imaging (EOB contrast-enhanced MRI, dynamic CT, or Sonazoid contrast-enhanced ultrasonography), and biopsy or treatment may be considered if they are found to have grown. Particularly, if early contrast-enhancement appears during follow-up, the nodule may be treated as hypervascular hepatocellular carcinoma.

**Background/objective**

The frequency of detection of nodules that show no early contrast-enhancement on contrast-enhanced imaging studies (hypovascular nodules) in high risk groups for hepatocellular carcinoma is considered to be increasing due to the recent improvements in the performance of imaging modalities. Hypovascular nodules include benign lesions such as hyperplastic nodules and regenerative nodules, precancerous lesions, and early hepatocellular carcinoma, and their management is controversial.

**Comments**

According to a retrospective study of 130 hypovascular nodules that were hypointense in the hepatocyte phase of EOB•Primovist contrast-enhanced MRI, the 2- and 3-year cumulative incidences of the development into classic hepatocellular carcinoma were 11.1 and 15.9%, respectively. Hypovascular nodules are unlikely to affect the life prognosis in a short period. However, as they include precancerous lesions and hepatocellular carcinomas at considerable percentages, if hypovascular nodules are detected in patients with chronic liver disease, histological diagnosis or subsequent follow-up is necessary.

There have been few studies that provide sufficient evidence concerning the diagnostic principles for hypovascular nodules, and the diagnostic/therapeutic algorithms shown in the Scientific-Evidence-Based Clinical Practice Guidelines for Hepatocellular Carcinoma published in Japan and domestic and international guidelines including those of the American Association for the Study of Liver Diseases (AASLD), Asian Pacific Association for the Study of the Liver, and European Society for Medical Oncology are based on experts’ opinions. All these guidelines recommend follow-up by biopsy or, after a short period (3 months by the Japanese and AASLD guidelines), contrast-enhanced imaging (CT, MRI, ultrasonography) if early contrast enhancement and washout, which are findings of classic hepatocellular carcinoma, are not detected by contrast-enhanced CT or MRI. According to the guidelines of the Japan Society of Hepatology, masses 2 cm or less in diameter that do not show typical imaging findings of hepatocellular carcinoma are not detected by contrast-enhanced CT or MRI. According to the guidelines of the Japan Society of Hepatology, masses 2 cm or less in diameter that do not show typical imaging findings of hepatocellular carcinoma are not detected by contrast-enhanced CT or MRI. According to the guidelines of the Japan Society of Hepatology, masses 2 cm or less in diameter that do not show typical imaging findings of hepatocellular carcinoma are not detected by contrast-enhanced CT or MRI. According to the guidelines of the Japan Society of Hepatology, masses 2 cm or less in diameter that do not show typical imaging findings of hepatocellular carcinoma are not detected by contrast-enhanced CT or MRI. 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development into hypervascular hepatocellular carcinomas more likely are reported to include (1) hypointensity in the hepatocyte phase of EOB•Primovist contrast-enhanced MRI, (2) hyperintensity on T2-weighted MRI, (3) presence of fat components, and (4) a diameter of 10-15 mm or larger at detection.\textsuperscript{7,11-14} Examination of these factors are considered to contribute to the judgment of whether or not hypovascular nodules should be biopsied or treated. Additionally, for the evaluation of the presence or absence of early contrast enhancement, images should always be evaluated with attention to the appropriateness of imaging conditions of dynamic study (injection rate of the contrast agent, imaging timing).

Index words and secondary materials used as references
A search of PubMed was performed using “hypovascular” and “hepatocellular carcinoma” as key words. The Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 was also used as a reference.

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Background/objective

Classic hepatocellular carcinoma is defined as advanced hepatocellular carcinoma with a macroscopically clear border and is hypervascular on imaging. The usefulness of Sonazoid contrast-enhanced ultrasonography, contrast-enhanced dynamic CT, EOB•Primovist contrast-enhanced MRI, and angiography including CTAP and CTHA for the diagnosis of classic hepatocellular carcinoma is evaluated on the basis of the latest evidence.

Comments

For the imaging diagnosis of hepatocellular carcinoma, in addition to conventional contrast-enhanced CT, contrast-enhanced ultrasonography using Sonazoid, a second-generation ultrasound contrast agent, began to be covered by insurance in January 2007. Regarding MRI, EOB•Primovist (gadoxetate disodium preparation), a hepatocyte-specific contrast agent, began to be covered by insurance in December 2007.

For contrast-enhanced dynamic CT, MDCT has spread to many facilities, and it is superior to MRI in consistency of image quality and time required for imaging (10-15 min/examination). Since each scan can be finished in several seconds, deterioration of image quality is unremarkable even in patients incapable of breath-holding. Its diagnostic power is also sufficient for the diagnosis of classic hepatocellular carcinomas 1 cm or greater in diameter.\(^1,2\)

EOB•Primovist contrast-enhanced MRI has been reported to be superior to contrast-enhanced dynamic CT for the diagnosis of hypervascular hepatocellular carcinoma by a comparative study using AFROC analysis.\(^1\) Also, many comparative studies on the diagnostic ability of EOB•Primovist contrast-enhanced MRI and contrast-enhanced dynamic CT for hepatocellular carcinoma not restricted to classic hepatocellular carcinoma have been performed, all reporting superiority of MRI with or without statistical significance.\(^2-6\)

However, reports on the diagnostic performance of Sonazoid contrast-enhanced ultrasonography are still scarce. In a study comparing the diagnostic performance of Sonazoid contrast-enhanced ultrasonography, contrast-enhanced dynamic CT, and EOB•Primovist contrast-enhanced MRI for hepatocellular carcinoma, the diagnostic accuracy was 72, 74, and 86%, respectively, with no significant difference.\(^7\) Also, when the diagnostic power for liver tumors was compared between Sonazoid contrast-enhanced ultrasonography and contrast-enhanced dynamic CT, the number of hepatocellular carcinomas (not restricted to classic hepatocellular carcinomas) detected was 261 and 257, and the discrimination rate of hepatocellular carcinoma was 92.6 and 89.3%, respectively, neither with a significant difference.\(^8\)

On the other hand, in a comparative study using malignant tumors of the liver, of which hepatocellular carcinoma was dominant (90/108 nodules), the detection sensitivity was 95.4 and 85.2%, and the diagnostic accuracy was 94.7 and 82.3%, by contrast-enhanced ultrasonography and contrast-enhanced dynamic CT, respectively, indicating significant superiority of ultrasonography.\(^9\)

Angiography has been used for the diagnosis of hepatocellular carcinoma from early days of diagnostic imaging. Recently, the IVR-CT system integrating a flat panel detector angiography machine with an MDCT machine has been applied clinically. The diagnostic ability for hepatocellular carcinoma by CTAP and double-phase CTHA using a 4-channel MDCT system has been reported to be excellent with a sensitivity of 93% and a specificity of 97%.\(^10\)

However, recent reports of comparisons with other modalities are few.\(^11\) In a study comparing angiography and contrast-enhanced dynamic CT using single-slice CT, the detection sensitivity of CTAP+CTHA (99%) was superior to that of contrast-enhanced dynamic CT (68%).\(^12\) EOB•Primovist contrast-enhanced MRI shows a very high diagnostic ability due partly to the marked improvements in the performance of recent MRI systems. However, to obtain sufficiently diagnostic images, high-end equipment with a magnetic field strength of 1.5T or higher is essential, and
appropriate determination of the imaging sequence and parameters and conditions for injection of the contrast agent is also important. Therefore, the modality does not necessarily ensure excellent diagnostic performance at all facilities. Furthermore, MRI requires 30-45 minutes for one examination, and, at many facilities, it is considered difficult to perform MRI in all high-risk patients for hepatocellular carcinoma. The diagnostic ability of contrast-enhanced ultrasonography has been improved further, particularly, since second-generation contrast agents became available. Presently, reports on comparative evaluation of contrast-enhanced ultrasonography for hepatocellular carcinoma are limited but are expected to increase for the future.

While angiography including CTAP and CTHA is very useful for the diagnosis of classic hepatocellular carcinoma, it is more invasive than other modalities as it requires selective catheterization of the hepatic or superior mesenteric artery. Therefore, with improvements in the diagnostic performance of other modalities, situations in which CTHA and CTAP are performed exclusively for diagnostic purposes have decreased, and they are mostly performed recently with therapeutic procedures such as TACE.

In conclusion, all modalities are sufficiently useful for the diagnosis of classic hepatocellular carcinoma, but it is unnecessary to perform all examinations, and appropriate ones should be selected depending on the circumstances of the facility and patient’s condition. Also, it may be necessary to combine multiple examinations depending on the situation.

Index words and secondary materials used as references


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9) Hatanaka K et al: Sonazoid-enhanced ultrasonography for diagnosis of hepatic malignancies: comparison with contrast-enhanced CT. Oncology 75 (suppl 1): 42-47, 2008 (Level 4)
Is CTHA/CTAP or angiography appropriate as a preoperative examination for hepatocellular carcinoma?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>C1</th>
<th>CTHA/CTAP</th>
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CTHA/CTAP may be considered when preoperative evaluation by non-invasive modalities such as CT and MRI is judged to be insufficient. It is not recommended to perform angiography alone for examination.

### Background/objective

Angiography used to be a standard preoperative examination for liver tumors. CT during hepatic arteriography (CTHA) and CT during arterial portography (CTAP) are techniques developed primarily in Japan and were performed for the evaluation of multiple lesions, detection of intrahepatic metastases, and diagnosis of portal and hepatic vein invasion. A combination of CTHA and CTAP (CTHA+CTAP) has been regarded the most precise of the preoperative examinations for liver tumors, but it has limitations including high invasiveness, radiation exposure, and need for special equipment such as IVR-CT. The positions of angiography and CTHA/CTAP have changed with the recent development of the technique of contrast-enhanced CT, increases in the number of detector rows, and advent of liver-specific contrast agent for MRI. The significance of these modalities as preoperative examinations is evaluated.

### Comments

Angiography including digital subtraction angiography (DSA) is an invasive examination. Although it was a standard preoperative examination in the 1980s (Figure 1), its diagnostic performance has recently become inferior to that of contrast-enhanced dynamic CT regarding hypervascular hepatocellular carcinoma alone (number of nodules detected out of 98 nodules: 92 by CT, 53 by DSA),11 (sensitivity/specificity: 86.8 and 92.8% by CT; 69 and 91.5%, respectively, by DSA),23 and the sensitivity has been reported to be 33% by comparison with findings in all hepatectomy samples.31 Also, by comparison with findings in all hepatectomy samples, the sensitivity was inferior to that of CTAP (85% for CTAP, 67% for DSA)5 (Figure 2) and particularly low in well-differentiated lesions3 and lesions 2 cm or less in diameter. The use of the modality for examination alone is not recommended by the guidelines of the American Association for the Study of Liver Diseases (AASLD) or European Association for the Study of the Liver (EASL) concerning the diagnosis and treatment of hepatocellular carcinoma or the Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 of Japan.

Intra-arterial contrast-enhanced CT (CTHA and CTAP) is a technique of performing CT during selective angiography by injecting a contrast agent into an artery via a catheter. The technique, also called intra-arterial CT or angiographic CT, was developed primarily in Japan and was also regarded as the most precise preoperative examination primarily for metastatic liver tumors in Western countries in the 1980s to the early 1990s. Recently, however, it has nearly ceased to be used due to the improvements in non-invasive examinations. For hepatocellular carcinoma, the Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 mention the procedure as an optional examination without clearly defining its role or significance, and it has not been recommended as a preoperative examination by international guidelines. However, there have been a number of reports indicating its usefulness for the differentiation of small lesions and estimation of the degree of differentiation of hepatocellular carcinoma,13 and the procedure is performed at many facilities in Japan.

The diagnostic ability of CTHA+CTAP for hepatocellular carcinoma has often been reported to be superior to that of contrast-enhanced dynamic CT regarding hypervascular hepatocellular carcinoma alone (sensitivity: 99% vs. 68%9) (sensitivity/specificity in non-tumor-bearing liver segments: 90.6/97.4% vs. 75.4/94.9%),11 but there are also reports that the two modalities are comparable (sensitivity/specificity: 60/99.7% vs. 58/98.8%) and that the significance of the addition of CTHA+CTAP to dynamic CT is meager (sensitivity of dynamic CT and dynamic CT+ CTHA+CTAP: 94 vs. 97%).11 The difference in the diagnostic performance may be narrowed by the recent increase in the number of detector rows of CT devices and development of the imaging technique in contrast-enhanced dynamic CT, but data available for the evaluation are deficient.

As for comparison with dynamic MRI using an extracellular gadolinium-based contrast agent, there are reports that CTHA+CTAP is superior to dynamic MRI5,10,14 (sensitivity/positive predictive value: 99/83 vs. 76/91%)9 (sensitivity in tumor-bearing liver segments: 89 vs. 75%)14 and that they are comparable (sensitivity in tumor-bearing liver segments/specificity in non-tumor-bearing liver segments: 94/92 vs. 90/99%).13 Compared with MRI using superparamagnetic iron oxide (SPIO) nanoparticles as a liver-specific contrast agent, CTHA+CTAP has been reported to be superior (sensitivity/specificity in non-tumor-bearing liver segments: 90.6/97.4 vs. 77.2/98.5%)13 and to be comparable (sensitivity...
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in tumor-bearing liver segments/specificity in non-tumor-bearing liver segments of CTHA+CTAP and SPIO contrast-enhanced MRI: 90.8/96.2 vs. 89.7/98.5%).

There is also a report that the diagnostic performance can be improved by a combination of contrast-enhanced dynamic CT and SPIO contrast-enhanced MRI to a level comparable to CTHA+CTAP (sensitivity/positive predictive value of CTHA+CTAP and SPIO contrast-enhanced MRI+ dynamic CT: 92.4 vs. 95.5%).

The diagnostic performance of CTAP alone has also been reported to be comparable to that of SPIO contrast-enhanced MRI.

While the diagnostic performance of a combination of dynamic MRI using an extracellular gadolinium-based contrast agent and SPIO contrast-enhanced MRI has been reported to exceed that of CTHA+CTAP, this combination remains a problem in reimbursement under the medical insurance system in Japan.

Concerning comparison with the liver-specific contrast agent Gd-EOB-DTP, the use of which has recently been approved, the ability of Gd-EOB-DTPA contrast-enhanced MRI to discriminate between hepatocellular carcinoma 2 cm or less in diameter and atypical nodules has been reported to exceed that of CTHA+CTAP, but data presently available for the evaluation are scarce. Gd-EOB-DTPA contrast-enhanced MRI is considered to have an improved diagnostic ability primarily for well-differentiated hepatocellular carcinoma. While confusion in pathological diagnostic criteria for well-differentiated hepatocellular carcinoma has been gradually resolved, whether or not the detection of well-differentiated hepatocellular carcinoma improves the outcome remains controversial, and the clinical significance of nodules detected only in the hepatocyte phase 20 minutes after the contrast agent administration has not been established. Compared with conventional extracellular contrast agents, Gd-EOB-DTPA has lower gadolinium content, which may reduce the ability to detect hypervascularization of tumors or hypervascular intrahepatic metastases. Further accumulation of data is necessary for comparison between CTHA+CTAP and Gd-EOB-DTPA contrast-enhanced MRI.

In CTHA and CTAP, the equipment of the facility and skill of image readers must be considered. By CTAP alone, false
positive results have been reported to increase (sensitivity/specificity by CTAP and CTAP+DSA: 75/60 vs. 84/81%)\textsuperscript{20} and the diagnostic performance is considered to be improved by combining CTHA and CTAP. IVR-CT integrating angiographic and CT systems is desirable, but a combination of arteriography and CTAP may also be considered depending on the composition of diagnostic modalities at the facility. Also, on CTAP, intra-arterial injection of a vasodilator immediately before injection of the contrast agent reportedly increases the contrast of the normal hepatic parenchyma, reduces unevenness of contrast enhancement, and improves the contrast relative to the tumor. On CTHA, the diagnostic ability has been reported to be improved by examining the early and late phases.\textsuperscript{21,22} In both CTHA and CTAP, the evaluation of optimization or individualization of the contrast-enhancing and imaging protocols is insufficient. Moreover, in both modalities, contrast enhancement is poor in vessels other than the hepatic artery, portal vein, and hepatic vein and organs other than the liver. The modalities are inappropriate for the evaluation of lymph node metastasis, tumor embolism of the inferior vena cava, metastasis to other organs, and concurrence of other diseases, for which separate evaluation usual contrast-enhanced CT or dynamic CT is necessary.

Recently, the clinical application of CTAP and CTHA by cone-beam CT using a flat panel detector (FPD) angiography machine has been initiated. The technique has been reported to be useful as a method to assist manipulations and diagnosis and examine the drug distribution in treatments using an intra-arterial catheter but has not been evaluated as a preoperative examination. Presently, its usefulness as a preoperative examination for hepatocellular carcinoma is unknown.

Index words and secondary materials used as references

A search of PubMed was performed using “angiographically assisted CT”, “CT during arterial portography”, “CT during arteriopertography”, “CT during hepatic angiography”, “digital subtraction angiography”, “detection”, “EOB”, “gadoxetic acid”, “hepatocellular carcinoma”, “preoperative”, “primovist”, “sensitivity”, “superparamagnetic iron oxide”, and “SPIO” as key words. Also, the AASLD and EASL guidelines and the Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 were also used as references. Reports in which CTHA/CTAP was used as a standard reference were excluded. The evidence level of papers evaluating the diagnostic ability for liver tumors in general was reduced by 1 grade.

References

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Which modality is appropriate to discriminate pseudotumors due to arterioportal shunting from hepatocellular carcinoma?

**Recommendation grade**

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<th>Grade</th>
<th>Contrast-enhanced MRI using the liver-specific contrast agent SPIO (Resovist) or EOB is recommended as useful for the diagnosis of pseudotumors due to arterioportal shunting.</th>
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**Background/objective**

Arterioportal (AP) shunting is a condition in which arterial blood enters the hepatic sinusoids via the portal vein, which may be idiopathic or caused by liver cirrhosis, hepatectomy, biopsy, or tumor (hepatocellular carcinoma, hepatic angioma, metastatic liver tumor, etc.). Particularly, if an AP shunt complicating liver cirrhosis is detected as early contrast enhancement by dynamic contrast-enhanced CT or dynamic contrast-enhanced MRI using an extracellular gadolinium-based contrast agent, it must be discriminated from hepatocellular carcinoma. Therefore, if a mildly invasive examination that can accurately diagnose AP shunts can be selected, unnecessary treatments and excessive examinations can be avoided.

**Comments**

Typical images of AP shunts complicating liver cirrhosis are isoechic on B mode ultrasonography, isoattenuation on plain CT, isointense on T1- and T2-weighted imaging of MRI, wedge-shaped early staining on the liver margin in the arterial phase, and isoenhancement with the surrounding liver parenchyma in the late phase, on dynamic contrast-enhanced CT or dynamic contrast-enhanced MRI. They are imaged as a poorly contrasted area on CT during arteriportography (CTAP), and as a more intensely or equally contrasted area on CT during hepatic arteriography (CTHA), compared with the surrounding liver parenchyma. AP shunts can be readily diagnosed if such characteristic findings are obtained. However, they may be visualized, though infrequently, as hyperintense areas on T2-weighted imaging. Moreover, if an AP shunt is delineated as nodular early contrast enhancement in the liver parenchyma (Figure A), or if a hepatocellular carcinoma shows unclear washout in the equilibrium phase of dynamic contrast-enhanced CT or MRI, the differentiation between AP shunt and hepatocellular carcinoma may be difficult. In addition, the concentration of AFP, a tumor marker, may increase in patients with multiple AP shunts complicating chronic liver disease, also making their differentiation by blood tests difficult.

Takayasu et al. observed that many of multiple AP shunts complicating chronic liver disease disappear within 4 months and reported the importance of follow-up. Early delineation of the portal branches in the area of early contrast enhancement in the arterial phase of dynamic contrast-enhanced CT is considered to be a finding specific to AP shunting, but there has been no recent report concerning its delineation rate in a considerable number of cases. Kim et al. reported that early delineation of portal branches in the area of early staining on CTHA is a finding specific to AP shunting, but the delineation rate was low at 34.6%. Regarding findings on diffusion-weighted imaging of MRI, Motosugi et al. reported that all 32 nodular hepatic pseudolesions were isointense with the surrounding liver parenchyma but that 83 (67%) of the 123 hepatocellular carcinomas were hyperintense. Therefore, if a lesion is delineated as a hyperintense area on diffusion-weighted imaging, it is unlikely to be an AP shunt, but if it is detected as an isointense area, the differentiation with well-differentiated or hypovascular hepatocellular carcinoma is required. Moreover, a defect of diffusion-weighted imaging is a low detection rate as a result of susceptibility artifact due to air in the lung or intestine or motion artifact due to cardiac pulsation. Thus, contrast-enhanced MRI using the liver-specific contrast agent SPIO or EOB•Primovist attracts attention. SPIO is a superparamagnetic iron oxide preparation, and if it is taken up by Kupffer cells contained in the normal liver parenchyma or a region with an AP shunt, it causes hypointensity on T2- and T2*-weighted imaging while hepatocellular carcinoma, which contains no Kupffer cells, is presented as a relatively hyperintense area. On the other hand, EOB•Primovist, a paramagnetic gadolinium preparation, is taken up by normal hepatocytes contained in the normal liver parenchyma or an area with an AP shunt and causes iso- or hyperintensity in the hepatocyte phase (Figure B) and delineates hepatocellular carcinoma with no normal hepatocytes as a hypointensity. Mori et al. reported that areas with AP shunts complicating liver cirrhosis showed decreases in signal intensity comparable to those in the surrounding liver parenchyma in 5 of the 6 patients on SPIO contrast-enhanced T2*-weighted imaging. In addition, Motosugi et al. reported that EOB•Primovist contrast-enhanced MRI visualized 29 (87%) of the 32 hepatic pseudolesions as iso- or hyperintensities compared with the surrounding liver parenchyma but 116 (94%) of the 123 hepatocellular carcinomas as hypointensities, in the hepatocyte phase, contributing to the differential diagnosis. For these reasons, contrast-enhanced MRI using the liver-specific contrast agent SPIO or EOB•Primovist is recommended as a mildly invasive and highly accurate examination for the diagnosis of AP shunts.
The lesion showed early contrast enhancement (→) in the arterial phase (A) but was isointense with the surrounding liver parenchyma in the hepatocyte phase (B) of EOB Primovist contrast-enhanced MRI and was diagnosed as AP shunt.

Figure: AP shunting after radiofrequency ablation of hepatocellular carcinoma

Index words and secondary materials used as references

A search of PubMed was performed using “liver”, “pseudolesion”, “arterioportal shunting”, “US”, “CT”, “MRI”, and “CT angiography” as key words. Japana Centra Revuo Medicina was searched using “AP shunt”, “arterioportal shunting”, and “hepatic pseudolesion” as key words.

References

4) Kim HC et al: Preoperative evaluation of hepatocellular carcinoma: combined use of CT with arterial portography and hepatic arteriography. AJR 180: 1593-1599, 2003 (Level 4)
6) Mori K et al: Arterioportal shunts in cirrhotic patients: evaluation of the difference between tumorous and nontumorous arterioportal shunts on MR Imaging with superparamagnetic iron oxide. AJR 175: 1659-1664, 2000 (Level 5)
What imaging modalities are appropriate for the staging of hepatocellular carcinoma?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Imaging modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Chest CT, bone scintigraphy, PET (patients with hepatocellular carcinoma with risk factors of extrahepatic metastasis)</td>
</tr>
<tr>
<td>C1</td>
<td>Head CT/MRI (patients with hepatocellular carcinoma with neurological findings or lung metastasis)</td>
</tr>
</tbody>
</table>

In patients with hepatocellular carcinoma with risk factors of extrahepatic metastasis (tumor embolus in the portal vein, AFP>200 ng/mL, PIVKA-II ≥300 mAU/mL, platelet count ≤130x10^3/μL, age<65 years), it is recommended to perform chest CT, bone scintigraphy, and PET. In patients with hepatocellular carcinoma with neurological findings or lung metastasis, head CT/MRI may be considered for the diagnosis of brain metastasis.

Background/objective

Circumstances that prompt search for distant metastasis, target areas, and examinations used in staging hepatocellular carcinoma were evaluated.

Comments

The presence or absence of extrahepatic metastasis is important for the evaluation of need for local treatments for hepatocellular carcinoma. The frequency of the presence of extrahepatic metastasis of hepatocellular carcinoma is low at 1.0-2.3% at its diagnosis, but the frequency of the appearance of extrahepatic metastasis during follow-up after treatment increases to 21-24%. The frequency of the occurrence of extrahepatic metastasis according to the site is 6-29% in the lung, 5-20% in lymph nodes, 2-10% in bones, 1-10% in the adrenal gland, and 0.2-0.6% in the brain. An age of less than 65 years, progression of intrahepatic lesions, tumor thrombus of the portal vein, AFP>200 ng/mL, PIVKA-II ≥300 mAU/mL, and platelet count ≤130x10^3/μL have been reported as risk factors of extrahepatic metastasis. PET has an excellent ability to diagnose extrahepatic metastases including bone metastases of hepatocellular carcinoma between bone scintigraphy and PET is insufficient.

PET has an excellent ability to diagnose extrahepatic metastases including bone metastases of hepatocellular carcinoma, and it is reasonable to perform it aggressively if an elevation of a tumor marker that cannot be explained by abdominal lesions or lung metastasis is observed.

Bone scintigraphy is a procedure useful for the search of the whole body for bone metastasis, and it has also been reported to be useful in hepatocellular carcinoma (Figure). However, some bone metastases of hepatocellular carcinoma are known to show low radionuclide uptake. PET is likely useful for the evaluation of bone metastases that show low uptake on bone scintigraphy. Bone metastases of hepatocellular carcinoma are generally osteolytic, and about 50% of the sites of its metastasis are vertebral bodies. By PET/CT, not only metastasis but also the risk of compression fracture and vertebral canal stenosis may be evaluated, but research directly comparing the diagnostic ability for extrahepatic metastases including bone metastases of hepatocellular carcinoma between bone scintigraphy and PET is insufficient.

PET has an excellent ability to diagnose extrahepatic metastases including bone metastases of hepatocellular carcinoma, and it is reasonable to perform it aggressively if an elevation of a tumor marker that cannot be explained by abdominal lesions or lung metastasis is observed.

Contrast-enhanced CT or MRI is useful for the search for brain metastases, but the frequency of brain metastasis of hepatocellular carcinoma is low, and most brain metastases are accompanied by lung metastasis. Patients with symptoms, neurological signs, or lung metastasis, head CT or MRI may be worth considering for the search for brain metastasis.
Index words and secondary materials used as references

A search of PubMed was performed using “neoplasm staging”, “neoplasm metastasis”, “extrahepatic”, “brain”, “cerebral”, “cerebrum”, “bone”, “skeletal”, “hepatocellular carcinoma”, “bone scan”, and “scintigraphy” as key words. The Japan Society of Hepatology ed: Clinical Practice Guidelines for Hepatocellular Carcinoma 2009 was also used as a reference.

References

3) Bae HM et al: Protein induced by vitamin K absence or antagonist-II production is a strong predictive marker for extrahepatic metastases in early hepatocellular carcinoma: a prospective evaluation. BMC Cancer 11: 435, 2011 (Level 2)
9) Lin CY et al: 18F-FDG PET or PET/CT for detecting extrahepatic metastases or recurrent hepatocellular carcinoma: a systematic review and meta-analysis. Eur J Radiol 81: 2417-2422, 2011 (Level 3)
Which modalities are appropriate for the evaluation of the effects of TACE and RFA for hepatocellular carcinoma?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Modality</th>
</tr>
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<tbody>
<tr>
<td>B</td>
<td>Dynamic CT or dynamic MRI</td>
</tr>
<tr>
<td>C</td>
<td>Sonazoid contrast-enhanced ultrasonography</td>
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</table>

Dynamic CT or dynamic MRI is effective and is recommended. If only one or a few hepatocellular carcinomas have been treated, Sonazoid contrast-enhanced ultrasonography may also be considered.

**Background/objective**

Ultrasonography, CT, and MRI are all used for the evaluation of the therapeutic effects of TACE and RFA. For contrast-enhanced ultrasonography, Levovist and Sonazoid can be used in Japan, but contrasted enhanced ultrasound is not performed presently at all facilities. However, as ultrasonography has higher spatial and temporal resolutions than CT or MRI and is very useful for the visualization of one or a few hepatocellular carcinomas, it may be used as a guide for RFA. Dynamic CT, on the other hand, currently plays a central role for the evaluation of the therapeutic effects on hepatocellular carcinoma as it can be performed at nearly all facilities with CT equipment and a contrast agent injector in a short examination time (high throughput). Dynamic MRI using a gadolinium-based extracellular or EOB contrast agent can also be performed at facilities with a relatively high-performance MRI system. Recently, EOB Primovist contrast-enhanced MRI, which can visualize hepatocellular carcinoma in both the dynamic and hepatocyte phases, is rapidly spreading due to its high detecting ability. Which modalities should be selected for the evaluation of the effects of TACE and RFA for hepatocellular carcinoma was evaluated.

**Comments**

After TACE, non-contrast-enhanced CT is performed to examine the degree of lipiodol accumulation. At facilities where TACE is performed using IVR-CT, non-contrast-enhanced CT can be performed immediately after the treatment, but the degree of lipiodol accumulation is generally examined within 1 month after TACE. The treatment is expected to be effective when lipiodol is accumulated in the hepatocellular carcinoma without defects, but the strong hyperdensity of lipiodol may prevent the detection of recurrent lesions on CT, and contrast-enhanced MRI using a gadolinium-based extracellular contrast agent or EOB Primovist is useful. Since the treatment is also expected to be effective when the diameter of the hepatocellular carcinoma showing lipiodol accumulation has evenly decreased after TACE, follow-up using CT is also recommended. According to De Santis et al., lipiodol accumulation in hepatocellular carcinoma after TACE is observed as a hyperintensity on T1-weighted imaging a few days after treatment, but no signal that affects images of dynamic MRI is observed 3 months or more after the treatment. Therefore, it is necessary to confirm contrast enhancement of the recurrent and residual lesions in the arterial phase or defect (decrease) of uptake of EOB Primovist in the hepatocyte phase or wash-out of a gadolinium-based extracellular contrast agent in the equilibrium phase in T1-weighted images of dynamic MRI using such contrast agents. Hunt et al. and Murakami et al. reported that contrast-enhanced MRI is superior to contrast-enhanced CT for the evaluation of residual hepatocellular carcinoma after TACE. Levovist contrast-enhanced ultrasonography is also considered effective for the evaluation of the effect of TACE for hepatocellular carcinoma and may also be selected as an option that allows the evaluation of the site of recurrence without effects of Lipiodol accumulation. In Japan, Sonazoid contrast-enhanced ultrasonography, in which the duration contrast enhancement is long, is often selected, but, to the present, there has been no report of a large-scale study of the effectivenes of Sonazoid contrast-enhanced ultrasonography for the evaluation of the therapeutic effect after TACE, and further research is necessary.

The therapeutic effect after RFA for hepatocellular carcinoma is secured by a sufficient peripheral margin. According to Nakazawa et al. and Kim et al., a margin of about 5 mm or more is desirable, but a sufficient margin may be technically difficult to obtain depending on the site of hepatocellular carcinoma (near a large blood vessel, in the margin of the liver, sites difficult to puncture). The therapeutic effects after RFA can be evaluated by ultrasonography, dynamic CT, or dynamic MRI (using EOB Primovist or a gadolinium-based extracellular contrast agent), but the usefulness of
5. Gastrointestinal tract

3DCT for the evaluation of the safety margin has been suggested by Kim et al.\textsuperscript{7} Also, analysis of a case series showed that the therapeutic effect on hepatocellular carcinoma can be assessed by CT even immediately after RFA (after 1 week).\textsuperscript{8}

Ueda et al. reported that corona-like staining of hepatocellular carcinoma represents outflow tracts of the tumor blood flow.\textsuperscript{9} This report has great significance in the determination of the area of involvement of hepatocellular carcinoma and suggests the importance of the area of corona-like staining as a possible marker of the safety margin. According to case-control studies, hepatocellular carcinoma after RFA shows hyperintensity on T1-weighted imaging of MRI due to the effect of ablation.\textsuperscript{10,11} Therefore, on dynamic contrast-enhanced imaging for residual tumors, the T1-shortening effect of a gadolinium-based contrast agent (which also causes hyperintensity) may become difficult to judge. Another case-control study reported that the results of evaluation of the ablated area and residual tumors of hepatocellular carcinoma after RFA were in close agreement between Sonazoid contrast-enhanced 3D ultrasonography and 3DCT,\textsuperscript{12} but CT and MRI are less examiner-dependent than ultrasonography and facilitate the objective evaluation of changes in the tumor diameter and whether or not the safety margin is sufficient. At present, no report of a large-scale study concerning the evaluation of the effects of RFA using EOB Primovist can be found, and further research is necessary.

### Index words and secondary materials used as references

A search of PubMed was performed using “HCC”, “TACE”, “RFA”, “therapeutic effect”, and “imaging” as key words, and relevant reports were selected.

### References


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6) Kim YS et al: The minimal ablative margin of radiofrequency ablation of hepatocellular carcinoma (> 2 and < 5 cm) needed to prevent local tumor progression: 3D quantitative assessment using CT image fusion. AJR 195: 758-765, 2010 (Level 2)


Which modalities are appropriate for the diagnosis of liver metastases (metastatic liver tumors)?

**Recommendation**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Modality</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Dynamic MRI (EOB)</td>
</tr>
<tr>
<td>B</td>
<td>Dynamic CT</td>
</tr>
<tr>
<td>C1</td>
<td>Ultrasonography</td>
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</tbody>
</table>

There are evidences that MRI using a liver-specific contrast agent is superior to ultrasonography or contrast-enhanced CT in terms of diagnostic performance, and therefore the procedure is strongly recommended. Contrast-enhanced CT has a high diagnostic ability and is recommended. Contrast-enhanced ultrasonography has a higher ability than B mode ultrasonography for detecting liver metastases, but scientific evidence is insufficient as to whether or not its diagnostic performance is higher than that of contrast-enhanced CT or MRI. Therefore, contrast-enhanced ultrasonography may be worth considering, but it is not recommended to diagnose liver metastases by this modality alone, and it should be used in combination with other imaging techniques.

**Background/objective**

Metastatic liver tumor (liver metastasis) is observed more frequently than primary liver cancer, and it is the most frequent malignant tumor of the liver. Conventionally, B mode ultrasonography and contrast-enhanced CT have been generally considered necessary for the diagnosis of liver metastases. Today, however, the modalities used for the diagnosis of liver metastases are diverse, including contrast-enhanced ultrasonography, dynamic contrast-enhanced CT using MDCT, dynamic contrast-enhanced MRI using a gadolinium-based extracellular contrast agent, contrast-enhanced MRI using a liver specific contrast agent such as SPIO and Gd-EOB-DPTA, PET, and PET/CT. Improvements in these diagnostic imaging techniques have made detection of minute liver masses possible, and liver metastases have begun to be diagnosed before or after the beginning of treatment for primary lesions more frequently than before. In this article, a basic clinical question in diagnosing liver metastases was addressed by reviewing the literature.

Clinically, how the diagnosis leads to treatment is important in diagnosing liver metastases. The benefit of hepatectomy differs among primary lesions, and various studies and guidelines have reached the consensus that the meaning of diagnosis differs between cancers such as colon cancer, in which the benefit of maximum possible resection of liver metastases as well as the primary lesion has been established, and those such as pancreatic cancer and biliary tract cancer, in which the presence or absence of liver metastases is a factor in the judgment of whether the primary lesion should be resected. Therefore, it must be noted that imaging modalities are expected to provide information that helps with the accurate diagnosis of the presence or absence, number, and extent of liver metastases for the former type of tumors in anticipation of resection but information that contributes to the accurate presence diagnosis of liver metastasis alone for the latter. On the basis of the literature reviewed for this article, the clinical significance of imaging modalities in different types of cancer could not be evaluated in detail, and it is not discussed separately for colon cancer and other cancers to avoid complexity, but many references were related to colon cancer.

**Comments**

Concerning the diagnostic performance of various modalities, there are a large number of reports ranging from meta-analyses to case-control studies. Four meta-analyses were reported in the 2000s. Nielke et al.,1 in their meta-analysis of 39 reports (3,391 cases) evaluating the diagnostic performance of CT, MRI, and PET (PET/CT) for liver metastases of colorectal cancer, reported that the sensitivities of CT and MRI were 74.4 (68.7-79.3)% and 80.3 (74.6-85.0)%, respectively, showing no significant difference, but suggested the usefulness of a liver-specific contrast agent, which increased the sensitivity to 84.9 (79.3-89.2)%. They also reported that, in lesions less than 10 mm in diameter, the sensitivities of CT and MRI were 47.3 (40.1-54.5)% and 60.2 (54.4-65.7)%, respectively, being significantly higher for MRI. Bipats et al.2 performed a similar meta-analysis and reported that the sensitivity by patient was significantly higher for PET (94.6%), that the sensitivities by tumor of contrast-enhanced helical CT and 1.5T MRI were 63.8 and 64.4%, respectively, showing no marked difference, but that the sensitivities of contrast-enhanced MRI and SPIO contrast-enhanced MRI were significantly higher than that of non-contrast-enhanced MRI or contrast-enhanced CT using 45 g or less iodinated contrast agent, and that the sensitivity for tumors 1 cm or greater in diameter was significantly higher for SPIO contrast-enhanced MRI. Also, in their meta-analysis of reports concerning gastrointestinal cancers including esophageal, stomach, and colon cancers, Kinkel et al.3 reported that the sensitivity was 55 (95% CI: 41-68)% for US,
The sensitivity of the liver parenchymal phase (portal venous-dominant phase) was high (81-91%) in many reports and regarded the modality as a standard for the preoperative imaging diagnosis. Concerning the imaging timing, the excellent diagnostic performance of contrast-enhanced CT (liver parenchymal phase alone) with a sensitivity of 85.1% using an extracellular contrast agent is also considered high. There have been a large number of reports on the diagnostic performance of SPIO contrast-enhanced MRI since its first report in 1995, including ultrasonography, contrast-enhanced CT, and PET have been reported. There is a report that no difference was observed between non-contrast-enhanced MRI and dynamic contrast-enhanced MRI using an extracellular contrast agent, but recent studies have reported higher diagnostic performance compared with non-contrast-enhanced MRI or its improvement by the addition of contrast-enhanced MRI to non-contrast-enhanced MRI. As for contrast agents for MRI, there are extracellular contrast agents such as Gd-DTPA and SPIO and EOB as liver-specific contrast agents, which are specifically taken up by the reticuloendothelial system or hepatocytes, that can be used in Japan. While Ward et al. reported that Gd-DTPA-enhanced MRI and SPIO-enhanced MRI were superior to CT but that there was no significant difference between contrast-enhanced MRI and dynamic contrast-enhanced MRI using an extracellular contrast agent, but recent studies have reported higher diagnostic performance compared with non-contrast-enhanced MRI or its improvement by the addition of contrast-enhanced MRI to non-contrast-enhanced MRI. For contrast agents for MRI, there are extracellular contrast agents such as Gd-DTPA and SPIO and EOB as liver-specific contrast agents, which are specifically taken up by the reticuloendothelial system or hepatocytes, that can be used in Japan. While Ward et al. reported that Gd-DTPA-enhanced MRI and SPIO-enhanced MRI were superior to CT but that there was no significant difference between contrast-enhanced MRI and dynamic contrast-enhanced MRI using an extracellular contrast agent, but recent studies have reported higher diagnostic performance compared with non-contrast-enhanced MRI or its improvement by the addition of contrast-enhanced MRI to non-contrast-enhanced MRI. As for contrast agents for MRI, there are extracellular contrast agents such as Gd-DTPA and SPIO and EOB as liver-specific contrast agents, which are specifically taken up by the reticuloendothelial system or hepatocytes, that can be used in Japan. While Ward et al. reported that Gd-DTPA-enhanced MRI and SPIO-enhanced MRI were superior to CT but that there was no significant difference between them, all the above meta-analyses reported, regarding the diagnostic performance by tumor, no significant difference in the specificity but a significantly higher sensitivity for MRI using a liver-specific contrast agent. Therefore, the use of a liver-specific contrast agent is recommended, but the diagnostic ability of MRI using an extracellular contrast agent is also considered high. There have been a large number of reports on the diagnostic performance of SPIO contrast-enhanced MRI since its first report in 1995, and high sensitivities (80.6-97.2%) have been reported. There is also a report that the positive predictive value by SPIO contrast-enhanced MRI (91%) was significantly higher in MRI using a liver-specific contrast agent than in contrast-enhanced CT.

In the past reports, the sensitivity of ultrasonography was lower than that of contrast-enhanced CT or MRI, and the usefulness of this modality has not been demonstrated. Concerning contrast-enhanced ultrasonography, it has been a report by Bernatik et al. that 97% of the lesions detected by CT were visualized by contrast-enhanced ultrasonography, with a report that while contrast-enhanced ultrasonography may be more useful than B mode ultrasonography for the diagnosis of liver metastasis, there is no point in adding contrast-enhanced ultrasonography to MRI. Generally, ultrasonography has defects such as that it requires skill in scanning and shows wider individual variation but has advantages such as that it is simple and causes a less burden to medical economy, but the evidence that supports its superiority or performing it alone for the diagnosis of liver metastasis is deficient.

Since MDCT can simultaneously evaluate the liver and entire abdominal and thoracic regions by one scan, it is considered to be a primary modality for staging or follow-up. The 4 meta-analyses mentioned above included many reports that the diagnostic performance of contrast-enhanced CT was inferior to that of MRI using a liver-specific contrast agent. Clinically, however, there may be problems with the throughput and medical economy in performing all screening for liver metastasis with MRI. In a prospective study of 247 nodules in surgical cases, Valls et al. reported excellent diagnostic performance of contrast-enhanced CT (liver parenchymal phase) with a sensitivity of 85.1% (95% CI: 80.8-89.3%), positive predictive value of 96.1% (92.9-98.1%), and false positive rate of 3.9% (1.9-7.1%) and regarded the modality as a standard for the preoperative imaging diagnosis. Concerning the imaging timing, the sensitivity of the liver parenchymal phase (portal venous-dominant phase) was high (81-91%) in many reports. Scott et al. compared dual-phase imaging and imaging of the liver parenchymal phase alone and reported that dual-phase imaging was significantly superior with a sensitivity of 75.3 vs. 69.7% and Az value on ROC analysis of 0.84 vs. 0.82. There are reports supporting and refuting the usefulness of the addition of the arterial-dominant phase to the liver parenchymal phase, and the evidence concerning the usefulness of multiphasic imaging for the diagnosis of liver metastases is still unclear. After the introduction of MDCT, there have been reports of the usefulness of thin-slice scanning, and the technique may be worth considering.

Regarding the usefulness of MRI for the diagnosis of liver metastases, many comparative studies using modalities including ultrasonography, contrast-enhanced CT, and PET have been reported. There is a report that no difference was observed between non-contrast-enhanced MRI and dynamic contrast-enhanced MRI using an extracellular contrast agent, but recent studies have reported higher diagnostic performance compared with non-contrast-enhanced MRI or its improvement by the addition of contrast-enhanced MRI to non-contrast-enhanced MRI. As for contrast agents for MRI, there are extracellular contrast agents such as Gd-DTPA and SPIO and EOB as liver-specific contrast agents, which are specifically taken up by the reticuloendothelial system or hepatocytes, that can be used in Japan. While Ward et al. reported that Gd-DTPA-enhanced MRI and SPIO-enhanced MRI were superior to CT but that there was no significant difference between them, all the above meta-analyses reported, regarding the diagnostic performance by tumor, no significant difference in the specificity but a significantly higher sensitivity for MRI using a liver-specific contrast agent. Therefore, the use of a liver-specific contrast agent is recommended, but the diagnostic ability of MRI using an extracellular contrast agent is also considered high. There have been a large number of reports on the diagnostic performance of SPIO contrast-enhanced MRI since its first report in 1995, and high sensitivities (80.6-97.2%) have been reported. There is also a report that the positive predictive value by SPIO contrast-enhanced MRI (91%) was significantly higher in MRI using a liver-specific contrast agent than in contrast-enhanced CT.
significantly higher than that by CT (82%) while there was no difference in sensitivity.\textsuperscript{18}

There have also been a large number of reports on the usefulness of EOB contrast-enhanced MRI, and high diagnostic performance similar to that of SPIO contrast-enhanced MRI has been documented.\textsuperscript{17,19-21} Muhi et al.\textsuperscript{17} reported that the sensitivity for lesions 1 cm or less in diameter was higher in EOB- (92%) than SPIO- (63%) enhanced MRI but that both were superior to contrast-enhanced CT. Many of these studies were about liver metastases from colorectal cancer, but there is a report that the sensitivity of EOB contrast-enhanced MRI (92-94%) was higher than that of contrast-enhanced CT (74-76%) also for liver metastases from pancreatic cancer (Figure).\textsuperscript{20} Although MRI with a high magnetic field intensity has been reported to be more useful,\textsuperscript{21} evaluations concerning differences in the magnetic field strength have been few, and no clear evidence exists at present.

### References

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8. Sheafor DH et al: Comparison of unenhanced, hepatic arterial-dominant, and portal venous-dominant phase helical CT for the detection of liver metastases in women with breast carcinoma. AJR 172: 961-968, 1999\textsuperscript{(Level 2)}
11. Wicherts DA et al: Incremental value of arterial and equilibrium phase compared to hepatic venous phase CT in the preoperative staging of colorectal liver metastases: an evaluation with different reference standards. Eur J Radiol 77: 305-311, 2011\textsuperscript{(Level 3)}
19. Seo HU et al: Gadodextrate disodium-enhanced magnetic resonance imaging versus contrast-enhanced 18F-fluorodeoxyglucose positron emission tomography/computed tomography for the detection of colorectal liver metastases. Invest Radiol 46: 548-555, 2011\textsuperscript{(Level 2)}
Are CT during angiography (CTAP, CTHA) and PET appropriate for the diagnosis of liver metastases?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>C1</td>
<td>PET (including PET/CT)</td>
</tr>
<tr>
<td>C2</td>
<td>CT during angiography</td>
</tr>
</tbody>
</table>

PET is not sufficiently evidenced to be superior to other imaging modalities and cannot be recommended for the diagnosis of liver metastases, but because of its high specificity, it may be considered when the definitive diagnosis is impossible by other modalities. While CT during angiography has high sensitivity, it is not recommended not only as the evidence that its diagnostic ability is higher than that of MRI or CT is deficient but also because it is an invasive examination. MRI using a liver-specific contrast agent is more recommendable. If it cannot be performed, CT during angiography may be considered.

**Background/objective**

For diagnosing liver metastases, a wide variety of imaging modalities such as contrast-enhanced ultrasonography, dynamic contrast-enhanced CT using MDCT, dynamic contrast-enhanced MRI using a gadolinium-based extracellular contrast agent, contrast-enhanced MRI using a liver-specific contrast agent such as SPIO and Gd-EOB-DPTA, PET, PET/CT, and CT during angiography are available today. While ultrasonography, CT, and MRI are simple procedures performed on a routine basis, CT during angiography or PET are regarded as special rather than standard examinations. However, no guidelines that mention the use of CT during angiography or PET for the diagnosis of liver metastases are available, and the role of these modalities are unclear. In this article, therefore, the recommendation grades of CT during angiography and PET were evaluated on the basis of the literature.

**Comments**

There have been many reports on the diagnostic performance of various modalities from meta-analyses to case control studies. Four meta-analyses were reported in the 2000s. According to the meta-analysis of 39 reports (3,391 cases) evaluating the diagnostic performance of various modalities for liver metastases of colorectal cancer by Niekel et al., the sensitivities by lesion of CT, MRI, and PET were 74.4, 80.3, and 81.4%, respectively, with no significant difference, but the sensitivities by patient of CT, MRI, and PET (PET/CT) were 83.6, 88.2, and 94.1%, respectively, being significantly higher for PET. In a similar meta-analysis, Bipat et al. also reported that the sensitivity by patient of PET (94.6%) was higher than that of CT or MRI (60.2-75.8%) but that its sensitivity by lesion was higher, though not significantly, compared with CT or MRI. According to this meta-analysis, the sensitivity for tumors 1 cm or greater in diameter was significantly higher in SPIO-contrasted MRI. In the meta-analysis by Kinkel et al., in which the review was restricted to reports on cancer of the digestive organs with a specificity of 85% or higher, the sensitivity of PET was high at 90% (95%CI: 80-97%), exceeding that of CT or MRI, but the difference compared with MRI was not significant. In the meta-analysis by Floriani et al., also, the sensitivities by patient of ultrasonography, contrast-enhanced CT, MRI, and PET were 63.0, 74.8, 81.1, and 93.8%, respectively, and the specificities were 97.6, 95.6, 97.2, and 98.7%, respectively, being high in PDG-PET, but the sensitivities by tumor were 86.3, 82.6, 86.3, and 86.0%, respectively, showing no difference compared with MRI using a liver-specific contrast agent. Therefore, the diagnostic performance of PET is high by patient but not by tumor. In addition, according to the report by Ruers et al., PET was useful for the determination of the therapeutic approach to liver metastases, but its sensitivity for liver metastases varied with the size of the lesion, and the sensitivity of contrast-enhanced CT was higher for lesions 1.5 cm or less in diameter. The liver has been known to show physiologic accumulation of FDG, and there have been many reports that the diagnosis of liver metastases depends on their size. By the systematic review by Wiering et al., also, the sensitivity and specificity for extrahepatic lesions were very satisfactory at 91.2 and 98.4%, but those for liver metastases were at 88.0 and 96.1%, respectively, showing a decrease in the sensitivity. This defect may be corrected by the development of combined PET/CT or PET/MRI devices, evidence concerning whether or not these modalities are superior to MRI using a liver-specific contrast agent in detecting liver metastases is currently unclear. However, PET is considered useful for whole body scanning and, because of its high specificity, as an supplementary examination when the definitive diagnosis of liver metastasis is impossible by other modalities.

While there is no meta-analysis or systematic review on the usefulness of CT during angiography, there have been a large number of reports on studies comparing it with contrast-enhanced CT or MRI using a liver-specific contrast agent. The diagnostic performance has been reported to have improved by combining CTAP and CTHA compared...
with CTAP alone.\textsuperscript{13)} Although CT during angiography has been reported to be superior to MRI using a liver-specific contrast agent or CT due to its high sensitivity,\textsuperscript{11,12,21)} it has also been reported to be inferior or similar to contrast-enhanced CT\textsuperscript{14-17)} or MRI using a liver-specific contrast agent (SPIO).\textsuperscript{18-20)} Therefore, CT during angiography is not recommended from the standpoints of cost and invasiveness for the diagnosis of liver metastases when MRI using a liver-specific contrast agent is performed. No report comparing CT during angiography with EOB-enhanced MRI was found by our review of the literature, and which modality is superior is unclear, but as there are many reports that EOB-enhanced MRI has a diagnostic ability comparable to, or higher than, SPIO-enhanced MRI, substituting EOB for SPIO is considered acceptable.

Index words and secondary materials used as references
A search of PubMed was performed using “liver”, “hepatic metastasis”, “CT arterial portography”, “CT hepatic arteriography”, “sensitivity”, “specificity”, “PET”, and “PET/CT” as key words.

References
1) Niekel MC et al: Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG PET, and/or FDG PET/CT: a meta-analysis of prospective studies including patients who have not previously undergone treatment. Radiology 257: 674-684, 2010 (Level 1)
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7) Coenegrachts K et al: Comparison of MRI (including SS SE-EPI and SPIO-enhanced MRI) and FDG-PET/CT for the detection of colorectal liver metastases. Eur Radiol 19: 370-379, 2009 (Level 2)
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14) Valls C et al: Helical CT versus CT arterial portography in the detection of hepatic metastasis of colorectal carcinoma. AJR170: 1341-1347,
1998 (Level 2)


16) Kouwenhoven ST et al: The pre-operative stratification of patients with colorectal liver metastases: computed tomography arterial portography (CTAP) has no added value. Eur J Surg Oncol 36: 36-42, 2010 (Level 2)


18) Lencioni R et al: Detection of colorectal liver metastases: prospective comparison of unenhanced and ferumoxides-enhanced magnetic resonance imaging at 1.5 T, dual-phase spiral CT, and spiral CT during arterial portography. MAGMA 7: 76-87, 1998 (Level 3)


Although CT during angiography has been reported to be superior to MRI using a liver-specific contrast agent or CT due to its high sensitivity,11,12,21) it has also been reported to be inferior or similar to contrast-enhanced CT14-17) or MRI using a liver-specific contrast agent (SPIO).18-20) Therefore, CT during angiography is not recommended from the standpoints of cost and invasiveness for the diagnosis of liver metastases when MRI using a liver-specific contrast agent is performed. No report comparing CT during angiography with EOB-enhanced MRI was found by our review of the literature, and which modality is superior is unclear, but as there are many reports that EOB-enhanced MRI has a diagnostic ability comparable to, or higher than, SPIO-enhanced MRI, substituting EOB for SPIO is considered acceptable.
Background/objective

The biological nature and prognosis of intrahepatic cholangiocarcinoma (cholangiocellular carcinoma) evaluated by imaging modalities differ from those of HCC, and it is treated primarily by surgery. When intrahepatic cholangiocarcinoma is suspected, imaging examinations are performed for the presence diagnosis, qualitative diagnosis, and staging, and modalities must be selected for each objective.

Comments

Intrahepatic cholangiocarcinoma accounts for 3.6% of primary liver cancers, being the second most frequent following hepatocellular carcinoma. It is macroscopically classified into the mass-forming, bile-duct-infiltrating, and intraductal growth types. The mass-forming type forms a clear elliptical mass, has a distinct border, and typically shows ring-like staining of its irregular enhancement margin. In the delayed phase, the interior of the tumor is stained. The bile-duct-infiltrating type involves the blood vessels and connective tissue around the bile duct and shows dendritic extension in the longitudinal direction. The histological extent may be longer than the extent captured by imaging modalities, and caution is needed. The intraductal-growth type shows papillary or granular growth into the bile duct lumen but occasionally exhibits extension with dilation of the superficial layer or intrabiliary tumor embolus.

1) US

Ultrasonography, which is non-invasive and readily permits arbitrary selection of imaging planes, should be performed first. Generally, tumor-forming type cholangiocarcinoma can be recognized as a mass, but the bile-duct-infiltrating type is often overlooked, and this modality is not considered appropriate for the evaluation of tumor extent. On contrast-enhanced ultrasonography, ring-like staining in the arterial to portal-venous phases and defect in the parenchymal phase are findings characteristic of mass-forming cholangiocarcinoma and metastatic liver cancer. Reportedly, its diagnostic power is high with sensitivity, specificity, and positive predictive value of 90, 95, and 88%, respectively, and the modality is useful for the qualitative diagnosis.1)

2) CT

CT is useful for the localization of lesions and evaluation of the presence or absence of arterial or portal venous invasion and intrahepatic biliary duct dilation. While the mass-forming type is characterized by ring-like enhancement of the margin and enhancement in the delayed phase, some lesions show early enhancement. Figure 1 shows images of mass-forming type intrahepatic cholangiocarcinoma. A mass with irregular ring-like marginal enhancement was noted in S8 of the liver in the hepatic arterial dominant phase, and delayed enhancement was observed in the equilibrium phase. Lesions that show delayed enhancement have been reported to be rich in fibrous stroma, often invade adjacent nerves, and have poorer prognosis than lesions that show early enhancement.2,3) In the bile-duct-infiltrating type, the evaluation of the extent of intrabiliary invasion is generally considered difficult. However, a study using a 16-row MDCT showed diagnostic accuracies of 80.9 and 100% concerning the horizontal and vertical extents of involvement, respectively, but the ability of the modality for the diagnosis of N2 lymph node metastasis was limited.4) In CT after biliary drainage procedures such as endoscopic nasobiliary drainage (ENBD) and biliary stenting, the accuracy of the evaluation is limited due to enhancement of inflammation, and the evaluation before the biliary draining procedure is considered important. Figure 2 shows bile-duct-infiltrating type intrahepatic cholangiocarcinoma. Intrahepatic biliary duct dilation

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Which imaging modalities are appropriate when intrahepatic cholangiocarcinoma is suspected?

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Modality</th>
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<tbody>
<tr>
<td>A</td>
<td>Dynamic CT</td>
</tr>
<tr>
<td>B</td>
<td>Dynamic MRI (including EOB)</td>
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<tr>
<td>C1</td>
<td>Ultrasonography</td>
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</tbody>
</table>

Dynamic CT, which has a high diagnostic ability, is strongly recommended to be performed.

Dynamic MRI using an extracellular contrast agent provides blood flow information. EOB contrast-enhanced MRI is useful for staging while it may fail to show delayed enhancement characteristic of cholangiocarcinoma. So, these modalities are recommended.

Ultrasonography has no sufficient scientific evidence for its superiority to CT or MRI in diagnostic performance, but the diagnostic ability of contrast-enhanced ultrasonography is considered high, and it should be performed in combination with other imaging modalities.

---

1) US

Ultrasonography, which is non-invasive and readily permits arbitrary selection of imaging planes, should be performed first. Generally, tumor-forming type cholangiocarcinoma can be recognized as a mass, but the bile-duct-infiltrating type is often overlooked, and this modality is not considered appropriate for the evaluation of tumor extent. On contrast-enhanced ultrasonography, ring-like staining in the arterial to portal-venous phases and defect in the parenchymal phase are findings characteristic of mass-forming cholangiocarcinoma and metastatic liver cancer. Reportedly, its diagnostic power is high with sensitivity, specificity, and positive predictive value of 90, 95, and 88%, respectively, and the modality is useful for the qualitative diagnosis.1)

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is observed in the lateral segment of the left lobe with a region showing indistinctly bordered delayed enhancement on its proximal side (→).

3) MRI

MRI is useful for the localization of lesions and can also be used for the evaluation of the presence or absence of arterial or portal venous invasion, degree of intrahepatic biliary duct dilation, and sites of stenosis. Cholangiocarcinoma is hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Hypointensity of the interior represents fibrosis. On dynamic MRI using an extracellular contrast agent, ring-like enhancement of the margin and delayed enhancement are findings characteristic of the mass-forming type similarly to CT.

EOB-contrasted MRI has been reported to be excellent in detecting intrahepatic metastatic foci and is useful for designing treatments after the diagnosis of cholangiocarcinoma. For the qualitative diagnosis, however, it must be noted that the modality often fails to exhibit delayed enhancement, which is observed by imaging using an extracellular contrast agent, and may make distinction of the disease from other malignant tumors difficult. Also, MRCP, which allows non-invasive evaluation of the bile duct anatomy and has a high sensitivity of 96% concerning the extent of malignant tumors, is recommended.

Index words and secondary materials used as references


References

If a cystic lesion of the liver is detected, which imaging modalities are appropriate for the discrimination of benign and malignant diseases?

### Background/objective

Various modalities including ultrasonography, contrast-enhanced CT, and contrast-enhanced MRI have been reported to be useful for the discrimination of benign and malignant cystic lesions of the liver. The ability of each modality to discriminate benign and malignant cystic lesions of the liver was evaluated.

### Comments

Cystic lesions of the liver vary widely from congenital liver cysts including those derived from the liver parenchyma such as simple liver cysts and those derived from the bile duct such as Caroli disease to inflammation-derived and tumoral cysts. Malignant cystic tumors of the liver are frequently derived from tumoral cysts, but there have been a number of reports of malignant lesions developing from other cystic lesions, and they cannot be lumped together. In this section, of these cystic lesions, the discrimination between benign and malignant lesions of mucinous cystic neoplasm and intraductal papillary neoplasm of the bile duct, which are often malignant, is primarily discussed.

Ultrasonography, contrast-enhanced CT, and contrast-enhanced MRI are all useful for the examination of septa and solid areas. Contrast enhancement of septa and solid areas and mural nodules are observed in both benign and malignant diseases, but papillary solid tumors and nodular thickening of the septa are findings suggestive of malignancy (sensitivity: 67-100%)\(^1\)\(^-\)\(^8\) (Figure). However, the ability of each modality in detecting small solid parts or tumors along walls is limited.\(^1\)\(^,\)\(^7\)\(^,\)\(^9\) Also, benign and malignant diseases cannot be discriminated according to the presence or absence of calcification, and bleeding is reported to be a highly sensitive but non-specific sign of malignancy.\(^5\)\(^,\)\(^8\) Also, there have been few reports concerning EOB contrast-enhanced MRI.

Ultrasonography is the optimal examination for the evaluation of internal properties of cysts such as mucus and septa as a characteristic of the modality.\(^2\)\(^,\)\(^4\)\(^,\)\(^6\)\(^,\)\(^7\) It is also useful for the diagnosis of solid tumors that appear cystic on CT and MRI such as undifferentiated sarcoma.\(^10\)\(^,\)\(^11\) However, there have been reports that biliary sludge, mucus plugs, and calcification foci are occasionally difficult to distinguish from solid parts by ultrasonography and that CT is superior in delineating solid parts.\(^3\)\(^,\)\(^12\)\(^,\)\(^13\) Ultrasonography is also more dependent on the examiner’s skill.\(^7\) Contrast-enhanced CT has excellent spatial resolution and is useful for the determination of the size and anatomical location of lesions and evaluation of bile duct and vascular invasion.\(^2\)\(^,\)\(^4\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^14\)\(^,\)\(^15\) Similarly to CT, MRI is useful for the evaluation of the size, vascular invasion, and hepatic involvement and for the examination of internal properties such as bleeding.\(^5\)\(^,\)\(^8\)\(^,\)\(^14\)

Despite insufficiency of evidence and limitation of the discrimination ability, each modality has different characteristics in diagnostic performance, and the diagnosis by their combined use is recommended.

### Index words and secondary materials used as references

A search of PubMed was performed using “liver”, “cyst”, “diagnosis”, “malignant”, “biliary cystadenocarcinoma”, “intraductal papillary neoplasm of the bile duct”, and “imaging” as key words.

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2) Choi BI et al: Biliary cystadenoma and cystadenocarcinoma: CT and sonographic findings. Radiology 171: 57-61, 1989 (Level 4)
5) Buetow PC et al: Biliary cystadenoma and cystadenocarcinoma: clinical-imaging-pathologic correlations with emphasis on the importance of
5. Gastrointestinal tract

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13) Han JK et al: Intrahepatic intraductal cholangiocarcinoma. Abdom imaging 29: 558-564, 2004 (Level 5)


Figure: Intraductal papillary neoplasm of the bile duct

A Contrast-enhanced CT (liver parenchymal phase) Transverse section
B Contrast-enhanced CT (liver parenchymal phase) Coronal section

A cystic mass 3.5 cm in long diameter is observed in the caudate lobe of the liver. A papillary solid area is noted along the wall in the right part of the mass and shows contrast enhancement (→), which is a finding suggestive of malignancy.
## Background/objective

Cavernous hemangioma is the most frequent benign tumor of the liver. It is sometimes difficult to discriminate from primary liver cancer in patients with chronic liver disease and liver metastasis in tumor-bearing patients. It is often detected incidentally also in healthy individuals. Since it rarely ruptures or transforms into a malignant disease, unnecessary treatment can be avoided if it is definitively diagnosed by a minimally invasive and highly accurate method. This also avoids invasive procedures and cost of unnecessary additional examinations or follow-up.

## Comments

A majority of liver hemangiomas are cavernous hemangomas, which are benign liver diseases that form localized liver masses due to tumorous growth of large and small vascular lumens, in which flattened endothelial cells are arranged. In the interior of vascular lumens, degeneration such as new and old thrombus formation, necrosis, scars, fibrosis, and calcification is observed. As degeneration advances, the lesion becomes sclerosed hemangioma. It is necessary to diagnose liver hemangioma using imaging modalities by understanding these tissue architectures and degeneration.

1) Until the early 1990s, liver hemangiomas were occasionally diagnosed definitively by angiography, but invasive angiography has been completely obviated as a diagnostic procedure due to the recent development of less invasive imaging techniques. Similarly, while radionuclide studies using $^{99m}$Tc-labeled erythrocytes used to be performed, it has fallen into disuse due to the unsatisfactory accuracy and difficulty of diagnosing small hemangiomas. The performance of ultrasound devices began to improve since the late 1980s with improvements in the detection sensitivity for hemangiomas, but their differentiation from malignant tumors was not easy by ultrasonography without contrast enhancement. In the late 1980s, MRI became increasingly available, and its usefulness for the diagnosis of liver hemangiomas was reported. According to comparisons of ultrasonography with non-contrast CT and MRI performed in this period, MRI showed higher detection sensitivity. Thereafter, there was also a report that non-contrast MRI was superior to contrast-enhanced CT. From the early 1990s, the development of helical CT and high magnetic field strength MRI progressed, and contrast-enhanced dynamic study became possible with both CT and MRI, resulting in marked improvements in the diagnostic ability for liver hemangioma and reports of diagnostic performance exceeding that by ultrasonography.

2) In this period, Doppler ultrasonography was reported to be useful for the diagnosis of liver hemangioma, but the procedure has not been established as a method for the definitive diagnosis. Recently, also, with the introduction of contrast-enhanced ultrasonography, more detailed analysis of the hemodynamics of liver hemangiomas has become possible, causing improvements in the diagnostic performance of ultrasonography.

3) However, the reliability of contrast-enhanced ultrasonography for the diagnosis of liver hemangioma has not been securely established due to the presence of dead angles, difficulty in simultaneous evaluation of multiple lesions, and variability of the results depending on the examiner’s skill and the patient’s physique. In MRI, many hemangiomas show hyperintensity on T2-weighted imaging, and lesions about 4 mm in diameter has become detectable. On gadolinium contrast-enhanced MRI, usual staining type hemangiomas, in which marginal nodular staining extends internally with time, account for about 70% of the lesions. Some hemangiomas are those with arteriportal (AP) shunts, early enhancing type hemangiomas, which show intense enhancement of the whole lesion from the early phase of contrast enhancement, and delayed staining hemangiomas, which show partial dot-like staining (bright-dot sign) or only pale staining in the margin until the late phase of contrast enhancement. With improvements in the understanding of these atypical findings, it has become possible to diagnose liver hemangiomas with a high level of confidence. Moreover, radiation exposure cannot be ignored on contrast-enhanced multiphasic CT, and, particularly, on secondary

## Which imaging modalities are appropriate as for the reliable diagnosis of liver hemangiomas?

<table>
<thead>
<tr>
<th>Recommendation Grade</th>
<th>Imaging Modality</th>
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<tbody>
<tr>
<td>A</td>
<td>Extracellular gadolinium contrast-enhanced dynamic MRI</td>
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<tr>
<td>B</td>
<td>EOB contrast-enhanced MRI, contrast-enhanced dynamic CT</td>
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<tr>
<td>C1</td>
<td>Ultrasonography and contrast-enhanced ultrasonography</td>
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</tbody>
</table>

MRI including extracellular gadolinium contrast-enhanced dynamic MRI is the most reliable and is strongly recommended. EOB contrast-enhanced MRI and contrast-enhanced dynamic CT also have a sufficient diagnostic ability and are recommended to be performed. The diagnostic performance of ultrasonography is improved by the use of a contrast agent, and the modality should be considered.

Recommendation grade

A: Extracellular gadolinium contrast-enhanced dynamic MRI
B: EOB contrast-enhanced MRI, contrast-enhanced dynamic CT
C1: Ultrasonography and contrast-enhanced ultrasonography

MRI including extracellular gadolinium contrast-enhanced dynamic MRI is the most reliable and is strongly recommended. EOB contrast-enhanced MRI and contrast-enhanced dynamic CT also have a sufficient diagnostic ability and are recommended to be performed. The diagnostic performance of ultrasonography is improved by the use of a contrast agent, and the modality should be considered.

Recommendation grade

A: Extracellular gadolinium contrast-enhanced dynamic MRI
B: EOB contrast-enhanced MRI, contrast-enhanced dynamic CT
C1: Ultrasonography and contrast-enhanced ultrasonography

MRI including extracellular gadolinium contrast-enhanced dynamic MRI is the most reliable and is strongly recommended. EOB contrast-enhanced MRI and contrast-enhanced dynamic CT also have a sufficient diagnostic ability and are recommended to be performed. The diagnostic performance of ultrasonography is improved by the use of a contrast agent, and the modality should be considered.
examination of hemangiomas incidentally detected in healthy individuals, MRI with the benefit of no radiation exposure even on contrast-enhanced multiphasic imaging, is recommended. Recently, EOB Primovist contrast-enhanced MRI has begun to be performed widely for close evaluation of liver masses, but it often fails to present clear hyperintensity of blood pools in the late to delayed phase of contrast enhancement, its diagnostic ability for small hemangiomas is considered to be limited.\[15\-19\]

Index words and secondary materials used as references

A search of PubMed was performed using “liver”, “hemangioma”, “diagnosis”, “CT”, “US”, “MRI”, “angiography”, “scintigraphy”, and “EOB” as key words.

References

1) Yamashita Y et al: Cavernous hemangioma of the liver: pathologic correlation with dynamic CT findings. Radiology 203: 121-125, 1997 (Level 3)
16) Berrington de Gonzalez A, Darby S: Risk of cancer from diagnostic X-rays: estimates for the UK and 14 other countries. Lancet 363: 345-351, 2004 (Level 5)
Background/objective

Focal nodular hyperplasia (FNH) is a hypervascular lesion that arises in the background liver without chronic liver disease (so-called normal liver), and it is considered a reactive lesion due to regional abnormality (increase) of the blood flow. There are a large number of papers concerning the imaging diagnosis of FNH, and many of them regard “findings on pathological examination or dynamic CT/MRI” as the gold standard. This suggests that typical findings on dynamic CT/MRI are sufficient as the basis for the diagnosis of FNH on the clinical level. Practically, however, there are instances in which the diagnosis is uncertain, and how much the reliability of the diagnosis can be increased is a point in such cases.

Comments

Typical imaging findings of FNH can be summarized as follows:

1) Dynamic CT/MRI
   Homogeneous (isodense or hypodense) interior on plain CT, lobulated margin, enhancement in the arterial phase (nearly 100%), more intense enhancement in the arterial phase than hepatocellular adenoma, isodensity/isointensity with the surrounding liver parenchyma in the portal venous-delayed phase, and central scar that is hypodense/hypointense in the early phase, but contrast-enhanced in the late phase or thereafter, and hyperintense on T2-weighted imaging.

2) Liver-specific phase of MRI using a liver-specific contrast agent
   Iso-/hyperintensity compared with the surrounding liver parenchyma in the arterial phase of EOB contrast-enhanced MRI (91%) (Figure A), hypointense central scar in the hepatocyte phase of EOB contrast-enhanced MRI (100% when central scar is identified) (Figure B), and isointensity with the surrounding liver parenchyma in the Kupffer cell phase of SPIO contrast-enhanced MRI (83%).

3) Abdominal ultrasonography
   Diverse echogenicity, delineation of spoke-wheel blood flow signals or central vessels on Doppler or contrast-enhanced ultrasonography (Figure C), and staining of the entire nodule in the early phase of contrast-enhanced ultrasonography.

As mentioned above, FNH is often diagnosable by dynamic CT/MRI, and there have been few reports with a high evidence level genuinely comparing the diagnostic accuracy among various imaging modalities. In 2008, Zech et al. reported that FNH could be diagnosed with confidence more frequently by EOB contrast-enhanced MRI than by non-contrast-enhanced MRI or contrast-enhanced dynamic CT. Grazzioli et al. compared the frequency of the appearance of various findings on gadoxetic acid-enhanced MRI in 68 lesions of FNH and 43 lesions of hepatocellular adenoma and reported that 93% (40/43) of the hepatocellular adenomas were hypointense in the hepatocyte phase of EOB contrast-enhanced MRI, but that 91% (62/68) of the FNHs were iso-/hyperintense, and that the findings were useful for their differential diagnosis. Bartolotta et al. compared non-contrast-enhanced and contrast-enhanced ultrasonography and reported that findings characteristic of FNH (spoke-wheel, central scar, feeding vessel) are easier to confirm by contrast-enhanced ultrasonography.

As observed above, characteristic findings are more often reported by contrast-enhanced ultrasonography, and the use of a contrast agent is recommended when the diagnosis is made by ultrasonography. Since there has been no study comparing contrast-enhanced ultrasonography and dynamic CT/MRI, their performance cannot be compared, but if ultrasonography has demonstrated characteristic features allowing the diagnosis, further examination is unnecessary.

Which imaging modalities are appropriate for the definitive diagnosis of focal nodular hyperplasia (FNH)?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>A</th>
<th>Dynamic MRI (EOB)</th>
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<tbody>
<tr>
<td>A</td>
<td></td>
<td>Dynamic CT, dynamic MRI using an extracellular contrast agent</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td>Ultrasonography (non-contrast-enhanced)</td>
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</tbody>
</table>

Since iso-/hyperintensity compared with the surrounding liver parenchyma is a finding characteristic of FNH in the hepatocyte phase of EOB contrast-enhanced MRI, the modality is strongly recommended. Dynamic CT or dynamic MRI using an extracellular contrast agent is also recommended as modalities sufficiently capable of diagnosing FNH. FNH is often difficult to diagnose by ultrasonography, but should be considered because of its convenience.
While FNH can be sufficiently diagnosed by conventional dynamic CT/MRI, findings in the hepatocyte phase of EOB contrast-enhanced MRI are useful for the definitive diagnosis, and the modality should be selected as the first choice.

Index words and secondary materials used as references
A search of PubMed was performed using “focal nodular hyperplasia”, “magnetic resonance imaging”, “CT”, and “ultrasound” as key words.

References
8) Zech CJ et al: Diagnostic performance and description of morphological features of focal nodular hyperplasia in Gd-EOB-DTPA-enhanced liver magnetic resonance imaging: results of a multicenter trial. Invest Radiol 43: 504-510, 2008 (Level 4)
Which imaging modalities are appropriate for the diagnosis of liver tumors in patients with kidney or liver dysfunction?

**Recommendation grade**

**B** Non-contrast-enhanced MRI, ultrasonography

**C1** Contrast-enhanced CT, contrast-enhanced MRI (contrast agent to be used selected according to kidney function)

**B** Non-contrast-enhanced MRI including diffusion-weighted imaging and ultrasonography including Sonazoid-enhanced imaging are recommended. For contrast-enhanced CT or MRI in patients with kidney dysfunction, EOB-enhanced MRI may be considered when the eGFR is 30-60 mL/min/1.73 m², Resovist-enhanced MRI when it is less than 30 mL/min/1.73 m², and Resovist-enhanced MRI or contrast-enhanced CT for dialysis patients.

Concerning contrast-enhanced CT/MRI for patients with liver dysfunction corresponding to Child-Pugh class C, research on the appropriate selection of examinations and contrast agents is insufficient.

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### Background/objective

Since kidney dysfunction restricts the use of iodine- or gadolinium-based contrast agents, and since liver dysfunction reduces the contrast-enhancing effect of EOB-Primovist or Resovist, limitation of indications and decline in the diagnostic performance of examinations are expected in patients with kidney or liver dysfunction.

### Comments

Since Sonazoid, an ultrasound contrast agent, and Resovist, a liver-specific superparamagnetic iron oxide (SPIO) contrast agent for MRI, do not affect the kidney function and are not known to increase adverse events associated with kidney dysfunction, it permits contrast-enhanced imaging also in kidney dysfunction patients as usual.

In patients with an eGFR of less than 60 mL/min/1.73 m², the risk of contrast-induced nephropathy due to the administration of an iodine-based contrast agent increases, and contrast-enhanced CT is difficult to perform. The risk is considered to be aggravated further by the concurrence of risk factors including diabetes, dehydration, congestive heart failure, gout, an age of 70 years or above, and being under medication with NSAIDs.

In patients with kidney dysfunction, the risk of nephrogenic systemic fibrosis (NSF) due to gadolinium-based contrast agents is increased. For this reason, the administration of an extracellular gadolinium-based contrast agent or EOB-Primovist is avoided, in dialysis patients, patients with chronic kidney disease with an eGFR of less than 30 mL/min/1.73 m², and patients with acute renal failure. If the use of a gadolinium-based contrast agent is desirable after the evaluation of benefits and risks, Gadodiamide (Omniscan) and Gadopentetate dimeglumine (Magnevist), which have often been reported to induce NSF, should be avoided. Since EOB-Primovist is excreted via the liver as well as the kidney, it appears to be advantageous compared with an extracellular gadolinium-based contrast agent. In practice, however, its administration to dialysis patients cannot be recommended as clearance and contrast enhancement of the liver parenchyma are known to be significantly reduced in dialysis patients.

The evidence of the selection of an appropriate contrast agent or examination according to the eGFR for contrast-enhanced CT or MRI in patients with kidney dysfunction is insufficient. Therefore, recommendations of the present guidelines are provisional. When the eGFR is 30-60 mL/min/1.73 m², contrast-enhanced MRI using EOB-Primovist with a high diagnostic ability is recommended, because the risk of NSF is not very high. When the eGFR is less than 30 mL/min/1.73 m², the risk of NSF increases, and which of EOB-Primovist or Resovist should be recommended for contrast-enhanced MRI is difficult to judge, but Resovist contrast-enhanced MRI is recommended as the package insert of EOB-Primovist says, “Avoid the administration of this preparation,” and as the administration is likely to be repeated. For dialysis patients, it is recommended to avoid gadolinium-based contrast agents and to select Resovist-enhanced MRI or contrast-enhanced CT using an iodine-based contrast agent, which can be eliminated by dialysis, according to the circumstances of the facility.

Patients with liver dysfunction show attenuation of the contrast-enhancing effect of EOB-Primovist in the hepatocyte phase (Figure 1) and of Resovist in the so-called Kupffer phase. Research on the appropriate selection of contrast-enhanced CT or MRI for patients with liver dysfunction corresponding to Child-Pugh class C is insufficient, and even provisional recommendations are difficult.

Diffusion-weighted imaging has been reported to have some usefulness although it does not surpass that of contrast-enhanced MRI (Figure 2). In patients with compromised kidney or liver function, diffusion-weighted imaging has...
greater importance than usual.

**Index words and secondary materials used as references**


**References**


2) Kopp AF et al: MRI imaging of the liver with Resovist: safety, efficacy, and pharmacodynamic properties. Radiology 204: 749-756, 1997 (Level 2)


5) Japan Radiological Society and Japanese Society of Nephrology eds.: Guidelines for Administering Gadolinium-Based Contrast Agents to Patients with Renal Dysfunction (Second Edition). Joint Committee on NSF and the Use of Gadolinium-Based Contrast Agents, 2009 (Level 5)


Background/objective

Acute cholangitis is an infection in which the bile duct is obstructed, preventing the flow of bile and allowing abnormal proliferation of bacteria in bile. Severe acute cholangitis rapidly progresses to sepsis, which may be fatal, and prompt diagnosis and treatment are needed. The significance of imaging modalities in acute cholangitis is high, and they are performed for the evaluation of the presence or absence of bile duct obstruction/dilation and determination of the cause of obstruction. As for assessment of severity of acute cholangitis, routine clinical information is usually used and local imaging findings are not useful, except when an apparent abscess is formed.

Comments

Since there is no finding specific to acute cholangitis on plain radiography, it is impossible to diagnose the disease by this modality alone. It should be regarded as an examination for the diagnosis of other diseases that must be differentiated from acute cholangitis such as pneumonia, gastrointestinal perforation, and ileus.\(^1,2\) If CT has been performed, plain radiography is unnecessary.

In patients suspected to have acute cholangitis, ultrasonography is the examination to be performed first as it is the most convenient and least invasive.\(^3,4\) The findings of ultrasonography include biliary dilation, bile duct wall thickening, and pneumobilia, but they are all non-specific.\(^5\) In addition to these findings, if a stone is delineated, it provides additional support for the diagnosis. However, the sensitivity of ultrasonography for common bile duct stones is 20-60% and is unsatisfactory.\(^6\)

CT is superior to ultrasonography in that a wider area can be scanned. CT findings of cholangitis itself are non-specific, including biliary dilation, pneumobilia, and bile duct wall thickening, but uneven staining of the entire liver on dynamic CT has recently been reported as an additional finding suggestive of active inflammation.\(^7\) Dynamic CT is also useful for the determination of the cause of obstruction and the presence or absence of complications such as liver abscess and peribiliary abscess. Examinations including non-contrast CT are useful for the diagnosis of stones as a cause of obstruction.\(^8\) (See CQ77 and CQ78)

By MRI, it is possible to visualize bile duct dilation, edema of the bile duct mucosa, peribiliary edema, and fluid retention,\(^9\) but comprehensive evaluation based on findings including clinical information is still important. Hypointensity on heavily T2-weighted imaging and moderate signal intensity on fat-suppressed T1-weighted imaging are considered to be findings specific to pus in the bile duct,\(^9\) but its discrimination from biliary sludge is a problem.

### Which imaging examinations are appropriate when acute cholangitis is suspected?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>A</th>
<th>Ultrasonography, CT</th>
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<tr>
<td>B</td>
<td></td>
<td>MR/MRCP</td>
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<tr>
<td>C1</td>
<td></td>
<td>Plain radiography</td>
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<tr>
<td>C2</td>
<td></td>
<td>ERCP</td>
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Ultrasonography is strongly recommended for all patients suspected to have acute cholangitis because of its convenience and high diagnostic performance. CT is also strongly recommended as it is excellent in determining the cause of acute cholangitis and, particularly, delineating common bile duct stones that are difficult to visualize by ultrasonography and the mechanism of obstruction by tumor and is useful for the evaluation of the presence or absence of complications including abscess. MRI/MRCP is recommended as it is useful for the determination of the cause of acute cholangitis. Particularly, the delineation rate of common bile duct stones that are difficult to visualize by ultrasonography is high.

While acute cholangitis cannot be diagnosed by plain radiography itself, it may be considered for the differential diagnosis from other diseases. ERCP is basically performed for drainage and is not recommended to be used for purely diagnostic purposes. However, ERCP is performed preferentially for the diagnosis as well as treatment of moderate to severe acute cholangitis, which may be fatal.
Although hyperintensity along the portal tract observed on T2-weighted imaging, which suggests inflammation, is also observed frequently but is non-specific.\(^{10}\) MRCP satisfactorily visualizes biliary stones and malignant diseases that can cause obstruction.\(^{12,13}\) Since it allows the evaluation of the entire biliary system, it is useful as a guide for drainage. While its sensitivity and specificity are both 90% or higher for delineation of stones,\(^{11,12,14}\) its diagnostic performance for small (≤ 6 mm) stones is reportedly limited.\(^{11,15}\)

ERCP is very important as it has the highest ability for diagnosing the cause of obstruction in acute cholangitis and is also used therapeutically for drainage. The above non-invasive examinations are performed if the disease is clinically mild, but ERCP is selected preferentially with drainage in mind if the disease is moderate or severe and can be lethal.\(^{16}\)

**Index words and secondary materials used as references**

A search of PubMed was performed using “cholangitis”, “radiography”, “ultrasonography”, “computed tomography”, “magnetic resonance imaging”, and “endoscopic retrograde cholangiopancreatography” as key words. Committee for the Preparation of Tokyo guidelines for the management of acute cholangitis ed: Tokyo guidelines for the management of acute cholangitis and cholecystitis, 1st edition, 2005, and Evidence-Based Imaging, 2011 were also used as references.

**References**

7) Arai K et al: Dynamic CT of acute cholangitis: early inhomogeneous enhancement of the liver. AJR 181: 115-118, 2003 (Level 2)
Which examinations are appropriate when choledocholithiasis accompanied by biliary obstruction is suspected?

**Recommendation grade**

- **A** Ultrasonography
- **B** MRI/MRCP
- **C1** CT
- **C2** ERCP

### Background/objective

When choledocholithiasis accompanied by biliary obstruction is suspected, which examinations should be performed and at what timing? For the efficient diagnosis and prompt initiation of treatment, characteristics and roles of 4 diagnostic modalities were evaluated in this section.

### Comments

1) **Ultrasonography**

   Its specificity for detecting choledocholithiasis is nearly 100%, but its sensitivity is 68% at the highest and is less than 50% in many reports. This low sensitivity is due to limitations of delineation of stones in the common bile duct depending on their size, skill of the examiner, and various other factors. Also, according to a study comparing the common bile duct diameter measured by ultrasonography and intraoperative cholangiographic findings, stones were detected in 6% of the patients with a normal common bile duct diameter (≤ 5 mm) but 37.5% of those with a diameter of >5 mm. Therefore, a dilated common bile duct can be a marker for suspecting choledocholithiasis. Since ultrasonography is easy to perform and non-invasive, it should be the imaging examination of choice and is one of the predictive factors when choledocholithiasis is suspected. In addition, the detection of choledocholithiasis has been reported to be facilitated further by tissue harmonic imaging.

2) **CT**

   Non-contrast CT plays the primary role (See the standard imaging techniques for imaging techniques to be performed when stones are suspected). The sensitivity of CT for the detection of choledocholithiasis has been reported to be 65-88%. Stones may be isodense depending on their composition, and the sensitivity decreases to 24-26%, making their detection difficult.

3) **MRI/MRCP**

   According to a meta-analysis of 67 papers (4,711 cases), both the sensitivity and specificity of MRCP for the detection of choledocholithiasis are high at 92 (80-97) and 97 (90-99)% respectively. As shown in the figure, MRI/MRCP can clearly visualize stones in the common bile duct and is considered to be the most reliable non-invasive examination. While the sensitivity of MRCP for biliary obstruction is 95%, its sensitivity for choledocholithiasis is lower at 92%, and that for malignant diseases is even lower at 88%. One of the causes of this decrease in sensitivity for choledocholithiasis is the size of stones. There are reports that the sensitivity decreased from 100 to 64% in common bile duct stones 3 mm or less in diameter and that 100% of common bile duct stones 5 mm or greater in diameter but only 62% of stones less than 5 mm in diameter could be detected. EUS is an examination as reliable as MRI/MRCP for the diagnosis of choledocholithiasis. A systematic review comparing EUS and MRCP reported no difference in the detection power for common bile duct stones.

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4) ERCP

Since ERCP has been regarded as the standard for the diagnosis of choledocholithiasis, reports of the results by ERCP alone are limited. Recently, its sensitivity and specificity have been reported to be 93 and 100%, respectively. 

Incidental events such as pancreatitis, infection, bleeding, and perforation as well as unsuccessful attempts have been reported. If moderate or severe signs of infection are observed in the initial diagnostic procedure, diagnostic ERCP with treatment in mind is recommended to be performed without additional examinations.

Index words and secondary materials used as references

A search of PubMed was performed using “biliary obstruction”, “choledocholithiasis”, “US”, “CT”, “MRI”, and “ERCP” as key words limited to reports up until July, 2012. ASGE guideline 2010 and Springer Evidence-based imaging, 2011 were also used as references.

References

8) Baron RL et al: CT evaluation of gallstones in vitro: correlation with chemical analysis. AJR 151: 1123-1128, 1988 (Level 2)
Which modalities are appropriate for the diagnosis of gallstones/bile duct stones?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>A</th>
<th>Ultrasonography (recommended as the initial examination)</th>
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<tr>
<td></td>
<td>A</td>
<td>MRI/MRCP (recommended when bile duct stones are suspected)</td>
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<td></td>
<td>C1</td>
<td>CT</td>
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<td></td>
<td>C1</td>
<td>DIC (performed as DIC-CT)</td>
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<td>Plain radiography</td>
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</table>

Ultrasonography is strongly recommended as the initial examination. MRI/MRCP is also strongly recommended when bile duct stones are suspected. CT is inferior to MRI/MRCP in sensitivity for bile duct stones, but its use may be worth considering. DIC may also be worth considering if it is performed as DIC-CT using MDCT. ERCP is not recommended for pure diagnostic uses, but it should be performed preferentially if it is necessary for treatment. Plain radiography is not recommended because of the radiation exposure and low detection power.

Comments

1) Plain radiography

Of biliary tract stones, 15-20% are considered to have calcification sufficient to be visualized by plain radiography. While the modality is inexpensive, it is not recommended for the detection of gallstones/bile duct stones due to radiation exposure and low detection sensitivity. In non-traumatic abdominal pain, plain radiography is often ineffective for acute abdomen, and its effectiveness is limited to the detection of ileus and foreign bodies.

2) Ultrasonography

Ultrasonography is an inexpensive and safe examination. Its sensitivity, specificity, and accuracy for gallstones were about 75, 62, and 72%, respectively, in an early study, but the accuracy improved to 93% in subsequent evaluations. In the diagnosis of gallbladder disorders in general, the overall accuracy was 98.9%, false negative rate was 2.2%, and false positive rate was 2.8%. The accuracy of ultrasonography for all diseases was 93%, false negative rate was 11%, and unclear diagnosis rate was 4%. According to a meta-analysis of the diagnostic ability of emergency unit bedside ultrasonography for gallstones (8 papers, 710 cases), the sensitivity was 89.8% (95% CI: 86.4-92.5%), and the specificity was 88% (95% CI: 83.7-91.4%). For common bile duct stones, its sensitivity and specificity were 25 and 89%, or 63 and 95%, respectively.

In conclusion, ultrasonography is recommended as the initial imaging examination for the presence diagnosis of bile duct stones/gallstones although its detection ability for bile duct stones remains questionable.

3) CT

According to an evaluation in 1987, gallstones were detected by CT at a sensitivity of 79.1%, specificity of 100%, and accuracy of 89.8%. By another report published in the same year, the sensitivity of CT for bile duct stones was 76% and considered insufficient (Figure). A study comparing the usefulness of plain radiography and non-contrast-enhanced CT for the examination of non-traumatic acute abdomen including gallstones reported that the sensitivity of plain radiography was low, and that non-contrast-enhanced CT was accurate. CT can replace plain radiography as the initial imaging examination.

In a relatively new report concerning bile duct stones, the sensitivity and specificity of non-contrast-enhanced CT were 65 and 84%, respectively, and the sensitivity, specificity, and accuracy of CT with MPR for common bile duct stones were 88.9, 92.6, and 90.7%, respectively.

CT for the presence diagnosis of stones is typically non-contrast-enhanced.

4) MRI/MRCP

According to a meta-analysis reviewing 67 reports with appropriate diagnostic criteria (4,711 cases), the sensitivity and...
specificity of MRCT for biliary tract diseases were 95 and 97%, respectively, the sensitivity for gallstones was 92%, and the sensitivity for malignant tumors was 88%. MRCP was concluded as a non-invasive and appropriate examination for biliary tract diseases.

Two meta-analyses of papers comparing MRCP and EUS (301 and 405 cases) reported no significant difference in the diagnostic ability between the two modalities. While there is a report that patients in whom ERCP can be spared by the information obtained by MRCP are limited, MRCP is recommended as a non-invasive examination for gallstones/bile duct stones in symptomatic patients.

5) DIC

There is no clear report about the ability of conventional 2-dimensional DIC to detect gallstones/bile duct stones. Contrast agents used for DIC tend to more often cause adverse events than "other" iodine-based contrast agents. Also, the biliary tract may not be visualized depending on its patency or liver function. The sensitivity and specificity of CT cholangiography using 8-detector-row MDCT were 78 and 100% for gallstones/bile duct stones, and those of MRCP performed simultaneously were 94 and 88%, respectively. DIC cannot be a standard examination for gallstones/bile duct stones due to side effects of iodine-based contrast agents, radiation exposure, and reduced delineation ability in the presence of hyperbilirubinemia.

6) ERCP

The detection power of ERCP for bile duct stones is high, and the modality has been used as a standard examination in many studies. There is also a report that patients in whom ERCP can be spared by the information obtained by MRCP are limited. However, ERCP is associated with risks that cannot be ignored such as pancreatitis and cholangitis. Even when ERCP is performed for the diagnosis alone, 3-5% of the patients develop pancreatitis with a mortality rate of 0.2-0.5%. Also, ERCP is reported to be unnecessary in gallstone patients who are normal on biliary ultrasonography and liver function tests.

While ERCP is not recommended for purely diagnostic purposes, it should be performed preferentially when treatment is necessary.

Index words and secondary materials used as references
A search of PubMed was performed using “gallstone”, “cholecystolithiasis”, “choledocholithiasis”, “detection”, “abdominal radiograph”, “US”, “CT”, “MRI”, “MRCP”, “DIC”, and “ERCP” as key words.

References
4) Ahn SH et al: Acute nontraumatic abdominal pain in adult patients: abdominal radiography compared with CT evaluation. Radiology 225: 159-164, 2002 (Level 2)
5) Goldberg BB et al: Ultrasonic and radiographic cholecystography, a comparison. Radiology 111: 405-409, 1974 (Level 4)
15) Chung WS et al: Diagnostic accuracy of multidetector-row computed tomography for common bile duct calculi: is it necessary to add non-contrast-enhanced images to contrast-enhanced images? J Comput Assist Tomogr 31: 508-512, 2007 (Level 2)
Which imaging modalities are appropriate when acute cholecystitis is suspected?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Imaging Modality</th>
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<tr>
<td>A</td>
<td>Ultrasonography</td>
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<tr>
<td>B</td>
<td>CT, MRI/MRCP</td>
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<tr>
<td>C1</td>
<td>Plain radiography</td>
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<tr>
<td>C2</td>
<td>Biliary scintigraphy, DIC</td>
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</table>

**Ultrasonography** is strongly recommended to be performed first in all patients suspected to have acute cholecystitis. CT need not be performed in all patients but is recommended as it is useful when the definitive diagnosis is difficult by other examinations or for the evaluation of local complications. Plain radiography should be considered for the differentiation from other diseases. MRI/MRCP is recommended to be performed as it is useful for the diagnosis of acute cholecystitis and shows high delineation rate for stones in the neck of gallbladder and cystic duct. However, biliary scintigraphy and DIC, which used to be used for the diagnosis of acute cholecystitis, are scarcely performed in Japan today. It is also not recommended from the viewpoint of convenience.

**Background/objective**

Acute cholecystitis is a collective term for all inflammatory diseases of the gallbladder. It is reported to be caused by gallstones in 90-95% of the patients and to occur in every 2 of 3 patients with gallstones. It may also occur after surgery, trauma, or burn injury or be caused by long-term intravenous alimentation, malignant neoplasms, hepatic arterial infusion therapy, diabetes, drugs, or infection (non-calculous cholecystitis), and these conditions are reportedly more difficult to diagnose and more often follow a serious or lethal course than acute cholecystitis due to gallstones.

Acute cholecystitis is diagnosed comprehensively on the basis of clinical symptoms such as fever, right upper quadrant pain, and Murphy sign, blood test results such as elevated WBC and CRP, and imaging findings. Although the total mortality rate due to acute cholecystitis is low, being less than 10%, severe conditions such as gangrenous cholecystitis, purulent cholecystitis, gallbladder perforation, and emphysematous cholecystitis are occasionally observed, and the urgency and contents of treatment vary with the condition. Imaging examination plays an important role in the severity evaluation.

**Comments**

Ultrasonography is the examination that should be performed first in patients suspected to have acute cholecystitis as it is the most convenient and least invasive.1,2) Findings suggestive of acute cholecystitis include pain on compression of the gallbladder with a probe (sonographic Murphy sign), gallbladder enlargement, gallbladder wall thickening of 3 mm or more, gallstones, biliary sludge, free fluid around the gallbladder, and hypoechoic zones showing irregular multilaminate structures.2,3) Among them, a combination of the presence of gallstones and sonographic Murphy sign is considered to be the most sensitive.3,4) Gallbladder wall thickening of 3 mm or more and hypoechoic zones showing irregular multilaminate structures are also findings with relatively high diagnostic value.5) However, as stones in the neck of gallbladder or cystic duct causing acute cholecystitis are occasionally difficult to visualize by ultrasonography, careful examination by scanning from multiple angles and with changes in the body position is necessary. There is also a report that the sensitivity, specificity, and accuracy could be improved to 95, 100, and 99%, respectively, surpassing the usual diagnostic ability of ultrasonography (86, 99, and 92%, respectively), by evaluating increases in the blood flow of the gallbladder wall by (color or power) Doppler ultrasonography.5,6)

It has been reported that CT has lower diagnostic power than ultrasonography and that acute cholecystitis was diagnosed in 82% of the patients by ultrasonography but in only 36% by contrast-enhanced CT.5) CT findings suggestive of acute cholecystitis include gallbladder enlargement, gallbladder wall thickening, increased radiodensity of bile, fluid around the gallbladder, fat stranding around the gallbladder, and suberosal edema (Figure 1).5) However, the modality is considered useful for the diagnosis of local complications such as perforation and abscess, and tear of the gallbladder wall was reported to be difficult to detect by ultrasonography with an accuracy of 39% but to be detected more often by contrast-enhanced CT with an accuracy of 69%.7) Also, as the evaluation of gallstones by non-contrast CT is essential, a combination of non-contrast and contrast-enhanced CT is appropriate for the diagnosis of acute cholecystitis.

By MRI, gallbladder enlargement, wall thickening, and inflammatory changes around the gallbladder can be visualized. Hyperintensities around the gallbladder on T2-weighted imaging correspond to fluid retention and edema. MRI is
useful for the diagnosis of acute cholecystitis (Figure 2). However, it must be noted that hyperintensities around the gallbladder in T2-weighted images are false positive findings in patients with liver cirrhosis. In addition, MRCP showed an accuracy of 97%, which was higher than the accuracy by ultrasonography (77%), for stones in the neck of gallbladder and cystic duct.

Plain radiography is useful for the discrimination of diseases that must be differentiated from acute cholecystitis such as gastrointestinal perforation and ileus, but there is no finding specific to acute cholecystitis.

On biliary scintigraphy, acute cholecystitis can be diagnosed if the gallbladder is not delineated despite nearly normal technetium hepatobiliary iminodiacetic acid uptake by the liver or excretion into the common bile duct. In 1982, the accuracy of biliary scintigraphy (85%) was comparable to that of ultrasonography (88%), and the modality used to be the first choice examination for acute cholecystitis in Western countries, but its priority has presently been reduced due to the long scanning time and radiation exposure.

Drip infusion cholangiography (DIC) is a simple method to visualize the bile duct and gallbladder that used to be used for the diagnosis of acute cholecystitis and gallstones as the only technique for biliary tract imaging other than intraoperative cholangiography, but is has been mostly eliminated due to the low diagnostic performance and high frequency of allergic reactions to the contrast agent.

**Index words and secondary materials used as references**

A search of PubMed was performed using “cholecystitis”, “radiography”, “ultrasonography”, “CT”, “MRI”, “scintigraphy”, and “intravenous cholangiography” as key words.

**References**

Is CT appropriate when cholangiocarcinoma is suspected?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tr>
<td>B</td>
<td>CT is useful or the diagnosis of cholangiocarcinoma and is recommended.</td>
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</table>

**Background/objective**

For the diagnosis of cholangiocarcinoma, CT and MRI as well as abdominal ultrasonography are generally performed as non-invasive examinations, and there have been a number of reports on their usefulness. Recently, the excellence and reliability, particularly, of MDCT as a first-line examination are being established at many facilities. The usefulness of CT for the diagnosis of cholangiocarcinoma is evaluated.

**Comments**

CT is superior to ultrasonography in the delineation of obstruction or dilation of intra- and extrahepatic bile ducts and is useful for the presence diagnosis of bile duct obstruction. Particularly, in ultrasonography of obese patients and patients with gas in the gastrointestinal tract, the middle/lower biliary tract is often difficult to evaluate but can mostly be visualized clearly by CT.

Also, contrast-enhanced CT is an examination appropriate for the diagnosis of bile duct obstruction and can provide clear visual information necessary for this purpose including information concerning the site of the tumor or obstruction and adjacent anatomical structures. For the diagnosis of malignant neoplasms in patients with bile duct obstruction, the sensitivity, specificity, and accuracy of CT are reported to be 77, 63, and 83%, respectively.

CT has also been reported to be useful for the staging of malignant neoplasms and superior to other modalities in diagnosing vascular invasion, with an accuracy of 85%.

While its diagnostic ability for cancer of the ampulla of Vater and invasive cholangiocarcinoma is limited, it has recently become possible to obtain high-quality images by the introduction of MDCT with high spatial resolution, resulting in improvements in the delineation of bile duct and vascular structures. In the evaluation of the longitudinal extent of invasion of cholangiocarcinoma, the accuracy of MDCT was reported to be 90-100%.

Moreover, in the evaluation of morphological subtypes of cholangiocarcinoma (nodular, periductal infiltrating, and intraductal growing types), exact typing was reportedly possible by MDCT with an accuracy of 78.6%. Particularly, as a combination of transverse and coronal images more accurately reflects pathological features of the tumor than transverse images alone, high-quality multiplanar reconstruction (MPR) images in MDCT have been suggested to facilitate the evaluation of the anatomy of the biliary system and extent of tumor invasion, and the evaluation with the addition of MPR images is recommended.

**Index words and secondary materials used as references**

A search of PubMed was performed using “CT” and “extrahepatic cholangiocarcinoma” as key words. Evidence-Based Imaging (Springer), 2011 was also used as a reference.

**References**

Figure: Invasive cholangiocarcinoma

A  On MDCT/MPR imaging, contrast enhancement of the thickened wall is observed from the upper biliary tract to the right and left hepatic ducts (→).

B  In the transverse image of MDCT, circumferential wall thickening is noted with dilatation of the intrahepatic bile duct (→).
Are MRI and MRCP appropriate when cholangiocarcinoma is suspected?

MRI and MRCP are useful for the diagnosis of cholangiocarcinoma and are recommended.

Background/objective

Generally, for the diagnosis of cholangiocarcinoma, CT and MRI as well as abdominal ultrasonography are performed as non-invasive examinations, and there have been a number of reports on their usefulness. MRI of the abdominal region has continued to be improved with the recent innovations in hardware and software. The role of MRI and MRCP in the diagnosis of cholangiocarcinoma is evaluated.

Comments

MRCP can clearly visualize the entire biliary system compared with ultrasonography and is excellent in identifying the site of obstruction. It can also delineate the normal common bile duct in 98% or more of the patients. According to a meta-analysis concerning the presence diagnosis of benign or malignant bile duct obstruction and determination of the sites of obstruction, the sensitivity was 97 and 98%, respectively. In other studies, also, the accuracy was 95-100% and 97-100%, respectively. Also, unlike other techniques for direct imaging of the bile duct such as ERCP and PTC, MRCP is useful for imaging of the dilated bile duct proximal to the site of stenosis and excels, particularly, in the visualization of the stenotic area and diagnosis of multiple bile duct stenoses. While MRCP is highly accurate in the diagnosis of bile duct obstruction and identification of the obstruction sites, its accuracy in the qualitative diagnosis of bile duct obstruction is presently not considered sufficient. There have been a report that the sensitivity of MRCP for the discrimination of benign and malignant diseases was 88% and another report that its sensitivity, specificity, and accuracy for the detection of cholangiocarcinoma were 74.3, 71.4, and 73.2%, respectively. The recent improvements in the performance of MR devices and development of imaging techniques including parallel imaging have contributed to the shortening of the scanning time and improvements in the SNR and spatial resolution and have advanced the MRI diagnosis in the abdominal region.

Particularly, diffusion-weighted imaging is widely applied today to clinical practice. The detection rate of cholangiocarcinoma by this modality has been reported to be significantly higher than that by MRCP with sensitivity, specificity, and accuracy of 94.3, 100, and 96.4%, respectively. According to an evaluation concerning the delineation of cholangiocarcinoma by dynamic study combined with 3D fat-suppressed imaging at 3T, tumors and surrounding structures could be clearly visualized, and the procedure was useful for the evaluation of vascular obstruction/stenosis and tumor invasion and, with the addition of coronal images, contributed to the evaluation of the growth pattern of tumors and longitudinal extent of tumor invasion. Although the diagnostic ability of MRI for cholangiocarcinoma is suggested to be improved by diffusion-weighted imaging and fat-suppressed dynamic study using 3D imaging technique including coronal views as well as MRCP (Figure), further evaluation is considered necessary.

Index words and secondary materials used as references

A search of PubMed was performed using “MRI” and “extrahepatic cholangiocarcinoma” as key words. Evidence-Based Imaging (Springer), 2011 was also used as a reference.
Figure: Invasive cholangiocarcinoma
A MRCP/3D showed a defect in the hilar bile duct and marked dilatation of the intrahepatic bile duct (→).
B On LAVA (3T)/coronal imaging, contrast enhancement is observed in the thickened wall from the upper bile duct to the left and right hepatic ducts (→).
C On DWI, a hyperintense area is noted at the site of the tumor (→).

References
9) Xing-Yu Cui et al: Role of diffusion-weighted magnetic resonance imaging in the diagnosis of extrahepatic cholangiocarcinoma. World J Gastroenterol 16: 3196-3201, 2010 (Level 4)
10) Li N et al: MRCP and 3D LAVA imaging of extrahepatic cholangiocarcinoma at 3 T MRI. Clin Radiol 67: 579-586, 2012 (Level 4)
Are CT and MRI appropriate for the discrimination between cholangiocarcinoma and cholangitis?

**Recommendation grade**

No clear evidence has been reported regarding the usefulness of CT/MRI for the discrimination between cholangiocarcinoma and cholangitis. However, it is important to detect tumors and evaluate findings suggestive of cholangiocarcinoma such as metastatic foci including lymph node metastasis and vascular invasion.

**Background/objective**

Reports on the discrimination between benign and malignant diseases by CT/MRI in patients suspected to have biliary tract stenosis are few, and the discrimination is often clinically difficult. The usefulness of these modalities for the discrimination of benign and malignant diseases is evaluated on the basis of reports on CT/MRI findings in cholangiocarcinoma and cholangitis.

**Comments**

Generally, for the diagnosis of biliary tract stenosis due to malignant tumors, it is important to detect tumors and metastatic foci including lymph node metastases and vascular invasion.\(^1\) Also, it has been reported that many benign stenoses including traumatic and non-traumatic ones are characteristically short in extent, smooth, and symmetric, but dilatation of the bile duct proximal to the site of stenosis is more notable in malignant biliary tract stenoses and the extent of stenosis tends to be longer than in benign stenoses.\(^2\) On the other hand, primary sclerosing cholangitis causing diffuse bile duct stenosis has been reported to be characterized by multifocal bile duct stenoses/dilatations and to have been accurately diagnosed by MRCP in 90% or more of the patients.\(^5\) Clinically, however, the discrimination of benign and malignant diseases is not always easy, and the discrimination of primary sclerosing cholangitis and sclerosing cholangitis related to autoimmune (IgG4-related) pancreatitis from cholangiocarcinoma is often difficult.\(^7\) Concerning sclerosing cholangitis related to autoimmune pancreatitis, in particular, it has recently been reported that the disease shows significant differences in the extent of stenosis and maximum diameter of the part of the bile duct showing wall thickening, that wall thickening is eccentric in cholangiocarcinoma but concentric in cholangitis, and that this difference contributes to their discrimination.\(^10\) According to another report, however, no significant difference was noted in these respects, the extent of the area of wall thickening was significantly longer in cholangitis, and the area of stenosis was not necessarily in agreement with the area of wall thickening, contradicting with previous reports.\(^11\) Moreover, the frequency of skip lesions has been reported to be higher in cholangitis than in cholangiocarcinoma,\(^11\) but there have been no consistent findings concerning the discrimination between the two disorders.

Recently, with technological innovations in hardware and software of CT/MRI, high-quality MPR and 3D images of MDCT and diffusion-weighted imaging and fat-suppressed 3D dynamic study including coronal views have been suggested to contribute to improvements in the diagnosis of disorders of the biliary system (Figure).\(^12\) Further evaluation is considered necessary for the future.

**Index words and secondary materials used as references**

A search of PubMed was performed using “CT”, “MRI”, “extrahepatic cholangiocarcinoma”, and “cholangitis” as key words. Evidence-Based Imaging (Springer), 2011 was also used as a reference.
The Japanese imaging guideline 2013

References

1) Choi SH et al: Differentiating malignant from benign common bile duct stricture with multiphasic helical CT. Radiology 236: 178-183, 2005 (Level 4)
2) Rosch T et al: A prospective comparison of the diagnostic accuracy of ERCP, MRCP, CT, and EUS in biliary strictures. Gastrointest Endosc 55: 870-876, 2002 (Level 4)
3) Park MS et al: Differentiation of extrahepatic bile duct cholangiocarcinoma from benign stricture: findings at MRCP versus ERCP. Radiology 233: 234-240, 2004 (Level 4)
6) Textor HJ et al: Three-dimensional magnetic resonance cholangiopancreatography with respiratory triggering in the diagnosis of primary sclerosing cholangitis: comparison with endoscopic retrograde cholangiography. Endoscopy 34: 984-990, 2002 (Level 4)
7) Hayashi K et al: Autoimmune sclerosing cholangiopancreatitis with little pancreatic involvements by imaging findings. Hepatogastroenterology 54: 2146-2151, 2007 (Level 4)
14) Ahmetoglu A et al: MDCT cholangiography with volume rendering for the assessment of patients with biliary obstruction. AJR 183: 1327-1332, 2004 (Level 4)
16) Xing-Yu Cui et al: Role of diffusion-weighted magnetic resonance imaging in the diagnosis of extrahepatic cholangiocarcinoma. World J Gastroenterol 16: 3196-3201, 2010 (Level 4)
Is CT appropriate when gallbladder cancer is suspected?

**Background/objective**

While abdominal ultrasonography (US) is commonly used for screening of gallbladder lesions, MDCT has recently become widely available in clinical practice to provide images with high spatial resolution, and the degree of contribution of CT to the diagnosis of gallbladder lesions has increased. When gallbladder cancer is suspected, the usefulness of CT for the differentiation of benign and malignant diseases and determination of the therapeutic strategy was evaluated.

**Comments**

When gallbladder cancer is suspected, it is the most important first to differentiate benign and malignant diseases. According to a report comparing CT and EUS, the sensitivity and specificity of EUS were 86 and 87%, and those of CT were 72 and 91%, respectively, being in favor of EUS. Particularly, CT shows a high specificity of 94% for early intramural gallbladder cancer but a considerably low sensitivity of 33%, and the diagnosis is difficult even with the exhaustive use of MPR images by multislice CT. While polypoid lesions can be diagnosed with relatively high accuracy using morphological criteria (size>1 cm, wide-based), the ability of CT is insufficient to distinguish benign and malignant lesions with diffuse wall thickening.

The evaluation of the local depth of the lesion is important for the determination of the surgical procedure and prognosis. According to reports to date, the accuracy of T staging by CT is relatively high at 71-93%, but EUS, which visualizes the laminar structure of the gallbladder wall, is superior in evaluating intramural lesions (≤ T2) (Figure). However, concerning T3 or more advanced lesions showing invasion beyond the serosa such as direct intrahepatic invasion and invasion to the bile duct side, there are many reports that CT is superior with a sensitivity of 80-100% and a specificity of 81-95% compared with EUS, which has limitations in the scanning area, and that it is useful for the determination of the surgical procedure.

CT is superior to other modalities in evaluating the presence or absence of involvement of the portal vein or arteries and distant metastases including lymph node and liver metastases, which is important for the determination of the therapeutic approach to advanced cancers. However, concerning lymph node metastases, judgments are presently dependent on the size (≥ 1 cm) and morphology (round), and the accuracy has been less than 80% in many reports to date.

To summarize the above observations, if gallbladder cancer is intramural (≤ T2), the usefulness of CT, with a limited ability to delineate the laminar structure of the gallbladder wall, is insufficient for its discrimination from benign diseases or evaluation of its depth. However, if the lesion has spread beyond the serosa (≥ T3), CT is equally or more useful than other modalities for the evaluation of involvement of surrounding organs, lymph node metastasis, and distant metastasis. It is indispensable for the determination of the surgical procedure or therapeutic strategy for advanced cancers.

**Index words and secondary materials used as references**

A search of PubMed was performed using “gallbladder”, “cancer”, “carcinoma”, and “CT” as key words. Papers considered useful among those cited in the initially selected materials were adopted as additional references.
Figure: Gallbladder cancer Dynamic contrast-enhanced CT

A Early phase  B Delayed phase: An elevated lesion protruding into the lumen is observed in the wall of the gallbladder body on the abdominal cavity side. The tumor was relatively well-enhanced in the early phase, and delayed enhancement was noted at the base of the elevated lesion (→). Such findings on MRI have been reported to be possible signs of subserosal invasion, but those on CT may also be useful. (Yoshimitsu K et al: Magnetic resonance differentiation between T2 and T1 gallbladder carcinoma: significance of subserosal enhancement on the delayed phase dynamic study. Magn Reson Imaging, 2012)

References

2) Yoshimitsu K et al: Helical CT of the local spread of carcinoma of the gallbladder: evaluation according to the TNM system in patients who underwent surgical resection. AJR 179: 423-428, 2002 (Level 2)
5) Kim SJ et al: Accuracy of preoperative T-staging of gallbladder carcinoma using MDCT. AJR 190: 74-80, 2008 (Level 4)
8) Sadamoto Y et al: Preoperative diagnosis and staging of gallbladder carcinoma by EUS. Gastrointest Endosc 58: 536-541, 2003 (Level 3)
When gallbladder cancer is suspected, MRI provides information useful for the qualitative diagnosis of the lesion and determination of the therapeutic strategy and should be considered.

**Background/objective**

While extracorporeal ultrasonography (US) is widely used for screening of gallbladder lesions, MRI has also become a more routine examination than before with improvements in spatial resolution due to advances in MRI technology. The high contrast resolution characteristic of MRI may contribute to the diagnosis of gallbladder lesions. The usefulness of MRI for the differentiation of benign and malignant lesions and determination of treatment when gallbladder cancer is suspected is summarized.

**Comments**

When gallbladder cancer is suspected, it is the most important first to discriminate benign and malignant lesions. In polyoid lesions, it has been reported that the lesions are suspected to be malignant when delayed phase enhancement is observed on dynamic contrast-enhanced imaging, but the diagnosis presently depends on morphological criteria (size>1 cm, wide-based). Concerning lesions showing diffuse wall thickening, MRI is not considered to have a sufficient ability for qualitative diagnosis except for lesions that show clear extramural invasion. According to a recent evaluation, the ability of diffusion-weighted imaging to discriminate benign and malignant lesions is presently considered insufficient, with sensitivity and specificity being both 78%. However, the delineation of Rokitansky-Aschoff sinus (RAS) by MRCP is useful for the differentiation of gallbladder cancer from gallbladder adenomyomatosis.

The evaluation of the local depth is important for the determination of the surgical procedure and prognosis. In lesions showing extraserosal spread such as direct intrahepatic invasion and invasion to the bile duct side, the sensitivity and specificity of MRI are high at 67-100 and 86-100%, respectively, which are similar to those of CT, and many reports suggest the usefulness of MRI for the determination of the surgical procedure. Regarding intramural lesions, the evaluation has been conventionally considered difficult by MRI as well as CT, but, due to the recent improvements in spatial and temporal resolutions in addition to the high contrast resolution, it has been reported that T1 and T2 lesions could be diagnosed with sensitivity and specificity of 86 and 88%, respectively, based on delayed phase enhancement of the subserosal layer on dynamic contrast-enhanced MRI.

Similarly to CT, MRI excels other modalities in the evaluation of the presence or absence of portal and arterial invasion and distant metastases such as lymph node and liver metastases, which are important for the determination of surgical indications in advanced cancers. However, MRI is slightly inferior to CT in the area that can be scanned at a time and preoperative evaluation of detailed anatomical orientation of the lesion.

To summarize the above observations, MRI is excellent in the evaluation of extraserosal spread of lesions such as invasion to surrounding organs and lymph node and distant metastases similarly to CT, but it is slightly inferior to CT in the scanning area and preoperative evaluation of detailed anatomical orientation of the lesion. While its usefulness does not surpass that of CT at present, improvements in its usefulness for the qualitative diagnosis are expected due to dynamic contrast-enhanced imaging by diffusion-weighted and 3D imaging techniques (Figure).

**Index words and secondary materials used as references**

A search of PubMed was performed using “gallbladder”, “cancer”, “carcinoma”, and “MRI” as key words. Also, papers considered useful among those cited in the initially selected materials were used as additional references.
References

2) Ogawa T et al: High b-value diffusion-weighted magnetic resonance imaging for gallbladder lesions: differentiation between benignity and malignancy. J Gastroenterol 47: 1352-1360, 2012 (Level 4)

Figure: Gallbladder cancer with liver invasion
A Contrast-enhanced MRI  B Contrast-enhanced CT: A lesion showing irregular diffuse wall thickening is observed in the fundus of the gallbladder. Contrast enhancement of the mucosa is interrupted, and direct invasion to the liver bed is noted.
Are CT and MRI appropriate for the discrimination between gallbladder cancer and cholecystitis?

The diagnosis of diffuse wall thickening type gallbladder cancer and cholecystitis, particularly xanthogranulomatous cholecystitis, by CT and MRI is still often difficult. However, discriminating findings have been reported, and these modalities should be considered.

**Background/objective**

Symptoms and clinical findings of gallbladder cancer and cholecystitis often overlap, and their differential diagnosis is frequently difficult. However, they are diseases completely different in treatment and prognosis, and it is very important to more accurately discriminate them. The usefulness of CT and MRI for the discrimination between gallbladder cancer and cholecystitis is summarized on the basis of the reports to date.

**Comments**

If gallbladder cancer presents as a polypoid lesion, it poses little problem in the discrimination from cholecystitis, and its differentiation from benign polyps is a greater problem. However, if it is a diffuse wall thickening type, it is important to discriminate it from cholecystitis. Regarding points of differentiation, uneven wall thickening, interruption of contrast enhancement on the mucosal surface, and invasion to surrounding tissues have been reported to suggest gallbladder cancer, and the presence of gallstones and intramural defects of contrast enhancement suggesting intramural abscesses as findings indicating cholecystitis.\(^1\,2\) It has also been reported that gallbladder cancer is more often visualized in the early phase of dynamic imaging,\(^3\) shows uneven contrast enhancement of the wall, presents stronger contrast enhancement on the luminal side of the thickened wall,\(^4\) or is hyperintense (reduced ADC) at diffusion-weighted imaging.\(^5\) In practice, however, its discrimination from chronic cholecystitis is often difficult, and its differentiation from xanthogranulomatous cholecystitis in particular is even more difficult. According to reports to the present, diffuse wall thickening (sensitivity: 89%, specificity: 65%), continuity of the mucosa (sensitivity: 61%, specificity: 71%), hypodensity in the thickened wall (sensitivity: 67%, specificity: 71%), lack of invasion to the liver bed (sensitivity: 72%, specificity: 77%), and lack of intrahepatic bile duct dilatation (sensitivity: 67%, specificity: 71%) have been useful for the differentiation between gallbladder cancer and xanthogranulomatous cholecystitis, and the sensitivity and specificity were 83 and 100%, respectively, when at least 3 of these findings were present.\(^6\,8\) There are also reports that fat in xanthogranuloma could be detected by chemical shift imaging.\(^9,10\) In practice, however, findings frequently overlap, making their differential diagnosis difficult. It is also important to note that the presence or absence of metastatic foci such as lymph node metastasis can be a point of differentiation although it is an indirect finding.

At present, CT and MRI allow the discrimination between gallbladder cancer and cholecystitis, particularly xanthogranulomatous cholecystitis, to some extent, but the findings often overlap (Figure). Therefore, it is often impossible to exclude gallbladder, and the dependence on surgical resection persists due to the difficulty in precise differentiation.

**Index words and secondary materials used as references**

A search of PubMed was performed using “gallbladder”, “cancer”, “cholecystitis”, and “CT or MRI” as key words. Papers considered useful among those cited in the initially selected materials were also adopted as additional references.
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Figure: Xanthogranulomatous cholecystitis
A Contrast-enhanced CT  B Contrast-enhanced MRI  C MRI T2-weighted imaging
Marked wall thickening and a large number of defects of contrast enhancement suggestive of intramural abscesses are observed. Gallstones are noted in the areas considered to be the lumen. The disease was confirmed as xanthogranulomatous cholecystitis by surgery.

References

5) Ogawa T et al: High b-value diffusion-weighted magnetic resonance imaging for gallbladder lesions: differentiation between benignity and malignancy. J Gastroenterol 47: 1352-1360, 2012 (Level 4)
Is contrast-enhanced CT appropriate for diagnosis and assessment of severity in acute pancreatitis?

**Recommendation grade**

Contrast-enhanced CT is strongly recommended for the diagnosis and severity assessment of acute pancreatitis.

- **Background/objective**

  Acute pancreatitis is classified as acute abdomen. It is acute inflammation of the pancreatic parenchyma and is divided into mild cases that can be managed by conservative treatment and severe cases in which inflammation is not localized in the pancreatic parenchyma but spreads to tissues and organs not only around, but also distant from, the pancreas, and fatal complications such as systemic circulatory insufficiency, multiple organ failure, and severe infections develop due to systemic inflammatory response syndrome (SIRS). Imaging modalities play an important role in the evaluation of complications affecting the whole body as well as the state of the pancreas itself. If the disease follows a serious course, the mortality rate is very high, and the assessment of disease severity is closely related to the appropriateness of the selection of treatments.

- **Comments**

  Acute pancreatitis is frequently manifest as an edematous pancreas and responds to conservative treatments. However, about 20% of the cases are classified as severe acute pancreatitis, showing systemic inflammatory changes and subsequently developing various complications, with a high mortality rate. If the diagnosis of acute pancreatitis cannot be confirmed, or if the cause of pancreatitis cannot be identified by clinical findings, blood tests, and urinalysis, CT should be performed readily.

  CT provides objective images of a wide area of the body without being affected by gas in the gastrointestinal tract or adipose tissue in the abdominal wall or cavity and is suitable for the evaluation of not only pancreatic necrosis and changes around the pancreas but also complications extending to other parts. CT is used for the severity assessment as well as diagnosis of acute pancreatitis as mentioned below, and contrast-enhanced CT is recommended, if possible. If the condition is mild edematous pancreatitis, the only findings on contrast-enhanced CT are homogeneous delineation of the pancreatic parenchyma, normal-sized or only mildly enlarged pancreatic parenchyma itself (Figure 1), and slight hyperdensity of the adipose tissue around the pancreas. Local edema extends along the mesentery, mesocolon, and hepatoduodenal ligament to the abdominal cavity, and typical CT findings are enlargement of the pancreas, increased fat density in tissues around the pancreas to the retroperitoneal cavity (primarily, the anterior pararenal space), mesocolon, and mesentery proper, exudate retention (Figure 2), pseudocyst formation, heterogeneous density of the pancreatic parenchyma, pancreatic necrosis (Figure 3), fat necrosis of the retroperitoneal cavity and mesentery, hematoma, and pancreatic rupture on injury. Gas in and around the pancreas is often caused by fistula formation to the intestine or infection by gas-producing microorganisms (Figure 4). In more distant areas, bilateral pleural effusion and atelectasis may also occur. Indications of contrast-enhanced CT should be evaluated in consideration of the history of allergy to contrast agents and renal function.

  The criteria for assessment of severity in acute pancreatitis by the Ministry of Health, Labour and Welfare (2008) consist of 9 prognostic factors and also mention the contrast-enhanced CT grade as an independent item. These assessment criteria are also adopted in the guidelines for the management of acute pancreatitis: JPN guidelines 2010, and the disease is judged to be severe when the prognostic factor score is 3 or higher, or the contrast-enhanced CT grade is 2 or higher. Since the presence or absence of pancreatic necrosis and extrapancreatic spread of inflammation are closely related to the frequency of the occurrence of complications and mortality rate, these factors are incorporated in the contrast-enhanced CT grade. For contrast-enhanced CT grading, the pancreatic parenchyma is divided into 3 segments for convenience, i.e. the head, body, and tail, poorly enhanced areas are regarded as necrotic areas, and the extent of necrotic areas is reflected in the grade. Also, the extent of extrapancreatic spread of inflammation is added to the assessment as another factor, and the grade elevates as inflammation extends to the anterior pararenal space, to the base of the mesocolon, and to areas beyond the lower pole of the kidney. Advantages of contrast-enhanced CT are its usefulness for the diagnosis of complications such as pseudocysts, abscesses, mesenteric hemorrhage, non-obstructive mesenteric ischemia, false aneurysms, and portal thrombosis and its excellence in delineation of pancreatic duct stenosis due to small pancreatic cancers, which may cause acute pancreatitis, in addition to the evaluation of the area of intra- and extra-pancreatic spread mentioned above.
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Index words and secondary materials used as references


References

4) O’Connor OJ et al: Imaging of acute pancreatitis. AJR 197: W221-225, 2011 (Level 5)

Figure 1: Acute edematous pancreatitis (CT Grade 1)
On contrast-enhanced CT, the entire pancreatic parenchyma is enlarged, but no clear hypo-enhanced area is noted. Effusion (*) is observed around the pancreas, and a diagnosis of acute pancreatitis with a CT Grade of 1 can be made.

Figure 2: Severe acute pancreatitis (CT Grade 2)
While the entire pancreatic parenchyma is enlarged, no clear hypo-enhanced area is noted. Fat necrosis (*) is observed in the transverse mesocolon and anterior pararenal space and extends beyond the lower pole of the kidney. A diagnosis of severe acute pancreatitis of CT Grade 2 can be made.
5. Gastrointestinal tract

Figure 3: Severe acute pancreatitis (CT Grade 3)
The entire pancreatic parenchyma is enlarged, and hypo-enhanced areas are observed in the body and tail of the pancreas. Fat necrosis (*) extends beyond the lower pole of the kidney, and a diagnosis of severe acute pancreatitis of CT Grade 3 can be made.

Figure 4: Infectious pancreatic necrosis
The head of the pancreas is enlarged, and hypo-enhanced areas are observed in the body. Gas (→) is noted in the area of necrosis, and infectious pancreatic necrosis was demonstrated by FNA.

Is CT appropriate for the diagnosis of chronic pancreatitis?

CT is useful and is recommended. However, close examination by modalities such as EUS is necessary for the diagnosis of early chronic pancreatitis.

Background/objective

In Japan, the Clinical Diagnostic Criteria for Chronic Pancreatitis have been used for the diagnosis of chronic pancreatitis. The criteria were revised in 2009, incorporating the concept of early chronic pancreatitis. The usefulness of CT for the diagnosis of chronic pancreatitis is evaluated in consideration of the revised diagnostic criteria.

Comments

Chronic pancreatitis is defined as “a pathological condition in which chronic changes such as irregular fibrosis, cell infiltration, parenchymal loss, and granulation occur in the interior of the pancreas and cause pancreatic exocrine and endocrine dysfunctions.” The disease is often irreversible and is classified into alcoholic and non-alcoholic depending on the etiology. Autoimmune and obstructive pancreatitis, which are reversible, are presently handled separately as chronic inflammation of the pancreas.

According to international reports on the diagnosis of chronic pancreatitis, the sensitivity and specificity of CT for the diagnosis of chronic pancreatitis are 74-91 and 78-98%, respectively.1-3) The sensitivity and specificity for diffuse calcification of the pancreas have been reported to be 53 and 94%, and those for pancreatic calculus to be 43 and 88%, respectively.4) Because of the high specificity, CT is considered useful for the diagnosis (Figure).

The pathological concept of early chronic pancreatitis was incorporated in the diagnostic criteria during the last revision on the basis of the Rosemont classification, international endoscopic ultrasound (EUS)-based criteria for the diagnosis of chronic pancreatitis. According to these criteria, patients who cannot be diagnosed with definite or probable chronic pancreatitis are diagnosed to have suspected chronic pancreatitis when two or more of 4 clinical findings are fulfilled: “Recurrent attacks of upper abdominal pain”, “abnormal blood or urinary pancreatic enzyme levels”, “pancreatic exocrine insufficiency”, and “sustained drinking of 80 g/day or more as pure ethanol”. For such patients with suspected chronic pancreatitis, early (within 3 months) further examination by EUS or ERCP is recommended, and a diagnosis of early chronic pancreatitis is made when imaging findings shown in the table are obtained. The Rosemont classification is based on EUS findings, and CT findings are not included in the diagnostic criteria for early chronic pancreatitis in this revision. In foreign countries CT has been reported to be less sensitive5,6) and to have limited diagnostic ability7,8) for early chronic pancreatitis compared with EUS or ERCP. By the Clinical Diagnostic Criteria for Chronic Pancreatitis 2009, EUS is performed first for the imaging diagnosis of early chronic pancreatitis in consideration of incidental diseases, and ERCP is performed when necessary for symptomatic patients strongly suspected to have pancreatic lesions. Therefore, close examination by modalities such as EUS is useful for the imaging diagnosis of early chronic pancreatitis. While the new diagnostic criteria are epoch-making in that they opened the way to the early diagnosis/early treatment by the introduction of the concept of early chronic pancreatitis, the diagnostic criteria for early chronic pancreatitis are not based on sufficient data, and the diagnostic value and validity of CT also need further evaluation through accumulation of cases.

Index words and secondary materials used as references

5. Gastrointestinal tract

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Figure: Chronic pancreatitis
A Non-contrast CT (axial view): The pancreatic parenchyma is atrophied, and the main pancreatic duct is dilated (→). Calcification foci are scattered over the pancreatic parenchyma (small →). B Contrast-enhanced CT (arterial phase, oblique image): A pancreatic calculus is observed in the main pancreatic duct (→).

Table: Imaging findings of early chronic pancreatitis (cited from the Japanese clinical diagnostic criteria for chronic pancreatitis 2009)

<table>
<thead>
<tr>
<th>Either a or b is observed.</th>
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</thead>
<tbody>
<tr>
<td>a. Of the 7 EUS findings shown below, 2 or more including at least one of (1)-(4) are noted.</td>
</tr>
<tr>
<td>(1) Lobularity, honeycombing type</td>
</tr>
<tr>
<td>(2) Nonhoneycombing lobularity</td>
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<tr>
<td>(3) Hyperechoic foci (non-shadowing)</td>
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<tr>
<td>(4) Stranding</td>
</tr>
<tr>
<td>(5) Cysts</td>
</tr>
<tr>
<td>(6) Dilated side branches</td>
</tr>
<tr>
<td>(7) Hyperechoic MPD margin</td>
</tr>
<tr>
<td>b. Irregular dilatation of 3 or more side branches on ERCP.</td>
</tr>
</tbody>
</table>

References
8) Aoun E et al: Rapid evolution from the first episode of acute pancreatitis to chronic pancreatitis in human subjects. JOP 8: 573-578, 2007 (Level 4)
Is CT appropriate for the diagnosis and severity assessment of pancreatic fistula?

While the evidence is deficient, CT is used widely for the severity assessment of pancreatic fistula and should be considered. (There is no relevant literature concerning the diagnosis.)

Background/objective
Pancreatic fistula is a pathologic condition in which pancreatic juices leak out of the pancreatic duct. The degrees of contribution of CT to the diagnosis and severity assessment were evaluated.

Comments
Pancreatic fistula occurs primarily as a postoperative complication or is caused by chronic pancreatitis, acute pancreatitis, or pancreatic injury. Pancreatic fistulae are classified into external and internal fistulae (extra- and intracorporeal leakage of pancreatic juices, respectively).

Since pancreatic fistulae frequently develop as a postoperative complication, the usefulness of CT primarily for the evaluation of postoperative pancreatic fistulae is discussed in this article.

There used to be no standard diagnostic criteria for pancreatic fistulae, but the International Study Group on Pancreatic Fistula (ISGPF) first showed clinical diagnostic criteria in 2005.¹

According to these criteria, pancreatic fistula is defined as “a condition in which the amylase level in the drained fluid is 3 or more times higher than the normal serum amylase level on the third postoperative day or thereafter.”

Fistulae in agreement with these diagnostic criteria are also classified into Grades A (no clinical symptom), B (there are signs of infection, but the management by conservative treatment is possible), and C (serious pancreatic fistula complicated by intraperitoneal hemorrhage or sepsis, and care in the ICU or re-operation is necessary).

Performing CT postoperatively for the evaluation of the presence or absence of pancreatic fistula is controversial. Some perform routine postoperative CT examination, but others refute it, because the discrimination between postoperative fluid retention and pancreatic fistula is impossible. Recently, there have been positive reports about the usefulness of CT due to its contribution to the clinical diagnosis of pancreatic fistula.²⁻³ Hashimoto et al. maintained that retention of fluid, particularly fluid containing air bubbles, at the site of pancreaticojejunal anastomosis or drainage from the pancreatic bed demonstrated by CT after pancreaticoduodenectomy strongly suggests pancreatic fistula.² Bruno et al. reported that fluid retention after surgery is likely to suggest pancreatic fistula and that CT occasionally suggests clinically unclear pancreatic fistula.³

There was no mention as to whether or not CT is useful for the severity assessment of pancreatic fistula in the papers found by our search.

Index words and secondary materials used as references
A search of PubMed was performed using “pancreas”, “fistula”, and “CT” as key words.

References
2) Hashimoto M et al: CT features of pancreatic fistula after pancreaticoduodenectomy. AJR 188: 323-327, 2007 (Level 4)
What are imaging modalities appropriate for the detection of pancreatic cancer?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td><strong>B</strong></td>
<td>Dynamic CT is recommended. The evaluation should be made by dynamic CT, using pancreatic-parenchymal and portal-venous phase images at a slice thickness of 2-3 mm. If only secondary signs are observed, the addition of delayed phase imaging, dynamic imaging using MRI or US, EUS, or PET is desirable.</td>
</tr>
</tbody>
</table>

**Background/objective**

Resection is the only curative treatment for pancreatic cancer. However, small pancreatic cancers are often asymptomatic and are overlooked by imaging studies. Many lesions are unresectable at the diagnosis, and this is the primary reason for the poor prognosis. Imaging modalities useful for the detection of pancreatic cancer in patients suspected to have, or at a high risk for, the disease are evaluated.

**Comments**

Relatively non-invasive imaging modalities used for detecting pancreatic cancer include US, CT, and MRI dynamic studies. While all these methods are generally satisfactory for the detection of cancers 20 mm or greater in diameter showing extrapancreatic spread, CT is commonly regarded as the first choice, unless there are contraindications, because of the consistency of the image quality and high objectivity of MDCT.

To find a hypoattenuating mass, which is the finding on contrast-enhanced CT most useful for detecting pancreatic cancer, pancreatic-parenchymal and portal-venous phase imaging is recommended. Since image reading experiments have shown that the concomitant use of the coronal view and curved MPR significantly improves the diagnostic performance for pancreatic cancer, it is desirable to perform MDCT at a detector thickness of 1.25 mm or less and prepare 2-3 mm thick horizontal views and MPR images for the evaluation.

Pancreatic-parenchymal phase imaging, in which the pancreas shows maximum enhancement, is important to obtain satisfactory contrast between cancer and pancreatic parenchyma. While satisfactory pancreatic-parenchymal phase images can be usually obtained by injecting a contrast agent at 300 mgI/mL at a volume of 1.5-2 mL/kg of body weight over 30 seconds and scanning about 40 seconds after the beginning of the administration of the contrast agent, bolus tracking is frequently employed to cope with individual variation in hemodynamics. At image reading, it is important to check whether the images are adequate pancreatic-parenchymal phase images, the marks of which are enhancement of the aorta slightly after the peak and strong enhancement of the splenic-portal veins.

Regarding overlooking of pancreatic cancer by CT, images suggestive of cancer were reportedly obtained 6-18 months before it was diagnosed in more than 50% of the patients, and the detection rate of pancreatic cancer 20 mm or less in diameter by dynamic CT was 77% (14/18). By dynamic studies using MDCT, 5.4% (35/644) of cancers and 27% (16/59) of those 20 mm or less in diameter were reported to be isoattenuating with the surrounding parenchyma, making diagnosis impossible. Histological characteristics of such cancers are considered to be a diameter of 20 mm or less, high degree of differentiation, and persistence of acinar tissue and islet cells in the tissue. Staining in the delayed phase is useful for their detection, and attention to findings such as interruption of the main pancreatic duct, dilatation of the pancreatic or bile duct or atrophy of the parenchyma in the upstream of the mass, and changes in the morphology at the mass is necessary. It has been reported that 79.2% (19/24) and 73.7% (14/19) of isoattenuating tumors were detected by MR and PET/CT, respectively (Figure).

The abilities of MRI and US dynamic studies to detect pancreatic cancer are reported to be comparable to, or higher than, that of CT, and that EUS, which is more invasive, is reported to have higher detecting ability than MDCT, but there is no study that strictly compared their abilities to detect resectable cancers 20 mm or less in diameter with that of MDCT, and further evaluation is needed with this respect. However, as US and MRI are more sensitive than CT due to the difference in contrast enhancement, they should be performed when only secondary signs have been detected by CT. The sensitivity and specificity of PET/CT for the detection of pancreatic cancer have been reported to be 89% (41/46) and 69% (9/13), respectively, and, despite problems with the detection of small cancers and uptake by inflammatory masses, it is worth attempting in patients showing equivocal CT images.

**Index words and secondary materials used as references**

A search of PubMed was performed using “pancreatic adenocarcinoma”, “computed tomography”, “magnetic resonance imaging”, “ultrasonography”, and “positron emission tomography” as key words.
Figure: Dynamic CT of pancreatic cancer
In the pancreatic parenchymal phase (A), the entire area is evenly enhanced, and the hypoattenuating mass is unclear. In the delayed phase (B), a mass that shows more intense enhancement than the pancreatic parenchyma (→) is clearly observed.

References
7) Gangi S et al: Time interval between abnormalities seen on CT and the clinical diagnosis of pancreatic cancer: retrospective review of CT scans obtained before diagnosis. AJR 182: 897-903, 2004 (Level 3)
9) Kim JH et al: Visually isoattenuating pancreatic adenocarcinoma at dynamic-CT: frequency, clinical and pathologic characteristics, and diagnosis at imaging examinations. Radiology 257: 87-96, 2010 (Level 2)
10) Yoon SH et al: Small (<20mm) pancreatic adenocarcinoma: analysis of enhancement patterns and secondary signs with multiphasic multidetector CT. Radiology 259: 442-452, 2011 (Level 2)
11) Ishigami K et al: Diagnostic value of the delayed phase image for iso-attenuating pancreatic carcinoma in the pancreatic parenchymal phase on multidetector computed tomography. Eur J Radiol 69: 139-146, 2009 (Level 3)
Background/objective
For pancreatic cancer, surgery is the only curative treatment. The assessment of the local spread, lymph node metastasis, and distant metastasis by imaging modalities is very important in evaluating the need for surgery. The usefulness of CT, MRI, and PET/CT for the staging of pancreatic cancer was evaluated.

Comments
For the T staging (General Rules for the Study of Pancreatic Cancer), the size of the tumor and invasion to the intrapancreatic bile duct, duodenum, peripancreatic tissue, extrapancreatic nerve plexus, neighboring major vessels, and other organs must be evaluated. The assessment of invasion to posterior tissues, extrapancreatic nerve plexus, and blood vessels, which affects the therapeutic strategy and prognosis, is of particular importance. Regarding the diagnostic performance of dynamic CT, Mazzeo et al.\(^1\) reported that retroperitoneal fat tissue invasion could be diagnosed with a sensitivity of 80%, specificity of 84%, and accuracy of 82%, and, according to Mochizuki et al., those for extrapancreatic nerve plexus invasion were 100, 83, and 95%, respectively.\(^2\) Also, Lu et al.\(^3\) reported that the diagnostic sensitivity, specificity, and accuracy for vascular invasion, which was defined as contact with tumor over half the circumference or more of the vessel, were 84, 98, and 94%, respectively, suggesting high precision of CT for local staging of the disease. There is also a report that the diagnostic performance for local spread or vascular invasion was improved by the addition of MPR.\(^4\) Concerning MRI, peripancreatic tissue or vascular invasion was reported to have been diagnosed by 3D GRE dynamic MRI similarly to CT.\(^5\)\(^6\)

Concerning N staging, small regional lymph nodes may be metastatic and conversely large ones may be reactively enlarged. Roche et al.\(^7\) compared CT images and resected specimens of regional lymph nodes in resectable pancreatic cancer patients and reported that the sensitivity, specificity, and accuracy of the diagnosis of lymph node metastasis were 14, 85, and 73%, respectively, when lymph nodes with a short diameter of 10 mm or greater were assumed to be metastatic, indicating the low sensitivity of CT. Kauhanen et al.\(^8\) also reported the sensitivities of CT, MRI, and PET/CT for lymph node metastasis to be 30, 9, and 30%, respectively, with all these modalities being unsatisfactory in sensitivity.

As for M staging, the assessment of liver metastasis and peritoneal dissemination is particularly important. Motosugi et al.\(^9\) reported that the sensitivity for liver metastasis was 92-94% by Gd-EOB-DTPA contrast-enhanced MRI and 74-76% by CT (P=0.030-0.044), so the concomitant use of CT with more sensitive MRI is recommended for detecting liver metastasis. Regarding PET/CT, Kauhanen et al.\(^9\) reported its usefulness for the detection of distant metastasis with sensitivities of CT, MRI, and PET/CT being 38, 38, and 88%, respectively. Heinrich et al.\(^10\) also reported that unnecessary radical surgery could be avoided in 16% by performing PET in patients with pancreatic cancer judged to be resectable by modalities such as CT. However, according to Frohlich et al.,\(^11\) the sensitivity of PET for metastatic foci 1 cm or less in diameter was low at 43%, and Wakabayashi et al.\(^12\) also reported that the sensitivity of PET was not superior to that of CT for liver metastasis (53% by PET vs. 74% by CT) or peritoneal dissemination (43 vs. 57%). PET/CT is worth attempting for lesions difficult to assess by CT or MRI, but its necessity as a routine examination is controversial from the viewpoints of cost-effectiveness and exposure.

In predicting the resectability of pancreatic cancer, the abilities of CT and MRI have been reported to be comparable (Table). MRI may be used as a substitute for CT for local assessment, but as the thoracic to pelvic regions can be scanned at one time by CT, and as the vascular anatomy necessary for surgery can be readily evaluated by CTA, dynamic CT is considered to be the procedure to be performed first.

Index words and secondary materials used as references
A search of PubMed was performed using “pancreatic cancer”, “CT”, “MRI”, and “PET” as key words.
### Table: Resectability predicted by various modalities

<table>
<thead>
<tr>
<th>Author/year of report</th>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>Positive predictive value (%)</th>
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<td>63 ~ 75</td>
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<td>Lee JK et al&lt;sup&gt;13&lt;/sup&gt; 2010</td>
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<td>71 ~ 75</td>
<td>74 ~ 78</td>
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<tr>
<td></td>
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<td>90</td>
<td>59 ~ 65</td>
<td>80 ~ 82</td>
<td>83 ~ 85</td>
<td>71 ~ 73</td>
</tr>
</tbody>
</table>

### References

12. Wakabayashi H et al: Role of 18F-fluorodeoxyglucose positron emission tomography imaging in surgery for pancreatic cancer. World J Gastroenterol 14: 64-69, 2008 (Level 4)
Which are imaging modalities appropriate for the detection of pancreatic endocrine tumors?

Ultrasonography, endoscopic ultrasonography, dynamic CT, and dynamic MRI are recommended.

Background/objective

Pancreatic endocrine tumors can be divided into functional and non-functional types. Non-functional tumors are often detected after they have grown to a considerable size. Functional tumors are smaller in size and often multiple. CT is performed first when endocrine tumor is suspected. MRI and ultrasonography is frequently used for the qualitative diagnosis of lesions.

Comments

1) Ultrasonography

(1) Extracorporeal ultrasonography

Insulinoma is the most frequent functional endocrine tumor (accounting for about 60% of all endocrine tumors), and it is mostly a solitary lesion. It is often small, and the preoperative detection rate was reported to be 60%. Recently, its detection rate has been reported to have improved to about 80% due to the development of new technology.

(2) Endoscopic ultrasonography

In 2012, Fiebrich et al. reviewed the literature concerning pancreatic endocrine tumors published in 1995-2010 and evaluated their detectability by (1) examinations performed when hormonal abnormalities were present, (2) those performed to closely examine the pancreas when endocrine carcinoma had been demonstrated at sites other than the pancreas but as the primary lesion had not been identified, and (3) those performed for screening when gene abnormalities (such as MEN type 1 and Von Hippel Lindau disease) had been suggested. They concluded that endoscopic ultrasonography showed the highest detection performance in all 3 situations.

(3) Intraoperative ultrasonography

Small insulinomas that are isoechoic on extracorporeal ultrasonography are often difficult to detect preoperatively. Intraoperative ultrasonography may be indicated when endocrine tumor is clinically suspected due to symptoms but cannot be detected by extracorporeal ultrasonography, CT, or MRI. Intraoperative ultrasonography could reportedly detect such lesions in 86-100% of the patients.

2) Dynamic CT

Some authors are skeptical about the role of dynamic CT for the preoperative search for endocrine tumors. By MDCT, however, the detection of endocrine tumors has been facilitated by combining its high temporal and spatial resolutions with an intravenous bolus injection of the contrast agent (Figure), and preoperative detection sensitivities surpassing 80% have been reported. Particularly, imaging in the late arterial phase (also called pancreatic-parenchymal phase) performed about 40 seconds after the beginning of intravenous injection of the contrast agent has a high detection ability.

3) MRI

Contrast-enhanced dynamic MRI, reportedly with a preoperative sensitivity exceeding 80%, has been suggested to be an excellent modality. A manganese-based contrast agent, which cannot be used in Japan, has also been reported to be useful for detecting small insulinomas of the pancreas.

Each of the above examinations is useful for the detection of pancreatic endocrine tumors. In clinical practice, abdominal ultrasonography, dynamic CT, or dynamic MRI is recommended to be performed first when pancreatic endocrine tumor is suspected, followed by endoscopic or intraoperative ultrasonography if more detailed evaluation is considered necessary.

Index words and secondary materials used as references

A search of PubMed was performed using “pancreas, tumor, and ultrasound”, “pancreas, tumor, and CT”, and “pancreas,
tumor, and MRI as key words

References

2) Angeli E et al: Value of abdominal sonography and MR imaging at 0.5 T in preoperative detection of pancreatic insulinoma: a comparison with dynamic CT and angiography. Abdom Imaging 22: 295-303, 1997 (Level 4)
7) King AD et al: Dual phase spiral CT in the detection of small insulinomas of the pancreas. BJR 71: 20-23, 1998 (Level 4)
Background/objective
With recent improvements in the imaging diagnosis, the detection rate of asymptomatic cystic masses of the pancreas has risen, and patients treated by surgery have increased. Guidelines for the management of small asymptomatic cystic masses about 2-3 cm in diameter have not been established, and as many cystic tumors are mildly malignant, they are often resected. This makes the role of imaging modalities important. Which modality is the most useful for the discrimination of cystic masses of the pancreas was evaluated.

Comments
It is indisputable that CT and MRI are useful for the diagnosis of cystic masses of the pancreas. Many case reports have suggested the usefulness of MRI for the diagnosis of cystic masses of the pancreas, emphasizing the advantages of MRI such as high tissue contrast resolution, usefulness for the diagnosis of hemorrhage, and applicability of MRCP. However, according to recent retrospective studies using a large number of patients, the diagnostic performance of MRI has been reported more often to differ significantly than to be superior compared with CT. The diagnostic ability of CT has been enhanced by the high spatial resolution and usefulness of reconstructed 3D images of multislice CT. Although there have also been sporadic reports discussing the usefulness of diffusion-weighted MR imaging and the apparent diffusion coefficient, restriction of diffusion of intracystic fluid should be regarded as a relative finding as it can also occur due to various causes in non-tumoral lesions and serous cysts.

According to a relatively old report comparing the usefulness of CT, MRI, and EUS for the diagnosis of pancreatic tumors in general, EUS was superior, particularly, for masses 3 cm or less in diameter. However, the image quality of current CT or MRI is clearly improved, and this report cannot be endorsed at present. By our search, there has been only 1 report each making comparison between CT and EUS concerning the differentiation of cystic pancreatic masses, and no significant difference was observed in the diagnostic performance in either report. Due to the lack of multiple reports, the evidence concerning the usefulness of EUS compared with CT or MRI must be deemed to be absent. It is also unrealistic to attempt to diagnose cystic masses of the pancreas by EUS alone.

Index words and secondary materials used as references
A search of PubMed was performed using “pancreas”, “cystic mass”, “differential diagnosis”, “CT”, “MRI”, and “EUS” as key words.

References
2) Sahani DV et al: Pancreatic cysts 3 cm or smaller: how aggressive should treatment be? Radiology 283: 912-919, 2006 (Level 3)
Figure: Serous cystic neoplasm

A  Early phase contrast-enhanced CT  B  T2-weighted MRI  The lesion appears solid on CT but is clearly diagnosed to be an aggregation of microcysts on T2-weighted imaging. With experience, however, the lesion is sufficiently diagnosable also by CT.
Which is the imaging modality most appropriate for the assessment of the degree of malignancy of intraductal papillary mucinous neoplasm (IPMN)?

CT and MRI are recommended. Their diagnostic abilities are nearly equal. EUS is also useful when intramural nodules are suspected.

Background/objective
IPMN, which can be classified into the main duct and branch duct types, is a tumor that grows slowly, following the adenoma-carcinoma sequence, and has been considered to have a better prognosis than common pancreatic cancer. With accumulation of knowledge, however, its prognosis has been suggested to be worse than was initially reported. The main duct type is frequently malignant and is invariably an indication of surgery, but the branch duct type is often benign and may be observed in some patients. Therefore, the differentiation of benign and malignant diseases is of clinical importance in branch duct IPMN. The diagnostic performance of each modality, particularly its precision in the assessment of the degree of malignancy, was evaluated.

Comments
Pathologically, IPMN is often a mixed type, in which lesions are present in both the main pancreatic duct and its branches, but it is basically a mucosal disease and is nearly impossible to accurately diagnose by imaging modalities. Clinically, it is practical to classify the disease into the main duct and branch duct types depending on the relative dominance in images. MRCP is generally considered useful for the evaluation of the overall picture of IPMN, but it is not considered to be clearly superior to CT or EUS. Thus, there is no difference in the usefulness among the 3 modalities for the differential diagnosis between the main duct and branch duct types.

The international consensus guidelines for the management of IPMN underwent a major revision in 2012. Notable points of revision include the reduction of the criterion of dilatation of the main pancreatic duct to 5 mm to detect main duct (MD) type IPMN with less missed diagnosis, classification of MD-IPMN with dilatation to 5-9 mm as a “worrisome feature” and dilatation to 10 mm or more as “high-risk stigmata”, recommendation of 2-stage classification also of branch duct (BD) IPMN into a “worrisome feature” and “high-risk stigmata”, and approval of observation even when the diameter exceeds 3 cm, which was conventionally an indication for resection, if no “high-risk stigmata” are observed. Thus, highly malignant MD-IPMN was regarded as a surgical indication, and the surgical indication of less malignant BD-IPMN was reserved. According to the guidelines, dilatation of the main pancreatic duct and the cyst diameter may be evaluated by either multislice CT or MRCP, but EUS is necessary for the evaluation of intramural nodules.

While there have been a number of reports that MRI is useful for the diagnosis of IPMN including the differentiation between benign and malignant diseases, CT has recently been reported to show high diagnostic performance by the use of multislice CT and image reconstruction techniques such as curved-reformation, and reports suggesting an ability comparable to that of MRI have increased. Although there have been many reports emphasizing high diagnostic performance of EUS, those comparing it with CT or MRI are extremely few. Clinically, IPMN is rarely evaluated by EUS alone. According to a report in 1998, there was no difference in the abilities of CT, MRI, and EUS to discriminate benign and malignant diseases. Recently, it has been reported that there is no difference in the diagnostic ability between EUS and CT and that EUS may be unnecessary. However, the study population was small in these reports, and the usefulness of EUS for the evaluation of small intramural nodules is readily understood in consideration of its high spatial resolution. As the guidelines mention, EUS is still considered necessary for detailed evaluation (Figure). It must be noted, however, that the findings on EUS depend on the examiner’s skill and are unsatisfactory in objectivity.

Index words and secondary materials used as references
A search of PubMed was performed using “IPMN”, “CT”, “MRI”, and “EUS” as key words.
Figure: EUS of branch duct type IPMN
An intramural nodule is clearly delineated in a multilocular cyst (→). The lesion was difficult to detect by CT or MRI. Pathologically, the disease was non-invasive carcinoma.

References

7) Sahani DV et al: Intraductal papillary mucinous neoplasm of pancreas: multi-detector row CT with 2D curved reformations-correlation with MRCP. Radiology 238: 560-569, 2006 (Level 2)
12) Cone MM et al: Endoscopic ultrasound may be unnecessary in the preoperative evaluation of intraductal papillary mucinous neoplasm. HPB (Oxford) 13: 112-116, 2011 (Level 4)
Which imaging modalities are appropriate for preoperative examination of esophageal cancer?

CT and PET/CT are useful for staging of the disease and are recommended. Esophagography is useful for the preoperative determination of the site and assessment of the severity of stenosis and is recommended.

**Background/objective**

In the management of esophageal cancer, accurate preoperative staging is important for the selection of treatment. The effectiveness of esophagography, CT, MRI, and PET/CT as a preoperative examination for esophageal cancer was evaluated.

**Comments**

The visualization rate by esophagography decreases when the depth of invasion is slight. There is no report comparatively evaluating the invasion depth of superficial cancers determined by esophagography and that determined by endoscopy or endoscopic ultrasound (EUS). Regarding advanced esophageal cancer, the positive predictive value and imaging sensitivity of esophagography performed for esophageal and cardiac cancer have been reported to be 42% and higher than 90%, respectively. While there has been no report concerning the effectiveness of esophagography for the diagnosis of advanced esophageal cancer, esophagography is superior to endoscopy in the determination of the site and evaluation of the severity of stenosis, objectivity of findings, delineation of the tumor area even when the lesion does now allow the passage of the endoscope. And it is more cost-effective (Figure). According to a report comparing esophagography and CT, the delineation of esophageal cancer did not significantly differ between the two modalities, but the accuracy of the diagnosis of the longitudinal extent of the lesion was higher by esophagography (59%) than by CT (32%). Therefore, in advanced esophageal cancer, barium contrast radiography is very useful as it is superior to other examinations in comprehensive evaluation of the lesion including its resectability and spatial relationship with the adjacent organs.

CT is used as the first choice for the diagnosis of distant metastasis in preoperative examination of esophageal cancer. CT particularly allows the evaluation of the liver, lungs, and bones, which are frequent sites of distant metastasis, and is highly useful. Concerning the liver, the sensitivity of CT for liver metastases 1 cm or greater in diameter has been reported to be about 90%. For lung metastases, also, CT has been reported to be very sensitive. However, histopathological examination may be necessary in smokers, because there is the possibility of primary lung cancer.

As for the evaluation of the primary lesion (T staging), the ability of CT in the determination of the depth of invasion is limited. Many esophageal cancers are visualized by CT as wall thickening, but the differential staging of T1-T3 is impossible by CT alone. In the literature comparing CT and EUS, there have been some reports that the accuracy of T staging by CT was inferior to that by EUS. Therefore, the most important role of CT in the diagnosis of the depth of invasion is to discriminate T3 lesions, which can be radically resectable, and T4 lesions, which are not indications for surgical treatment. The evaluation of the fat layer between the tumor and adjacent organs is of particular importance. In fact, the sensitivity and specificity of CT for mediastinal invasion have been reported to be 88-100 and 85-100%, respectively, suggesting that the modality is useful for diagnosing T4 lesions. Also, it has recently become possible to perform MRP or prepare detailed 3D images due to the increased availability of MDCT, but there is no evidence of its usefulness.

On the other hand, the assessment of lymph node metastasis by CT has a number of problems. Generally, lymph nodes in the thoracic or abdominal cavity are considered to be enlarged when they are 10 mm or greater in diameter, and supraclavicular lymph nodes to be enlarged when they are 5 mm or greater in short diameter. However, many metastatic lymph nodes are normal in size, and this is a major factor for the poor accuracy of the staging of esophageal cancers. According to early reports, the sensitivity and specificity of CT for lymph node metastasis with a criterion of 10 mm or greater were 30-60 and 60-80%, respectively, and nearly all metastatic lymph nodes 7 mm or less in diameter were indistinguishable from normal nodes.

Concerning the ability of MRI and CT to stage advanced esophageal cancers, while there was a report that MRI showed higher sensitivity, specificity, and accuracy in the evaluation of the depth of invasion and lymph node metastasis than CT, more reports denied significant differences between the two modalities. Also, as MRI is more expensive, has a narrower scanning area, and is more susceptible to artifacts due to respiration and cardiac pulsation than CT, it cannot be recommended as a preoperative examination.

PET, by which the whole body can be searched for distant metastases at one time, is not utilized for staging (T staging)
of the primary lesion, because it is difficult to evaluate the degree of tumor invasion by PET alone despite its high sensitivity for the presence of disease compared with CT.\textsuperscript{12,17} It is also difficult to visualize early esophageal cancer by PET, and no correlation between FDG uptake and degree of tumor invasion has been demonstrated.\textsuperscript{18,19}

PET is considered to be very useful for the diagnosis of lymph node metastasis as it permits functional assessment regardless of the size (Figure). The sensitivity/specificity of PET for lymph node metastasis have been reported to be 65.5/100, 57/90, and 51/84\%.\textsuperscript{20,21} In all these reports, the specificity was sufficiently high, and the modality, which can reliably detect lymph node metastasis, if there is uptake, is considered to be a useful examination, while the discrimination of false positives due to conditions such as chronic inflammation is still necessary.\textsuperscript{20} The low sensitivity is related to the difficulty in the assessment of metastatic lymph nodes adjacent to the tumor. By PET/CT, the evaluation based on both the uptake and size is possible, and the sensitivity may well be improved. When compared with CT or EUS, PET has a significantly higher specificity,\textsuperscript{18} and the diagnostic specificity for lymph node metastasis can be improved by the addition of PET to conventional examination by CT and EUS.

Concerning the diagnostic performance of PET for distant metastasis, the sensitivity and specificity were reported to be 69 and 95\%, respectively, but its detection power is insufficient for lesions 6-7 mm or less in diameter, and MDCT has higher spatial resolution. There is also a report that PET has no major significance in the evaluation of early esophageal cancer and is not recommended.\textsuperscript{18} At any rate, the assessment of distant metastasis is insufficient by PET alone, and a combination of contrast-enhanced CT and PET or PET/CT is necessary.

**Index words and secondary materials used as references**

A search of PubMed was performed using “esophageal cancer”, “esophagogram”, “CT”, “MRI”, “PET”, “diagnosis”, and “staging” as key words. The Japan Radiological Society and Japan College of Radiology (JCR) Joint Guideline Committee eds: Guidelines for Diagnostic Imaging of the Digestive Tract 2007 and Evidence-based Guideline Recommendations on the Use of Positron Emission Tomography Imaging in Oesophageal Cancer (Clin Oncol 24: 86-104, 2012) were also used as references.
5. Gastrointestinal tract

References

1) Sugimachi K et al: Clinicopathologic study of early stage esophageal carcinoma. Surgery 105: 706-710, 1989 (Level 4)
5) Kuszyk BS et al: Portal phase contrast-enhanced helical CT for the detection of malignant hepatic tumors: sensitivity based on comparison with intraoperative and pathologic findings. AJR 168: 91-95, 1996 (Level 3)
9) Daffner RH et al: CT of the esophagus. II. Carcinoma. AJR 133: 1051-1055, 1979 (Level 5)
Which imaging modalities are appropriate for the postoperative follow-up of esophageal cancer?

**Recommendation grade**

C1

While CT, PET, and esophagography are performed for postoperative follow up, there are no clear grounds for recommending any of these modalities.

**Background/objective**

Although the therapeutic results of esophageal cancer are improving, advanced cancer still frequently recurs. It is important to detect local recurrence and metastases to lymph nodes and other organs as early as possible by scheduled and careful postoperative surveillance. Which modalities are useful for postoperative surveillance was evaluated.

**Comments**

Since the prognosis of esophageal cancer has been reported to be more favorable in the asymptomatic than symptomatic group at recurrence, early detection may improve the outcome.

There is a report that esophagography is effective for the diagnosis of local recurrence in the esophageal lumen. While mucosal changes in anastomotic recurrence can be detected by esophagography, extramural recurrence and lymph node enlargement cannot, limiting the usefulness of the modality. Endoscopic ultrasound is effective for diagnose them, but postoperative changes such as fibrosis are difficult to differentiate from recurrence.

Some reports have recommended PET as useful for the diagnosis of recurrence, reporting its diagnostic accuracy to be 87.2% (sensitivity: 93.1%, specificity: 75.7%). The literature on CT is scarce, but its accuracy has been reported to be 84 and 87%, being comparable to that of PET. Regarding the diagnosis of local recurrence by PET, the sensitivity is high, but the specificity is further reduced (50%) due to false positive findings. Also, PET has been reported to be sensitive for bone metastases but less sensitive than CT for lung metastases, and CT has been suggested to be superior depending on the recurrence pattern. The two modalities are expected to cover for each other’s weaknesses when combined as PET/CT.

While there is no scientific report concerning the interval or duration of surveillance, follow-ups are generally performed every 6 months over 5 years. Some patients in the high-risk group for recurrence are followed up every 3-4 months.

**Index words and secondary materials used as references**

A search of PubMed was performed using “esophageal cancer”, “surveillance”, “postoperative”, “CT”, “PET”, and “esophagogram” as key words. The Japan Esophageal Society ed: Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus, 2012 (3rd edition) was also used as a reference.

**References**

2) Revathy B et al: Diagnosis, Staging, and Follow-Up of Esophageal Cancer. AJR 181: 785-793, 2003 (Level 5)
Background/objective

The prevalence of gastric cancer is high world-wide, and the TNM classification is used for its preoperative staging. Primarily, endoscopy is performed for preoperative examination for gastric cancer, but CT is also employed widely (Figure). Imaging techniques involving radiologists are evaluated.

Comments

Upper GI tract radiography is widely recognized to be useful as a preoperative examination for gastric cancer, and there have been many reports from Japan concerning the usefulness of close radiographic examination of the stomach for the evaluation of the depth and extent of early gastric cancer.

CT (primarily contrast-enhanced CT) is performed as a routine preoperative examination for gastric cancer at many facilities because it allows the evaluation of the presence or absence of distant metastases to organs including the liver and lung and peritoneal dissemination as well as lymph node metastasis and comprehensive assessment of the presence or absence of extraserosal spread (invasion to surrounding organs), which is difficult to diagnose by gastroscopy. Kim and Chen et al. reported that MPR and 3D images prepared by MDCT improved the accuracy of preoperative T-staging of gastric cancer.1,2 In a study to evaluate the depth of gastric cancer by CT performed after inflating the stomach with water or air, Kumano et al. reported that the accuracy of the diagnosis of the depth was high at 91% with both water and air.3 Other reports also suggested the usefulness of T-staging by CT.4 Recently, the assessment using virtual endoscopy such as CT gastrography has been reported to be useful for the evaluation of the site and depth of the lesion.5 The accuracy of the diagnosis of lymph node metastasis by CT has also been reported at 51-83.8%.6,7 Kim et al. further reported that MPR improved the accuracy of the diagnosis of lymph node metastasis in early gastric cancer.8 The site of distant metastasis of gastric cancer is most frequently the liver, and the frequency of hematogenous metastases to organs such as the lung, adrenal gland, bone, and brain is also high, but many reports suggested the usefulness of CT for the diagnosis of metastases to all these sites.9 Also, the diagnosis of peritoneal dissemination is important to avoid unnecessary open surgery.10 On CT, ascites is a vital finding suggesting peritoneal metastasis, and, according to Chang et al., the probability of peritoneal dissemination is 75% or higher if 50 mL or more ascites is detected by CT.11 Yajima et al. reported that the sensitivity and specificity of ascites demonstrated by CT were 51 and 97%, respectively, for the diagnosis of peritoneal dissemination.12

Many reports supported the usefulness of PET and PET/CT for the preoperative staging of gastric cancer.8,13 For the diagnosis of lymph node metastasis, however, the sensitivity of PET alone is reportedly low.12 Kim et al. also reported that PET/CT was superior to contrast-enhanced CT except for the sensitivity and accuracy in the diagnosis of lymph node metastasis of advanced gastric cancer,13 so the addition of PET is recommended if lymph node metastasis is suspected on CT.

Index words and secondary materials used as references

A search of PubMed was performed using “gastric cancer”, “preoperative”, and “staging” as key words.
The Japanese imaging guideline 2013

Figure: Preoperative images of advanced gastric cancer (type II)
A Endoscopy: A type II lesion primarily occupying the anterior wall from the lower body to the antrum of the stomach is noted. B Contrast-enhanced CT: An irregular mass shadow is observed in the anterior wall of the stomach with obvious invasion to the serosal surface. C Gastrography (compression method): A mass shadow is observed in the lower body to the antrum of the stomach. The mass shows ulceration in the center and a circumferential ridge. D PET/CT: FDG uptake is observed at the tumor.

References
7) Kim YN et al: Gastric cancer staging at isotropic MDCT including coronal and sagittal MPR images: endoscopically diagnosed early vs. advanced gastric cancer. Abdom Imaging 34: 26-34, 2009 (Level 3)
8) Lee MH et al: Gastric cancer: imaging and staging with MDCT based on the 7th AJCC guidelines. Abdom Imaging 37: 531-540, 2012 (Level 5)
11) Ozkan E et al: The role of 18F-FDG-PET/CT in the preoperative staging and posttherapy follow up of gastric cancer: comparison with spiral CT. World J Surg Oncol 9: 75, 2011 (Level 4)
Which imaging modalities are appropriate for postoperative follow-up of advanced gastric cancer?

### Background/objective

While the results of surgery for gastric cancer are improving, advanced gastric cancer has a high risk of recurrence and is often followed-up over a long period of time after surgery. The number of examinations to evaluate for postoperative recurrence is increasing, but there is no clear consensus about a reasonable follow-up method by imaging examinations. The usefulness of CT and PET in patients after surgery for gastric cancer was evaluated.

### Comments

Postoperative recurrence of gastric cancer is observed as local recurrence at the surgical site, peritoneal dissemination, or distant metastasis including the liver. Therefore, patients are followed up generally by endoscopy for local evaluation and CT or contrast-enhanced CT for both local recurrence and distant metastasis (Figure A). However, there have been few reports evaluating the usefulness of CT after surgery for gastric cancer. Also, CT reportedly lacks the specificity for small and localized foci of lymph node metastasis, and early peritoneal dissemination is often difficult to detect.

Recently, there have been a large number of reports about the usefulness of PET for the postoperative follow-up of gastric cancer (Figure B). According to Shimada et al., while PET has limitations such as that it often shows false negative results in signet ring cell carcinoma and non-solid-type poorly differentiated carcinoma, it is useful for the evaluation of distant metastasis and therapeutic responses and contributes to the selection of more appropriate treatments. Also, meta-analysis by Wu et al. (9 studies, a total of 526 patients who underwent PET) suggested the usefulness of PET/CT with sensitivity and specificity of 0.72 and 0.84 by PET alone, 0.74 and 0.85 by contrast-enhanced CT alone, and 0.75 and 0.85, respectively, by PET/CT. Therefore, PET or PET/CT will be recommended in the future for patients suspected to have recurrence.

Concerning the period until recurrence, it has been reported that early gastric cancer recurred within 2 years in 50% and within 3 years in 88.9% of the patients and that advanced gastric cancer recurred within 2 years in 79.2% and within 3 years in 90.7%. On the other hand, the frequency of recurrence 5 years or longer after surgery has been reported to be 8.6%, and that of recurrence 10 years or more after surgery to be less than 1%, in all cases of recurrence. From these observations, the follow-up period after surgery for gastric cancer, which is usually 5 years, is considered appropriate.

Lastly, whether or not periodic follow-up after surgery for gastric cancer is beneficial for patients or socially and economically reasonable is a very important question. Kim et al. reported that the prognosis was poor in patients who were symptomatic and had recurrence but that periodic postoperative follow-up did not contribute to the outcome. Also, Eom et al. followed up 1,767 patients after surgery for gastric cancer by periodic examinations (for 3 years by CT, hematological tests, and endoscopy) and reported that recurrence was observed in 310 patients (17.5%), that abnormalities were observed on periodic examinations in 75.2% (233) of these patients, but that no significant difference was noted in the overall survival between these patients and those in whom no abnormality was observed. Further accumulation of cases and evaluation are considered necessary with regards to the usefulness of periodic examinations and a socially and economically reasonable follow-up schedule. Particularly, for patients with early gastric cancer and those considered to be at a low risk, the approach of avoiding unnecessary examinations and examining only symptomatic patients may be worth evaluating.

### Index words and secondary materials used as references

Guidelines for diagnosis, treatment and follow-up 2010 were also used as references.

References

2) Ha HK et al: Local recurrence after surgery for gastric carcinoma: CT findings. AJR 161: 975-977, 1993 (Level 4)
5) Ozkan E et al: The role of 18F-FDG-PET/CT in the preoperative staging and posttherapy follow up of gastric cancer: comparison with spiral CT. World J Surg Oncol 9: 75, 2011 (Level 4)
Which imaging modalities are appropriate for preoperative examination of colorectal cancers?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Imaging modalities</th>
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<tbody>
<tr>
<td>B</td>
<td>CT, MRI (for rectal cancer alone)</td>
</tr>
<tr>
<td>C1</td>
<td>PET, barium enema, CT colonography</td>
</tr>
<tr>
<td>B</td>
<td>CT is recommended for the search for metastases. There is no clear evidence to recommend PET.</td>
</tr>
<tr>
<td>C1</td>
<td>MRI (and transrectal ultrasound) is recommended for the evaluation of local invasion of rectal cancer.</td>
</tr>
</tbody>
</table>

**Background/objective**

Lower gastrointestinal (GI) endoscopy is generally performed for the diagnosis of colon cancer, but CT and MRI are also performed (Figure), because the degree of extramural spread and invasion to other organs, lymph node metastasis, and distant metastasis cannot be evaluated by lower GI endoscopy. The usefulness of imaging modalities (barium enema, CT, MRI, and PET) for the diagnosis of colon cancer was evaluated.

**Comments**

For creating a therapeutic strategy and determining the prognosis of colon cancer, it is important to evaluate the degree of invasion (T stage), lymph node metastasis (N stage), and metastasis (M stage). In many guidelines including the NCCN Guidelines recommend the examination of the pelvic region, abdominal region including the liver, and abdominal region by CT. This examination is recently performed frequently using MDCT, which permits imaging of the whole body as thin slices with a thickness of 5 mm or less and visualization of small lymph nodes and metastatic foci 5 mm in diameter. However, according to studies in which preoperative abdominal CT was performed as a routine examination in patients with colorectal cancer the therapeutic strategy was changed in only 19% (13/70).\(^1\)\(^2\) Also, as lung metastasis is observed infrequently at the initial examination, some authors are skeptical about the necessity of CT.\(^3\) Regarding local evaluation of rectal cancer, local staging by CT or MRI is suggested except in cases where tumors are clearly T1/2, N0.\(^4\) Particularly for the evaluation of mesorectal invasion, MRI is considered to be superior to CT.\(^5\) According to a meta-analysis evaluating transrectal ultrasound, MRI using a transrectal coil, and CT,\(^6\) transrectal ultrasound and transrectal coil MRI were superior to CT in the evaluation of invasion to the propria muscularis and are comparable in sensitivity, but ultrasound was more specific than MRI (86 vs. 69%). In the evaluation of invasion to pararectal tissues, ultrasound has been reported to be superior to CT or MRI (US: 90%, CT: 79%, MRI: 82%). In Japan, however, transrectal ultrasound or transrectal coil MRI is rarely used for the staging of rectal cancer. Also, intrarectal MRI has been removed from the NCCN Guidelines, 2012. In Japan, MRI is performed using a phased array coil instead of a transrectal coil, but both procedures are generally considered to have nearly comparable diagnostic abilities and are recommended as methods for the evaluation of local invasion. On the other hand, local evaluation by CT is considered difficult, but the accuracy of the diagnosis of intramural invasion and invasion to other organs by MDCT is expected to be improved by preparing high-resolution MRP images perpendicular to the plane in which the colon cancer is in contact with the intestinal wall or other organs.\(^7\)

The sensitivity of imaging modalities for the evaluation of lymph node metastasis has been reported to be only 60%,\(^8\) and the above meta-analysis also concluded that transrectal ultrasound, transrectal coil MRI, and CT are similar in sensitivity for invasion to other organs and lymph node metastasis.\(^5\)

PET is considered to be useful for the evaluation of the presence or absence of local recurrence, lymph node metastasis, and distant metastasis.\(^9\) It is more sensitive than CT to detect intraabdominal lymph node metastasis. PET has also been reported to be superior in the evaluation of liver metastasis.\(^10\) (See CQ69 on liver metastasis). Also, contrast-enhanced CT+PET has been shown to be more sensitive than PET or CT alone.\(^11\)\(^12\) However, PET is expensive, and the accumulation of the evidence of its usefulness for the diagnosis of metastasis is still insufficient.

Barium enema has advantages such as the ease of evaluation of the entire picture of the lesion compared with endoscopy, but endoscopy was reported to be superior in the diagnosis of colon cancer with submucosal invasion,\(^13\) and opportunities to perform barium enema have decreased. Images resembling those of barium enema can be prepared by CT colonography, but the clinical evaluation of the modality remains insufficient.

**Index words and secondary materials used as references**

A search of PubMed was performed using “colon cancer”, “rectal cancer”, “colorectal cancer”, “preoperative”, and
**Figure: Preoperative images of advanced rectal cancer**

A Barium enema: A circumferential type II lesion is observed in the part of the rectum below the peritoneal reflection (→).  
B Endoscopy: Circumferential stenosis is noted, and the passage of the endoscope is difficult.  
C MRI: Circumferential wall thickening is observed in the rectum (→). While the lesion clearly spreads beyond the propria muscularis, no invasion to the prostate is observed.

“staging” as key words. The NCCN guidelines Colon Cancer Ver.2. 2012 and Schmiegel W et al: S3 guidelines for colorectal carcinoma: results of an evidence-based consensus conference on February 6/7, 2004 and June 8/9, 2007 (for the topics IV, VI and VII). Z Gastroentero 48: 65-136, 2010 were also used as references.

**References**

5) Mathur P et al: Comparison of CT and MRI in the pre-operative staging of rectal adenocarcinoma and prediction of circumferential resection margin involvement by MRI. Colorectal Dis 5: 396-401, 2003 (Level 2)  
Which imaging modalities are appropriate for postoperative follow-up of colorectal cancer?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Imaging modality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B</strong></td>
<td>Contrast-enhanced CT</td>
</tr>
<tr>
<td><strong>C1</strong></td>
<td>MRI (rectal cancer), PET (PET/CT)</td>
</tr>
</tbody>
</table>

Contrast-enhanced CT is recommended. While the evidence is insufficient, MRI and PET/CT are also useful in some patients and may be considered.

Background/objective

While the therapeutic results of cancer of the digestive tract are improving, the recurrence rate of advanced cancer remains high. Local recurrence, lymph node metastasis, and metastasis to other organs may be detected early by designed, careful postoperative surveillance. Which imaging modalities are useful for postoperative surveillance of colorectal cancer was evaluated on the basis of the literature.

Comments

Regarding the method for postoperative surveillance of colon cancer, multiple randomized controlled trials (intensive vs. non-intensive) and their meta-analysis have been carried out internationally, and the early detection of recurrence was shown to be possible with an improvement in the prognosis in the intensive group. In Western countries, guidelines have been issued successively since 2005, and the Guidelines for the Treatment of Colorectal Cancer prepared for the standardization of the diagnosis and treatment of colorectal cancer were published in Japan, but the surveillance method varies among the guidelines (Table).

According to a follow-up study of colorectal cancer patients after curative resection by the Japanese Society for Cancer of the Colon and Rectum, recurrence occurred within 3 years after surgery in 80% or more, and within 5 years after surgery in 95%, but more than 5 years after surgery in less than 1%, of all patients. Recurrence was observed most frequently in the liver, followed by the lung, and locally in the colon. This suggests that surveillance should be continued over 5 years after surgery at shorter intervals during the first 3 years.

The detection rate for resectable lung metastases on postoperative surveillance of colon cancer patients with plain chest radiography is low at about 1%, and the modality is not recommended in Western countries for periodic follow-up. Moreover, as it is possible today to scan from the thoracic to pelvic region in one session by multislice CT, the importance of plain chest radiography in surveillance has decreased.

According to the ASCO Guidelines, annual thoracoabdominal CT scans are recommended for 3 years after surgery in groups at high-risk for recurrence. The guidelines also recommend that pelvic CT should be considered, particularly for previously unirradiated patients after surgery for rectal cancer. There is a report that the discrimination between postsurgical scarring and recurrent lesions is difficult and that baseline pelvic CT images early after surgery are useful for this purpose. Also, if intrapelvic recurrence is suspected, diffusion-weighted MRI, EUS, and PET/CT of the pelvic region have been reported to be useful. The ESMO Clinical Practice Guidelines recommend thoracoabdominal CT examination every 6-12 months over 3 years after surgery for the high-risk group. According to the guidelines, the usefulness of other imaging modalities has not been demonstrated, and they should be applied only to patients in whom recurrence is suggested by symptoms.

The usefulness of periodic colonoscopy has not been established due to the low incidence of anastomotic recurrence after surgery for colon cancer. In rectal cancer, however, the local recurrence rate is higher than in colon cancer, and there has been a report recommending colonoscopy for surveillance. Recently, the availability of CT-colonography (CTC), which can be performed more easily than colonoscopy, is increasing. The sensitivity and specificity of CTC for the diagnosis of local recurrence of colorectal cancer are reportedly 81.8 and 93.1%, respectively, and contrast-enhanced CTC is expected to be useful for future colorectal cancer surveillance.

See CQ69 for liver metastasis of colorectal cancer.

Index words and secondary materials used as references

A search of PubMed was performed using “colorectal cancer”, “surveillance”, “recurrent”, and “postoperative” as key words. The ASCO Guidelines 2005, ESMO Clinical Practice Guidelines 2010, NCCN Guidelines 2012, and the
Japanese Society for Cancer of the Colon and Rectum ed: JSCCR Guidelines for the Treatment of Colorectal Cancer 2009 were also used as references.

Table: Postoperative surveillance methods for colorectal cancer recommended by the JSCCR Guidelines for the Treatment of Colorectal Cancer and international guideline

<table>
<thead>
<tr>
<th></th>
<th>JSCCR Guidelines (Stage I mp, Stage II)</th>
<th>JSCCR Guidelines (Stage III)</th>
<th>ASCO</th>
<th>ESMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical interview</td>
<td>Every 3 months for the first 2.5 years and every 6 months thereafter</td>
<td>Every 3 months for the first 3 years and every 6 months thereafter</td>
<td>Every 3-6 months for the first 3 years and every 6 months thereafter</td>
<td>When appropriate</td>
</tr>
<tr>
<td>Tumor marker (CEA)</td>
<td>Every 3 months for the first 2.5 years and every 6 months thereafter</td>
<td>Every 3 months for the first 3 years and every 6 months thereafter</td>
<td>Every 3 months (started after the end of chemotherapy in patients undergoing 5FU adjuvant chemotherapy)</td>
<td>When there are symptoms suggestive of recurrence</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Every 6 months for the first 3 years and annually thereafter</td>
<td>Every 6 months</td>
<td>Chest X-ray is not recommended</td>
<td>When there are symptoms suggestive of recurrence</td>
</tr>
<tr>
<td>Chest CT</td>
<td>When necessary</td>
<td>Annually</td>
<td>Annually</td>
<td>When there are symptoms suggestive of recurrence</td>
</tr>
<tr>
<td>Abdominal US</td>
<td>After 6, 18, and 30 months</td>
<td>After 6, 18, 30, 42, and 54 months</td>
<td>No mention</td>
<td>Annually for 3 years after surgery</td>
</tr>
<tr>
<td>Abdominal CT</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually</td>
<td>When there are symptoms suggestive of recurrence</td>
</tr>
<tr>
<td>Pelvic CT (rectal cancer)</td>
<td>After 1, 2, 3, and 5 years</td>
<td>Every 6 months for the first 2 years and annually thereafter</td>
<td>Considered for previously unirradiated patients</td>
<td>Not recommended to be performed periodically</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>1 and 3 years after surgery*</td>
<td>1, 2, and 3 years after surgery*</td>
<td>3 years after surgery and every 5 years thereafter*</td>
<td>Every 5 years</td>
</tr>
</tbody>
</table>

* For the evaluation of anastomotic recurrence, when necessary.
# Flexible sigmoidoscopy performed every 6 months in rectal cancer patients non-irradiated for 5 years.

References
2) Kim HJ et al: CT Colonography for combined colonic and extracolonic surveillance after curative resection of colorectal cancer. Radiology 257: 697-704, 2010 (Level 2)

87
Is diagnostic imaging appropriate for reducing negative appendectomy?

There is a strong evidence that negative appendectomy can be reduced by diagnostic imaging, particularly by CT, and it is strongly recommended.

Background/objective

Acute appendicitis lacks characteristic symptoms or findings early after the onset and often leads to perforation due to a delay of diagnosis. Once the appendix is perforated, the frequency of complications such as intraperitoneal abscess, subcutaneous abscess, and adhesive ileus increases. Therefore, unnecessary appendectomy, also called negative appendectomy, tends to be performed due to fear of perforation. Its incidence was considered about 20% but has markedly decreased recently to 5% or less presumably due largely to contribution of imaging techniques (Figure).

Comments

Concerning adults, a study of 3,540 cases of appendectomy (with a preoperative diagnosis of appendicitis) in Washington State showed that negative appendectomy was seen in 9.8% of the patients without imaging examination but in 8.1% with ultrasonography and 4.5% with CT. The results of other reports were similar. A healthcare cost-cutting effect has also been reported. However, on a population basis, the negative appendectomy rate reportedly showed no change after the introduction of diagnostic imaging or laparoscopy.

In children, according to a retrospective study by Rao et al. of 129 cases, the negative appendectomy rate was 10% in boys and 18% in girls but decreased after the introduction of CT to 5 and 12%, respectively, and the incidence of appendiceal perforation also decreased from 22 to 14%. Garcia Peña et al. reported that the negative appendectomy rate was 14.7% before the introduction of imaging examination but significantly decreased to 4.1% by a protocol of performing prospective ultrasonography with CT in suspected cases alone. It has been reported from the same facility that the rate decreased from 11 to 5.5% also when imaging examination was performed by limiting the indications using a clinical practice guideline. However, factors other than imaging examination may have been involved in the results.

From various reports including those cited above, negative appendectomy appears to be clearly decreasing due to diagnostic imaging. However, the diagnosis is still reported to be difficult even by CT in patients with sparse visceral fat, those with ileus, and those in whom the appendix cannot be identified as it is complicated by perforation or abscess.

Index words and secondary materials used as references

A search of PubMed was performed using “appendicitis”, “CT”, “negative appendectomy”, “diagnosis”, and “effect” as key words.

References

2) Lee CC et al: Routine versus selective abdominal computed tomography scan in the evaluation of right lower quadrant pain: a randomized controlled trial. Acad Emerg Med 14: 117-122, 2007 (Level 2)
5) Flum DR et al: Has misdiagnosis of appendicitis decreased over time? A population-based analysis. JAMA 286: 1748-1753, 2001 (Level 4)
9) Levine CD et al: Why we miss the diagnosis of appendicitis on abdominal CT: evaluation of imaging features of appendicitis incorrectly diagnosed on CT. AJR 184: 855-859, 2005 (Level 4)
Figure: Acute appendicitis
A  Plain CT  B  Contrast-enhanced CT  C  Coronal MPR  D  Sagittal MPR: An enlarged appendix accompanied by wall enhancement and thickening (→) is observed in the right lower abdominal region. The density of the surrounding adipose tissue is increased, and free fluid is noted, suggesting abscess formation. Surgery was performed, and the diagnosis of acute appendicitis was confirmed. Intraoperatively, pus was collected in the mesoappendix and mesocecum.
When is CT appropriate in patients suspected to have acute appendicitis?

**Background/objective**

Appendicitis is first diagnosed from physical findings and laboratory data, but it is often missed or alternatively unnecessarily treated by surgery due to misdiagnosis. When appendicitis is strongly suspected clinically, diagnostic imaging is useful for decision making, but performing diagnostic imaging in all such patients is inappropriate from the viewpoints of exposure and medical economy. What kind of patients should undergo imaging studies?

**Comments**

There are various diagnostic scoring systems for acute appendicitis due to the difficulty in its initial diagnosis. Among them, the Alvarado score is the most commonly used,\(^1\) and there have been a number of reports that a score of 6 or above strongly suggests appendicitis in children.

On the other hand, Kharbanda et al. reported an attempt to identify children who are unlikely to have appendicitis and, thus, require no diagnostic imaging using clinical findings and laboratory results as triage tools.\(^2\) As a result, the sensitivity and negative predictive value for acute appendicitis were 98 and 32%, respectively, if there is at least one of (1) a neutrophil count of 6,750 or above, (2) nausea, and (3) tenderness most intense in the right lower abdominal region, and the use of CT could be reduced to 20% by applying this rule. However, the diagnostic power of this method is low and variable in adults. Presently, no method has been sufficiently shown to be useful for discriminating patients who require diagnostic imaging.

In the retrospective study by Garcia Peña et al., patients were divided into 3 groups according to the risk level based on symptoms and laboratory data, a management guideline was presented, and the outcome was evaluated.\(^3\) They reported that, by following this guideline, the negative appendectomy (false positive) and false-negative rates could be minimized. Nathan et al. reported that information obtained by CT is very limited when an emergency physician judged the possibility of appendicitis to be low.\(^4\) Also, Blackmore et al. reported that false positives may increase if CT is used when appendicitis is unlikely.\(^5\) These results suggest that CT should be used when the possibility of appendicitis is high or moderate. Kondo et al. considered that CT may be omitted if half a day or longer has passed from the onset to the initial examination and muscular guarding is observed, because appendicitis is highly likely. However, CT should be performed in other cases.\(^6\) On the other hand, Nathan et al. state that CT should be performed in all patients preoperatively.\(^7\)

**Index words and secondary materials used as references**

A search of PubMed was performed using “appendicitis” and “diagnosis” as key words.

**References**

4) Nathan RO et al: Therapeutic impact of CT of the appendix in a community hospital emergency department. AJR 191: 1102-1106, 2008 (Level 4)
Which imaging modality is appropriate for acute appendicitis in adults?

CT is recommended as there is an evidence that CT has higher sensitivity and specificity than ultrasonography for adult acute appendicitis.

**Background/objective**

Acute appendicitis is the most frequent of the diseases that require emergency surgery, and about 7% of all people reportedly suffer from the disease in their lifetime. Ultrasonography can be performed readily at the bedside and has high diagnostic accuracy, but it is dependent on the examiner’s skill and affected by intestinal gas. CT, on the other hand, has been reported to have a high diagnostic ability and can objectively scan a wide area in a short time, but it is not performed in all patients due to radiation exposure, cost, and accessibility.

**Comments**

In treating appendicitis, complications including abscess formation and peritonitis are observed, but the appendix is often found to be normal on surgery, and the frequency of such events used to be about 20%, because the therapeutic approach was determined on the basis of physical findings and the WBC. Recently, more exact diagnosis using imaging modalities such as ultrasonography and CT is necessary.

According to meta-analysis by Terasawa et al. of 12 prospective trials using CT, the sensitivity was 94% (95% confidence interval: 91-95%), and the specificity was 95% (93-96%). According to meta-analysis by Doria et al. of pooled data from 31 prospective and retrospective trials using CT, they were 94 (92-95) and 94 (94-96)%, respectively. However, meta-analysis by Terasawa et al. of 14 prospective trials using ultrasonography reported sensitivity and specificity of 86 (83-88) and 81 (78-84)%, respectively. According to pooled date from 26 studies using ultrasonography reported by Doria et al., they were 83 (78-87) and 93 (90-96)%, respectively, indicating significant superiority of CT in sensitivity. In all analyses, considerable variation was observed in the background of patients, prevalence, and presence or absence of contrast enhancement (intravenous, oral, rectal) among the reports, the criteria for surgery or follow-up and exact criteria for the diagnosis were unclear, and there is the possibility these studies overestimate of the sensitivity and specificity. However, CT clearly had high sensitivity and specificity and was superior to ultrasonography in adults. Since many of these reports were about Western populations, the diagnostic performance of ultrasonography is estimated to be higher in Japanese with a generally smaller physique, but perforation is difficult to diagnose by ultrasonography, CT is recommended to be performed as much as possible in adults. Many papers in Japanese were case reports or case collections, and none with a high evidence level was found.

**Index words and secondary materials used as references**

A search of PubMed was performed using “appendicitis”, “CT”, and “US” as key words. Blackmore CC et al: Imaging in acute abdomen in evidence based imaging, written and edited by Medina LS & Blackmore CC, Springer 2006 was also used as a reference.

**References**

Which modalities are appropriate for diagnostic imaging of acute appendicitis in children?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Ultrasonography</td>
</tr>
<tr>
<td>C1</td>
<td>CT</td>
</tr>
<tr>
<td>C2</td>
<td>Abdominal plain radiography</td>
</tr>
</tbody>
</table>

In the diagnosis of acute appendicitis in children, CT has higher sensitivity and similar specificity compared with ultrasonography but has problems such as radiation exposure and accessibility. Therefore, it is recommended to perform ultrasonography first and to perform CT when abnormality cannot be detected, or the diagnosis is difficult, by ultrasonography. The significance of abdominal plain radiography is unclear, and this modality is not recommended.

Background/objective

In children, appendicitis is a frequent disease that progresses rapidly and leads to perforation in many patients. Therefore, prompt diagnosis and treatment are necessary. However, CT involves radiation exposure. Imaging modalities for acute appendicitis in children were evaluated.

Comments

In children, acute appendicitis is the most frequent form of acute abdomen and is a typical disease that requires emergency surgery. Symptoms are of their equivocal in children, particularly young children, occasionally making the diagnosis difficult. In addition, the disease progresses rapidly and often results in perforation, so it must be diagnosed and treated promptly. The disease occurs more frequently in older children, being rare in those aged 5 years or less and most frequent in those in their 10s-20s. The male-female ratio of patients is 3:2, and the disease occurs with a slight predominance in boys. Postoperative complications still occur frequently in those who suffered perforation, and it is of clinical importance not to overlook perforation and perform effective treatments. Particularly, in the diagnosis, attention to exposure is necessary in consideration of the characteristic of children.

Doria et al. performed meta-analysis of 26 prospective and retrospective studies performed by ultrasound alone, CT alone, and their combination. According to pooled data from 8 prospective studies using CT, the sensitivity was 94% (95% confidence interval: 92-97%), and the specificity was 95% (94-97%). In 23 prospective trials using ultrasonography, they were 88 (86-90) and 94 (92-95)%, respectively. Similarly to adults, CT was superior in sensitivity, and the two modalities were comparable in specificity. These studies varied in the patients’ background, prevalence, and presence or absence of contrast enhancement as in studies using adults. Also, while CT tended to be used more often in the United States, ultrasonography was used more often in reports from Europe and Asia. Moreover, the number patients aged 5 years or less was limited.

Two prospective studies were carried out using the design of performing ultrasonography first and adding CT only when the appendix could not be identified, or a definitive diagnosis could not be made, by ultrasonography, and reported a sensitivity of 77-97% and a specificity of 89-99%. In a randomized trial using 600 patients examined by a combination of CT and ultrasonography or ultrasonography alone, the sensitivity and specificity were 99 and 89% by the combination but 86 and 95%, respectively, by ultrasonography alone. It has also been reported that the appendix could not be visualized by ultrasonography in 25% of underweight children, 33% of normal-weight children, but 79% of overweight children. However, in these meta-analyses, the criteria for surgery or follow-up, which serve as grounds for the diagnosis, were unclear, similar to reports concerning adults, and the possibility of overestimation of the sensitivity and specificity has been suggested. Many of the papers in Japanese were case reports or case collections, and none with a high evidence level was found.

For these reasons, CT is considered to have higher diagnostic ability as in adults (Figure). However, in consideration of radiation exposure and accessibility, it is recommendable to perform ultrasonography first and to perform CT when no abnormality can be detected or the diagnosis is difficult by ultrasonography.

Index words and secondary materials used as references

A search of PubMed was performed using “appendicitis”, “CT”, “US”, and “children” as key words.
The Japanese imaging guideline 2013

Figure: Acute appendicitis in children
Contrast-enhanced CT (coronal image)
An enlarged appendix showing wall thickening and enhancement is observed in the right lower abdominal region. The density of the surrounding adipose tissue is elevated, indicating acute appendicitis.

References
When appendicitis is suspected, what is the appropriate CT scan protocol?

For the diagnosis of appendicitis, there is no consensus about whether non-contrast CT suffices or whether contrast enhancement should be used, there is no consensus for the appropriate scanning area and slice thickness.

Background/objective

The usefulness of CT for the diagnosis of acute appendicitis has recently become evident, but the scanning protocol varies. While acute appendicitis is considered to be sufficiently diagnosable by non-contrast CT, methods using intravenous contrast agents, oral or enteral gastrointestinal contrast agents, or their combinations are also performed. The scanning area may also be wide, covering the abdominal to pelvic region, or be focused to avoid radiation exposure.

Comments

Many studies using CT with oral or rectal administration of a contrast agent have been reported in Western countries, but intravenous contrast enhancement is more common in Japan. The sensitivity and specificity have been reported to be 90 and 97%, respectively, even by non-contrast CT, and according to a study in Japan, its diagnostic performance was comparable to that of contrast-enhanced CT. However, there are also reports that the diagnostic performance was improved by the use of a contrast agent. From Boston University, it has been reported that the use of an oral contrast agent could be omitted by performing 64-row multislice CT using an intravenous contrast agent with MPR.

Concerning the slice thickness, the rates of appendix identification and definitive diagnosis were reportedly improved as the slice thickness was thinner, and image reconstruction at a slice thickness of at least 5 mm or less is necessary. Reconstruction in the coronal and sagittal planes is also considered useful. Some authors have recommended focused CT for children to reduce the exposure. Scanning of the entire abdominal region is not always necessary to examine whether the condition is appendicitis or not, and the diagnostic precision is not considered to differ even by focused CT limited to the area below the lower pole of the right kidney. According to a report on the diagnosis of appendicitis using low-dose CT, the diagnostic performance did not differ compared with normal-dose CT. The significance of low-dose CT, particularly, in children should be evaluated in the further study.

Index words and secondary materials used as references

A search of PubMed was performed using "appendicitis", "CT", "diagnosis", "unenhanced", and "enhanced" as key words.

References

2) Lane MJ et al: Unenhanced helical CT for suspected acute appendicitis. AJR 168: 405-409, 1997 (Level 4)
6) Anderson SW et al: Abdominal 64-MDCT for suspected appendicitis: the use of oral and IV contrast material versus IV contrast material only. AJR 193: 1282-1288, 2009 (Level 2)
9) Seo H et al: Diagnosis of acute appendicitis with sliding slab ray-sum interpretation of low-dose unenhanced CT and standard-dose i.v. contrast-enhanced CT scans. AJR 193: 96-105, 2009 (Level 4)
Is MRI appropriate when a pregnant woman is suspected to have appendicitis?

**Recommendation**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Non-contrast MRI</td>
</tr>
<tr>
<td>D</td>
<td>Contrast-enhanced MRI</td>
</tr>
</tbody>
</table>

In pregnant women, MRI has some diagnostic value and may be considered. Contrast enhancement should be avoided in MRI of pregnant women.

**Background/objective**

While the incidence of acute appendicitis during pregnancy is lower than in the non-pregnant period, the disease is the most frequent acute abdomen during pregnancy. Generally, the appendix, which is considered to be displaced in upper and lateral directions with enlargement of the uterus, is particularly difficult to identify by ultrasonography, preventing the diagnosis. Also, the effectiveness of the modality depends largely on the examiner’s skill. The diagnostic power of ultrasonography in pregnant women vary among reports.\(^1\)\(^-\)\(^3\) In patients with suspected appendicitis difficult to diagnose by ultrasonography, CT has been reported to be useful.\(^4\)\(^,\)\(^5\) However, MRI, which is free of radiation exposure and is less operator dependent, is expected to be useful in pregnant women.

**Comments**

Reports of the usefulness of MRI in pregnant women are limited to those of a few retrospective studies.\(^3\)\(^,\)\(^6\)\(^-\)\(^8\) The sensitivity and specificity of MRI have been reported to be 90-100 and 93-98%, respectively, indicating a relatively high diagnostic ability, but its diagnostic performance has not been assessed strictly or in comparison with other modalities. Pedrosa et al. reported that the sensitivity and specificity of ultrasonography were 36 and 99%, but those of MRI were 100 and 93%, respectively.\(^9\) MRI also shows a negative predictive value of 100% and is excellent in excluding appendicitis. Contrast-enhanced imaging should not be performed, because there is no report of its usefulness, and because the contrast agent is transferred to fetuses.

**Index words and secondary materials used as references**

A search of PubMed was performed using “appendicitis”, “diagnosis”, and “pregnancy” as key words.

**References**

1) Lim HK et al: Diagnosis of acute appendicitis in pregnant women: value of sonography. AJR 159: 539-542, 1992 (Level 4)
5) Lazarus E et al: CT in the evaluation of nontraumatic abdominal pain in pregnant women. Radiology 244: 784-790, 2007 (Level 4)
6) Oto A et al: MR imaging in the triage of pregnant patients with acute abdominal and pelvic pain. Abdom Imaging 34: 243-250, 2009 (Level 4)
Which imaging modalities are appropriate for the diagnosis of ileus?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>CT</td>
</tr>
<tr>
<td>C1</td>
<td>Ultrasonography</td>
</tr>
</tbody>
</table>

CT and ultrasonography are more sensitive and specific than plain radiography, and there modalities are recommended. Additionally, CT is useful for the diagnosis of intestinal ischemia. Since CT is more sensitive than ultrasonography, examination by CT is preferable.

**Background/objective**

In digestive tract obstruction, the early diagnosis of the site and cause of obstruction and the presence or absence of intestinal ischemia is important. Digestive tract obstruction used to be diagnosed by abdominal plain radiography alone after physical examination. Recently, however, modalities such as ultrasonography and CT are used frequently. In this section, the significance of CT and ultrasonography compared with plain radiography was evaluated.

**Comments**

According to pooled data of 4 papers including some prospective studies (199 patients), the sensitivity and specificity of plain radiography were 65 and 75%, respectively.\(^1-4\) In studies comparing 2 modalities, plain radiography was inferior in both sensitivity and specificity to ultrasonography\(^1,2\) and MRI.\(^3\) Compared with CT, plain radiography was also reported to be either inferior in both sensitivity and specificity\(^2,3\) or inferior in sensitivity but similar in specificity.\(^4\) From these results, if the diagnosis is uncertain by plain radiography in patients with acute abdomen, CT or ultrasonography is considered necessary.

The sensitivity and specificity of ultrasonography were 92 and 95%, respectively, according to pooled data of 4 studies,\(^1,2,5,6\) and those of CT were 94 (71-100) and 78 (57-100)%, respectively, according to pooled data of 7 studies.\(^2,3,7-11\) In a small prospective study of Suri et al. evaluating 32 patients by plain radiography, CT, and ultrasonography, CT showed high sensitivity (93%) and specificity (100%) for the diagnosis of ileus, was superior to other modalities, and allowed the evaluation of the cause of ileus in 87% (23% by US and 7% by plain radiography).\(^2\) While reports concerning MRI are limited, it has been reported to be highly sensitive and specific.\(^3,11\) Beall et al. reported that it is superior to CT,\(^11\) but the number of cases was very limited.

The presence or absence of intestinal ischemia (strangulation) is important for the selection of treatment for ileus. Physical findings are important, but they are insufficient in sensitivity or specificity, and imaging evaluation, particularly, using CT is considered significant (Figure). On CT, findings such as an increase or decrease in contrast enhancement of the intestinal wall, the target sign, closed loop formation, changes in the intestinal wall, mesenteric free fluid, congestion of the mesenteric vein, and the beak sign are important. Concerning the diagnostic performance of CT, the sensitivity was 95 (83-100)%, and the specificity was 90%, based on the pooled data of 399 cases in 5 reports.\(^7-9,12,13\) The negative predictive value in particular was 98%, suggesting that strangulation is unlikely with a negative CT. Reports regarding the effect of CT findings on the outcome are deficient, but, according to a prospective study of 57 cases by Taourel et al., the treatment was changed in 21% of the patients by performing CT.\(^14\)

**Index words and secondary materials used as references**

A search of PubMed was performed using “small bowel obstruction”, “plain radiography”, “CT”, “US”, and “MRI” as key words. Blackmore CC et al: Imaging in acute abdomen in evidence-based imaging, Medina LS & Blackmore CC ed, Springer 2006 was also used as a reference.

**References**

4) Frager D et al: CT of small-bowel obstruction: value in establishing the diagnosis and determining the degree and cause. AJR 162: 37-41, 1994 (Level 4)
Figure: Strangulation ileus CT
A  Non-contrast  B Portal-venous phase: The small intestine forms a closed loop and is hyperdense on non-contrast CT (→). Enhancement of the intestine is poor on contrast-enhanced CT. Surgery revealed that part of the greater omentum near the transverse colon and the mesentery formed a cord-like structure, and the small intestine was trapped in it. Since the intestine showed necrosis-like discoloration over a 20 cm segment, a 60 cm enterectomy was performed.

12) Zalcman M et al: Helical CT signs in the diagnosis of intestinal ischemia in small-bowel obstruction. AJR 175: 1601-1607, 2000 (Level 4)
14) Taourel PG et al: Value of CT in the diagnosis and management of patients with suspected acute small-bowel obstruction. AJR 165: 1187-1192, 1995 (Level 4)
**Background/objective**

Diverticulitis of the colon is often treated conservatively, but the differentiation of right-sided diverticulitis from appendicitis poses a problem. Also, as complications such as abscess formation may be observed, early and accurate diagnosis is vital. Colonic diverticulitis has long been diagnosed by abdominal plain radiography and barium enema, but the use of modalities such as CT (Figure) and ultrasonography has recently increased. The diagnostic value of these modalities was evaluated.

**Comments**

Concerning the diagnostic performance of CT for colonic diverticulitis, the sensitivity, specificity, positive predictive value, and negative predictive value were reported to be 89, 99, 99, and 90%, respectively, according to pooled data of 414 patients in 4 studies, with high specificity and positive predictive value. As for ultrasonography, the sensitivity, specificity, positive predictive value, and negative predictive value were reported to be 91, 92, 92, and 91%, respectively, based on pooled data of 526 patients in 4 studies.

According to a report by Pradel et al., who prospectively evaluated the diagnostic performance of ultrasonography and CT, more information could be obtained by CT in 11%, by US in 5%, and similar amount of information could be obtained by the two modalities in 84%, suggesting that ultrasonography may be the modality of choice. However, as the diagnosis of complications such as peritonitis is difficult by ultrasonography, the addition of CT is recommended depending on the necessity.

CT has also been reported to be useful for the management of diverticulitis. In a prospective study of 542 patients by Ambrosetti et al., surgery was often necessary, and the complication rate was higher, in patients with findings of severe diverticulitis.

Thus, while CT and ultrasonography are useful for the diagnosis of colonic diverticulitis, it should be noted that the differentiation from colorectal cancer is difficult in many patients by imaging findings alone.

**Index words and secondary materials used as references**

A search of PubMed was performed using “diverticulitis”, “CT”, “US”, and “MRI” as key words. Blackmore CC et al, Imaging in acute abdomen in evidence based imaging, Medina LS & Blackmore CC ed, Springer 2006 was also used as a reference.

**References**

6) Hollerweger A et al: Sigmoid diverticulitis: value of transrectal sonography in addition to transabdominal sonography. AJR 175: 1155-1160, 2000 (Level 3)
Figure: Colonic diverticulitis  Contrast-enhanced CT  MPR images
A diverticulum is observed in the proximal ascending colon. The density of the surrounding adipose tissue is increased, indicating diverticulitis (→).

06
Gynecology
In what situations is MRI appropriate for the diagnosis and follow-up of endometriosis?

**Recommendation grade**

Transvaginal ultrasonography is recommended as the initial examination. MRI is recommended for the diagnosis of ovarian and pelvic endometrioses, when the presence of solid components suggestive of malignant tumor is suspected by direct observation and transvaginal ultrasonography, when the differentiation from other tumors is difficult, when the lesion itself is difficult to visualize by transvaginal ultrasonography, and for the preoperative evaluation of the severity of adhesions.

**Background/objective**

Endometriosis is a disease that may cause dysmenorrhea and sterility and is a common disease observed in 6-10% of women of reproductive age. Ovarian endometriosis may underlie diseases including endometrioid adenocarcinoma and clear cell carcinoma and has been known to be related to borderline malignant tumors. Pelvic endometriosis also causes adhesions, may induce pain or infertility, and is an indication for medication and lysis of adhesions. Situations in which MRI is useful for the diagnosis and follow-up of ovarian and pelvic endometriosis were evaluated.

**Comments**

When endometriosis is suspected, transvaginal ultrasonography is the first choice screening modality. If an ovarian tumor is suggested by transvaginal ultrasonography, and the differentiation between endometriomas and other adnexal masses by MRI is very high at 96%. Signal intensity of cyst contents are characteristic, being hyperintense on both T1- and T2-weighted imaging or hyperintense on T1-weighted imaging but partially hypointense, a pattern called “shading”, on T2-weighted imaging. Cysts may be irregular in shape and show sharp angles due to adhesions to surrounding structures, and cysts of various sizes containing hemorrhage of various ages may be aggregated (multiplicity). According to the General Rules for Clinical Management of Endometriosis of Japan, these findings are a reliable basis for the determination of a therapeutic strategy.

Pelvic endometriosis is classified into peritoneal endometriosis present on the peritoneal surface and deep endometriosis invading 5 mm or more into neighboring organs. The disease usually involves the uterine ligament, rectovaginal septum, pouch of Douglas, and peritoneum but may also affect various sites including the intestinal tract, ureter, and inguinal region. On MRI, lesions are hypointense on T2-weighted imaging, reflecting fibrosis, but hyperintense on T1-weighted imaging and may or may not be accompanied by smaller lesions. The gold standard for the final diagnosis of pelvic endometriosis is laparoscopy, which allows histological evaluation, but there have been a number of reports on the preoperative diagnosis by transvaginal ultrasonography and MRI. It has been reported that transvaginal ultrasonography shows slightly higher sensitivity, specificity, and accuracy for deep endometriosis but should be performed complementarily with MRI, that MRI is relatively well correlated with surgery in deep pelvic endometriosis, that its sensitivity and specificity for deep endometriosis are comparable to those of transvaginal ultrasonography, but that MRI is more reliable than other preoperative examinations, and that the accuracy of MRI for endometriosis spreading to parauterine tissues was 96.4%. Despite variation in diagnostic performance in pelvic endometriosis with the site and examiner’s experience in image reading, MRI is considered to contribute to the preoperative diagnosis and mapping of pelvic endometriosis.

Similarly, transvaginal ultrasonography is recommended for periodic follow-up. Since ovarian endometriosis may be origin of borderline malignant or malignant tumors, periodic follow-up is important. Cancers arising from ovarian endometriosis preferentially occurs after menopause, and surgery is recommended for masses with a maximum diameter of 9 cm or greater. An increase in the tumor size, a high CA125 level or its rapid increase, transvaginal ultrasound findings suggesting a solid structure, and changes in the echo level of the contents to that of water due to exudate production associated with cancerization have been reported as signs of malignant change. If such signs are observed, further evaluation by MRI is necessary (See CQ112 for the discrimination from ovarian cancer).

**Index words and secondary materials used as references**

A search of PubMed was performed using “endometriosis”, “endometrioma”, “endometriotic cyst”, “MRI”, “diagnosis”, “sensitivity”, and “specificity” as key words. The Japan Society of Obstetrics and Gynecology, the General Rules for Clinical Management of Endometriosis (The 2nd Edition), 2010 was also used as a reference.
**References**


6) Abrao MS et al: Comparison between clinical examination, transvaginal sonography and magnetic resonance imaging for the diagnosis of deep endometriosis. Hum Reprod 22: 3092-3097, 2007 (Level 3)


10) Bazot M et al: Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. Fertil Steril 92: 1825-1833, 2009 (Level 2)


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**Figure: Chocolate cyst of the left ovary MRI**

A  Transverse T2-weighted image   B  T1-weighted image  Multilocular cystic tumor of the left ovary, presenting with homogeneous hyperintensity on T1-weighted imaging and heterogeneous hypointensity (shading) on T2-weighted imaging. Diagnosed as endometrioma of the left ovary.
Is MRI appropriate for the diagnosis of uterine fibroids?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>In patients who cannot be diagnosed by bimanual palpation or ultrasonography, MRI is recommended as it contributes to the qualitative diagnosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>In patients undergoing uterus-preserving invasive treatments (myomectomy, UAE, FUS, etc.), MRI is useful for the accurate determination of the location, site, and number of fibroids and is recommended.</td>
</tr>
</tbody>
</table>

**Background/objective**

For the diagnosis of uterine fibroids, bimanual palpation and ultrasonography by a gynecologist are the first choice, but MRI may be ordered if the diagnosis is uncertain. Also, in patients scheduled to undergo invasive treatments (myomectomy, UAE, FUS, etc.) assuming uterine preservation, MRI is recommended for the accurate determination of the location, site, and number of fibroids. The usefulness of MRI for the diagnosis of uterine fibroids was evaluated.

**Comments**

Uterine fibroid is diagnosed mostly by bimanual palpation and ultrasonography (TVUS) by a gynecologist, and it is uncommon to perform MRI for screening.\(^1\),\(^2\) MRI is ordered primarily for (1) further evaluation of patients not diagnosable by ultrasonography and (2) preoperative evaluation of patients undergoing uterus-preserving invasive treatments (myomectomy, UAE, FUS, etc.). According to a report of comparison with surgical specimens of submucosal fibroids, the diagnostic performance of MRI (sensitivity: 100%, specificity: 91%) was superior to those of TVUS (sensitivity: 83%, specificity: 90%) or hysteroscopy (sensitivity: 82%, specificity: 87%).\(^3\) In another study of comparison with surgical specimens, the sensitivity of MRI (80%) was 2-fold higher than that of TVUS (40%), and MRI was more reproducible (k=0.97) than TVUS (k=0.74).\(^4\) Evaluation of MRI and TVUS findings in fibroids before UAE showed that they were closely correlated concerning the lesion size, but that the correlation was low with regards to the location or number (R=0.17), and that MRI could detect more lesions and was useful for more exact determination of location (submucosal, intramyometrial, subserosal).\(^5\) Another study on fibroids before UAE by MRI, the diagnosis was changed in 18%, and the therapeutic strategy was changed in 22%, of the patients after MRI.\(^6\) From these evaluations, MRI is recommended for the accurate determination of the location, site, and number of fibroids in patients undergoing invasive treatments (Figures 1, 2).

A typical manifestation of fibroids on T2-weighted MRI is a hypointense mass with a clear border, but it may be visualized as a hyperintensity in T2-weighted images depending on degenerations and histological subtypes, posing difficulty in the discrimination from malignant tumors.\(^7\)-\(^9\) While some lesions such as red degeneration and lipoleiomyoma can be diagnosed due to characteristic imaging features,\(^10\),\(^11\) edema, necrotic degeneration, and cellular leiomyoma are often difficult to diagnose by routine MRI, and the diagnostic performance is not improved even by the addition of usual contrast-enhanced T1-weighted imaging.\(^12\),\(^13\) The discrimination of histological subtypes and benign and malignant diseases has been attempted using contrast-enhanced dynamic studies and diffusion-weighted imaging, and future evaluations are awaited.\(^12\),\(^14\) Also, both subserosal fibroid and ovarian fibrous tumor often present low intensity signals on T2-weighted imaging, posing problems with the differentiation. On MRI, there have been reports that delineation of flow voids of feeding vessels continuous from the uterine body was useful for the diagnosis of myoma\(^15\) and that the evaluation of the enhancement pattern on contrast-enhanced dynamic studies was useful for the differential diagnosis.\(^16\)

**Index words and secondary materials used as references**

A search of PubMed was performed using “leiomyoma”, “myoma”, “fibroid”, “uterus”, “uterine”, “MRI”, and “magnetic resonance” as key words.

**References**

8) Ha HK et al: MR imaging analysis of heterogeneous leiomyomas of the uterus. Front Biosci 2: 4-12, 1997 (Level 3)
Is MRI appropriate for the diagnosis of uterine adenomyosis?

If abnormalities suggestive of adenomyosis are noted in the myometrium by transvaginal ultrasonography, MRI is recommended to confirm the diagnosis and evaluate complicating lesions.

**Background/objective**

Since symptoms of uterine adenomyosis vary widely and are non-specific, it is difficult to definitively diagnose by clinical criteria alone. Transvaginal ultrasonography is often performed first in routine gynecological examination. The usefulness of MRI for the diagnosis of uterine adenomyosis was evaluated using transvaginal ultrasonography as a reference.

**Comments**

The sensitivity and specificity of MRI for the diagnosis of uterine adenomyosis are 70-89 and 86-93%, and those of transvaginal ultrasonography are 65-89 and 65-98%, respectively, indicating no significant difference in diagnostic performance. However, for the diagnosis of adenomyosis, which complicates uterine myoma in about 50% of the patients, MRI with a sensitivity of 67% and a specificity of 87% is more accurate than transvaginal ultrasonography with a sensitivity of 33% and specificity of 98%. Concerning uterine enlargement, also, MRI has been reported to show high accuracy in the discrimination between leiomyoma and uterine adenomyosis as its cause.

Diffuse or localized thickening of the junctional zone (JZ) observed on T2-weighted imaging has been reported by many authors as an MRI finding that serves as the basis of a diagnosis of uterine adenomyosis. This finding reflects smooth muscle hyperplasia associated with ectopic endometrium. The thickness of the JZ is reported to be normally 8 mm or less, and 12 mm or thicker is generally accepted as a criterion for the diagnosis of adenomyosis. With this criterion, the sensitivity and specificity have been reported to be 63-93 and 91-96%, respectively. Punctate hyperintensities observed in the myometrium on T2-weighted imaging have also been reported by many to be of diagnostic use. This finding reflects cystic dilatation of gland ducts in ectopic endometrium in the lesion and is a specific finding (99%) while it is observed in about half the patients (Figures 1, 2).

When uterine adenomyosis is complicated by endometrial cancer, it must be noted that the border between cancer and adenomyosis is unclear on T2- or contrast-enhanced T1-weighted imaging and that the presence diagnosis of uterine body cancer and evaluation of the degree of myometrial involvement are difficult. In such circumstances, there is a report that the border between lesions of uterine body cancer and adenomyosis could be clearly visualized by diffusion-weighted imaging. Expectations for the modality are high, but further evaluation is necessary before its usefulness is established.

**Index words and secondary materials used as references**

A search of PubMed was performed using “MRI” and “adenomyosis” as key words.

**References**

1) Bazot M et al: Ultrasonography compared with magnetic resonance imaging for the diagnosis of adenomyosis: correlation with histopathology. Hum Reprod 16: 2427-2433, 2001 (Level 3)
6) Kang S et al: Adenomyosis: specificity of 5mm as the maximum normal uterine junctional zone thickness in MR images. AJR 166: 1145-1150, 1996 (Level 4)
Figure 1: Uterine adenomyosis Sagittal T2-weighted image
The junctional zone, showing low signal intensity, is thickened in the posterior wall of the uterine body (→), with many punctate hyperintensities observed in the interior. A typical image of uterine adenomyosis.

Figure 2: Uterine adenomyosis complicated by fibroids Sagittal T2-weighted image
Uterine adenomyosis complicated by myoma. A lesion of adenomyosis primarily affecting the posterior wall of the body of uterus is delineated as a hypointense area with an unclear border containing punctate hyperintensities (→). In the anterior wall, a fibroid is visualized as a hypointense mass with a clear border (M).
Background/objective

In diagnostic imaging for the staging of ovarian cancer, invasion to surrounding pelvic organs, peritoneal dissemination, and lymph node metastasis are major concerns. Since accurate information about these conditions is an important basis for complete resection and optimal debulking (maximum diameter of residual tumor<1 cm), which are important for the treatment of ovarian cancer, its diagnostic value is high. The usefulness of US, CT, MRI, and PET/CT for the staging of ovarian cancer was evaluated.

Comments

A multicenter joint study evaluating the performance of US, CT, and MRI in staging ovarian cancer reported that all these modalities accurately evaluated the extent of tumor involvement in the extraovarian pelvic region, abdominal region, and outside the abdominal/pelvic region with no significant difference among the modalities. According to an evaluation of peritoneal dissemination and lymph node metastasis on the basis of the above study, the area under the ROC curve concerning the detection of peritoneal dissemination was significantly larger by MRI (0.96) than by US (0.86), and MRI was particularly useful in the infradiaphragmatic space, but the ability to detect small lesions 2 cm or less in diameter was low in both modalities. Therefore, it was concluded that CT and MRI are useful for the staging of ovarian cancer and that US can be used complementarily.

Thus, CT and MRI are useful for the staging of ovarian cancer, but CT is a more practical choice today, when MDCT is widely available and allows imaging in a short period. When sagittal and coronal views are evaluated together by MDCT, peritoneal dissemination has been reported to be diagnosed with a specificity of 94-100% (Figure). MRI is defined as the second imaging modality in the ACR and ESUR guidelines and is recommended when contrast-enhanced CT cannot be performed due to contraindications to contrast agents or pregnancy or when a definitive diagnosis is impossible by CT. However, in the diagnosis of intrapelvic invasion such as invasion to the uterus, sigmoid colon, bladder, and pelvic wall, MRI with higher spatial resolution is reportedly superior to CT, and it should be considered for the evaluation of intraperitoneal tumor invasion. Also, diffusion-weighted imaging is useful for the detection of peritoneal dissemination and should be considered for its close evaluation.

A recommended area of CT examination is from the bottom of the lung to the inguinal region. The inclusion of the bottom of the lung allows the evaluation of the presence or absence of supradiaphragmatic lymph node enlargement and pleural effusion. Chest CT is considered when chest plain radiography showed thoracic abnormalities such pleural effusion, or when supraclavicular lymph nodes are suspected to be enlarged.

Concerning PET/CT, there have been reports that PET/CT showed significantly higher sensitivity (69 vs. 38%) and accuracy (94 vs. 90%) than CT alone for the detection of lesions, and that it showed more favorable results than CT alone despite the absence of significant difference. Since the detectability of small peritoneal disseminations and metastases outside the abdominal/pelvic region such as supraclavicular lymph node metastasis is improved in PET/CT, the modality should be considered when the objective of examination is the detection of such lesions.

Index words and secondary materials used as references

A search of PubMed was performed using “CT”, “MRI”, “PET (PET/CT)”, “US”, “ovarian cancer or ovarian carcinoma”, and “staging” as key words. The ACR Appropriateness Criteria® (Staging and follow-up of ovarian cancer) and ESUR guidelines: ovarian cancer staging and follow-up were also used as references.
Figure: Left ovarian serous carcinoma

A-C Contrast-enhanced CT  D Contrast-enhanced CT (coronal MPR image) Left ovarian cancer (C) is observed with multiple peritoneal disseminations in areas including the perihepatic space, Morrison’s pouch, mesentery, greater omentum, paracolic sulcus, and pelvis (A-D). On the coronal view, dissemination is clear in the right infradiaphragmatic space and Morrison’s pouch.

References

7) Nam EJ et al: Diagnosis and staging of primary ovarian cancer: correlation between PET/CT, Doppler US, and CT or MRI. Gynecol Oncol 116: 389-394, 2010 (Level 2)
Is MRI appropriate for the qualitative diagnosis of ovarian mass?

**Recommendation grade**

For patients not diagnosable by ultrasonography, which is the first choice, MRI contributes to the qualitative diagnosis of ovarian masses and is recommended. Contrast-enhanced MRI improves the accuracy of the differentiation of benign and malignant ovarian masses and is recommended.

**Background/objective**

While ultrasonography by a gynecologist is the first choice for the diagnosis of ovarian mass, MRI is frequently ordered for undiagnosable patients. Also, incidental detection of ovarian masses during screening by ultrasonography or examination for other diseases by modalities such as CT is increasing. The usefulness of MRI for the differentiation between benign and malignant ovarian masses was evaluated.

**Comments**

Most of ovarian tumors are benign cystic masses and are diagnosable by ultrasonography. The accuracy of ultrasonography (TVUS) for the differentiation between benign and malignant ovarian tumors is 80-83%, and while it improves by the addition of color Doppler imaging, the diagnosis of lesions in which solid and cystic parts are mixed is often reported to be difficult.\(^1\,2\) There have been multiple reports that MRI was useful, with accuracies of 83-93%, for the diagnosis of patients undiagnosable by ultrasonography.\(^3\,4\) Findings suggestive of malignancy in ovarian tumors include a large tumor diameter (≥4 cm), bilateral involvement, tumor consisting primarily of solid components, tumor showing necrosis in the solid part, cystic tumor with a cyst wall or septal thickness of 3 mm or greater, and cystic mass accompanied by papillary intramural nodules (Figure), and, as secondary findings, ascites, intraperitoneal dissemination, and lymph node enlargement.\(^5\,9\) Necrosis of the solid part and intramural nodules accompanying a cystic mass are considered to contribute most to the diagnosis of malignancy. Also, as the diagnostic accuracy is improved by contrast enhancement,\(^5\) the procedure is recommended in patients without contraindications. On the other hand, the detection of fat, which suggests teratoma, a hemorrhagic cyst accompanied by shading on T2-weighted imaging, which suggests an endometrioma, and strong hypointensity on T2-weighted imaging, which suggests fibrous tumor, are considered to be findings associated with a high possibility of benignancy.\(^1\,10\,11\) Recently, there have been reports that diffusion-weighed imaging and dynamic MRI are useful for the differentiation of benign and malignant lesions,\(^12\,14\) and hyperintense solid parts with lower apparent diffusion coefficient and hypervascularity of the solid part on dynamic MRI were shown to be correlated with malignancy, but further validation is necessary about the possibility of their contribution to improvements in the accuracy.

Various benign and malignant tumors and tumor-like lesions occur in the ovary. Characteristic MRI findings reflecting histological features frequently lead to specific diagnoses as well as the differentiation of benign and malignant diseases. CT is inferior to MRI in contrast resolution, and while the detection of calcification may contribute to the qualitative diagnosis of ovarian masses, its indications should be carefully evaluated in young females because of problems including gonadal exposure.

**Index words and secondary materials used as references**

A search of PubMed was performed using “ovary”, “ovarian”, “adnexa”, “adnexal”, and “MRI” as key words, and relevant references cited in the selected literature were also adopted. The ESUR guidelines (Spencer JA et al: ESUR guidelines for MR imaging of the sonographically indeterminate adnexal mass: an algorithmic approach. Eur Radial 20: 25-35, 2010) was also used as a reference.

**References**

Figure: Clear cell carcinoma of the ovary  MRI
A  Fat-suppressed contrast-enhanced T1-weighted image: A unilocular cystic mass is observed in the ovary, accompanied by multiple enhancing intramural nodules. B  Diffusion-weighted image: The intramural nodules are markedly hyperintense.

6. Gynecology

Is diagnostic imaging appropriate for the staging of uterine cervical cancer?

**Background/objective**

Treatment for cervical cancer has two pillars, i.e., surgery and radiation therapy, and the treatment is selected according to the General Rules for Clinical and Pathological Study of Uterine Cervical Cancer (3rd edition: Japan Society of Obstetrics and Gynecology). This edition clearly states, “Imaging modalities such as CT and MRI can be used for the evaluation of the spread and size of tumor,” and diagnostic imaging plays an important role in the clinical staging of cervical cancer. In this section, the usefulness of imaging modalities for staging cervical cancer was evaluated.

**Comments**

Used for the staging according to the General Rules for Clinical and Pathological Study of Uterine Cervical Cancer vary in effectiveness among examiners and have limitations in the evaluation of intrapelvic lymph nodes. In Japan, CT or MRI is performed before treatment in most patients with cervical cancer, and PET/CT is also used at some facilities. Ultrasonography is often performed at gynecological outpatient clinics simultaneously with pelvic examination and is useful due to its simplicity and low cost. While the results of transvaginal or transrectal ultrasonography concerning the local spread have been reported to be similar or relatively good compared with CT or MRI,\(^1\)\(^\text{,}\)\(^2\) it is inferior to these modalities in the evaluation of lymph node metastasis and objectivity.

CT and MRI have been suggested since early times to be useful for the staging, and a multicenter meta-analysis reported that MRI is more sensitive than CT for parametrial invasion (55% by CT, 74% by MRI) (Figure) and that they are nearly equal in diagnosing lymph node metastasis.\(^3\) According to a joint multicenter research conducted by the American College of Radiology Imaging Network (ACRIN) and Gynecologic Oncology Group (GOG), the sensitivities of MRI and CT for stage IIb or more advanced cancer were relatively low (42% by CT, 53% by MRI), but their specificities were high (82% by CT, 85% by MRI).\(^3\) Regarding invasion to other organs such as the bladder and rectum, MRI was more sensitive than CT and is useful for the selection of treatment.\(^4\) Cystoscopy, rectoscopy, and excretory urography are considered to be substitutable with MRI or CT.\(^5\) Also, the evaluation of the tumor volume is important for the prognosis and evaluation of the therapeutic effect, and the tumor volume and its shrinkage due to radiation therapy can be evaluated objectively by MRI.\(^6\)

Concerning gadolinium contrast enhancement, no sufficient universal consensus has been reached. Staging is made basically by T2-weighted imaging, and while the contrast between the tumor and normal myometrium is reportedly improved in contrast enhanced MRI with a consequent improvement in the diagnostic ability,\(^7\) its indications are limited, and the modality does not necessarily contribute to improvements in diagnostic performance.

Diffusion-weighted imaging has also begun to be used more extensively in the abdomen and pelvis due to improvements in MRI equipment. Cervical cancer is hyperintense on diffusion-weighted imaging and shows a low apparent diffusion coefficient (ADC).\(^8\) Concerning the usefulness of the modality, greater attention is directed to the prediction of the therapeutic effect\(^9\) and delineation ability of lymph node metastasis\(^10\) than to the diagnosis of local invasion.

CT or PET/CT is used for close evaluation of distant metastasis and paraaortic lymph node metastasis. According to analysis by the ACRIN/GOG, both CT and MRI show a low sensitivity (37% by CT, 31% by MRI) but a high specificity (94% by CT, 56% by MRI) when a short diameter of the node of \(\geq\)1 cm was used as the criterion of lymph node metastasis.\(^11\) A meta-analysis reported that PET and PET/CT were more sensitive than CT or MRI (82% by PET and PET/CT, 50% by CT, 56% by MRI), but lymph node metastasis is not taken into consideration in staging and, presently, is not an essential item.\(^12\)

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**Recommendation**

- **B** MRI, CT
- **C1** PET (PET/CT)

**Recommendation grade**

- **B**
- **C1**

MRI is recommended for the measurement of the tumor diameter and evaluation of the depth of local invasion, invasion to surrounding organs, and intrapelvic lymph node metastasis. While CT is inferior to MRI in the ability to determine the depth of invasion, it is recommended when MRI cannot be performed and for the diagnosis of metastasis.

PET or PET/CT can be performed as it is useful for the evaluation of lymph node and distant metastases, but it does not affect the staging.

References

2) Testa AC et al: Transvaginal ultrasonography and magnetic resonance imaging for assessment of presence, size and extent of invasive cervical cancer. Ultrasound Obstet Gynecol 34: 335-344, 2009 (Level 3)
Is diagnostic imaging appropriate for the staging of endometrial cancer?

**Background/objective**

The prognosis of endometrial cancer depends on the histological type, degree of malignancy, and stage of the tumor. In advanced stages, diagnostic imaging contributes greatly to the evaluation of myometrial and cervical invasion, adnexal spread, and lymph node and distant metastasis. More accurate preoperative diagnosis concerning these features helps with the selection of the surgical procedure and determination of the therapeutic strategy. Myometrial invasion, in particular, is strongly correlated with lymph node metastasis, and its accurate preoperative diagnosis is highly significant. The usefulness of TVUS, CT, MRI, and PET/CT for the diagnosis of preoperative staging of endometrial cancer was evaluated.

**Comments**

Evidence-based guidelines for treatment of uterine body neoplasm in Japan recommend preoperative assessment of myometrial and cervical invasion by MRI and lymph node and distant metastasis by various imaging modalities (recommendation grade: C1).

Concerning the preoperative staging of endometrial cancer, Kinkel et al. reported a meta-analysis in 1999 that there was no significant difference among TVUS, CT, and MRI. In the same report, however, contrast-enhanced MRI was shown to be significantly more useful than non-contrast MRI, TVUS, or CT for the evaluation of myometrial invasion (Figures 1, 2).

Regarding myometrial invasion, many reports showed that the sensitivity and specificity of TVUS were high and did not significantly differ compared with those of MRI, but reports indicating MRI is highly sensitive and specific and more useful are increasing. Particularly, there have been many reports indicating the usefulness of contrast-enhanced MRI, and the accuracy of the diagnosis of myometrial invasion was 92% by contrast-enhanced MRI compared with 78% by T2-weighted imaging. The ACR Appropriateness Criteria also recommend MRI, particularly contrast-enhanced MRI, unless there are contraindications. Dynamic contrast-enhanced MRI is preferred if possible. Internationally, it appears common to perform MRI only when the evaluation is difficult by TVUS because of the cost, but as there are problems such as the risk of dissemination by the scanning procedure and dependence of the precision on the examiner’s skill, MRI, which is more objective, is very useful.

However, there is a report that the sensitivity of MRI was 87% for shallow myometrial invasion but 56% for deep myometrial invasion, suggesting a decline in the diagnostic ability for the latter. High magnetic field MRI (3T) has been reported to be superior to conventional MRI in evaluating deep myometrial invasion, but no significant difference has been demonstrated by overall evaluation including cervical invasion and lymph node metastasis.

MRI is also useful for the evaluation of cervical invasion. However, while its sensitivity (67%), specificity (95%), and accuracy (91%) have been reported to be higher than those of TVUS, the sensitivity (19%) and accuracy (84%) have also been reported to be low, suggesting limitations in the evaluation, and the results have not been consistent.

The diagnostic performance of imaging modalities for lymph node metastasis is low with a sensitivity of about 50% due to the presence of micrometastases by imaging modalities using the lymph node size (short diameter ≥1 cm) as a diagnostic criterion. PET/CT has been reported to be relatively superior to other imaging modalities in the evaluation of lymph node metastasis, but it shows only slightly higher sensitivity, and its sensitivity to unenlarged lymph nodes with a diameter of 10 mm or less is low similarly to other modalities.

Also, while PET/CT is reportedly useful for the detection of distant metastasis, its value has not been sufficiently established. According to a report comparing PET/CT and CT/MRI, the sensitivity of PET/CT for distant metastasis...
was 83.3% and was higher than 66.7% for CT/MRI, but there was no difference in specificity.\textsuperscript{9}

Since many uterine body cancers are detected in an early stage without metastasis, some authors consider that examination to the thoracic region using CT for distant metastasis is unnecessary except in histological types with a poor prognosis such as serous adenocarcinoma and clear cell adenocarcinoma, highly malignant tumors at a high risk of metastasis, and tumors showing local invasion.

Diffusion-weighted MRI has recently begun to be employed widely for the examination of the abdomen and pelvis. Despite high frequency of overlapping findings, uterine body cancer is hyperintense and shows a lower apparent diffusion coefficient (ADC) compared with benign endometrial lesions on diffusion-weighted imaging. There is also a report that diffusion-weighted imaging is superior to contrast-enhanced MRI in the evaluation of myometrial invasion and staging.\textsuperscript{11}

Among modalities, CT shows lower contrast resolution and is less effective for delineating lesions in the uterine body than MRI. Therefore, it is not very useful for the assessment of local spread\textsuperscript{12} and is suited for the search for lymph node and distant metastasis. However, if MRI is not available, local spread can be evaluated by contrast-enhanced CT.

In the ACR Appropriateness Criteria, CT is recommended for the diagnosis of abdominal lymph node metastasis,
but abdominal MRI is also recommended in consideration of radiation exposure. However, as it is necessary to scan a relatively wide area to search for metastases, CT is considered preferable to MRI if performed for this purpose.

**Index words and secondary materials used as references**


**References**

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10) Park JY et al: Comparison of the validity of magnetic resonance imaging and positron emission tomography/computed tomography in the preoperative evaluation of patients with uterine corpus cancer. Gynecol Oncol 108: 486-492, 2008 (Level 3)
12) Hardesty LA et al: The ability of helical CT to preoperatively stage endometrial carcinoma. AJR 176: 603-606, 2001 (Level 2) but abdominal MRI is also recommended in consideration of radiation exposure. However, as it is necessary to scan a relatively wide area to search for metastases, CT is considered preferable to MRI if performed for this purpose.
Background/objective

Uterine sarcoma is often difficult to diagnose by cytological examination or biopsy, and it is often problematic to distinguish benign degenerated uterine leiomyomas and uterine sarcomas. Carcinosarcoma is recently considered to be metaplasia of endometrial cancer, however it is included as uterine sarcoma in many retrospective studies and also included in this evaluation. The usefulness of diagnostic imaging for the preoperative diagnosis and staging of uterine sarcoma is evaluated.

Comments

Ultrasonography, which is the first imaging modality of choice in the gynecologic disorders, was suggested to be useful for the differentiating between uterine leiomyoma and sarcoma in early reports, but this could not be confirmed in subsequent studies. MRI has high soft tissue contrast and is useful for the differential diagnosis of uterine masses. Sarcoma was reported to be a large mass with heterogeneous signal intensity due to hemorrhage and necrosis. However, Cornfeld et al. reported that there is no objective criteria in the differentiation between benign and malignant uterine mesenchymal tumors by MRI. Diffusion-weighted imaging is a recent developed technique in which malignant lesions tend to show high intensity because of high cellularity and allows quantitative evaluation by the measurement of the apparent diffusion coefficient (ADC). The diagnostic performance for uterine sarcoma was improved by the measurement of the ADC, and further accumulation of cases is awaited.

The clinical course and treatment of uterine sarcoma vary with the histological type. Reported MRI features of each histological type helps the diagnosis, although no reports with high evidence level exists due to rarity and lack of large-scale studies of uterine sarcomas. The presence of hemorrhage and necrosis which can be evaluated by MRI signals give clues to the diagnosis of uterine leiomyosarcoma. Contrast-enhanced MRI is useful for the evaluation of necrosis, and the accuracy has been reported to be improved by dynamic contrast-enhanced MRI with the measurement of LDH isozymes. Endometrial stromal sarcoma exhibits various invasion patterns, and MRI findings such as bands of low signal intensity on T2-weighted imaging and continuous tumor extent along the blood vessels and the ligaments are informative. Carcinosarcoma is difficult to differentiate from uterine body cancer, however on MRI it is a large mass that dilates the uterine cavity and shows characteristic MRI features such as heterogeneous hyperintensity on T2-weighted imaging, early and persistent enhancement and/or gradual and delayed strong enhancement.

Although the clinical staging of uterine sarcoma used to be made similarly to uterine body cancer, a new staging system was established by the FIGO in 2009. The diagnosis of uterine sarcoma may be difficult, however, MRI and CT are recommended for the assessment of local and distant metastasis.

Index words and secondary materials used as references

A search of PubMed was performed using “uterine sarcomas”, “endometrial stromal sarcomas”, “uterine leiomyosarcomas”, “uterine carcinosarcomas”, and “diagnostic imaging” as key words.
6. Gynecology

The Japanese imaging guideline 2013

References

5) Tamai K et al: The utility of diffusion-weighted MR imaging for differentiating uterine sarcomas from benign leiomyomas. Eur Radiol 18: 723-730, 2008 (Level 2)
8) Namimoto T: Combined use of T2-weighted and diffusion-weighted 3-T MR imaging for differentiating uterine sarcomas from benign leiomyomas. Eur Radiol 19: 2756-2764, 2009 (Level 2)
12) Teo SY et al: Primary malignant mixed Mullerian tumor of the uterus: findings on sonography, CT, and gadolinium enhanced MRI. AJR 191: 278-283, 2008 (Level 4)

Figure: Uterine leiomyosarcoma

A  T2-weighted image: A heterogeneously hyperintense mass is observed in the myometrium of the uterine body (→).  B  T1-weighted image: Irregular T1 hyperintensities are presented in the mass (→), suggesting hemorrhage due to necrosis, and leiomyosarcoma is likely based on the images.
Is PET appropriate for the diagnosis and follow-up of gynecological tumors?

**Recommendation grade**

<table>
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<tr>
<th>Grade</th>
<th>Restaging for uterine and ovarian cancers</th>
<th>Restaging for gynecological cancers other than uterine and ovarian cancers</th>
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PET is useful and recommended for the diagnosis of recurrence of uterine and ovarian cancers. It has been reported to be useful in recurrent gynecological malignancy other than uterine and ovarian cancers, although there is still limited evidence. For this reason, its clinical application may be considered.

**Background/objective**

Positron emission tomography (PET) using fluorodeoxyglucose (FDG) is one of the relatively new imaging modalities clinically applied to various malignant neoplasms. The usefulness of PET (PET/CT) in gynecological tumors was evaluated.

**Comments**

Since gynecological malignancies can be classified into uterine, ovarian, and fallopian tube cancers and other malignant neoplasms including sarcoma, the usefulness of PET is discussed in relation to the goal of its use, i.e., the diagnosis, differential diagnosis, staging, diagnosis of recurrence, and assessment of therapeutic effects. PET has no role in the diagnosis or differential diagnosis of primary uterine cervical and endometrial cancers because the uterine cavity can be observed directly with ease, cells and tissues can be sampled, and the endometrium shows physiologic uptake in some periods of the menstrual cycle.

In the staging, the sensitivity and specificity of PET (PET/CT) for intrapelvic lymph node metastasis of uterine cervical cancer have been reported to be 79 and 99%, and those for para-aortic lymph node metastasis to be 84 and 95%, respectively, suggesting that it is a modality that can complement CT or MRI. However, its sensitivity to Stage Ib1-IIa lesions with a primary focus 4 cm or less in diameter is low at 32%, and the modality exerts little effect on therapeutic strategy. In uterine body cancer, also, PET shows sensitivity and specificity of 73 and 95% for intrapelvic lymph node metastasis and 85 and 95%, respectively, for para-aortic lymph node metastasis, similarly to uterine cervical cancer. However, histological examination and follow-up are necessary for the definitive diagnosis, and lymph node dissection must not be omitted on the basis of negative PET findings. PET has sensitivity and specificity of 92-96 and 81-100% for the recurrent of uterine cervical cancer and 96-100 and 78-88%, for the recurrence of uterine body cancer, respectively, and shows satisfactory precision for both disorders.

A case of recurrence of uterine cervical cancer is presented in the figure.

The ovary shows physiologic FDG uptake as does the endometrium, and benign tumors may also show uptake. The sensitivity and specificity of PET for the detection of ovarian cancer have been reported to be 52-58 and 76-78%, respectively, so the modality is not recommended for the initial diagnosis or differential diagnosis. Reports on the preoperative staging are limited, but the sensitivity and specificity of PET (PET/CT) for lymph node or peritoneal metastasis have been reported to be 62 and 97% in intrapelvic lesions and 75 and 98%, in extrapelvic lesions, respectively being superior to those of CT alone. According to a multicenter study, the sensitivity and specificity of PET for the diagnosis of recurrent ovarian cancer were 90-96 and 80-88%, respectively, when it was clinically suspected from elevation of tumor marker levels and findings on other imaging modalities, similarly to recurrent uterine cancer, and PET affected the determination of the therapeutic approach in 60% of the patients.

On the basis of the above observations, the NCCN Guidelines 2008 concerning uterine and ovarian neoplasms described PET as a modality that should be considered when metastatic foci cannot be detected by conventional diagnostic imaging despite suspicion of recurrence due to clinical signs such as elevated tumor marker levels after the initial treatment or when a definitive diagnosis of recurrence is difficult.

Since metabolic changes of tumoral lesions after chemotherapy or radiation therapy precede morphological changes, i.e., changes in size, PET, which provides information about not only morphology but also metabolism, is expected to contribute to the evaluation of the therapeutic effect. However, various changes that lesions undergo after treatment, such as inflammatory change, or the appropriate timing of examination after treatment have not been adequately assessed. PET is still in the stage of clinical research, and the evidence that the modality should be performed clinically on a routine basis is deficient. As of spring, 2012, PET for the assessment of the therapeutic effect on gynecological tumors is not covered by the national medical insurance system.
Reports on the diagnosis of gynecological tumors other than uterine and ovarian cancers by PET are limited to those of the case series study level, but its diagnostic precision for lymph node metastasis before treatment and recurrence after treatment has been reported to be comparable to that in uterine and ovarian cancer. Therefore, the modality may also have similar usefulness in other gynecological tumors.

Index words and secondary materials used as references

References
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15) Fulham MJ et al: The impact of PET-CT in suspected recurrent ovarian cancer: a prospective multi-centre study as part of the Australian PET Data Collection Project. Gynecol Oncol 112: 462-468, 2009 (Level 1)
16) Cohn DE et al: Prospective evaluation of positron emission tomography for the detection of groin node metastases from vulvar cancer. Gynecol Oncol 65: 179-184, 2002 (Level 2)
Is periodic imaging need for the follow-up of gynecological malignancies?

There are still unsolved problems related to imaging indications and frequency of examination, versatility, cost-performance, and radiation exposure. While the usefulness of PET/CT for the diagnosis of recurrent gynecological malignancies has been established, abdominopelvic contrast-enhanced CT may be considered as an alternative.

Background/objective

Concerning the post-treatment follow-up of gynecological malignancies, the interval and examination protocols are addressed in the guidelines of the Japan Society of Gynecologic Oncology. It is recommended to perform CT every 6-12 months for ovarian cancer (grade C1), 1-2 times/year for uterine body cancer (grade C1), and plain chest radiography and other imaging examinations when appropriate for uterine cervical cancer (grade C1). However, guidelines concerning uterine cervical cancer also present the opinion that all diagnostic imaging should be performed when recurrence is suspected and is inappropriate as a routine examination. In consideration of these circumstances and the recent widespread use of PET equipment, imaging modalities appropriate for post-treatment follow-up were evaluated.

Comments

For the post-treatment follow-up of gynecological malignancies, various imaging modalities, particularly contrast-enhanced CT, are performed in addition to pelvic examination, measurement of tumor markers, and vaginal cytology. For the early detection of recurrence of ovarian cancer, the ability of PET/CT has recently come close to that of tumor marker (CA125) examination. As for imaging modalities, MRI has been reported to be more useful or equally useful compared with contrast-enhanced CT for the diagnosis of local recurrence, but the results of PET/CT surpass those of contrast-enhanced CT or MRI in detecting recurrence in general. In comparison with tumor markers, Rettenmaier et al. observed that routine imaging (abdominopelvic CT and plain chest radiography) is more sensitive than CA125 but that CA125 is superior in cost-performance. According to the ACR Appropriateness Criteria, which show the exposure dose as a reference for conducting imaging examinations, abdominopelvic contrast-enhanced CT is recommended but while routine chest CT is not. In Japan, the incidence of serous adenocarcinoma, which often shows an elevation in CA125, is lower than in Western countries, and PET/CT can only be performed in limited facilities. Under these circumstances, it is reasonable to perform PET/CT, if necessary and possible, by taking the histological type of the primary lesion and postoperative stage, tumor marker level, cost-performance, and risk of exposure into consideration and to select abdominopelvic contrast-enhanced CT as second line.

In uterine body cancer, also, the superiority of PET/CT has been largely established. According to the ACR Appropriateness Criteria, MRI rather than CT is recommended when PET is not available, probably from the viewpoint of reducing radiation exposure, but the evaluation of the diagnostic ability and cost-performance appears insufficient. In Japan, contrast-enhanced CT is considered a practical choice.

In uterine cervical cancer, the tumor marker SCC is useful for the follow-up in addition to the above-mentioned pelvic examination and vaginal cytology, but there is a report that the addition of conventional contrast-enhanced CT or plain chest radiography to these modalities does not contribute to the early detection of recurrence and that its significance is questionable. Here again, PET/CT has recently been reported to be useful for the early detection of asymptomatic recurrence and distant metastasis. Therefore, there seems to be some significance in carrying out PET/CT although its probable usefulness is lower than in ovarian or endometrial cancer. Also, while MRI is in wide routine clinical use for the follow-up of patients after uterus-preserving surgery, but its utility has not been sufficiently validated.

Index words and secondary materials used as references

A search of PubMed was performed using “CT”, “MRI”, “PET”, “uterine cervical carcinoma”, “endometrial carcinoma”, “ovarian carcinoma”, “recurrence”, “follow up”, and “after treatment” as key words. Guidelines of the Japan Society of Gynecologic Oncology (Treatment Guidelines for Cervical Cancer 2011, Treatment Guidelines for Uterine Body Cancer 2009, and Treatment Guidelines for Ovarian Cancer 2010), ACR Appropriateness Criteria (Staging and follow-up of ovarian cancer, pretreatment evaluation and follow-up of endometrial cancer of the uterus), and ESUR guidelines: ovarian cancer staging and follow up were also used as references.
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Which imaging modality is appropriate for imaging of acute abdomen in pregnant women?

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<thead>
<tr>
<th>Recommendation grade</th>
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<td>Non-contrast MRI, CT</td>
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For evaluation of acute abdomen in pregnant women, ultrasonography should be performed first.

If the diagnosis is difficult by ultrasonography, non-contrast MRI is recommended.

If the diagnosis is difficult even by non-contrast MRI, or if MRI cannot be performed, CT may be considered. Contrast-enhanced imaging is acceptable, if necessary.

Background/objective

Appendicitis is the most frequent cause of acute abdomen during pregnancy, and the diagnosis often depends on imaging. In pregnant women, early diagnosis and treatment are necessary, because abortion or premature delivery and maternal sepsis increase with the occurrence of appendiceal perforation or panperitonitis. Without a doubt, ultrasonography is the first choice imaging modality for acute abdomen in pregnant women. However, if a definitive diagnosis cannot be made, there is no consensus as to which of MRI and CT should be selected as the next modality. In Japan, this judgment is often left to the clinical staff.

Comments

Regarding the diagnostic performance of ultrasonography for appendicitis, which is the most frequent acute abdomen in pregnant women, the diagnosis was impossible in 88 (29/33), 96 (44/46), and 92% (11/12) of the patients, because the appendix could not be identified. Also, as a result of a prospective cohort study, Butala et al. reported that the sensitivity/specificity of ultrasonography in the 1st, 2nd, and 3rd trimesters were 40/100, 33/100, and 0/100%, respectively. Therefore, the diagnosis of acute abdomen other than appendicitis is also expected to be often difficult in pregnant women, and this tendency is more notable in late pregnancy, in which the uterus is enlarged.

The safety of MRI in early pregnancy has not been established, but there is presently no evidence that suggests it is unsafely, and its use in consideration of the period of pregnancy is recommended. The Guidelines for Diagnostic Imaging, 2003 of the Japan College of Radiology state that the long-term safety of MRI has not been sufficiently established and that careful evaluation of indications and avoidance of its application in the organogenic period (within 15 weeks) are necessary. According to the American College of Radiology (ACR), MRI can be performed in all periods including the 1st trimester. Therefore, there seems to be little controversy over the safety of the use of MRI for the diagnosis of acute abdomen in the 2nd trimester and thereafter, if diagnosis by ultrasonography is not possible.

MRI has been reported to be useful for the determination of the cause of acute abdomen in pregnant women in many diseases, allowing the diagnosis of gastrointestinal (inflammatory bowel diseases, diverticulitis, ileus), hepatobiliary (gallstones, choledocholithiasis, acute cholecystitis, pancreatitis, HELLP syndrome, and acute fatty liver), urinary (physiologic hydronephrosis, urolithiasis), vascular (venous thrombosis), and gynecological (uterine myoma, ovarian mass and torsion) diseases as well as acute appendicitis. While reports on the diagnosis of appendicitis by MRI are limited, it shows a high diagnostic ability with sensitivity and specificity of 90.5 and 98.6%, respectively, according to the meta-analysis by Blumenfeld et al. In Japan, however, CT is considered acceptable due to the limited availability of MRI in emergency situations. According to a questionnaire survey of radiology departments of general hospitals in the United States (85 respondents), 63 (74%) facilities had clear statements about principles of imaging diagnosis in pregnant women, and the percentage of preferential use of MRI/CT for the diagnosis of appendicitis was reported to be 39/32, 38/48, and 29/58% in the 1st, 2nd, and 3rd trimesters, respectively. A tendency to choose MRI in early pregnancy and CT in late pregnancy is observed. As mentioned in the Guidelines for obstetrical practice in Japan (Obstetrics edition 2011), radiation exposure at less than 50 mGy from 11 days after insemination to the 10th week of pregnancy does not increase the incidence of fetal anomalies. Exposure from the 10th-27th week of pregnancy may theoretically cause impairment of the central nervous system, but no effect has actually been documented at less than 100 mGy. In the diagnosis of acute abdomen, the radiation exposure does not exceed 50 mGy on a single series of abdominal CT with technical modifications including avoidance of multiple scans. Therefore, CT is an alternative if the benefit is judged to be greater than the risk after careful evaluation of the period of pregnancy and radiation dose (Figure). There has been no report evaluating the appropriateness of the use of a contrast agent in the diagnosis of acute abdomen during pregnancy. According to the United States Food and Drug Administration, intravenous iodine-based
contrast agents are classified in pregnancy as category B (a risk has not been demonstrated by animal reproduction studies or in pregnant women) and are more preferable to use in pregnant women than gadolinium-based contrast agents for MRI (category C: The use in pregnant women may be warranted despite potential risks). There has been a report that a single dose of an iodine-based contrast agent to a pregnant woman is unlikely to exert a significant effect on the fetal thyroid function, but thyroid function screening of neonates 1 week after birth is recommended. Therefore, CT may be considered if the diagnosis is difficult by ultrasonography or non-contrast MRI, or if MRI cannot be performed, and, for this purpose, CT may be performed with contrast enhancement, if necessary. If contrast-enhanced CT is clearly considered to have a higher diagnostic ability, it is recommended to perform contrast-enhanced CT alone by omitting non-contrast CT to reduce the exposure dose. Further reductions in exposure may be possible in the future through the development and application of novel CT technology such as low-dose CT using iterative processing and virtual non-contrast CT based on dual energy CT.

Index words and secondary materials used as references

A search of PubMed was performed using “acute abdominal pain”, “US”, “MRI”, “CT”, and “pregnancy” as key words.

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5) Japan College of Radiology: Guidelines for Diagnostic Imaging 2003, p197 (Level 5)
07
Urinary system
Is CT appropriate for immediate examination in adults suspected to have acute pyelonephritis?

**Recommendation grade**

C2

It is not recommended to immediately perform non-contrast or contrast-enhanced CT in adults with uncomplicated acute pyelonephritis.

**Background/objective**

Adult urinary tract infection is often restricted to the lower urinary tract and can be diagnosed on the basis of clinical symptoms and laboratory data. If inflammation has, or is suspected to have, spread to the kidneys (acute pyelonephritis), non-contrast or contrast-enhanced CT is indicated for the diagnosis and determination of the therapeutic strategy. However, performing CT in all patients is not reasonable from the viewpoints of radiation exposure and medical economy. Which patients, then, should undergo CT?

**Comments**

It is often easy to clinically diagnose acute pyelonephritis in patients without complicating factors such as diabetes, and appropriate antibiotic treatment usually leads to satisfactory resolution (complicated pyelonephritis is discussed in CQ120). Lim et al. evaluated the correlation between CT findings and clinical and laboratory data by dividing 130 adults with acute pyelonephritis or renal abscess who underwent contrast-enhanced CT into 3 groups: Mild acute pyelonephritis, severe acute pyelonephritis, and renal abscess.13 In the patients placed into the mild acute pyelonephritis group on the basis of CT findings, the mean duration of fever was reportedly 2.2 days, which was shorter than in the severe acute pyelonephritis (3.4 days) or renal abscess (5.4 days) group. Huang et al. divided patients with acute pyelonephritis into 3 groups (I-III) according to contrast-enhanced CT findings and compared clinical characteristics and outcome. Group I with mild CT findings promptly responded to antibiotic therapy and showed a mean duration of fever of 2.9 days, which was significantly shorter than in Groups II or III.20 Ha et al. and June et al. also reported that the mean duration of fever was 1.7-3.1 days in patients with no findings on contrast-enhanced CT and those with mild acute pyelonephritis.3,4 All these were retrospective studies, but the duration of fever was about 3 days in many patients with pyelonephritis showing mild CT findings (Figure).

According to the American College of Radiology (ACR) guidelines, CT is unnecessary in patients with uncomplicated acute pyelonephritis if they respond satisfactorily to antibiotic therapy, and non-contrast and contrast-enhanced CT are indicated when a satisfactory response is not observed within 72 hours.

**Figure: Acute pyelonephritis**

In this abdominal contrast-enhanced CT image, wedge-shaped and cord-like areas of poor contrast enhancement (→) are observed in the left and right kidneys, respectively.
The European Association of Urology (EAU) guidelines also recommend to perform non-contrast CT to exclude conditions such as renal and perinephric abscesses if patients with uncomplicated acute pyelonephritis exhibit fever persisting for 72 hours or longer after the initiation of treatment.

Adults showing poor response to treatment and those who have complications and are suspected to have acute pyelonephritis are discussed in CQ120.

Index words and secondary materials used as references

A search of PubMed was performed using “acute pyelonephritis” and “CT” as key words. The ACR guidelines 2008 and EAU guidelines 2009 were also used as references.

References

Is CT appropriate when patients suspected to have acute pyelonephritis show poor response to treatment?

**Recommendation grade**

**C1**

Contrast-enhanced CT may be considered in patients without renal dysfunction.

**Background/objective**

Uncomplicated acute pyelonephritis often responds promptly to antibiotic therapy. However, if the initiation of treatment is delayed, or if the patient is compromised or immunosuppressed such as diabetes, the disease may develop into renal or perinephric abscess. Drainage or surgery may be necessary for the management of renal or perinephric abscess, and non-contrast or contrast-enhanced CT is indicated for the diagnosis and determination of the therapeutic strategy. How should indications of CT be evaluated from the disease history, clinical symptoms, and laboratory data?

**Comments**

There have been a few studies attempting to predict renal abscess and severe pyelonephritis from clinical and laboratory data. Lim et al. divided 130 adult patients with acute pyelonephritis or renal abscess who underwent contrast-enhanced CT into 3 groups according to CT findings, i.e., mild acute pyelonephritis, severe acute pyelonephritis, and renal abscess, and evaluated their correlations with clinical and laboratory data. As a result, they reported that CT findings were correlated with clinical and laboratory data and that multivariate analysis identified diabetes, hypotension, acute renal failure or a leukocytosis of 20,000 or higher as significant risk factors of renal abscess. Most (97.9%) of the patients who showed severe pyelonephritis or renal abscess on CT had diabetes, hypotension, acute renal failure, or a leukocytosis 20,000 or higher. They also reported that since the remaining patients exhibited fever persisting for 72 hours or longer after the initiation of treatment, all patients with severe pyelonephritis or renal abscess can be identified by CT according to the European Association of Urology (EAU) guidelines.

The EAU guidelines recommend consideration of non-contrast CT to exclude renal and perinephric abscesses in patients with uncomplicated acute pyelonephritis showing fever persisting for 72 hours after the initiation of treatment. Huang et al. reported that close correlations were observed between 3 subgroups of acute pyelonephritis based on contrast-enhanced CT findings and the clinical severity. Significant differences were observed in the duration of fever, lateral abdominal pain, leukocytosis, and duration of pyuria, and, in the group with CT findings indicating severe pyelonephritis, septic shock, diabetic ketoacidosis, and acute renal failure were observed more frequently. While these studies were all retrospective, they showed association of renal abscess or severe pyelonephritis with diabetes, hypotension, and acute renal failure. Also, non-contrast CT is useful for the evaluation of gas, stones, and hemorrhage in the urinary tract, kidney enlargement, inflammatory masses, hydronephrosis, and stranding of perirenal fat tissue. However, these findings are often absent, and, in many instances, image findings suggestive of acute pyelonephritis are obtained by contrast-enhanced CT alone. The addition of contrast-enhanced CT is desirable if the patients have no

**Figure: Perinephric abscess**

Abdominal contrast-enhanced CT shows a mass with hypodense interior and a contrast enhanced margin (→) from the lower pole of the right kidney to the perinephric region.
contraindication of contrast medium such as renal dysfunction (Figure).

The American College of Radiology (ACR) guidelines recommend the evaluation using non-contrast and contrast-enhanced CT within 24 hours if diabetic or other immunocompromised patients respond poorly to treatment. The guidelines also consider CT to be worth performing in patients with a history of urological diseases such as urolithiasis, history of surgery for urological diseases, and episodes of recurrent pyelonephritis.

**Index words and secondary materials used as references**

A search of PubMed was performed using “acute pyelonephritis” and “CT” as key words. The ACR guidelines 2008 and EAU guidelines 2009 were also used as references.

**References**


Is CT appropriate for abdominal pain due to urolithiasis?

**Abdominal non-contrast CT is strongly recommended as there is evidence that it is useful for the diagnosis of not only lithiasis but also abdominal pain due to other causes.**

**Background/objective**

While abdominal pain (colic) is frequently observed in urolithiasis, causes of abdominal pain vary widely from urological to internal, surgical, and gynecological disorders, and prompt and accurate imaging diagnosis is required. Whether or not CT is useful when abdominal pain is suspected to be caused by urolithiasis was evaluated.

**Comments**

According to the Japanese Clinical Practice Guidelines for Urolithiasis revised edition (2005), plain radiography of the kidney-ureter-bladder region (KUB) and ultrasonography (US) are recommended as the initial examination for urolithiasis. Concerning the diagnostic performance for urolithiasis in patients with colic, the sensitivity and specificity by KUB alone are 54-64 and 67%,1,2 and those by US alone are 24-29.6 and 90-100%, respectively,3,4 but they improved to 79-96 and 91-100%, respectively, when they are combined,5 possibly with shortening of the time required for US and an improvement in diagnostic performance.6 There is also a report that urinary tract obstruction by kidney stones could be diagnosed with a sensitivity of 80% in pregnant patients by Doppler ultrasonography using the resistive index (RI) of the renal artery and that obstruction could be diagnosed even without hydronephrosis.7

Also, the sensitivity and specificity of excretory urography (intravenous pyelography or urography; IVP, IVU), which has been one of the important examinations of the upper urinary tract, have been reported to be 59.1-72.5 and 90-100%, respectively, for urolithiasis,1,2,5 but the frequency of its application is decreasing due to the recent propagation of CT and CT urography (CTU). As for comparison between non-contrast CT and IVP, the sensitivity and specificity of non-contrast CT are extremely high at 91-100 and 91-100%, respectively,1,3,7,8 and non-contrast CT has been reported to be useful by many authors. In patients with asymptomatic hematuria, it has been reported that there was no significant difference between CTU and IVU for detecting stones and other significant abnormalities of the urinary tract such as tumor, CTU was slightly superior to IVU.9 There is also a report that CT is more time- and cost-effective, including indirect cost on examination time and adverse effects than IVP,10 because it is useful for the diagnosis of abdominal disorders other than urolithiasis.1-3,7,8 While CT has been reported to be very useful by many authors, a randomized controlled trial comparing non-contrast CT and IVP showed that CT is superior in the initial diagnosis of urolithiasis but that there was no difference in the outcome, duration of hospitalization, or frequency of urological intervention.11 Recently, as the radiation exposure during CT examination has attracted attention, it is necessary to consider the fact that the exposure dose is 2-3 times higher by non-contrast CT than by IVP.10

MRI is an examination with minimum risk of radiation exposure. For the evaluation of urolithiasis in patients with colic, MRI urography (MRU) with heavily T2-weighted imaging shows a sensitivity of 53.8-57.2% and a specificity of 100%, but the sensitivity and specificity of contrast-enhanced MRU using 3D FLASH are 96.2-100 and 100%, respectively, so the addition also of contrast-enhanced MRU has been recommended.11 While CT has been reported to be very useful by many authors, a randomized controlled trial comparing non-contrast CT and IVP showed that CT is superior in the initial diagnosis of urolithiasis but that there was no difference in the outcome, duration of hospitalization, or frequency of urological intervention.11 Recently, as the radiation exposure during CT examination has attracted attention, it is necessary to consider the fact that the exposure dose is 2-3 times higher by non-contrast CT than by IVP.10

In order to reduce the radiation exposure on CT, high-pitch helical CT imaging14 and low-dose CT imaging. The sensitivity and specificity are both 90% or higher even by low-tube current CT imaging at 30-76 mAs,15,16 but the sensitivity tends to decrease (50-79%) for small stones 2 mm or less in diameter and in overweight patients with a BMI exceeding 30.15,17 The sensitivity and specificity have been reported to be 97 and 95%, respectively, even by ultra-low-dose CT (20 mA) with a radiation exposure similar to that by plain radiography.18

To summarize, when urolithiasis is suspected in patients with colic, it is recommended to perform abdominal non-contrast CT, which can be executed promptly and has a high diagnostic ability for not only urolithiasis but also other disorders. However, the importance of urinalysis and non-invasive examinations such as KUB and US as the initial examinations remains unchanged. While reports that CT is superior to these examinations are increasing, there have also been reports that diagnostic performance comparable to that of non-contrast CT can be obtained by a combination of US and KUB15,18 It is recommended to perform these less-invasive examinations for pregnant women and at facilities unequipped with CT, and an easy choice of CT should be avoided. However, US is highly dependent on the examiner’s skill, and the measurement of the RI is not very reproducible, restricting the ability of the modality. While MRI is free of radiation exposure, the image quality shows wide variation among facilities, and the examination time tends to be...
longer than CT.

Low-dose CT to reduce the radiation exposure is expected to be a standard imaging technique in near future. The compromised image quality, which limits the diagnostic ability, due to reduced radiation exposure compared with standard-dose CT is being compensated for by the recent advances of image reconstruction techniques such as iterative reconstruction.

Index words and secondary materials used as references

A search of PubMed was performed using “plain radiography”, “intravenous urography (IVU)”, “US”, “CT”, “MRI”, “renal or ureteral colic”, “renal or ureteral stone”, and “hematuria” as key words. The ACR appropriateness criteria were also used as a reference.

References

3) Rengifo AD et al: Diagnostic validity of helical CT compared to ultrasonography in renal-ureteral colic. Arch Esp Urol 63: 139-144, 2010 (Level 4)
5) Mitterberger M et al: Plain abdominal radiography with transabdominal native tissue harmonic imaging ultrasonography vs unenhanced computed tomography in renal colic. BJU Int 100: 887-890, 2007 (Level 4)
Is contrast-enhanced CT appropriate for the differentiation of benign and malignant cystic renal masses?

**Grade A**

The evaluation of the nephrographic phase using thin slices (≤5 mm) by a bolus injection of a contrast agent is useful for the differentiation of benign and malignant lesions and is strongly recommended.

### Background/objective

Cystic renal masses are observed frequently in routine imaging examinations, and most of them are simple cysts. While additional examination is unnecessary for patients in whom the definitive diagnosis is possible by ultrasonography, non-contrast CT, or usual contrast-enhanced CT, cystic masses showing wall thickening or septa may include renal cell carcinoma. The Bosniak classification is widely used as criteria prepared in consideration of the diagnosis of, and determination of the therapeutic strategy for cystic masses. Its usefulness is evaluated.

### Comments

In 1986, Bosniak reported a classification system for cystic renal masses based on CT findings. In consideration of the therapeutic approach, Bosniak initially proposed 4 categories from I to IV. Categories I and II are benign cysts that need no treatment, category III is cysts difficult to differentiate between benign and malignant by imaging examination and is an indication for surgery, and category IV is malignant and should be treated surgically. Thus, categories I and II can be left untreated, but categories III and IV require surgery, so the discrimination between categories II and III is important. Various retrospective studies have been conducted, and Aronson et al. concluded that categories I and II were non-malignant and that the Bosniak classification was useful, but Cloix et al. and Wilson et al. observed that malignant lesions are often included in categories I and II and expressed negative views on the Bosniak classification. However, these studies were carried out in a small number of patients (32 patients at most), and contrast enhancement could not be evaluated in some patients because non-contrast CT was not performed. In addition, the slice thickness was large at 10 mm in most patients. In subsequent reports such as those by Siegel et al. and Curry et al., the number of subjects was 70 or higher and the slice thickness was 5 mm or 7 mm or less in many patients. According to their reports, the percentage of malignant lesions in categories I and II combined was 3% (13% in category II, 0% in category I) and 0%, respectively, and that in categories III and IV combined was 78 and 70%, respectively, results that sufficiently supported the Bosniak classification.

To accurately apply the Bosniak classification, it is essential to use a thin slice thickness (≤5 mm), to inject the contrast agent in bolus at 2-3 ml/s, and to evaluate the nephrographic phase. It is also necessary to perform non-contrast CT to evaluate the presence or absence of contrast enhancement.

According to the conventional classification, categories I and IV could be diagnosed relatively easily, but the discrimination between categories II and III, which is the most important, was difficult and the interobserver agreement rate was low. Indeed, 16% of the patients judged to be category I or II were reportedly classified as category III or IV by another observer. Therefore, Bosniak added category II F (F stands for follow-up) as an intermediate category between II and III, and this 5-category classification is widely used at present. Categories I and II should be left untreated, category II F needs follow-up by imaging studies, and surgery is recommended for categories III and IV. In a retrospective study using MDCT, the percentage of malignant lesions was 4% in category I or II, 25% in category II F, 81% in category III, and 87% in category IV, suggesting the usefulness of the new classification system. However, in subsequent reports, the percentage of malignant lesions was 25% in category II F and 54% in category III, and there was a discrepancy between the two reports in the percentage of malignant lesions in category III (Figure, Tables 1,2).

The follow-up of II F lesions showed increased complexity such as an increase in the septal thickness in 5%, and they were reported to be malignant (mean follow-up period: 5.8 years). Moreover, there is a report that 13% of category II F lesions advanced to category III (median period: 6 months) and that about half these lesions were malignant. From these observations, the follow-up of category II F lesions is considered to be reasonable. Concerning the intervals of follow-up examinations, it is recommended to perform the first follow-up after half a year and, if there is no change, to continue the examination annually at least for 5 years.

### Index words and secondary materials used as references

A search of PubMed was performed using “renal”, “cystic”, “tumor”, “CT”, and “Bosniak” as key words. In addition, 2 papers were cited to understand the contents. The American College of Radiology guidelines (Israel GM et al: Clinical Condition: Indeterminate Renal Masses.
**Table 1: Bosniak classification (cited with modifications from Reference #8)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>A benign simple cyst with a hairline-thin wall that does not contain septa, calcifications, or solid components. It measures water density and does not enhance with contrast material.</td>
</tr>
<tr>
<td>Category II</td>
<td>A benign cyst that may contain a few hairline-thin septa. Fine calcification or a short segment of slightly thickened calcification may be present in the wall or septa. Uniformly high-attenuation lesions (&lt; 3 cm) that are sharply marginated and do not enhance are included in this group.</td>
</tr>
<tr>
<td>Category II F</td>
<td>These cysts may contain an increased number of hairline-thin septa. Minimal enhancement of a hairline-thin smooth septum or wall can be seen, and there may be minimal thickening of the septa or wall. The cyst may contain calcification that may be thick and nodular, but no contrast enhancement is present. There are no enhancing soft-tissue components. Totally intrarenal nonenhancing high-attenuation renal lesions that are 3 cm or larger are also included in this category. These lesions are generally well marginated.</td>
</tr>
<tr>
<td>Category III</td>
<td>These lesions are indeterminate cystic masses that have thickened irregular walls or septa in which enhancement can be seen.</td>
</tr>
<tr>
<td>Category IV</td>
<td>These lesions are clearly malignant cystic masses that not only have all the characteristics of category III lesions, but also contain enhancing soft-tissue components adjacent to but independent of the wall or septa.</td>
</tr>
</tbody>
</table>

**Figure: Bosniak categories III and II F**

Contrast-enhanced CT Sagittal reconstructed image (nephrographic phase)

The multilocular cystic mass at the lower pole has thick and irregular septa (▲) and is category III. However, the multilocular cystic mass in the upper pole has slightly enhanced and somewhat thickened septa (→) and is classified as category II F.
## Table 2  Frequency of malignant lesions among cysts of various Bosniak categories

<table>
<thead>
<tr>
<th>Four-category classification</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aronson et al(^2)</td>
<td>0/0</td>
<td>0/4</td>
<td>5/9 (56%)</td>
<td>7/7 (100%)</td>
<td>20</td>
</tr>
<tr>
<td>Cloix et al(^3)</td>
<td>1/2 (50%)</td>
<td>1/7 (14%)</td>
<td>4/13 (31%)</td>
<td>8/10 (80%)</td>
<td>32</td>
</tr>
<tr>
<td>Wilson et al(^4)</td>
<td>0/7</td>
<td>4/5 (80%)</td>
<td>4/4 (100%)</td>
<td>6/6 (100%)</td>
<td>22</td>
</tr>
<tr>
<td>Siegel et al(^5)</td>
<td>0/22</td>
<td>1/8 (13%)</td>
<td>5/11 (45%)</td>
<td>26/29 (90%)</td>
<td>70</td>
</tr>
<tr>
<td>Curry et al(^6)</td>
<td>0/4</td>
<td>0/11</td>
<td>29/49 (59%)</td>
<td>18/18 (100%)</td>
<td>82</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Five-category classification</th>
<th>I</th>
<th>II</th>
<th>IIF</th>
<th>III</th>
<th>IV</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al(^9)</td>
<td>0/30</td>
<td>2/25 (8%)</td>
<td>2/12 (17%)</td>
<td>22/27 (81%)</td>
<td>27/31 (87%)</td>
<td>125</td>
</tr>
<tr>
<td>Smith et al(^10)</td>
<td>-</td>
<td>-</td>
<td>4/16 (25%)</td>
<td>58/107 (54%)</td>
<td>-</td>
<td>123</td>
</tr>
</tbody>
</table>

Note) In\(^10\) category II F (69) and III (144) patients were selected and evaluated retrospectively.


### References


8) Israel GM et al: Follow-up CT of moderately complex cystic lesion of the kidney (Bosniak category II F). AJR 181: 627-633, 2003 *(Level 3)*


Is contrast-enhanced CT appropriate for the evaluation of solid renal masses?

**Recommendation grade**

**A** Contrast-enhanced CT (judgment of whether or not a renal mass is solid)

**B** Dynamic CT (qualitative differentiation of solid renal masses)

**A** Contrast-enhanced CT is strongly recommended for the judgment of whether or not a renal mass is solid.

**B** Dynamic CT is recommended, because clear cell renal cell carcinoma, which accounts for 70-80% of renal cell carcinomas, can be identified and because a homogeneous appearance suggests a benign entity not requiring surgery.

**Background/objective**

For the diagnosis of solid renal tumor, the lesion must first be confirmed a solid mass. Next, the discrimination of whether the lesion is benign or malignant is made. Angiomyolipoma (AML) and renal cell carcinoma (RCC) are the most important differential diagnoses in consideration of their frequency. If the lesion is malignant, it is also desirable to provide information concerning the histological type. Recently, from the viewpoint of molecular targeted treatment, the differentiation between clear cell RCC and other histological types is important. The usefulness of contrast-enhanced CT for the definitive diagnosis of solid renal mass and differentiation between benign and malignant diseases is evaluated below.

**Comments**

For the qualitative diagnosis of whether a renal mass is solid or cystic, it is important to perform contrast-enhanced as well as non-contrast CT to examine enhancement characteristics. Formerly, the lesion was judged to be solid when the CT value increased by 10 HU or more between before and after contrast enhancement, but, after the advent of helical CT, contrast enhancement is considered definitive with an increase in the CT value of 20 HU or more in consideration of the effect of pseudoenhancement. Also, while the qualitative diagnosis of masses 10 mm or less in diameter is difficult at a slice thickness of 5 mm, the ability to qualitatively diagnose masses 5-10 mm in diameter is markedly improved by the use of thin slices of about 3 mm. If a cyst is strongly suspected after non-contrast CT, usual contrast-enhanced CT (nephrographic phase) suffices. However, if a solid mass is suspected, dynamic CT is recommended to discriminate benign and malignant lesions.

For the discrimination of benign and malignant lesions, AML and RCC are the most important differential diagnoses. AML can usually be diagnosed by the detection of fat density at non-contrast CT, which is more accurate than contrast-enhanced CT for this purpose. The reported threshold of fat density at non-contrast CT has varied widely from -10 to -40 HU, but the diagnostic ability for AML has recently been reported to be maximum at a threshold of -10 HU. On the other hand, contrast-enhanced CT is useful for the diagnosis of solid tumors except for classic AML that contains fat density. Particularly, the homogeneity and pattern of contrast enhancement at dynamic CT are useful.

First, lesions that show heterogeneous marked enhancement in the corticomedullary phase of dynamic CT can be nearly identified as clear cell RCC, which confirms the malignancy (Figure 1). Generally, malignant lesions present with heterogeneous contrast enhancement due to hemorrhage or necrosis. In contrast, lesions that are homogeneous at dynamic CT are often benign. For example, AML with minimal fat (Fat poor AML, hyperattenuating type) shows a homogeneous appearance after contrast as it consists mostly of muscle components (Figure 2). This type of AML accounts for about 5% of all AML and is characterized by hyperdensity (more than 45 HU) compared with the renal parenchyma at non-contrast CT and hypointensity at T2-weighted MRI. Benign tumors such as leiomyoma, metanephric adenoma, and small oncocytoma are also homogeneous on contrast enhanced imaging. Particularly, those that are hyperdense at non-contrast CT and show homogeneous contrast enhancement (hyperattenuating homogeneously enhancing masses) are likely to be benign. However, as malignant tumors such as papillary renal cell carcinoma may also exhibit similar appearances, confirmation by biopsy is recommended.

There have been a number of reports that histological classification of RCC is also possible by dynamic CT. RCC has 3 major histological types: Clear cell type, chromophobe type, and papillary type. Although reports have varied in the dose or infusion rate of the contrast agent, scanning timing, and number of scans, clear cell RCC shows heterogeneous marked enhancement in the corticomedullary phase (about 30 seconds after the beginning of the contrast agent administration) and show fading in the nephrographic (after about 80-100 seconds) and early excretory (after about 180-300 seconds) phases. In chromophobe RCC, homogeneous moderate contrast enhancement is observed in the corticomedullary phase, but it diminishes thereafter. Papillary RCC shows only slight contrast enhancement in the corticomedullary phase and is usually gradually enhanced homogeneously to the early excretory phase.
These differences in the enhancement pattern reflect angiogenesis of the tumor.\(^5,16\) Thus, these 3 major histological types are distinguishable from one another. However, it is important to note that the imaging appearance of oncocytoma resembles those of clear cell and chromophobe RCCs\(^5,9-11,17,18\) and that that of metanephric adenoma also resembles that of papillary RCC.\(^5\)

### Index words and secondary materials used as references

### References
2. Curry NS: Small renal masses (lesions smaller than 3 cm): imaging evaluation and management. AJR 164: 355-362, 1995 (Level 5)
   (Level 5)
18) Kondo T et al: Spoke-wheel-like enhancement as an important imaging finding of chromophobe cell renal carcinoma: a retrospective analysis on computed tomography and magnetic resonance imaging studies. Int J Urol 11: 817-824, 2004 (Level 3)
The preoperative staging of renal cell carcinoma is indispensable for planning the treatment. As mentioned by the General Rule for Clinical and Pathological Study of Renal Cell Carcinoma, CT plays the primary role in the preoperative staging. The usefulness of CT along with MRI, bone scintigraphy, and PET is evaluated. The present 4th edition of the General Rule for Clinical and Pathological Study of Renal Cell Carcinoma (2011) are based on the TNM classification version 7 (2009) by the Union for International Cancer Control, and some revisions have been made from the previous staging system. Since the old classification was applied to the papers that we cited as references, caution is necessary.

**Comments**

1) **CT**

   In a prospective study on imaging techniques, a combination of 3 phases, i.e., non-contrast, corticomedullary, and nephrographic phases, showed a significantly higher staging ability (accuracy: 91%) than a combination of 2 phases, i.e., non-contrast and corticomedullary or nephrographic phase (accuracy: 82 and 86%, respectively). Dynamic CT is considered useful for not only the qualitative diagnosis but also staging of masses.

   It has been suggested that the greatest cause of a decrease in the accuracy of T factor staging of renal cell carcinoma is the low diagnostic ability for invasion to perirenal fat (distinction between T1/T2 and T3a). This is due to the difficulty in the discrimination of tumor invasion to fat tissue and benign changes such as those associated with inflammation. In fact, the accuracy of the diagnosis of perirenal fat invasion by 16-detector-row MDCT has been reported to be 64%. While there is one report that the accuracy was 95% by 4-detector-row MDCT with a slice thickness of 1.25 mm, other studies using 4-detector-row MDCT reported that the diagnosis of perirenal fat invasion was difficult, and it is reasonable to consider the diagnosis to be still difficult today. However, except for part of T1a lesions, which are indications for partial nephrectomy, T1, T2, and T3a are all indications for total nephrectomy. Therefore, at least, their exact preoperative diagnosis is not of great clinical importance. There is also a report that pT3a renal cell carcinomas underestimated as T1 by preoperative CT showed a recurrence-free survival rate similar to that of pT1 renal cell carcinoma.

   The diagnostic ability of CT for tumor thrombosis has been improved by the use of multiplanar reconstruction with the advent of MDCT (Figure). There have been reports that its sensitivity and specificity were 93 and 80%, respectively, and that the level of tumor thrombus could be accurately determined in 84% of the patients except for the segmental vein, contributing to the planning of surgery.

   Widely used diagnostic criteria for lymph node metastasis are a short diameter of 1 cm or greater and loss of the horseshoe shape, but they have long been considered insufficient. While reports on the diagnostic ability of MDCT for lymph node metastasis are few, there is a report that the accuracy, false positive rate, and false negative rate were 74, 19, and 7%, respectively, using 16-detector-row MDCT.

   The necessity of chest CT is considered high, because the lung is the most frequent site of distant metastasis of renal cell carcinoma. However, a retrospective study in 120 patients with renal cell carcinoma concluded that plain chest radiography was sufficient for T1-stage tumors and that chest CT is indicated when solitary masses have been detected by plain chest radiography, when there are respiratory symptoms, and for advanced tumors.

   There are also 2 reports that discussed the necessity of pelvic CT in preoperative staging. In both reports, the probability of the presence of significant lesions in the pelvis was very low at 2-3%, and the necessity of the inclusion of
the pelvis was excluded. However, very rarely, the renal artery divides from the common iliac artery, so the scan range covering the pelvis may be reasonable in the corticomedullary phase to preoperatively clarify the arterial anatomy by CT angiography.

2) MRI

The diagnostic ability of MRI for the T stage and tumor embolism has been reported to be nearly equal to that of 4-detector row MDCT. However, the role of MRI in the staging is limited as a wider area can be scanned in a shorter period, and as the diagnosis of distant metastases is possible, by MDCT.

MRI is considered useful for the judgment of whether or not nephron-sparing surgery is possible (discrimination between T1a and T3a lesions). Specifically, a high diagnostic ability (accuracy: 91%) can be obtained concerning perirenal fat invasion by a combination of pseudocapsule rupture and changes in the surrounding fat tissue on T2-weighted imaging.

Also, contraindication of contrast-enhanced CT are good indications for MRI. Recently, it has been reported that diagnostic performance similar to that of dynamic MRI was achieved for tumor thrombosis by implementing a steady-state free precession technique (such as TrueFISP, FIESTA, balanced FFE, and TrueSSFP).

3) Bone scintigraphy

According to the reports to date, bone scintigraphy may be performed in conditions strongly suggestive of bone metastasis such as bone pain, but its value as a routine examination for the staging is limited. In a retrospective study in 205 pathologically proved renal cell carcinoma patients, 34 (17%) had bone metastasis, and the sensitivity and specificity of bone scintigraphy were 94 and 86%, respectively, but the positive predictive value was low at 57%. Also, the bone metastasis rate in patients with T1-3aN0M0 renal cell carcinoma without bone pain was 5% or less, and it is concluded that bone scintigraphy is not recommended in such patients.

4) PET

Presently, PET or PET/CT is covered by health care insurance for evaluating all malignant tumors except for early gastric cancer when the staging and diagnosis of metastasis or recurrence cannot be determined by other examinations or imaging modalities. While the sensitivity and negative predictive value of PET for primary lesions, lymph node, and distant metastases are low, its specificity and positive predictive value are relatively high. It is reportedly not useful for the differentiation of benign and malignant renal masses but is considered likely to play a complementary role for lesions suspected to be metastases by other examinations. However, scientific evidence is lacking partly because of the small number of subjects, and further evaluation is necessary for the future.

Index words and secondary materials used as references

The Japanese imaging guideline 2013

16

al: American College of Radiology ACR Appropriateness Criteria® Clinical Condition: Renal Cell Carcinoma Staging. Available at: http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/RenalCellCarcinomaStaging.pdf) were also used as references.

References

3) Roberts WW et al: Pathological stage does not alter the prognosis for renal lesions determined to be stage T1 by computerized tomography. J Urol 173: 713-715, 2005 (Level 3)
12) Roy C Sr et al: Significance of the pseudocapsule on MRI of renal neoplasms and its potential application for local staging: a retrospective study. AJR 184: 113-120, 2005 (Level 3)
19) Safaei A et al: The usefulness of 18F deoxyglucose whole-body positron emission tomography (PET) for re-staging of renal cell cancer. Clin Nephrol 57: 56-62, 2002 (Level 4)
Is CT appropriate for patients suspected to have upper tract urothelial tumor?

Since CT urography, which refers to excretory phase imaging of contrast-enhanced CT, is useful for the detection of upper tract urothelial tumors, it is recommended for high-risk groups including patients known to have, and those with a history of, urothelial tumor, and middle-aged to aged patients with macroscopic hematuria.

Background/objective

Because urothelial carcinoma is characterized by simultaneous occurrence of multiple lesions and a high recurrence rate, it is required to thoroughly examine the entire urinary tract including the renal pelvis, ureter, and bladder. While bladder cancer can be diagnosed by cystoscopy, the diagnosis of upper tract urothelial carcinoma is difficult. Recently, primarily in Western countries, CT urography has begun to be used widely for further examination of upper tract urothelial tumor. Its usefulness and problems are evaluated.

Comments

Intravenous urography (IVU) has long been used as the first choice imaging examination that permits easy screening of the entire urinary tract, but, with the advent of multi-detector CT, CT urography (CTU), or the excretory phase imaging after the contrast administration, has been reported as useful. By partial MIP (or volume rendering), images of the pelvis and ureter resembling urograms can be prepared readily, and, using usual high-resolution transverse images, lesions in and outside of the urinary tract can be evaluated in detail. In Western countries, CTU has spread rapidly, and IVU has been nearly abandoned. Early papers reported that the detection sensitivity of CTU for upper tract urothelial carcinoma was very high at 91-97%.

According to papers that compared the diagnostic performances of upper tract urothelial carcinoma in hematuria patients between CTU and IVU, the sensitivity, specificity, and accuracy were 75-80, 81-86, and 81-85% for IVU, but 94-96, 95-100, and 94-99%, with for CTU, indicating superiority of CTU compared with intravenous urography.

The 2008 American College of Radiology (ACR) guidelines rated IVU at 6 (out of a full score of 9) but CTU at 9 (top rank) as an examination for hematuria patients. The 2011 European Association of Urology (EAU) guidelines regarded CTU as a gold standard and mentioned that it had completely replaced IVU.

However, there is the problem that CTU radiation doses are 2-3 times higher than that of IVU 15-30 mSv by CTU and 5-10 mSv by IVU. The 2008 European Society of Urogenital Radiology (ESUR) guidelines restricted the indications of CTU to patients with macroscopic hematuria aged 40 years and above, who are at a higher risk of urothelial cancer, and recommended IVU for patients with microscopic hematuria aged 40 years and above and patients with hematuria (microscopic and macroscopic) aged less than 40 years. For CTU to become prevalent in Japan, standardization of the imaging procedure and further reduction of the radiation exposure must be accomplished.

Index words and secondary materials used as references

A search of PubMed was performed using “CT” and “urothelial tumor” as key words. The following documents were also used as references.

Van Der Molen AJ et al: CT urography: definition, indications techniques, A guideline for clinical practice (Eur Radiol 18: 4-17) 2008

References

7. Urinary system


5) Jinzaki M et al: Comparison of CT urography and excretory urography in the detection and localization of urothelial carcinoma of the upper urinary tract. AJR 196: 1102-1109, 2011 (Level 3)

Figure: CT urography of a patient with urothelial cancer
CT urography was performed in a patient with asymptomatic macroscopic hematuria. In transverse (upper left) and coronal reconstructed images of the excretory phase, a lesion with soft tissue density showing a defect is noted in the right renal pelvis (→). In both the MIP (lower left) and volume rendered (lower right) images, defects are noted in the renal pelvis (▲). The lesion was pT1 renal pelvic cancer. These images of the excretory phase reconstructed for detailed evaluation of the urinary tract are all called CT urograms.
Is CT appropriate for the evaluation of T-stage of bladder cancer?

While CT is inferior to MRI in the diagnostic performance concerning muscle layer invasion, it is comparable to MRI in the diagnostic performance in perivesical fat tissue invasion, and its implementation may be considered.

Background/objective

Since the therapeutic approach to and prognosis of bladder cancer vary with its depth, accurate preoperative evaluation of the depth is important. Today, when MDCT is widely available, it is necessary to reevaluate the diagnostic ability of CT for the depth of bladder cancer.

Comments

According to studies comparing CT and MRI in the diagnosis of the presence or absence of muscle layer invasion of bladder cancer, the accuracy was 50-55% by CT and 77-85% by MRI, with CT showing inferior results (Table 1).\(^1,2\) Concerning the presence or absence of perivesical fat tissue invasion, the accuracy was 45-89% by CT and 65-85% by MRI, with CT being comparable or slightly inferior to MRI (Table 2).\(^1,2,3\) Regarding the evaluations using CT alone, also, the accuracy of CT before the advent of MDCT was similar at 55-87% (Table 3).\(^4,5\)

A drawback of CT, in which the axial plane is the default imaging plane, is that the evaluation of small lesions in the apex and neck of the bladder is difficult due to the partial volume effect. These defects of CT are being resolved by examining thin sections prepared by MPR.\(^6\) Regarding the diagnostic precision of MDCT for perivesical fat tissue invasion, the accuracy, sensitivity, and specificity have been reported to be 93, 89, and 95%, respectively (Table 3).\(^7\) Concerning the diagnostic precision of MRI for perivesical fat tissue invasion after 2000, the accuracy, sensitivity, and specificity were reported to be 85, 86, and 84% by Tekes et al.\(^8\) and to be 94, 80, and 97%, respectively, by Takeuchi et al.,\(^9\) indicating that MDCT had diagnostic precision comparable to that of MRI in the same period. It is necessary to perform CT before transurethral resection of bladder tumor (TUR-BT), but if it is impossible, it is desirable to perform CT at an interval of 1 week or longer after TUR-BT.\(^11\) Also, the upper urinary tract can be examined by the addition of the postcontrast excretory phase (CT urography).\(^14\)

Index words and secondary materials used as references

A search of PubMed was performed using “bladder”, “cancer”, “staging”, and “CT” as key words. Papers with generalized themes, case reports, papers in which the wall depth was not the main theme, and those in which the diagnostic accuracy of extramuscular invasion could not be calculated were excluded.

| Table 1 Diagnostic performance of CT and MRI (stage T1/T2) (%) |
|---------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                     | Accuracy        | Sensitivity     | Specificity     | Positive predictive value | Negative predictive value |
| CT\(^1,2\)          | 50-55           | 58-66           | 43-48           | 43-47                        | 50-70                        |
| MRI\(^1,2\)         | 77-85           | 83-94           | 71-83           | 67-76                        | 83-98                        |

| Table 2 Diagnostic performance of CT and MRI (stage T2/T3) (%) (values in parentheses are medians) |
|---------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                     | Accuracy        | Sensitivity     | Specificity     | Positive predictive value | Negative predictive value |
| CT\(^1,7\)          | 45-89 (70)      | 50-100 (80)     | 42-83 (60)      | 27-89 (67)                  | 43-94 (75)                  |
| MRI\(^1,7\)         | 65-85 (81)      | 71-100 (86)     | 55-83 (60)      | 63-90 (75)                  | 50-100 (93)                  |
References

1) Nishimura K et al: The validity of magnetic resonance imaging (MRI) in the staging of bladder cancer: comparison with computed tomography (CT) and transurethral ultrasonography (US). Jpn J Clin Oncol 18: 217-226, 1988 (Level 3)
14) Jinzaki M et al: Comparison of CT urography and excretory urography in the detection and localization of urothelial carcinoma of the upper urinary tract. AJR 196: 1102-1109, 2011 (No applicable level)
Is MRI appropriate for the evaluation of T-stage of bladder cancer?

**Recommendation grade**

There is a moderate level of evidence that, MRI is useful for T-staging of bladder cancer. We recommend to use MRI when the tumor shows a sessile non-papillary appearance on cystoscopy.

**Background/objective**

The therapeutic strategy and prognosis of bladder cancer vary with its T-stage. Particularly, to diagnose the presence or absence of muscle layer invasion is essential to identify an appropriate candidate for total cystectomy. MRI with a higher contrast resolution than CT is expected to be useful for T-staging of bladder cancer.

**Comments**

The diagnostic accuracy of MRI (30-98%, median: 68%) in T-staging of bladder cancer is slightly higher than that of CT (47-55%, median: 52%) in T-staging of bladder cancer. CT is usually performed before MRI to identify metastasis or upper urinary tract lesions. If an obvious invasion of the tumor into the perivesical fat or the prostate is observed on the CT, bladder MRI may be omitted. MRI may also be skipped when the tumor shows a superficial appearance (pedunculated/papillary tumor) on cystoscopy.

T2-weighted, dynamic contrast-enhanced, and diffusion-weighted imaging are useful for the evaluation of the T-stage. The image plane perpendicular to the bladder wall at the base of the tumor is optimal for staging because a partial volume effect which might degrade the staging accuracy is minimal at the plane. While Tekes et al. reported that there was no difference in the diagnostic accuracy between groups in which MRI was performed within 60 days versus after 60 days following transurethral resection of bladder tumor (TUR-BT) or biopsy, it is desirable to perform MRI preoperatively, because the extent of the tumor may be overestimated due to edema, scar, or granulation tissue that develops in the bladder wall after the surgery or biopsy.

Table 1 shows the diagnostic performance of MRI for detecting muscle layer invasion of bladder cancer (stage T2 or more). Since the difference in signal intensity is small between tumors and normal muscle layer, the diagnosis of muscle layer invasion is generally difficult when only T2-weighted imaging is used. Dynamic contrast-enhanced imaging can improve the sensitivity for the muscle invasion because bladder cancer enhances stronger than the bladder muscle layer in the early phase. Therefore, if the extent of the tumor unclear on T2-weighted imaging, the findings demonstrated on dynamic contrast-enhanced imaging are recommended to be regarded as more important. Major drawback of T2-weighted and dynamic contrast-enhanced imaging, is a low specificity for bladder muscle layer invasion; Diffusion-weighted imaging with a high b value (e.g. b=1,000) is as an option to improve the specificity.

Although the diagnostic accuracy for muscle layer invasion has been improved by the development of new MRI techniques, it has not been completely reliable yet. If the presence or absence of muscle layer invasion of bladder cancer cannot be determined by MRI, the T-stage is recommended to be diagnosed pathologically by transurethral bladder tumor biopsy before total cystectomy.

Table 2 shows the diagnostic performance of MRI for perivesical fat invasion (stage: T3 or more). While contrast-enhanced imaging contributes to improve the sensitivity, of perivesical fat invasion, an attention should be paid for the contrast enhancement of blood vessels or inflammatory reaction around the bladder which mimics bladder tumor and results in a false positivity. Diffusion-weighted imaging is a useful option to depict the extent of the tumor more accurately. Because of the limitation of spatial resolution, the discrimination between microscopic invasion to the perivesical fat (stage: T3a) and deep muscle layer invasion (stage: T2b) is generally difficult. The diagnostic performances of MRI and CT for perivesical fat invasion (T3 or more) are comparable.

**Index words and secondary materials used as references**

A search of PubMed was performed using “bladder”, “cancer”, “MRI”, and “staging” as key words. Papers on general themes, those in which the diagnosis of bladder cancer staging was not the primary theme, those in which the magnetic field intensity of the MRI device used was not 1.5T, and those in which a rectal coil was used were excluded.
### References

18) Nishimura K et al: Clinical application of MRI for urological malignancy. 2: Usefulness of various imaging modalities for local staging of bladder cancer; a comparison between MRI, CT and transurethral ultrasonography. Acta Urol Jpn 34: 2091-2096, 1988 (Level 3)
19) Nishimura K et al: The validity of magnetic resonance imaging (MRI) in the staging of bladder cancer: comparison with computed tomography (CT) and transurethral ultrasonography (US). Jpn J Clin Oncol 18: 217-226, 1988 (Level 3)
Is MRI appropriate for detecting prostate cancer?

**Recommendation grade**
C1

Since there is the possibility that highly malignant tumors can be detected efficiently, the implementation of MRI may be considered even before biopsy to focus the area to be biopsied or to evaluate indications for biopsy.

**Background/objective**

Recently, the incidence and the mortality of prostate cancer are rapidly increasing in Japan. The measurement of the serum prostate-specific antigen (PSA) has been established as a method effective for the detection of prostate cancer, leading to a decrease in the mortality rate. While PSA is highly sensitive, its specificity is relatively low, and problems such as false positives in the PSA gray zone (4-10 ng/ml) have been suggested. In this setting, prostate MRI is expected to play roles in not only staging of cancer but also the tumor detection and localization and evaluation of the tumor aggressiveness. In this section, the usefulness of MRI for the detection of prostate cancer was evaluated by reviewing primarily reports on T2-weighted, dynamic contrast-enhanced, and diffusion-weighted imaging using a 1.5T scanner.

**Comments**

Methods for detecting prostate cancer include digital rectal examination (DRE), serum PSA, transrectal ultrasonography (TRUS), and MRI. Among these examinations, MRI using an endorectal coil (T2-weighted imaging) has the highest tumor localization ability. When reports using a surface coil are included, however, the sensitivity and specificity of T2-weighted imaging for detecting tumors have been reported to be 54-96 and 21-91%, respectively, with some showing low specificities. On the other hand, both dynamic contrast-enhanced and diffusion-weighted imaging have shown relatively high specificities, and the addition of these techniques to T2-weighted imaging improves the sensitivity and area under the ROC curve (Az value). Evaluation methods in which multiple MRI sequences are used in combination are called multiparametric MRI. The diagnostic ability of multiparametric MRI is high for prostate cancers of the transitional as well as peripheral zone (Figure). However, it must be noted that hemorrhage due to prostate biopsy interferes with the tumor detection and that MRI should be performed before biopsy. To summarize the reports concerning patients in whom the mean serum PSA level was 20 ng/ml or less and MRI was performed before biopsy or a mean of 8 weeks or longer after biopsy (to reduce the influence of hemorrhage), the sensitivity, specificity, and Az value of multiparametric MRI using a surface coil at 1.5T were 53-95%, 69-94%, and 0.737-0.966, respectively. The sensitivity tended to be improved by the use of an endorectal coil at 1.5T (sensitivity: 73-100%, specificity: 63-92%, Az value: 0.76-0.94), and the specificity to be improved by the use of a surface coil at 3T (sensitivity: 76-81%, specificity: 93-96%).

Recently, there have been reports that the Gleason score, which is an index of the tumor aggressiveness, and various risk scores show significant correlations with the apparent diffusion coefficient (ADC) on diffusion-weighted imaging and signal intensity on T2-weighted imaging in the tumor region (primarily in the peripheral zone) on prostate MRI. Also, the detectability of tumors by MRI is higher as the tumor size is larger, and as the Gleason score is higher. Therefore, there is the possibility that, by using MRI, cancers that need therapeutic intervention (significant cancer: size: ≥0.5 cm³, Gleason score: ≥7) can be efficiently detected among prostate cancers showing multicentric carcinogenesis.

An example of such instances is an increase of the cancer detection rate using targeted biopsy on the basis of MR findings (T2-weighted imaging, dynamic contrast-enhanced imaging, and MR spectrocopy) in patients with persistently elevated PSA levels and prior negative random TRUS-guided biopsy. According to a report using diffusion-weighted imaging and T2-weighted imaging from another group, in patients without findings indicative of cancer who underwent only systematic biopsy, as compared with patients who underwent targeted biopsy based on MR imaging findings, tumor detectability was low, and about 80% of the detected tumors were insignificant cancer. Moreover, in the targeted biopsy group, even in patients with a PSA of 4-20 ng/ml, detection was significantly better. These results suggest the usefulness of targeted biopsy based on MR imaging findings, and in patients with prior negative biopsy, or those with gray zone PSA levels, such findings may serve as a guide to determine the indications for biopsy. However, many tumors can be detected by DRE or TRUS, and there is no ground for recommending MRI for all high-PSA patients. For the future, optimization of imaging techniques of prostate MRI (coil, combination of sequences, imaging parameters) and evaluation methods of MR images must be advanced further.

Finally, the ESUR guidelines 2012 proposed a method called the Prostate Imaging Reporting and Data System (PI-RADS), by which findings obtained by various imaging techniques of multiparametric MRI are scored to objectively detect tumors and evaluate extracapsular extension. It is a novel attempt, but as appropriate scoring is difficult, an
attitude to utilize this method while simultaneously evaluating it is considered necessary.

Index words and secondary materials used as references
A search of PubMed was performed using “prostate cancer”, “detection”, and “MRI” as key words. The ESUR prostate MR guidelines 2012 were also used as a reference.

References
16) Turckbey B et al: Is apparent diffusion coefficient associated with clinical risk scores for prostate cancers that are visible on 3-T MR images?
Radiology 258: 488-495, 2011 (Level 3)
Is MRI appropriate for the local staging of prostate cancer?

**Recommendation**

MRI is useful for the evaluation of extraprostatic extension and seminal vesicle invasion of medium- to high-risk prostate cancer and is recommended. (note)

**Background/objective**

Prostate cancer is increasing rapidly, and the standardization of diagnostic imaging techniques for prostate cancer is important. While MRI is regarded as a reliable imaging modality in the local staging of prostate cancer, it is not performed in all patients. In this section, whether or not MRI is useful for the local staging (extraprostatic extension, seminal vesicle invasion) of prostate cancer and under what circumstances its usefulness is augmented are evaluated.

**Comments**

MRI is regarded as the most reliable imaging modality for the local staging of prostate cancer (Figure). A endorectal coil was used in most reports evaluating extraprostatic extension using a 1.5T MRI system. Concerning the diagnostic ability of T2-weighted imaging for extraprostatic extension, the sensitivity, specificity, and accuracy were 22-82, 70-100, and 61-84%, respectively, showing wide variations among reports. Multivariate analysis suggested that asymmetry of the neurovascular bundle and obliteration of the rectoprostatic angle are reliable findings suggestive of extraprostatic extension. As for the diagnostic ability of MRI for seminal vesicle invasion, the sensitivity, specificity, and accuracy have been reported to be 23-100, 75-100, and 76-97%, respectively. While there have been few studies using dynamic contrast-enhanced imaging, the procedure has been reported to be superior to T2-weighted imaging in detecting not only prostate cancer but also extraprostatic extension (diagnostic accuracy: 87%) and seminal vesicle invasion (98%). There is also a report that the diagnostic ability of less experienced readers was improved by the addition of dynamic contrast-enhanced imaging.

For the management of prostate cancer, appropriate treatment is selected according to risk classification based on the clinical stage, PSA level, Gleason score, and percentage of the biopsy core occupied by cancer tissue. In Western countries, the selection of imaging modalities in consideration of the risk of tumor is widely recognized, and is also mentioned in guidelines (EAU guidelines 2010, and ACR guidelines 2009). However, the risk classification based on the clinical stage is inappropriate as the grounds for the application of MRI to stage prostate cancers. In retrospective evaluations, the diagnostic ability of MRI for extra-prostate spread was low in low-risk patients but was higher in medium- to high-risk patients. On the other hand, the specificity showed little difference among the risk levels. When a patient shows a PSA level of 10 ng/ml or higher, or a biopsy Gleason score of 7 or greater, he is judged to be moderate or higher risk, and the evaluation of extraprostatic extension and seminal vesicle invasion by MRI is beneficial.

In Japan, most of prostate MR images are acquired by using a surface coil such as a pelvic phased array coil. While the staging ability is improved by using an integrated system of both surface and endorectal coils, compared with a surface coil alone, endorectal coils are unlikely to become popular in Japan at present. If a surface coil is used alone, a comparable staging ability is considered to be secured by using an MRI system at 1.5T or higher magnetic field strength, eliminating rectal gas, which deteriorates the image quality, and maintaining spatial resolution by the use of a thin slice thickness of about 4 mm. Local staging of prostate cancer using a 3T MRI system has also been attempted, and the procedure is expected to provide high-spatial resolution images and improve the staging ability. No marked improvement in the staging ability has been reported to date.

Finally, there were no papers suggesting contribution of diffusion-weighted imaging to the local staging.

**Index words and secondary materials used as references**

A search of PubMed was performed using “prostate cancer”, “staging”, and “MRI” as key words. Also, the JRS/JCR Joint Guideline Committee eds: Guidelines for Diagnostic Imaging of Prostate Cancer 2007 were used as a basic reference, and the EAU guidelines and ACR prostate cancer guidelines were used as references.

**References**

1. Yu KK et al: Detection of extracapsular extension of prostate carcinoma with endorectal and phased-array coil MR imaging: multivariate feat-
ture analysis. Radiology 202: 697-702, 1997 (Level 2)
6) Ogura K et al: Dynamic endorectal magnetic resonance imaging for local staging and detection of neurovascular bundle involvement of prostate cancer: correlation with histopathologic results. Urology 57: 721-726, 2001 (Level 2)
7) Allen DJ et al: Does body-coil magnetic-resonance imaging have a role in the preoperative staging of patients with clinically localized prostate cancer? BJU Int 94: 534-538, 2004 (Level 3)
11) Brassell SA et al: Correlation of endorectal coil magnetic resonance imaging of the prostate with pathologic stage. World J Urol 22: 289-292, 2004 (Level 2)
14) Chandra RV et al: Endorectal magnetic resonance imaging staging of prostate cancer. ANZ J Surg 7: 860-865, 2007 (Level 3)
7. Urinary system

130 Which imaging modalities are appropriate for the staging of testicular tumors?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>A</th>
<th>CT</th>
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<td>PET</td>
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CT has strong evidence for the usefulness and is recommended. PET lacks sufficient scientific evidence, but its implementation may be considered.

Background/objective

Presently, the cure rate of testicular tumors is very high, being 99% or higher in the early stage. In the advanced stage with metastasis, also, it is 90% in the good risk group, 75-80% in the intermediate risk group, and 50% in the poor risk group by the International Germ Cell Cancer Collaborative Group Classification. One of the most important factors of a high cure rate is accurate staging, and the stage is determined according to the site and size of metastasis. With these in mind, imaging modalities, particularly CT and PET, for the staging of testicular tumors were evaluated.

Comments

Testicular tumors most often metastasize to the retroperitoneal and mediastinal lymph nodes. CT is mentioned as essential for the staging of testicular tumors in multiple guidelines including the latest editions of the American College of Radiology (ACR) and European Association of Urology (EAU) guidelines, and in most cases contrast-enhanced CT is recommended. For patients with contraindications for the contrast agent, MRI with excellent contrast resolution is suggested as an alternative, but scanning of a wide area is impossible. Therefore, non-contrast CT is considered useful in patients with contraindications for the contrast agent in clinical practice. In detecting lung metastases, chest CT is more sensitive than plain chest radiography, and scanning from the thoracic to pelvic regions is useful. However, caution is necessary as false positive results are often obtained in lung lesions 1 cm or less in diameter. Chest CT may be omitted, particularly, in stage I seminoma if no abnormality is noted on plain chest radiography. Therefore, non-contrast CT is considered useful in patients with contraindications for the contrast agent in clinical practice. In detecting lung metastases, chest CT is more sensitive than plain chest radiography, and scanning from the thoracic to pelvic regions is useful. However, caution is necessary as false positive results are often obtained in lung lesions 1 cm or less in diameter. Chest CT may be omitted, particularly, in stage I seminoma if no abnormality is noted on plain chest radiography.

No firm conclusion has been reached concerning the usefulness of PET for the staging. According to a prospective multicenter study reported in 2008, PET was performed for the staging in 72 patients with stage I or IIA/B non-seminomatous germ cell tumors, and the results were confirmed histologically by retroperitoneal lymph node dissection. As a result, the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were 41, 95, 71, 87, and 67%, respectively, for CT and 66, 98, 83, 95, and 78%, respectively, for PET. While both CT and PET showed a high specificity, PET was significantly superior in the sensitivity and NPV. However, it must be noted that the NPV was less than 80% even by the use of PET.

In another study, PET was performed for the staging of 46 patients with stage I non-seminomatous germ cell tumors, and the patients were followed up by examination of tumor markers and CT. The sensitivity, specificity, accuracy, PPV, and NPV of PET were 70, 100, 93, 100, and 92%, respectively, and the modality was suggested to be superior in NPV (78%) to conventional tumor marker measurement and CT alone. On the basis of these results, a multicenter study was organized, and 87 PET-negative patients out of the 111 patients with stage I non-seminomatous germ cell tumor positive for vascular invasion were followed up without treatment. The study was discontinued as recurrence was observed in 33 patients at a median observation period of 12 months. Considering that the disease recurred within 1 year in 37% of the PET-negative patients, being PET-negative does not warrant observation without treatment.

Reasons for false negatives on PET in the initial staging include the smallness of the lesion (≤0.5 or 1 cm) and the presence of mature teratoma.

From these observations, it is concluded that PET may improve the sensitivity and NPV compared with CT in the staging of non-seminomatous testicular tumors but that its diagnostic ability is still deficient to warrant observation of stage I patients without treatment on the basis of a negative PET result.

The literature on PET used for the staging of seminoma is insufficient. However, as PET is more useful for the assessment of residual masses after chemotherapy in seminomas than in non-seminomatous lesions (discussed in detail in CQ131), at present, its implementation in patients with seminoma as well as non-seminomatous testicular tumors may be considered.

2) de Wit M et al: [18F]-FDG-PET in clinical stage I/II non-seminomatous germ cell tumours: results of the German multicentre trial. Ann Oncol 19: 1619-1623, 2008 (Level 3)
Background/objective

Due to the recent development of chemotherapy, there have been marked improvements in the cure rate of even advanced testicular tumors with metastasis, but the therapeutic approach remains controversial if residual tumors are observed after chemotherapy. Residual tumors often consist of necrotic/scar tissues not containing viable tumor cells, and as retroperitoneal lymph node dissection (RPLND) in particular is highly invasive, expectations for the assessment using imaging modalities are high.

In this setting, post-chemotherapy imaging evaluation of testicular tumors with metastasis, particularly by CT and PET, is discussed separately concerning seminoma and non-seminoma.

Comments

For testicular tumors without metastasis, radical high orchitectomy is performed, and chemotherapy and radiation therapy are added if necessary. Periodic follow-up (surveillance) for recurrence by tumor marker monitoring and abdominal CT is strongly recommended by multiple guidelines abroad.

For seminoma with metastasis, chemotherapy is performed in addition to high orchitectomy. The post-chemotherapy assessment by tumor marker monitoring and abdominal CT is also strongly recommended. While residual tumors are observed in 55-80% of the patients after chemotherapy, many of them are necrotic or fibrotic tissue. Conventionally, a maximum tumor diameter of 3 cm or greater on CT was used as a cutoff value. Actually, however, only 11-37% of residual tumors 3 cm or greater are viable.

Concerning the viability assessment of post-chemotherapy residual masses of seminoma, PET has been reported to show a high ability, particularly, when the tumor diameter is 3 cm or greater. According to a multicenter study reported in 2004, PET showed very high sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 80, 100, 100, and 96%, respectively. Because of this report, PET began to be recommended for the assessment of post-chemotherapy residual masses of seminoma by multiple international guidelines. Thereafter, as there have been sporadic reports of a high false positive rate by PET, the largest ever retrospective study was conducted for the reevaluation, and the results were released in 2011. According to this report, the sensitivity, specificity, PPV, and NPV of PET were 67, 82, 42, and 93%, respectively, and although they were superior to the values with a tumor size of 3 cm as a cutoff value, they were slightly lower than those reported previously.

From these observations, PET is considered to be superior to CT in the assessment of seminoma after chemotherapy with a particularly high NPV (93-100%). If a residual tumor 3 cm or greater in diameter is PET-negative 6 or more weeks after chemotherapy, it is unlikely to be viable.

Concerning non-seminomatous testicular tumor, according to a prospective multicenter study in 641 patients reported in 2000, the percentage of postoperative masses consisting of necrotic tissue alone was higher as the residual tumor size on CT was small, and as the tumor volume reduction rate was higher. However, viable tumor cells (teratoma or carcinoma) persisted in 28% of residual masses 9 mm or less in diameter and 20% of those with a volume reduction rate of 85% or higher. Moreover, in 2003, when RPLND was performed in 87 patients with residual lesions 20 mm or less in diameter after BEP therapy, viable tumors were reported to have been detected in 33%. From these results, in non-seminomatous tumors, the possibility that an even post-chemotherapy small residual tumor is viable is considered to be relatively high.

Regarding PET, a prospective multicenter study was performed in patients with histologically confirmed results in 2008, and the sensitivity, specificity, PPV, and NPV were 70, 48, 59, and 51% respectively, with an accuracy of 56%. Since
the accuracy was 55% by CT and 56% by tumor marker monitoring, the addition of PET to CT and the tumor marker did not provide additional information for the prediction of postoperative histological results.\(^8\) Other studies have also suggested that residual mature teratomas may give false negative results,\(^9\) and the use of PET is not recommended also by international guidelines.

As observed above, PET is recommended for seminoma patients with post-chemotherapy residual masses. With a negative result, the possibility of viable residual tumor is low, and additional treatments may be spared. Presently, PET is not recommended as a routine examination for the postoperative assessment of non-seminomatous tumors.

### Index words and secondary materials used as references


### References

08

Breast region
Background/objective

With the increase in the screening rate using mammography, patients in whom calcified lesions requiring further evaluation are detected have been increasing. In Japan, if no abnormality is noted by ultrasonography, stereotactic vacuum-assisted breast biopsy (SVAB) is performed, but its indications are unclear, and as the availability of the device remains insufficient as it can only be performed at limited facilities. Also, the usefulness of MRI for the evaluation of calcified lesions is controversial, and the position of MRI in the diagnosis and treatment of calcified lesions has not been established (Figure). The usefulness of MRI for the evaluation of calcified lesions was evaluated.

Comments

Reports on the usefulness of MRI for the evaluation of calcified lesions began to appear in the late 1990s, but as the ability of MRI in the qualitative diagnosis of calcified lesions was insufficient, the benefit of MRI was refuted. In the 2000s, the diagnostic ability of MRI was improved due to technical developments, and the recent changes in the clinical procedures associated with the introduction of SVAB have led to increases in reports recommending MRI.

According to major reports on the ability of MRI for the qualitative diagnosis of calcified lesions published after 2000, the sensitivity was 73-90%, specificity was 76-100%, positive predictive value was 73-92%, negative predictive value was 71-97%, and the accuracy was 74.5-96%. Only 3 reports from Japan clearly mentioned that no abnormality was noted on ultrasonography, and ultrasonography was not mentioned, or was not performed, in the other reports. The categories of target calcification and diagnostic criteria by MRI also varied among reports.

Among the possible roles of MRI in the diagnosis of calcified lesions, it is expected to be most useful for the selection between SVAB and observation for calcified lesions with no abnormality on ultrasonography. While there have been positive reports that observation is possible if there are no malignant findings on MRI, a recent meta-analysis presented a negative view that the negative predictive value of MRI is not sufficiently high to justify avoidance of SVAB.

In conclusion, MRI is not a modality that can replace SVAB, but as it may help with the selection of the therapeutic approach, its implementation may be considered.

Recommendation

While scientific evidence is insufficient, implementing MRI as a means for the selection of the therapeutic approach may be considered.

Index words and secondary materials used as references

A search of PubMed was performed using “MRI”, “breast”, “screening mammography”, and “microcalcification” as key words.

References

Figure: Calcified lesions of microinvasive carcinoma and MRI
Microcalcification was noted in the L region on screening mammography (A). No abnormality was noted on ultrasonography, but MRI (B) showed enhancement in the area of calcification (→). Surgery was performed after SVAB, and a diagnosis of microvascular carcinoma was made.
Breast cancers undetectable by inspection, palpation, or mammography may be detected by ultrasonography, and this modality is excellent particularly in diagnosing solid tumors. Moreover, the standardization of the terminology for ultrasound findings and preparation of criteria for the discrimination of benign and malignant diseases have also been advanced. MRI is sensitive for breast cancer, but its specificity is relatively low (Figure). Guidelines have been proposed to standardize the terminology for findings and imaging procedures, and improvements in the specificity are expected. PET is excellent in detecting malignant tumors, and PET/CT has recently become more available. The usefulness of ultrasonography, CT, MRI, and PET (PET/CT) for the discrimination of benign and malignant tumoral lesions of the breast was evaluated.

### Comments

1) **Ultrasonography**

The precision of ultrasonography has been markedly improved due to the recent improvements in ultrasonographic devices and development of software, and analysis of the morphology (shape, margin, depth-width ratio) of solid masses and evaluation of their mobility and deformability have been reported to be useful for the diagnosis and discrimination of benign and malignant lesions. To the present, the precision of ultrasonography (B-mode) in discriminating benign and malignant lesions has varied with the tumor size and has been reported at 75.6-88.4%. The diagnostic accuracy of ultrasonography has been affected by the examiner’s skill, performance of the device, and examination conditions, the standardization of the terminology has been insufficient, and the ability to differentially diagnose benign and malignant lesions has been rated poorly. However, as the Breast Imaging Reporting and Data System (BI-RADS)-Ultrasound similar to that for mammography has been prepared, the standardization of the terminology for findings and quality of diagnosis has been advanced, and, in the discrimination of benign and malignant solid tumors, the accuracy and positive and negative predictive values have been reported to be 71.3, 67.8, and 92.3%, respectively. In Japan, also, the Guidelines for Breast Ultrasound were published in July, 2004, and a major revision was made in 2008 by including the breast ultrasound diagnostic tree. In this version, also, ultrasound is shown to be useful for the discrimination of benign and malignant tumoral lesions and is recommended.

2) **MRI**

As for the diagnostic performance of MRI for breast cancer, the sensitivity and specificity were 90 (52-100) and 72 (21-100)%, respectively, according to a meta-analysis, with the specificity being low compared to the sensitivity. While the positive predictive value of MRI has been reported to be higher than that of mammography, the negative predictive value has been reported to be insufficient for omitting biopsy. Since the lack of standardization of the imaging method and diagnostic criteria was considered to be a cause of the relatively low specificity of MRI, the BI-RADS-MRI was prepared to standardize the terminology for, and interpretation of, findings and final diagnosis. According to a single-facility study in which tumoral lesions were evaluated on the basis of the BI-RADS-MRI, high diagnostic performance with sensitivity, specificity, and positive and negative predictive values of 99, 89, 96, and 98%, respectively, was reported. Also, the frequency of malignant lesions among BI-RADS category 3 lesions, which are considered to be probably benign on contrast-enhanced MRI, was 0.9%, which consisted of non-tumoral lesions alone, and none
of the tumoral lesions was malignant.\textsuperscript{12,13} Thus, MRI shows a high negative predictive value in tumoral lesions with assessment based on the BI-RADS-MRI. While the specificity is still unsatisfactory, there is the possibility that invasive examinations such as surgical biopsy may be avoided by performing MRI for tumoral lesions.

3) CT

Although there has been no report on the diagnostic ability of CT in tumoral lesions, the sensitivity, specificity, positive and negative predictive values, and accuracy of the diagnosis of mammary gland diseases at a single facility were reported to be 89.6, 54.5, 93.2, 39.3, and 84.7\%, respectively,\textsuperscript{14} with the specificity and negative predictive value being lower than those of ultrasonography or MRI. There is also a report that the diagnostic performance of CT was high with sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 92.6, 100, 100, 100, and 95.7\%, respectively,\textsuperscript{15} but the number of patients was small, and the evidence that CT is useful for the differential diagnosis of tumoral lesions is insufficient. In addition, CT has the defect that the exposure increases if multiphasic imaging is performed for the assessment of the hemodynamics, and it is not recommended to perform CT exclusively for the differential diagnosis of benign and malignant tumoral lesions of the mammary glands.

4) PET

Concerning the diagnostic ability of PET for breast cancer, the sensitivity varies widely from 48-95.7\%, but the specificity is relatively high at 73.3-100\%.\textsuperscript{16} Its sensitivity for small breast cancers 1 cm or less in diameter is low at 48-76.2\%, and the false negative rate is high for lesions with low histological malignancy, invasive lobular carcinoma, and non-invasive ductal carcinoma.\textsuperscript{16-30} According to reports comparing the sensitivity of PET with those of existing modalities, it was 83.3-96\% for PET, 58.3-78.9\% for mammography, 86.6-88\% for ultrasound, and 89-100\% for MRI.\textsuperscript{18-25} However, the comparison was not performed in patients including a sufficient number of those with small tumors, so
Is MRI appropriate for patients with abnormal nipple discharge showing no mammographic or ultrasound abnormalities?

**Recommendation grade**

While scientific evidence is insufficient, MRI may be considered.

**C1**

**Background/objective**

Abnormal nipple discharge suggestive of breast cancer is often from a single opening, and close evaluation is usually not indicated if discharge is from multiple openings or bilateral. Generally, slightly less than 15% of discharge from a single opening is malignant, and slightly less than 10% of malignant discharge shows no abnormality on inspection, palpation, mammography, or ultrasonography, occasionally making the diagnosis difficult.

**Comments**

As mentioned above, the cause of slightly less than 10% of malignant abnormal nipple discharge cannot be identified by diagnostic imaging, but, including latent cases, about twice this percentage is unexplained and is followed up by nipple discharge cytology.

According to the recommendations compiled in 2010 by the European Society of Mastology (EUSOMA) concerning MRI of mammary glands, (1) there is no sufficient scientific evidence for the clinical benefit of MRI as an examination of abnormal nipple discharge, and, (2) in countries where ductography is regarded as a routine examination for patients with abnormal nipple discharge, T2-weighted imaging and contrast-enhanced MRI are considered when ductography is technically difficult or is rejected by the patient.10

In most of the other literature, MRI is suggested to have a very high ability to detect lesions (sensitivity: 89-100%) and to be useful also when no lesion can be detected by mammography or ultrasonography (Figure).2,7

In Japan, ductography is not yet established as a routine diagnostic procedure for patients with abnormal nipple discharge. In many of the references shown below, the definitive diagnosis could be made by 2nd look ultrasonography after MRI, so MRI may be considered in patients with abnormal nipple discharge showing no abnormality by other modalities.

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**Figure: Non-invasive ductal carcinoma MRI**

A Non-contrast T1-weighted MIP image: Dendritic hyperintensities suggestive of bloody discharge are observed on the medial side of the right breast.  
B Contrast-enhanced T1-weighted MIP image: Clumped enhancement is noted on the caudal side of the dendritic hyperintensities. Biopsy was performed under 2nd look ultrasonography, leading to a diagnosis of non-invasive ductal carcinoma.
Index words and secondary materials used as references

A search of PubMed was performed using “breast”, “MRI”, and “nipple discharge” as key words. Also, Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group. (1) was used as a reference.

References

### Background/objective

In breast cancer, the intraductal extent and presence of multiple foci are known as risk factors of local recurrence after breast-conserving surgery, and it is extremely important to make the resection stump negative for the prevention of local recurrence. Breast MRI, which has become prevalent in Western countries since the 1980s, has higher sensitivity than other imaging modalities in the delineation of breast cancer and is expected to be useful for the preoperative evaluation of the disease extent. Also, in Japan, helical CT has been used since early on for the preoperative evaluation of the extent of breast cancer, and there have recently been reports on the evaluation of the disease extent using multislice CT.

### Comments

Local extension including the intraductal spread and the presence or absence of separate foci in the ipsilateral breast are often evaluated together as the “extent” in the staging of breast cancer. This evaluation is important as it affects the choice of surgical procedure. It is difficult to clearly distinguish intraductal spread and ipsilateral foci, and these ipsilateral multiple foci are included in the evaluation of the local extent in some reports.

Breast MRI has been shown by a number of reports to have higher diagnostic precision than mammography or ultrasonography concerning the extent of breast cancer. In comparison with pathological findings in patients who underwent mastectomy, the tumor diameter was significantly underestimated by mammography and ultrasonography, but MRI showed no significant errors. Also, in detailed comparison with pathological findings in patients including those who underwent breast-conserving surgery, the correlation coefficients of mammography, ultrasonography, and MRI were 0.63, 0.55, and 0.78, respectively, and the diagnostic ability by a combination of mammography and ultrasonography (correlation coefficient: 0.69) was still lower than that of MRI. As for the effects of the preoperative assessment of the spread of breast cancer by MRI on the surgical procedure, the surgical procedure was reported to have been changed appropriately by preoperative MRI in 19-28% of the patients. On the other hand, a recent multicenter randomized controlled trial (COMICE trial) reported that no significant difference was noted in the reoperation rate between the groups that underwent (816 patients) and did not undergo (807 patients) MRI before surgery for breast cancer. In this study, also, unnecessary mastectomy was reportedly performed due to overestimation in 2% of the patients who underwent MRI.

In the evaluation of intraductal involvement including non-invasive ductal carcinoma in situ, the sensitivity, specificity, and accuracy of contrast-enhanced multislice CT have been reported to be 71.8-88.2, 67.8-85.7, and 72.2-97.3%, respectively. When compared with groups in which the evaluation was made by mammography and ultrasonography alone, multislice CT has been reported to have reduced the rate of positive resection stumps and increased the breast-conservation rate. According to a prospective study comparing the diagnostic ability of various modalities in the evaluation of the extent of breast cancer, the diagnostic accuracy of multislice CT (71%) was significantly higher than that of ultrasonography (56%) or mammography (52%), but that of MRI (76%) was significantly higher.

Presently, therefore, it appears evident that breast MRI is superior to other imaging modalities in the precision of preoperative diagnosis of the extent of breast cancer. However, because of problems including overestimation, whether or not the existing evidence is sufficient to support MRI as a routine preoperative examination for patients undergoing breast-conserving surgery is still unclear. Further evaluation of issues including improvements in the precision of image reading and methods to accurately reflect the results of image reading in surgery is awaited. The role of multislice CT in the diagnosis of the disease extent is no more than supplementary to conventional modalities such as mammography and ultrasonography in patients who do not tolerate contrast-enhanced MRI due to contraindications including claustrophobia, an implanted metal device, and adverse reactions to gadolinium-based contrast agents.

### Recommendation

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>MRI</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MRI is recommended. If MRI cannot be performed, CT may be considered as it may be more effective than conventional clinical examinations, mammography, or ultrasonography.
Index words and secondary materials used as references


References

3) Amano G et al: Correlation of three-dimensional magnetic resonance imaging with precise histopathological map concerning carcinoma extension in the breast. Breast Cancer Res Treat 60: 43-55, 2000 (Level 2)
The presence of multiple ipsilateral breast cancer sites (multifocality and multicentricity) is a factor important for the evaluation of indications for breast-conserving therapy. Since breast MRI is highly sensitive for breast cancer, it is also expected to be useful for the detection of multiple breast cancer sites (Figure). Also, with the standardization of simultaneous bilateral breast imaging, the detection of cancer sites in the contralateral breast has become possible. However, since CT is performed in the supine position, which is also the surgical position, and provides high-resolution images in a short period, it is occasionally applied in Japan to the preoperative examination for breast-conserving therapy. Whether or not MRI and CT are useful for the diagnosis of multiple breast cancer sites was evaluated.

MRI has long been recognized to be useful for the detection of multiple breast cancer sites in Western countries, and many reported have appeared. In the preoperative assessment of breast-conserving therapy, the frequency of detection by MRI of ipsilateral multiple breast cancer sites undetectable by mammography is reportedly 27.1-38.0%. When mammography and ultrasonography are used in combination, the percentage of ipsilateral multiple breast cancer sites detected by MRI alone has been 6.3-11.2%. According to 2 meta-analyses reported recently, additional lesions were detected in the ipsilateral breast in 16-20% of the patients by using MRI for the preoperative evaluation of breast cancers, but the positive predictive value for multiple breast cancer sites was 66-67%, and the results were false positive in about one-third of the patients. While MRI is superior to conventional clinical examinations or imaging modalities in the detection ability for multiple breast cancer sites, a considerable number of false positives occur simultaneously, and histological evaluation is recommended for lesions detected by MRI alone.

In meta-analyses concerning the detection of contralateral breast cancers, the frequency of detection of additional contralateral lesions by MRI before breast cancer surgery was 5.5-9.3%, and the positive predictive value for breast cancer was 37-47.9%.

Presently, there is no clear evidence that breast MRI should be performed as a routine preoperative examination in patients undergoing breast-conserving surgery for detecting multiple breast cancer sites. Further evaluation is necessary concerning false positive results and the management of lesions detected by MRI alone. However, it is evident that the detection rate of multiple breast cancer sites by MRI is higher than those by other imaging modalities.

On the other hand, the frequency of preoperative detection by multislice CT of ipsilateral multiple breast cancer sites undetectable by mammography has been reported to be 4.5-18.7%, which is lower than the detection rate by MRI. In the reports evaluating the diagnostic abilities concerning the extent of breast cancers showing multifocality or multicentricity by various modalities in the same patients, the accuracy was 77% by MRI, 64% by multislice CT, 36% by mammography, and 59% by ultrasonography, being higher in CT than in mammography or ultrasonography but lower than in MRI. Particularly, for intraductal lesions, the sensitivity of multislice CT is considered to be significantly lower, and the accuracy also to be lower, than those of MRI. Presently, therefore, MRI is recommended as the first choice for the diagnosis of multiple breast cancer sites. However, in patients who cannot tolerate MRI due to claustrophobia or implanted metal devices, CT may be used supplementarily to mammography or ultrasonography in the preoperative examination of patients undergoing breast-conserving surgery.

A search of PubMed was performed using “breast”, “MRI”, “CT”, “multifocal”, “multicentric”, “contralateral”, and “preoperative” as key words. The Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer Vol. 2 Epidemiology/Diagnosis, 2011, and Breast MRI: guidelines from the European Society of Breast Imaging 2008 were also used as references.
Background/objective

Whether or not there is axillary lymph node metastasis is important for the staging and risk classification. Also, while axillary lymph node metastasis contributes to the local control, it may cause a decline in the QOL due to causes such as edema of the upper extremities, and the accurate judgments concerning the presence or absence of metastasis and indication for dissection is considered necessary. Since the negative agreement rate between the clinical and pathological diagnoses is low by the current methods, pathological confirmation of the presence or absence of metastasis cannot be omitted. Recently, the pathological confirmation of negative lymph node metastasis by sentinel node biopsy and additional lymph node dissection with a positive biopsy result are becoming standard procedures for clinically N0 patients.

Comments

By ultrasonography, the axillary lymph nodes as well as the breast are evaluated (Figure). The diagnostic precision by ultrasonography has been reported to be improved by a combination of criteria concerning the size (regarded as positive when the diameter exceeds 5 mm) and morphology (round, hypoechoic, cortical thickening, disappearance of the hilum of lymph node, and lobulation) and simultaneous evaluation of the blood flow by color Doppler imaging. However, there is no established diagnostic method, and the diagnostic ability of ultrasound alone is limited.

CT is occasionally performed simultaneously with metastasis screening of the thoracic region or an area including the abdominal region, but the modality has not been shown to be effective for the diagnosis.

MRI is often performed for the diagnosis of intramammary lesions, and it may be performed as a secondary modality for the axilla. It has been reported that the evaluation using MR spectroscopy showed a sensitivity of 65% and a specificity of 100%. There is also a report that the diagnostic ability of even unenhanced MRI was improved by combining it with diffusion-weighted imaging. Presently, however, no appropriate diagnostic procedure has been established, and the diagnostic ability is insufficient.

There were many reports that the sensitivity of PET was high in the early years, but it is currently considered low. Particularly, small lymph node metastases (those with a diameter of less than 5 mm and micrometastases) are difficult to detect. However, the specificity of both PET and PET/CT is high. In patients with advanced breast cancer, lymph nodes showing positive findings on PET or PET/CT should be considered clinically positive, and performing axillary dissection without sentinel node biopsy is worth evaluating. The table shows the diagnostic performance of various modalities.

Index words and secondary materials used as references

A search of PubMed was performed using “breast”, “axillary” “lymph node”, “metastasis”, “PET”, “CT”, “MRI”, and “US” as key words. The Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer Vol. 2 Epidemiology/Diagnosis, 2011 CQ12 “Is diagnostic imaging recommended for the evaluation of axillary lymph nodes?” was also used as a reference.
Table: Diagnostic performance of various modalities

<table>
<thead>
<tr>
<th>Modality</th>
<th>Ultrasound (diameter)</th>
<th>Ultrasound (shape)</th>
<th>CT</th>
<th>MRI</th>
<th>PET or PET/CT</th>
<th>PET/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%) mean</td>
<td>69 (66-73)</td>
<td>81 (54-92)</td>
<td>n.a.</td>
<td>90 (79-90)</td>
<td>63 (65-100)</td>
<td>56 (44-67)</td>
</tr>
<tr>
<td>Specificity (%) mean</td>
<td>75 (44-98)</td>
<td>96 (88-98)</td>
<td>n.a.</td>
<td>90 (79-89)</td>
<td>94 (54-100)</td>
<td>96 (90-99)</td>
</tr>
<tr>
<td>Number of studies</td>
<td>631</td>
<td>706</td>
<td>354</td>
<td>307</td>
<td>2,591</td>
<td>862</td>
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<tr>
<td>n.a. : not available</td>
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</table>

**Figure: Ultrasonography performed for the preoperative staging of breast cancer**

Lymph nodes showing level I and II enlargement are noted in the maxilla. Their shape suggested metastasis, and the nodes were judged to be malignant by aspiration cytology. Axillary dissection was performed, and metastasis was also histopathologically confirmed.

References

Background/objective

In breast cancer, the presence or absence of distant metastasis is important for the determination of the therapeutic approach and prognosis. Conventionally, the whole body used to be searched for metastasis by modalities including chest plain radiography, bone scintigraphy, and ultrasonography of the liver, but CT and MRI began to be performed with the development of imaging devices and diagnostic techniques. Recently, instances in which PET or PET/CT is performed have also increased. However, patients with early breast cancer at a low risk of distant metastasis have increased due to increases in the screening rate, and the significance of performing a whole body search for metastasis in such patients as in patients with advanced breast cancer has become controversial. Thus, the usefulness of various examinations was evaluated according to the stage.

Comments

In a systematic review of 22 papers that evaluated distant metastasis using ultrasonography of the liver, bone scintigraphy, chest plain radiography, CT (thoracic, abdominal), PET, or PET/CT published in 1995-2011, metastasis was detected in 7.0% of breast cancer patients, but the frequency of patients with metastasis was very low at 0.2 and 1.2% in stages I and II, respectively, 13.9% in stage III, but high at 39.6% in inflammatory breast cancer. Also, the sensitivity and specificity for metastasis were higher in CT (thoracic, abdominal), PET, and PET/CT than in conventional examinations (ultrasonography of the liver, bone scintigraphy, chest plain radiography) (Figure).

Concerning ultrasonography of the liver and bone scintigraphy, the Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer Vol. 2 Epidemiology/Diagnosis, 2011 refer to a low metastasis detection rate despite a high false positive rate in stages I and II in CQ11 “Are bone scintigraphy and ultrasonography of the liver recommended for the preoperative evaluation?” Thus, the examinations are not considered very useful in stages I and II, in which distant metastasis is rare, and their consideration is recommended in patients with symptoms or positive findings or stage III breast cancer, in which the frequency of distant metastasis increases. The NCCN guidelines also do not recommend examinations in stage I or II but recommend consideration of performing them in patients with T3N1M0 (stage IIIA) or locally advanced breast cancer and those with symptoms or abnormal test results.

CT (thoracic, abdominal) is considered more useful for the detection of lung or liver metastasis than ultrasonography of the liver or chest plain radiography. In a study in which CT was performed preoperatively to search for lung or liver metastasis, false positive results were frequently obtained in stages I and II, but stage III was changed to stage IV in 6.0% of the patients due to detection of metastases undetected by ultrasonography of the liver or chest plain radiography. The usefulness of CT (thoracic, abdominal) is limited in stages I and II with few distant metastases but is considered to increase in stage III, in which distant metastasis is more frequent. The NCCN guidelines also do not recommend CT (thoracic, abdominal, pelvic) for stage I or II breast cancer patients and recommend consideration of its implementation in patients with T3N1M0 (stage IIIA) or locally advanced breast cancer and those with symptoms or positive test results.

PET and PET/CT have been reported to detect distant metastases with higher sensitivity and specificity than ultrasonography of the liver or chest plain radiography, or CT (Figure). However, many of these reports were targeted to high risk breast cancers such as those suspected to have metastases or inflammatory breast cancer, and those concerning stage I or II breast cancer were few. Also, the accuracy of PET has been reported to be high in osteolytic metastasis but low in osteoblastic metastasis compared with bone scintigraphy. However, as PET/CT can delineate osteosclerosis of osteoblastic metastasis by CT, the modality is considered to have higher diagnostic ability than PET for bone metastasis. According to the NCCN guidelines, PET or PET/CT is not applied to the staging of stage I-II and operable stage III breast cancer, and PET/CT is most useful in patients with locally advanced cancer.
or distant metastasis. As observed above, PET or PET/CT is considered to be recommendable for patients with locally advanced or stage III or more advanced breast cancer and those in whom the presence or absence of metastasis is equivocal by other imaging modalities.

Regarding liver MRI, there are data that liver metastases could be identified in 18% of stage III-IV patients by MRI, but no systematic report exists concerning preoperative search for metastasis in breast cancer patients. The NCCN guidelines recommend the implementation of liver MRI as well as CT in patients with T3N1M0 (stage IIIA) or locally advanced breast cancer or patients with symptoms or positive test results.

Concerning the preoperative search for metastasis by head CT or MRI, there have recently been few reports, and sufficient evaluation was impossible. Therefore, the modalities were not graded in the present edition. Generally, the abrupt occurrence of brain metastasis without metastasis to other organs is rare, and screening of asymptomatic patients is not recommended.

**Index words and secondary materials used as references**

A search of PubMed was performed using “breast cancer”, “metastasis”, “US”, “CT”, “MRI”, and “PET” as key words. The Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer Vol. 2 Epidemiology/Diagnosis, 2011 and the NCCN guidelines ver. 2. 2011 were also used as references.

**References**


Which imaging modalities are appropriate to evaluate the effects of preoperative chemotherapy for primary lesions of breast cancer?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Imaging Modalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>CT, MRI, PET (including PET/CT)</td>
</tr>
<tr>
<td>C1</td>
<td>Mammography, ultrasonography</td>
</tr>
</tbody>
</table>

While scientific evidence is insufficient, mammography and ultrasonography may be considered for the evaluation of the effects of preoperative chemotherapy. CT, MRI, and PET (including PET/CT) are useful for the evaluation of the effects of preoperative chemotherapy and are recommended.

**Background/objective**

Recently, preoperative chemotherapy has begun to be selected as an initial treatment for breast cancer, because, if a satisfactory reduction in the tumor size has been achieved, breast-conserving surgery becomes possible even for locally advanced breast cancer with no indication for breast-conserving surgery, and, if complete pathological remission has been achieved, a favorable prognosis can be expected even in patients with advanced breast cancer.

In the implementation of preoperative chemotherapy, it is necessary to clarify the residual lesion and the extent and accurately evaluate the therapeutic effect for the selection of treatment and evaluation of surgical indications after chemotherapy. For this, it is important to objectively assess the lesion by imaging modalities. While this CQ is focused on primary lesions of breast cancer, the same approach should also be applied to metastatic lesions.

**Comments**

According to the Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer, 2011, diagnostic imaging is more useful than inspection/palpation for the evaluation of the effectiveness of preoperative chemotherapy, and its recommendation grade is B. However, the selection of modalities and evaluation methods remain unconfirmed.

Mammography, ultrasonography, CT, MRI, and PET/CT are used for the evaluation of therapeutic effects on breast lesions. Compared with palpation, mammography has been reported to have higher diagnostic precision concerning complete remission, but there is also a report that it is inferior to palpation in the evaluation of the maximum tumor diameter after chemotherapy, and its position has not been settled. Mammography is useful for the assessment of calcification associated with malignant lesions, which is likely to be difficult by other modalities.

Ultrasound is reportedly superior to mammography in the assessment of therapeutic effects on breast cancer, and it is also used widely in Japan. However, as the precision of the examination varies among examiners, and as objective evaluation is difficult, it is not recommended by the RECIST 1.1. Caution is needed in its use.

The guidelines of the Japanese Breast Cancer Society consider that CT may be useful for the assessment of breast lesions when MRI cannot be used, and this principle is considered to apply to the evaluation of the therapeutic effects when breast lesions alone are the targets. However, advanced breast cancer is often accompanied by lymph node metastasis or distant metastasis, and CT is useful for their evaluation.

There have been a number of reports that MRI is useful for the assessment of breast lesions before and after chemotherapy. According to a meta-analysis reviewing 25 papers, MRI shows a relatively low sensitivity but a considerably high specificity in predicting complete remission.

Presently, PET is often performed as PET/CT. Concerning the evaluation of breast lesions, PET has limitations in the evaluation of small lesions due to its poor resolution, but it is sufficiently useful for the evaluation of advanced breast cancers that require preoperative chemotherapy. There have been a few reports comparing the diagnostic ability between PET/CT and MRI regarding the evaluation of therapeutic effects on breast lesions, and they suggested that the specificity was higher in MRI, but the sensitivity was higher in PET/CT, in the assessment of complete remission. PET/CT shows high diagnostic performance for metastatic lesions, with sensitivity and specificity being reported at 100 and 96%, respectively, in stage II and III patients. PET/CT, by which not only primary but also metastatic lesions can be evaluated, is considered to be highly useful when their simultaneous evaluation is necessary.

Scientific evidence concerning mammography and ultrasonography is insufficient, and patients in whom these modalities are useful are limited. Ultrasonography should be performed with attention to the observer dependence. While MRI, CT, and PET/CT are recommended, they need not be performed together, and the selection of modalities depending on the situation is necessary.
Index words and secondary materials used as references


References

6) Uematsu T et al: Neoadjuvant chemotherapy for breast cancer: correlation between the baseline MR imaging findings and responses to therapy. Eur Radiol 20: 2315-2322, 2010 (Level 2)
Are CT, MRI, and ultrasonography appropriate for the periodic follow-up for local recurrence of breast cancer after breast-conserving therapy?

### Background/objective

Recently, a meta-analysis by the Early Breast Cancer Trialist’s Collaborative Group (EBCTCG) has reported that the survival rate decreases with increases in the frequency of local recurrence and suggested the importance of the diagnosis and control of local recurrence. Also, a recent meta-analysis has evaluated whether or not the early detection of local recurrence of breast cancer affects the survival rate and reported that the survival rate was favorable when the recurrence was detected early by periodic mammography. According to the Evidence-based Clinical Practice Guidelines for Breast Cancer, periodic mammography after the primary treatment is useful for the detection of local recurrence after breast-conserving therapy (BCT) (Recommendation grade: A). Actually, however, various modalities have begun to be used for the follow-up after BCT. In this article, the usefulness of ultrasonography, MRI, and CT for periodic follow-up of the breast after BCT was evaluated.

### Comments

After BCT, a wide variety of histological changes including inflammation, edema, hemorrhage, and granulomatous change are observed in the breast due to surgery and radiation therapy. While these histological changes are mitigated with time from immediately after the treatment, they never disappear and make the detection of recurrent lesions difficult by influencing images.

Ultrasonography is performed routinely before and after surgery for breast cancer, and the Guidelines set its recommendation grade at B for the preoperative diagnosis of breast cancer. However, for the local recurrence (including recurrence in the contralateral breast) after BCT, ultrasonography alone is highly sensitive (87-90.9%) but slightly less specific (68.6-98.3%) and frequently shows false positives, so ultrasound-guided cytological or histological examination may be indicated. The addition of ultrasonography to inspection, palpation, and mammography, which are techniques currently recommended for the screening for local recurrence after BCT, reportedly improved the sensitivity and specificity. Therefore, ultrasonography is useful for the further evaluation as it plays a supplementary role to screening procedures such as inspection, palpation, and mammography.

For recurrent/residual lesions, the sensitivity, specificity, and positive and negative predictive values of MRI are reported to be 61.2-100, 69.7-96, 56.3-75, and 54.8-100%, respectively, with the positive predictive value being low. Concerning the diagnosis of recurrent lesions by MRI, recurrence is suggested by findings including the pattern, shape, and enhancement of staining and the appearance of new lesions. Of such latent or multiple lesions in the conserved affected breast, 12.2-64% were not detected by mammography but detected by MRI, and MRI caused changes in the therapeutic approach after recurrence in about 30% of the patients, indicating the usefulness of the modality. However, as lesions and mammary gland tissue enhance similarly during some periods after BCT, there are limitations in the detection of recurrent lesions in the breast or discrimination between benign and malignant lesions. By recent MRI, both breasts can be examined at one time, and latent breast cancers have been detected in the contralateral as well as affected breast after BCT at frequencies of 2-5%. However, in 2 retrospective studies, the positive predictive value of MRI for lesions in the contralateral breast was low at 67-47.9%, the true positive/false positive rate was 0.92, and the discrimination between benign and malignant lesions was difficult. Also, biopsy was recommended in 32% of the patients with suspected breast cancers detected by MRI in the contralateral breast, 5% of these lesions were cancers, and many of them were early treatable non-invasive ductal carcinoma or early breast cancer.

Thus, while the usefulness of MRI after BCT is recognized, the low recurrence rate, stress to the patients, and poor cost performance are considered to be disadvantages for the patients. Furthermore, how the detection of breast cancer in the contralateral breast by MRI affects the long-term prognosis of the patients presently remains unclear.

Advantages of CT are that the scanning time is shorter than in MRI, scanning can be made in the surgical position, and the cost is lower. In some retrospective studies, the sensitivity, specificity, positive and negative predictive values,
and accuracy of CT for the local recurrence after BCT have been reported to be 90-91, 85-90, 90-94, 90-98, and 88-90%, respectively, indicating a high diagnostic ability, but CT was performed for lesions suspected to be malignant by mammography or ultrasonography during the follow-up in all these studies. Also, these reports lacked criteria of the CT value for identifying lesions as recurrence. In consideration of the increase in X-ray exposure due to CT examination, the modality cannot be recommended for breast screening after BCT.

Index words and secondary materials used as references
A search of PubMed was performed using “breast conserving-therapy”, “MRI”, “CT”, “ultrasonography”, “ultrasound”, “local recurrence”, and “ecurrence” as key words. The Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer Vol. 2 Epidemiology/Diagnosis, 2011 were also used as a reference.

References

10) Kim MJ et al: Sonographic surveillance for the detection of contralateral metachronous breast cancer in Asian population. AJR 19: 221-228, 2009 (Level 4)
Which imaging modalities are appropriate for the periodic whole-body follow-up after surgery for breast cancer?

| Recommendation grade | Plain chest radiography, chest CT, ultrasonography of the liver, abdominal CT, MRI of the liver, bone scintigraphy, PET (including PET/CT), and head CT/MRI are not recommended unless clinical symptoms are present because scientific evidence recommending imaging examinations is deficient. |

**Background/objective**

Regarding which examinations should be performed at what frequency in the periodic whole-body follow-up (surveillance) for metastases after surgery for breast cancer, the usefulness of examinations currently performed routinely in clinical practice in Japan was evaluated.

**Comments**

As a result of a prospective study in which patients after surgery for breast cancer were followed up either by periodic physical examination and mammography alone or by combining these procedures with bone scintigraphy, ultrasonography of the liver, plain chest radiography, and blood tests, a prospective study using plain chest radiography and bone scintigraphy, and a 10-year follow-up study after the second prospective study, the survival rate was shown not to improve even by careful follow-up using additional imaging modalities. In an additional meta-analysis of these studies, no difference was noted in the survival rate or recurrence-free survival rate, and no significant difference was noted even by sub-group analysis according to age, tumor diameter, and state of lymph node metastasis. Further, in a prospective study in which patients diagnosed to have recurrence by liver function tests, tumor marker monitoring, plain chest radiography, CT, and bone scintigraphy and those diagnosed on the basis of the clinical history, symptoms, physical findings, and mammography were compared, the difference in the diagnostic method did not affect the survival rate. Although these studies were carried out before 2000, there have been few studies thereafter possibly because of their strong impact. To the present, various recurrence risk classifications have been reported, but there has been no study that compared the frequency or types of periodic follow-up according to differences in recurrence risk.

Regarding individual examinations, there has been no study that showed the usefulness of postoperative periodic plain chest radiography. In none of the prospective or retrospective studies evaluating periodic follow-up by means including plain chest radiography was the modality shown to be useful. The medical cost however reduced by performing plain chest radiography upon the appearance of symptoms.

There has been no prospective study concerning postoperative thoracoabdominal CT. In 2 retrospective studies, the effects of postoperative chest CT or CT of an area including the pelvic region were evaluated, but the modality was not shown to be useful in either study. In addition, no studies showing the usefulness of periodic CT examination in asymptomatic patients exist.

Concerning the liver, ultrasonography of the liver was included in the items of periodic follow-up in one prospective study, but neither the survival rate nor QOL were improved by periodic examinations. Also, there is no study that showed the usefulness of periodic ultrasonography of the liver in asymptomatic patients. No study has been conducted about periodic surveillance of the liver by MRI in asymptomatic patients.

As for bone scintigraphy, it has been reported that bone is the most frequent site of the first recurrence after treatment for breast cancer, and that the risk of recurrence can be classified according to the pathological tumor diameter, state of lymph node metastasis, and histological type, but no prognosis-improving effect of postoperative periodic bone scintigraphy has been demonstrated. According to a retrospective study in which the circumstances of detection of bone metastasis were compared between symptomatic and asymptomatic patients, no prolongation of the survival period was noted even when asymptomatic bone metastases were detected by periodic follow-up including bone scintigraphy. The NSABP reported that a symptomatic bone metastasis was in only 0.65% (52/7,984 scans), and the Ludwig Breast Cancer Study Group reported that initial bone metastases could be detected early by bone scintigraphy in only 2.4% of the patients positive for axillary lymph node metastasis. Currently, however, treatments for bone metastasis are changing due to improvements in the diagnostic precision of bone scintigraphy and the advent of bisphosphonate preparations. There is also a paper urging reevaluation of the clinical significance of bone scintigraphy in patients with advanced breast cancer, in which bone metastasis is considered to be frequent. Even if bone scintigraphy may not clearly prolong the survival period, further evaluation is considered necessary as it may reduce skeletal-related events. At present, however, there are no solid grounds for recommending periodic bone scintigraphy for asymptomatic patients.

No prospective study concerning postoperative PET exists. PET is more sensitive and specific in detecting recurrence
of breast cancer than conventional imaging modalities including mammography, ultrasonography, CT, MRI, radiography, and bone scintigraphy. However, its effects on the survival rate, QOL, or medical economy has not been studied. In one retrospective study, PET was compared with conventional imaging modalities concerning the detection of metastatic/recurrent breast cancer. PET showed higher sensitivity and negative predictive value but no difference in the specificity or positive predictive value compared with other imaging modalities. As observed above, PET is useful for the detection of recurrence of breast cancer, but there has been no study evaluating the usefulness of periodically performing PET in asymptomatic patients.

There has been no study about periodic head CT/MRI in asymptomatic patients. Thus, no effect of careful periodic follow-up incorporating various examinations after surgery for breast cancer on the survival rate or QOL has been demonstrated. Since there may be changes in the significance of early detection with changes in treatments, further observational studies should be carried out according to the principles of EBM, and examinations demonstrated to be useful should be mentioned in guidelines for periodic follow-up.

Index words and secondary materials used as references

A search of PubMed was performed using “breast”, “cancer”, “follow-up”, and “imaging” as key words, but few relevant papers were found. The Japanese Breast Cancer Society ed.: The Evidence-based Clinical Practice Guidelines for Breast Cancer Vol. 2 Epidemiology/Diagnosis, 2011 were also used as a reference.

References

1) The GIVIO Investigators: Impact of follow-up testing on survival and health-related quality of life in breast cancer patients. A multicenter randomized controlled trial. JAMA 271: 1587-1592, 1994 (Level 2)
09
Musculoskeletal
Is MRI appropriate for the diagnosis of cervical spondylotic myelopathy?

**Recommendation grade**

B

MRI is useful for the localization of lesions, evaluation of disease status, and prediction of prognosis. However, MRI alone is insufficient for the evaluation of spinal cord compression and should be performed in combination with plain radiography or CT.

**Background/objective**

MRI is an imaging modality indispensable for the diagnosis of cervical spine disorders. The usefulness of MRI for the diagnosis of cervical spondylotic myelopathy was evaluated.

**Comments**

Regarding the diagnosis of cervical spondylotic myelopathy, there have been a number of studies comparing the diagnostic ability between MRI (Figure) and other modalities or evaluating the correlation between MRI and neurological findings and between MRI findings and prognosis after treatment. Larsson et al. studied 26 patients with cervical radiculopathy or myelopathy and reported that MRI was recommendable along with plain radiography as the first choice imaging for the diagnosis of cervical spondylotic myelopathy but that the differentiation of whether cervical spine compression was caused by bony or soft tissues was reportedly difficult. Sengupta et al. also studied 41 patients with cervical myelopathy after surgical treatment and, comparing the surgical findings and imaging interpretations, concluded that the differentiation of spinal cord compression was difficult by MRI. Nagata et al. on the other hand, analyzed 115 patients with cervical spondylotic myelopathy and reported that the degree of spinal cord compression in sagittal T1-weighted MRI correlated with the clinical severity as defined by the evaluation criteria for the therapeutic results of cervical myelopathy by the Japan Orthopaedic Association (JOA score), and they concluded that MRI is useful for diagnosis and postoperative evaluation. Bucicero et al. calculated the ratio between the anteroposterior and lateral diameters of the spinal cord (anteroposterior compression ratio: APCR) in the transverse view of MRI in 35 patients with cervical spondylotic myelopathy and reported that neurological findings were mild in patients with an APCR of 40% or higher. In contrast, they found that neurological findings were severe and no postoperative improvements were observed in those with an APCR of 10% or less. Chung et al. also evaluated 37 surgically treated patients and reported that the degree of spinal cord compression in the transverse image correlated with the postoperative outcome. Moreover, according to a report by Wada et al. based on the postoperative results in 50 patients, the transverse area of the spinal cord at the site of maximum compression was most closely correlated with outcome, and it was 40 mm² or less in many patients who showed poor postoperative improvements. Thus, MRI, which directly visualizes spinal cord compression, has been confirmed as useful for the diagnosis of cervical spondylotic myelopathy, evaluation of the disease status, and prediction of postoperative prognosis. However, there have been reports that the diagnosis based on visual evaluation has limitations and that interobserver agreement is particularly poor.

In cervical spondylotic myelopathy, in addition to morphological change, i.e., flattening of the spinal cord due to compression, abnormal high signal intensity is often observed, particularly, on T2-weighted imaging, (T2-high signal intensity). This finding is considered to reflect some reversible or irreversible pathological condition, and while a number of studies have been conducted about its diagnostic significance, the conclusions have varied. Chung et al. evaluating 37 patients surgically treated for cervical spondylotic myelopathy, reported that T2-high signal intensity was not correlated with the postoperative outcome. Matsumoto et al. also studied 52 conservatively treated patients with cervical spondylotic myelopathy and concluded that T2-high signal intensity was not correlated with the clinical severity or therapeutic results. However, Chen et al. evaluated 64 patients surgically treated for cervical spondylotic myelopathy by dividing the T2-high signal intensity into types 1 (indistinctly bordered mild hyperintensity) and 2 (distinctly bordered marked hyperintensity) and observed that the outcomes were comparable to those showing no T2-high signal intensity in type 1 but were poor in type 2. Suri et al. analyzed the outcomes in 146 surgical patients and reported that the outcome was poor when areas of abnormal signal intensity were observed on T1- as well as T2-weighted imaging. Moreover, Chatley et al. evaluating 64 surgically treated patients, reported that the outcome was poor in patients who showed T2-high signal intensity in 2 or more vertebral bodies, and Wada et al. mentioned similar observations.

There have also been studies on the diagnostic significance of contrast-enhanced MRI. Ozawa et al. evaluated the relationship between preoperative contrast-enhanced T1-weighted images and clinical symptoms in 683 surgically treated patients with cervical spondylotic myelopathy and reported that no significant difference was observed in the preoperative JOA score between groups with and without intramedullary contrast enhancement but that the...
postoperative JOA score was significantly higher in the group without contrast enhancement.

In the diagnosis of cervical spondylotic myelopathy, MRI is useful for the localization of lesions, evaluation of disease status, and prediction of prognosis, but is insufficient for the evaluation of spinal cord compression, and is recommended to be used in combination with plain radiography or CT. However, problems including the lack of objectivity of findings (poor interobserver agreement rate) and ambiguousness of the significance of T2-high signal intensity are remaining issues.

Index words and secondary materials used as references

A search of PubMed was performed using “cervical spondylosis”, “cervical spondylotic myelopathy”, and “MRI” as key words. The Guidelines Committee of the Japan Orthopaedic Association/Committee for the Preparation of Guidelines for Cervical Spondylotic Myelopathy eds: Clinical Guidelines for Cervical Spondylotic Myelopathy, 2005 were also used as a reference.

References

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3) Nagata K et al: Clinical value of magnetic resonance imaging for cervical myelopathy. Spine 15: 1088-1096, 1990 (Level 4)


7) Cook C et al: Observer agreement of spine stenosis on magnetic resonance imaging analysis of patients with cervical spine myelopathy. J Manipulative Physiol Ther 31: 271-276, 2008 (Level 4)


Is myelography appropriate for the diagnosis of cervical spondylotic myelopathy/radiculopathy?

**Recommendation grade**

| C1 | In cervical spondylotic radiculopathy |
| C2 | In cervical spondylotic myelopathy |

**C1** In the diagnosis of cervical spondylotic radiculopathy, myelography may be useful, and its implementation may be considered. The addition of CT myelography is not recommended.

**C2** In the diagnosis of cervical spondylotic myelopathy, myelography is not recommended as it may be omitted by performing less invasive MRI with plain radiography or CT.

**Background/objective**

Indications for myelography have been gradually limited with the propagation of MRI. Whether or not myelography, which involves radiation exposure and is highly invasive, is still necessary for the diagnosis of cervical spondylotic myelopathy/radiculopathy was evaluated.

**Comments**

There have been multiple studies in which the diagnostic ability for cervical spondylotic myelopathy/radiculopathy was compared between myelography or CT myelography (Figure) and MRI. Larsson et al. compared the diagnostic performance of myelography, CT myelography, and MRI in 26 patients with cervical radiculopathy or myelopathy and reported that information concerning narrowing of the subarachnoid space and spinal cord compression can be obtained similarly by all modalities and that the accuracy of the diagnosis of nerve root compression was also comparable. While it is difficult to judge whether a bony or soft tissue structure is causing nerve compression by MRI alone, they reported that this judgment was possible by combining MRI with plain radiography and recommended this combination highly. Barlett et al. compared MRI (1 and 0.5T) and CT myelography in 23 patients with cervical myelopathy and reported that MRI was more useful for the evaluation of spinal cord compression but that CT myelography was more useful for the evaluation of nerve root compression. Song et al. compared CT myelographic and MRI findings with surgical findings in 50 patients surgically treated for degenerative disorders of the cervical spine and showed that MRI was superior for the evaluation of intervertebral disc hernia and nerve root compression but that CT myelography was superior for the evaluation of narrowing of the intervertebral foramina and bony changes. Shafaie et al. compared the disc-vertebral body junction, intervertebral joints, lateral recesses, size of the spinal cord, spinal canal, and neural foramen between CT myelography and MRI in 20 patients surgically diagnosed with cervical spondylotic radiculopathy or myelopathy and observed that there were moderate correlations but that changes in the intervertebral discs and bones were not in close agreement, and concluded that CT myelography and MRI play complementary roles. These reports suggest that MRI alone is insufficient for the evaluation of spinal cord/nerve root compression but that the evaluation of the source of compression is made possible by a combination of MRI with plain radiography or CT, which provide information concerning bone changes. Also, MRI has been shown to be equally or more useful compared with myelography or CT myelography for the assessment of spinal cord compression, and myelography may be omitted by performing MRI with plain radiography or CT for the diagnosis of cervical spondylotic myelopathy. However, there are situations in which myelography is necessary for the diagnosis of cervical spondylotic radiculopathy.

Regarding comparisons between myelography and CT myelography, Sobel et al. compared myelographic and CT myelographic findings in 30 surgically treated patients with cervical disorders and reported that information obtained by the two modalities was comparable. On the other hand, Scotti et al. compared myelography and CT myelography in 40 patients with symptoms/signs of cervical spondylotic radiculopathy or myelopathy and reported that spinal cord compression was delineated more clearly by CT myelography, allowing the discrimination between osteophytes and intervertebral disc hernia. Badami et al. made similar comparisons in 30 surgically treated patients with cervical spondylotic radiculopathy or myelopathy and by CT myelography obtained additional information (properties of the lesion, asymmetry, spinal cord atrophy, and narrowing of the neuroforamina) in 60% of the patients. Furthermore, Yu et al. compared CT, myelography, and CT myelography in 69 patients with cervical spondylotic myelopathy or radiculopathy and observed that additional CT myelography is occasionally necessary in myelopathy but only provides information similar to myelography in radiculopathy. The addition of CT myelography to myelography is considered to provide extra information in many patients, but there is little evidence that CT myelography should be added for the diagnosis of cervical spondylotic radiculopathy, so this addition is not recommended.
Index words and secondary materials used as references
A search of PubMed was performed using “cervical spondylosis”, “cervical spondylotic myelopathy”, “cervical spondylotic radiculopathy”, and “myelography” as key words. The Guidelines Committee of the Japan Orthopaedic Association/Committee for the Preparation of Guidelines for Cervical Spondylotic Myelopathy eds: Clinical Guidelines for Cervical Spondylotic Myelopathy, 2005 were also used as a reference.

References
1) Larsson EM at al: Comparison of myelography, CT and magnetic resonance imaging in cervical spondylosis and disk herniation. Pre- and postoperative findings. Acta Radiol 30: 233-239, 1989 (Level 4)
2) Bartlett RJ et al: Two-dimensional MRI at 1.5 and 0.5T versus CT myelography in the diagnosis of cervical radiculopathy. Neuroradiology 38: 142-147, 1996 (Level 4)
4) Shafaie FF et al: Comparison of computed tomography myelography and magnetic resonance imaging in the evaluation of cervical spondylotic myelopathy and radiculopathy. Spine 24: 1781-1789, 1999 (Level 4)
7) Badami JP et al: Metrizamide CT myelography in cervical myelopathy and radiculopathy: correlation with conventional myelography and surgical findings. AJR 144: 675-680, 1984 (Level 4)
Background/objective

As MRI is mildly invasive and involves no radiation exposure, it is indispensable for the imaging diagnosis of lumbar spine disorders. The usefulness of non-contrast MRI, contrast-enhanced MRI, and MR myelography for the diagnosis of lumbar disc herniation was evaluated.

Comments

Concerning the diagnosis of lumbar disc herniation, there have been studies comparing the diagnostic ability between non-contrast MRI (Figure) and other imaging modalities. Janssen et al.\(^1\) compared non-contrast MRI, myelography, and CT myelography in 60 surgically treated patients with suspected intervertebral disc herniation and reported that the accuracy was highest at 96% by non-contrast MRI compared with 81% by myelography, 57% by CT myelography, and 84% by a combination of myelography and CT myelography. Thornbury et al.\(^2\) compared non-contrast MRI, CT, and CT myelography in 95 patients with low-back pain (surgically treated in 56) and reported no significant difference in diagnostic performance among the modalities. Szypryt et al.\(^3\) compared non-contrast MRI and myelography in 30 patients who underwent surgery for suspected disc herniation and observed that the accuracy was slightly higher at 88% by non-contrast MRI compared with 75% by myelography. Non-contrast MRI showed diagnostic performance comparable or superior to other modalities, and as it also involves no radiation exposure and is less invasive, it is the most recommendable imaging modality.

There have also been studies on the usefulness of non-contrast MRI for the evaluation of radiculopathy, evaluating the relationships of disc herniation with the shape of the nerve root and degree of compression. Gorbachova et al.\(^4\) evaluated non-contrast MR images in 96 patients and reported no significant relationship between the short diameter of the nerve root and disc herniation. In contrast, Pfirrmann et al.\(^5\) reported a close correlation between the degree of nerve root compression by disc herniation (4-point classification) observed by non-contrast MRI and intraoperative findings in 94 surgically examined nerve roots. While correlations between lower limb pain and the degree of nerve root compression or severity of disc herniation have also been reported, no non-contrast MRI findings correlating to areas of complaint have been presented.\(^6,7\)

Concerning contrast-enhanced MRI, there have been studies indicating its usefulness for the follow-up of disc herniation. Komori et al.\(^8\) evaluated contrast-enhanced MR images of 48 patients with unilateral radiculopathy symptoms and reported that disc herniation that showed ring-like contrast enhancement was likely to be resorbed. Autio et al.\(^9\) studied contrast-enhanced MR images of 160 patients with unilateral sciatica and suggested that thick ring-like contrast enhancement, marked displacement, and an age of 41-50 years were related to the regression rate. Also, sequestrated disc herniation often presents with an appearance mimicking tumor, but contrast-enhanced MRI has been reported to be useful for its discrimination from tumors.\(^10,11\) Moreover, Hueftle et al.\(^12\) compared MRI and pathological findings in 17 patients who underwent surgery for failed back surgery syndrome and reported that early phase contrast-enhanced MRI within 10 minutes after the contrast agent injection was useful for the differential diagnosis of epidural fibrosis and recurrence of disc herniation. Contrast-enhanced MRI usually need not be performed for the diagnosis of intervertebral disc herniation, but it may be useful for the follow-up, discrimination from tumors, and diagnosis of postoperative recurrence.

MR myelography is used as an alternative for myelography due to its high delineation ability for the subarachnoid space and morphology of the nerve root and ganglia. Aota et al.\(^13\) evaluated 83 patients diagnosed by MRI with intervertebral disc herniation and reported that swelling and deformation of nerve roots and dorsal ganglia were clearly

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**Recommendation**

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<th>Recommendation grade</th>
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<td>B</td>
<td>Non-contrast MR</td>
<td>Contrast-enhanced MRI</td>
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Non-contrast MRI is useful and recommended. Contrast-enhanced MRI is useful in some situations for the follow-up, discrimination from tumors, and diagnosis of postoperative recurrence, and its implementation may be considered. MR myelography is not recommended as there is no evidence supporting its addition to non-contrast MRI.
visualized and that their degree was closely correlated with the severity of lower limb pain. However, Pui et al.\textsuperscript{14) evaluated 72 patients diagnosed with cervical or lumbar disc herniation by MRI and concluded that the diagnostic ability for herniation is not improved by the addition of MR myelography to non-contrast MRI. O’Connell et al.\textsuperscript{15) examined MR images of 207 patients with lumbar pain or radiculopathy symptoms and concluded that the addition of MR myelography to non-contrast MRI provided little extra information. MR myelography is not recommended as there is no evidence that it should be added to non-contrast MRI.

Index words and secondary materials used as references

A search of PubMed was performed using “back pain”, “sciatica”, “disk herniation”, and “MRI” as key words. Also, Medina LS and Blackmore C eds: Evidence-Based Imaging: Optimizing Imaging in Patient Care 2011 and the Guidelines Committee of the Japan Orthopaedic Association/Committee for the Preparation of Guidelines for Lumbar Disc Herniation eds: Clinical Guidelines for Lumbar Disc Herniation (2nd revised edition) 2011 were also used as references.

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Are discography and myelography recommended for the diagnosis of lumbar disc herniation?

**Recommendation grade**

<table>
<thead>
<tr>
<th>C1</th>
<th>Discography</th>
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<td>C2</td>
<td>Myelography</td>
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**C1** Discography may be useful for the diagnosis of lateral type disc herniation, and, as it may serve as a supplementary examination for the functional diagnosis by inducing and reproducing disc pain, its implementation may be considered.

**C2** Myelography is not recommended as it can be omitted by performing less invasive MRI and CT.

**Background/objective**

Myelography used to be considered the most reliable method for the diagnosis of disc herniation and spinal canal stenosis before the introduction of MRI into routine clinical practice. Discography has also been used for the morphological evaluation of the intervertebral discs and functional diagnosis by induction and reproduction of disc pain. Whether or not these highly invasive examinations involving radiation exposure are still necessary for the diagnosis of lumbar disc herniation currently, when MRI has become widely available, was evaluated.

**Comments**

1) **Myelography**

There have been studies in which the diagnostic ability of MR myelography and other imaging modalities for lumbar disc herniation was compared. Modic et al.\(^1\) compared MRI, CT, and myelography in 48 patients who underwent surgery for suspected disc herniation or spinal canal stenosis and showed that diagnostic performance of MRI was comparable to that of CT or myelography with an accuracy of 82.6% compared with 83% by CT, 71.8% by myelography, 92.5% by a combination of MRI and CT, and 89.4% by a combination of CT and myelography. Albeck et al.\(^2\) compared myelography, CT, and MRI in 80 patients surgically treated for suspected disc herniation and recommended CT or MRI as the first choice for the diagnosis of disc herniation, because myelography provided least information. Janssen et al.\(^3\) compared MRI, myelography, and CT myelography in 60 patients surgically treated for suspected disc herniation and reported that the diagnostic accuracy for disc herniation was highest at 96% by MRI, 81% by myelography, and 57% by CT myelography and that it was even higher than 84% by a combination of myelography and CT myelography. Myelography cannot be recommended as there is no evidence that it exceeds MRI or CT.

2) **Discography**

The ability for the morphological evaluation of the lumbar intervertebral discs has been compared between discography (Figure) and other imaging modalities. Birney et al.\(^4\) compared the diagnostic abilities of discography and MRI for degenerative disc disease in 90 patients with low-back pain and radiculopathy symptoms (surgically treated in 57) and reported that the sensitivity and specificity were 87.5 and 100% by discography and 100 and 92.86%, respectively, by MRI, with no significant difference. Segnarbieux et al.\(^5\) evaluated the usefulness of CT discography in 29 patients with lateral type disc herniation among patients who underwent discectomy for herniation. They reported that the discrimination between the foraminal and extraforaminal types was difficult by CT, myelography, CT myelography, or MRI in 15 of the 29 patients and that this discrimination and appropriate selection of the surgical procedure became possible by the addition of CT discography. Maroon et al.\(^6\) reported that the findings on discography and CT myelography were in agreement with surgical findings in all 25 surgically treated patients with lateral type disc herniation. For the diagnosis of lumbar disc herniation, discography is not always necessary but is occasionally useful for the diagnosis of lateral type herniation.

Discography has also been used for the functional diagnosis of disc pain based on the reproduction of pain after injection of the contrast agent and its alleviation by the addition of topical steroid injection. While there have been a number of studies showing its usefulness for the diagnosis of disc pain and determination of its intervertebral level,\(^7\) disc pain is not specific to disc herniation. In diagnosing disc herniation, provocation and reproduction of disc pain by discography can be a supplementary examination for the functional diagnosis.

**Index words and secondary materials used as references**

A search of PubMed was performed using “disk herniation”, “myelography”, and “discography” as key words. The Guidelines Committee of the Japan Orthopaedic Association/Committee for the Preparation of Guidelines for Lumbar Disc Herniation eds: Clinical Guidelines for Lumbar Disc Herniation (2nd revised edition) 2011 were also used as
The Japanese imaging guideline 2013

Figure: Lumber disc herniation

A  Discography (L4/5 level)  Lateral view: Leakage of the contrast agent from the intervertebral disc to the posterior direction is observed at the L4/5 level (→). B  CT discography (L4/5 level)  C  CT discography  Sagittal MPR image: Leakage of the contrast agent from the intervertebral disc to the left posterior direction is more clearly visualized (→).

References

Is MRI appropriate for the diagnosis of rotator cuff tears of the shoulder? Is MR arthrography also necessary?

<table>
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<th>Recommendation grade</th>
<th>B Non-contrast MRI</th>
<th>C1 MR arthrography</th>
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<tr>
<td>B</td>
<td>Non-contrast MRI is useful along with ultrasonography. While ultrasonography is superior to non-contrast MRI in cost-effectiveness, non-contrast MRI is recommended since ultrasonography is not widely used in Japan.</td>
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<tr>
<td>C1</td>
<td>MR arthrography has the highest diagnostic ability but is invasive. It may be considered when the diagnosis is impossible by other modalities or when detailed evaluation is necessary.</td>
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**Background/objective**

For rotator cuff tears of the shoulder, arthroscopy or direct observation by surgery is the gold standard. However, these procedures are invasive, and diagnostic imaging is performed first when rotator cuff tears are clinically suspected. Arthrography used to be the most effective diagnostic modality, but MRI is prevalent today. The usefulness of non-contrast MRI and necessity of MR arthrography for the diagnosis of rotator cuff tears were evaluated.

**Comments**

A number of studies have been carried out to evaluate the usefulness of imaging modalities for the diagnosis of rotator cuff tears of the shoulder. According to a meta-analysis by Jesus et al., the sensitivity and specificity for the diagnosis of partial/full-thickness tears of the rotator cuff were 87.0 and 81.7% by non-contrast MRI (Figure 1), highest at 92.3 and 94.5% by MR arthrography (Figure 2), and 85.1 and 86.1% by ultrasonography, respectively, with no significant difference between non-contrast MRI and ultrasonography. The Az value by ROC analysis was highest at 0.935 by MR arthrography, followed by 0.889 by ultrasonography and 0.878 by non-contrast MRI. On pairwise correlational analysis, no significant difference was observed between non-contrast MRI and ultrasonography. In a meta-analysis by Dinnes et al., also, the sensitivity and specificity for full-thickness tears were 87 and 96% by ultrasonography, 89 and 93% by non-contrast MRI, and highest at 95 and 93% by MR arthrography, respectively. However, the diagnostic ability for partial tears was reported to be low in all these modalities. MR arthrography is considered to have the highest ability for the diagnosis of rotator cuff tears, but as it is invasive, it is recommended only in special situations such as when the diagnosis is difficult by other modalities and when detailed evaluation is necessary in top athletes. Also, while ultrasonography is recommended for screening as the least expensive modality, it is greatly dependent on the examiner’s skill and is not performed widely in Japan. Being an imaging modality available at most facilities, non-contrast MRI is recommended most highly.

As for comparisons between direct and indirect MR arthrography, there have been reports that no significant difference was observed in the diagnostic ability between the two procedures, that the diagnostic ability did not differ between 3D and 2D imaging, and that 3D imaging is recommended to reduce the imaging time, but no large-scale research has been conducted. Regarding limb positioning, it has been reported that no significant difference was observed in the diagnostic ability between conventional and abduction and external rotation (ABER) positions and that the diagnostic ability was improved by the addition of ABER position to conventional position. Further evaluation is necessary regarding these points.

**Index words and secondary materials used as references**

A search of PubMed was performed using “rotator cuff injury”, “rotator cuff tear”, “diagnosis”, “MRI,” and “MR arthrography” as key words. Medina LS and Blackmore C eds: Evidence-Based Imaging: Optimizing Imaging in Patient Care 2011 was also used as a reference.

**References**


## Is MRI appropriate for the diagnosis of glenoid labral tears of the shoulder? Is MR arthrography also necessary?

<table>
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<th>Recommendation grade</th>
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<th>Non-contrast MRI</th>
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<td>C1</td>
<td>MR arthrography</td>
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Non-contrast MRI is useful and recommended. MR arthrography may have higher ability than non-contrast MRI to delineate labral fragments and degeneration, and its implementation may be considered. Particularly, the diagnostic ability is improved by the addition of abduction and external rotation (ABER) view.

## Background/objective

Shoulder disorders are diagnosed relatively accurately by physical examination by orthopedists with excellent clinical competence, but such injuries are occasionally difficult to diagnose, and imaging examinations are frequently employed. The usefulness of non-contrast MRI and necessity of MR arthrography for the diagnosis of glenoid labral tears were evaluated.

## Comments

There have been multiple meta-analyses that evaluated the usefulness of physical examination by orthopedists for the diagnosis of glenoid labral tears of the shoulder.\(^1\text{-}^3\) Some physical diagnostic tests have been suggested to be useful, but their precision varies,\(^1\text{-}^3\) and there seems to be no reliable physical examination at present.\(^4,5\) Some reports have suggested the usefulness of ultrasonography,\(^6,7\) but its diagnostic precision is questioned by many authors, unlike ultrasonography diagnosis of rotator cuff tears.

The diagnostic ability of non-contrast MRI (Figure) for glenoid labral tears using arthroscopy as a reference standard is relatively high with sensitivity, specificity, and accuracy of 88-98, 89.5-96, and 94-95.7%, respectively.\(^8,9\) According to the site of labral tears, the sensitivity and specificity have been reported to be 89-96 and 86-100% in the anterior part, 7.7-53 and 97-98% in the posterior part, and 40 and 100% in the lower part, respectively. However, only a few patients were evaluated in each report, and the data are not reliable.\(^10,11\)

Chandnani\(^12\) compared the delineation sensitivity of non-contrast MRI, MR arthrography (Figure), and CT arthrography for glenoid labral tears using arthroscopy as a reference standard in 28 patients with instability or unexplained pain of the shoulder and reported that non-contrast MRI (93%) and MR arthrography (96%) were comparable but were superior to CT arthrography (73%). The delineation sensitivity of these modalities for avulsion fragments and degeneration of the glenoid labrum were also reported to be 46, 96, and 52% and 11, 56, and 24%, respectively, with MR arthrography being the most sensitive. In patients with anterior instability, the diagnostic sensitivity and specificity of MR arthrography for labral tears were 91-92 and 92-93%, respectively.\(^13,14\) There has been a report that superior labrum anterior to posterior (SLAP) lesions and sublabral recess, which is a normal variation, could be discriminated with high precision by MR arthrography,\(^15\) but it has also been reported that labra appearing normal on arthroscopy presented various findings on MR arthrography,\(^16\) so SLAP lesions should be diagnosed carefully. Magee et al.\(^17\) suggested that MR arthrography may be more useful than non-contrast MRI in top athletes, in whom small, unusual site, or multiple tears of the supraspinatus tendon and labrum are often observed. Also, there have been multiple reports that the diagnostic ability of MR arthrography for labral tears was improved by the addition of abduction and external rotation (ABER) view.\(^18\text{-}20\) According to Cvitanic et al.,\(^20\) the sensitivity and specificity were 48 and 91% in conventional position, 89 and 95% in ABER position, and 96 and 97% with both positions combined, respectively. However, it was reported that ABER position could not be maintained in 1/7-1/5 of the patients, and its addition is not always possible.\(^9,20\)

Regarding comparisons between direct and indirect MR arthrography, Jung et al.\(^21\) compared the diagnostic abilities of the two procedures for SLAP lesions and rotator cuff tears using arthroscopy as a reference standard and reported no significant difference. However, there has also been a systematic review reporting that indirect MR arthrography (Figure) showed a high sensitivity of 90-100% but a specificity of 71-89%.\(^22\) Indirect MR arthrography has advantages such as no need for fluoroscopy and low invasiveness but disadvantages such as interference of image reading by contrast enhancement of soft tissues associated with intravenous administration of the contrast agent and insufficient extension of the joint space.

For the diagnosis of glenoid labral tears, non-contrast MRI is the most recommendable imaging modality. While there has been no report indicating that MR arthrography has higher diagnostic ability than non-contrast MRI, it may have
higher ability to delineate labral fragments and degeneration than non-contrast MRI. Since the diagnosability of labral tears is improved by the addition of ABER view, its addition is desirable, if possible.

Index words and secondary materials used as references

A search of PubMed was performed using “shoulder”, “labrum injury”, “labrum tear”, “labral injury”, “labral tear”, “MRI”, and “MR arthrography” as key words. Medina LS and Blackmore C eds: Evidence-Based Imaging: Optimizing Imaging in Patient Care 2011 was also used as a reference.

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18) Cvitanic O et al: Using abduction and external rotation of the shoulder to increase the sensitivity of MR arthrography in revealing tears of the anterior glenoid labrum. AJR 169: 837-844, 1997 (Level 4)
Is MRI of the wrist appropriate for the diagnosis of rheumatoid arthritis?

**Recommendation grade**

MRI of the wrist is useful and recommended, and contrast-enhanced MRI is preferable. MRI should be performed in combination with rheumatologist’s examination and serological tests.

**Background/objective**

Joint MRI findings in rheumatoid arthritis include synovial thickening, bone marrow edema, bone erosion, and joint effusion, but these findings lack specificity, as other inflammatory joint disorders may present with similar findings. In 2010, classification criteria for rheumatoid arthritis were jointly revised by the American College of Rheumatology and European League Against Rheumatism, but these criteria (2010-ACR/EULAR criteria) attached importance to arthralgia, distribution of subjective/objective findings such as swelling, and number of affected joints and included no items related to joint MRI. The usefulness of MRI of the wrist for the diagnosis of rheumatoid arthritis was evaluated.

**Comments**

The usefulness of wrist MRI (Figure) for the diagnosis of rheumatoid arthritis has been evaluated in multiple cohort studies. In most of these studies, the 1987 revision of the classification criteria for rheumatoid arthritis by the American College of Rheumatology (1987-ACR criteria) were used for the diagnosis. There have been reports that MRI of the wrist was not useful for the differentiation of early rheumatoid arthritis from other inflammatory joint disorders. On the other hand, Solau-Gervais et al. evaluated contrast-enhanced MRI of the bilateral wrists in 30 patients with inflammatory multi-joint pain and reported that bone erosion of the metacarpophalangeal joints was useful for this differentiation. Sugimoto et al. evaluated contrast-enhanced bilateral wrist MRI in 27 patients suspected to have rheumatoid arthritis and reported high diagnostic performance with sensitivity, specificity, and accuracy of 100, 73, and 89%, respectively, using synovitis of the bilateral wrists, metacarpophalangeal joints, and proximal interphalangeal joints as MRI diagnostic criteria. Narváez et al. evaluated 40 patients suspected to have early rheumatoid arthritis and reported that the sensitivity and specificity were 100 and 78% by non-contrast-enhanced/contrast-enhanced MRI of the unilateral wrist (using synovitis accompanied by bone erosion or bone marrow edema of the wrist, metacarpophalangeal, or proximal interphalangeal joints as diagnostic criteria) and 23 and 100%, respectively, by anticyclic citrullinated peptide (anti-CCP) antibody testing and that MRI of the wrist contributed more to the diagnosis than anti-CCP antibody.

The usefulness of combinations of MRI of the wrist with symptoms or other examinations was evaluated in some studies. Sugimoto et al. applied their original diagnostic criteria, in which MRI criteria (contrast enhancement of the bilateral wrists, metacarpophalangeal joints, and proximal interphalangeal joints) were added to the 1987-ACR criteria, to 48 patients suspected to have early rheumatoid arthritis and reported that the diagnostic sensitivity, specificity, and accuracy changed from 77, 91, and 83% to 96, 86, and 94%, respectively, with improvements in the sensitivity and accuracy. Tamai et al. evaluated the diagnostic ability of a combination of serum markers and non-contrast-enhanced bilateral wrist MRI for early rheumatoid arthritis in 113 patients and reported satisfactory results with a sensitivity of 82.5% and a specificity of 84.8% by diagnosing rheumatoid arthritis when two or more of 1) anti-CCP antibody or rheumatoid factor being positive, 2) symmetric wrist arthritis on MRI, and 3) bone erosion/bone marrow edema on MRI were observed. They also showed similar results in 129 patients with unclassified arthritis using contrast-enhanced MRI of the bilateral wrists and serum markers and reported that a combination of bone marrow edema demonstrated by MRI and positive anti-CCP antibody was particularly useful for the diagnosis. Duer et al. evaluated 41 patients with unclassified arthritis and observed that a combination of contrast-enhanced MRI of the hand showing the severest symptoms and bone scintigraphy contributed most to the differentiation between rheumatoid and non-rheumatoid arthritis.

According to a meta-analysis by Suter et al., diagnostic performance of MRI of the wrist for early rheumatoid arthritis differed widely depending on the diagnostic criteria, with the sensitivity and specificity varying from 20-100 and 0-100%, respectively. It is difficult to discuss the diagnostic ability of MRI of the wrist on the basis of these results, but, on closer analysis, synovitis and its combination with bone marrow edema or bone erosion showed relatively high sensitivity and specificity, and bone marrow edema or bone erosion alone tended to show a high specificity but a low sensitivity. Therefore, contrast-enhanced MRI, which is useful for the depiction of synovitis, is preferable to non-contrast MRI.

For the diagnosis of rheumatoid arthritis, MRI of the wrist is useful, and contrast-enhanced MRI is desirable. MRI
The Japanese imaging guideline 2013

The Japanese imaging guideline 2013 should be performed in combination with rheumatologist’s examination and serological tests rather than MRI of the wrist alone. However, most of the studies reviewed here were carried out using the 1987-ACR criteria, and those using the 2010-ACR/EULAR criteria are still few. In the future, it is necessary to clarify the usefulness of MRI of the wrist on the basis of the 2010-ACR/EULAR criteria.

Index words and secondary materials used as references
A search of PubMed was performed using “hand”, “wrist”, “rheumatoid arthritis”, “diagnosis”, and “MRI” as key words. The 1987-ACR and 2010-ACR/EULAR classification criteria were also used as references.

References

2) Duer-Jensen A et al: Bone edema on magnetic resonance imaging is an independent predictor of rheumatoid arthritis development in patients with early undifferentiated arthritis. Arthritis Rheum 63: 2192-2202, 2011 (Level 3)
5) Narváez J et al: Usefulness of magnetic resonance imaging of the hand versus anticyclic citrullinated peptide antibody testing to confirm the diagnosis of clinically suspected early rheumatoid arthritis in the absence of rheumatoid factor and radiographic erosions. Semin Arthritis Rheum 38: 101-109, 2008 (Level 3)
Which imaging modalities are appropriate for the diagnosis of osteonecrosis of the femoral head?

**Recommendation grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>B</td>
<td>Bone scintigraphy using SPECT, MRI, and plain radiography</td>
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<td>C1</td>
<td>CT</td>
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**Bone scintigraphy using SPECT and MRI are useful and recommended.** While the diagnostic ability of plain radiography is not high, it is a basic staging modality and is recommended.

**CT is excellent in the diagnosis of subchondral fracture in necrotic bone, and its implementation may be considered in disease staging.**

**Background/objective**

Histological examination is considered to be the gold standard for the diagnosis of osteonecrosis of the femoral head, but it is usually omitted because of its high invasiveness. Imaging modalities play an important role, and plain radiography, CT, bone scintigraphy, and MRI are used internationally in diagnostic criteria and staging. The usefulness of these modalities, and which of them should be selected, were evaluated.

**Comments**

A large number of studies have been performed to evaluate the usefulness of imaging modalities for the diagnosis of osteonecrosis of the femoral head. It has been reported that the sensitivity of plain radiography was 58-86\% \(^{(1,5)}\), that of CT (Figure) was 71-95\% \(^{(4,7)}\), the sensitivity and specificity of transverse bone scintigraphy were 81-91.3 and 74-100\%, respectively \(^{(2,4,6-10)}\), and those of MRI (Figure) were 98-100\% \(^{(2,4,8,9)}\) and 71-100\%, respectively \(^{(8,10)}\), with MRI being the most sensitive. In studies comparing bone scintigraphy using SPECT and MRI, \(^{(1,11)}\) the sensitivity was higher in bone scintigraphy (91 and 100\%) than in MRI (87 and 66\%). There has also been a study that compared an early phase of bone scintigraphy and MRI and reported that a decrease in the blood flow that was not visualized by MRI could be detected in an early phase of bone scintigraphy. \(^{(12)}\) According to a study comparing the diagnostic abilities of bone scintigraphy, CT, and MRI by ROC analysis, \(^{(13)}\) MRI was superior to bone scintigraphy with a confidence level of 99\%, and there was no significant difference between MRI and CT. However, the reference standard varied among studies from biopsy (histological diagnosis) to bone marrow pressure and MRI, and there were differences in the magnetic field intensity and imaging protocol of MRI, and this must be taken into consideration. In a multi-center study that investigated the diagnostic ability using the diagnostic criteria by the Ministry of Health and Welfare research committee, \(^{(14)}\) a sensitivity of 91\% and a specificity of 99\% were reported to be achieved when any 2 of the 5 criteria proposed on the basis of plain radiography, bone scintigraphy, MRI, and pathological findings were used in combination. Thus, while bone scintigraphy using SPECT and MRI show high diagnostic abilities, a combination of multiple modalities is considered desirable.

Staging of osteonecrosis of the femoral head is important for the determination of the therapeutic strategy and prognosis. Although a few staging methods have been proposed, they are based on plain radiographs, and bone scintigraphic, MRI, and pathological findings are taken into consideration. Among the items included, subchondral fracture in necrotic bone is often difficult to diagnose, and the usefulness of imaging modalities for its diagnosis was evaluated. In a multi-center study using CT as a reference standard, \(^{(15)}\) the sensitivity and specificity of plain radiography were reported to be 71 and 97\%, and those of MRI to be 38 and 100\%, respectively. According to other studies using CT as a reference standard, \(^{(16)}\) the sensitivity, specificity, false positive rate, and false negative rate of MRI were 88-92.9, 28.6, 71.4, and 7.1\%, respectively. CT is the most useful for the diagnosis of subchondral fracture.

For the diagnosis of osteonecrosis of the femoral head, bone scintigraphy using SPECT and MRI show high diagnostic abilities and are recommended. Although the diagnostic ability of plain radiography is not high, it is a basic staging modality and is recommended. CT is excellent in diagnosing subchondral fracture in necrotic bone, and its implementation may be considered in disease staging.

**Index words and secondary materials used as references**

A search of PubMed was performed using “femoral head”, “osteonecrosis”, “avascular necrosis”, “aseptic necrosis”, “radiography”, “CT”, “MRI”, and “scintigraphy” as key words. The ARCO staging system, diagnostic criteria/staging system by the Research Committee on Idiopathic Osteonecrosis of the Femoral Head, Ministry of Health and Welfare, and Steinberg classification were also used as references.
The Japanese imaging guideline 2013

Figure: Osteonecrosis of the femoral head
A  Coronal T1-weighted MRI  B  Sagittal T2-weighted MRI: Osteonecrosis is observed primarily in the anterosuperior portion of the femoral head, and band-like hypointensity suggesting the border of necrotic region is noted (→). Linear hypointensity parallel to the articular surface is observed in the subchondral region of the femoral head (▲), indicating subchondral fracture. C  Sagittal MPR image of CT: The margin of necrotic bone is observed as band-like sclerosis (→). Subchondral fracture is identified as a linear radiolucent area in the anterior portion (▲).

References
4) Thickman D et al: Magnetic resonance imaging of avascular necrosis of the femoral head. Skeletal Radiol 15: 133-140, 1986 (Level 4)
8) Totty WG et al: Magnetic resonance imaging of the normal and ischemic femoral head. AJR 143: 1273-1280, 1984 (Level 4)
15) Stevens K et al: Subchondral fractures in osteonecrosis of the femoral head: comparison of radiography, CT, and MR imaging. AJR 180: 363-368, 2003 (Level 4)
16) Yeh LR et al: Diagnostic performance of MR imaging in the assessment of subchondral fractures in avascular necrosis of the femoral head. Skeletal Radiol 38: 559-564, 2009 (Level 4)
Is MRI appropriate for the diagnosis of meniscus/cruciate ligament tears of the knee?

**Background/objective**

MRI is frequently used for the diagnosis of tears of the menisci and cruciate ligaments, which are intra-articular structures of the knee. Physical examination by orthopedists is also regularly performed, and some orthopedists undervalue MRI. While arthroscopy is regarded as the most reliable diagnostic method, it is more invasive and expensive than MRI, so MRI is preferable to diagnostic arthroscopy. The usefulness of MRI for the diagnosis of meniscus/cruciate ligament tears was evaluated.

**Comments**

There have been a number of studies that evaluated the usefulness of physical examination by orthopedists for the diagnosis of meniscus/cruciate ligament tears of the knee using arthroscopy as a reference standard. According to meta-analyses of these studies, the diagnostic ability varied in individual physical tests, and it was improved by a composite physical examination. There have also been many studies that evaluated the diagnostic ability of MRI using arthroscopy as a reference standard. According to a meta-analysis by Oei et al., the sensitivity and specificity of MRI were 93 (92-95) and 88 (85-91) % for the medial meniscus tears, 79 (74-84) and 96 (95-97) % for the lateral meniscus tears, 94 (92-97) and 94 (93-96) % for the anterior cruciate ligament tears, and 91 (83-99) and 99 (99-100) % for the posterior cruciate ligaments tears, respectively. By a meta-analysis by Crawford et al., the sensitivity, specificity, and accuracy of MRI were 91.4, 81.1, and 86.3% for medial meniscus tears, 76.0, 93.3, and 88.8% for lateral meniscus tears, and 86.5, 95.2, and 93.4% for anterior cruciate ligament tears, respectively. MRI shows high diagnostic performance for meniscus/cruciate ligament tears, but its sensitivity is the lowest for lateral meniscus tears, so more attention to subtle findings is necessary in the lateral meniscus than in the medial meniscus or cruciate ligaments. The MR units used in the reports were diverse from 0.1 to 1.5T systems, but there have been reports suggesting no marked difference in the diagnostic ability according to the magnetic field strength. It must be noted that arthroscopy is not perfect as a reference standard due to some defects: the accuracy is dependent on the examiner’s skill, there are areas difficult to examine such as the peripheries and posterior segment of the meniscus, and only the surface of intra-articular clinical structures can be examined.

Regarding whether or not MRI should be performed after clinical examination by an orthopedist, there have been many studies using arthroscopy as a reference standard, most of which suffered a limitation that only patients with clinically suspected meniscus or ligament tears were included. There have been reports that the diagnostic ability of clinical examination were comparable to, or higher than, that of MRI, suggesting a supplemental diagnostic rule of MRI. On the other hand, there have also been reports that the diagnostic ability of MRI was higher than that of clinical examination, or that the diagnostic ability was improved by performing MRI. It has also been reported that MRI could reduce the need of diagnostic arthroscopy in 27.3-51.4% of the patients. Vincken et al. evaluated 293 patients who underwent MRI and arthroscopy after orthopedist’s examination, observed that the sensitivity and specificity for the selection of patients requiring arthroscopic treatment were 93.2 and 79.2%, respectively, and 87.3 and 88.4% after adjustment for verification bias, and concluded that MRI was useful for the selection of patients for arthroscopic treatment.

For the diagnosis of meniscus/cruciate ligament tears, it is recommended to perform MRI in combination with clinical examination by an orthopedist rather than alone. It is useful for reducing diagnostic arthroscopy and selecting patients who require arthroscopic treatment.

**Index words and secondary materials used as references**

A search of PubMed was performed using “knee”, “meniscus injury”, “meniscus tear”, “ligament injury”, “ligament tear”, “MRI”, and “arthroscopy” as key words. Medina LS and Blackmore C eds: Evidence-Based Imaging: Optimizing Imaging in Patient Care 2011 was also used as a reference.
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1) Solomon DH et al: The rational clinical examination. Does this patient have a torn meniscus or ligament of the knee? Value of the physical examination. JAMA 286: 1610-1620, 2001 (Level 3)
7) Vellet AD et al: Anterior cruciate ligament tear: prospective evaluation of diagnostic accuracy of middle- and high-field-strength MR imaging at 1.5T and 0.5T. Radiology 197: 826-830, 1995 (Level 4)
Is MRI appropriate for the diagnosis of bone tumors/tumor-like lesions?

Recommendation grade

The first choice imaging modality is plain radiography. MRI is useful for detecting lesions and evaluating the disease state and local invasion. It is recommended when malignant tumors are suspected or the therapeutic approach cannot be determined by plain radiography.

Background/objective

Plain radiography is recommended as first choice imaging for the evaluation of bone tumors/tumor-like lesions, but MRI is also performed frequently. The usefulness and indications of MRI for the diagnosis of bone tumors/tumor-like lesions were evaluated.

Comments

Various imaging modalities are used for the diagnosis of bone tumors/tumor-like lesions, but plain radiography is the least expensive and most accessible modality that can be performed at many facilities for the detection and analysis of histological properties of lesions. Many benign lesions are typical and can be diagnosed by plain radiography alone, and the addition of other imaging modalities is unnecessary for such lesions except when invasive treatments are considered. Ma et al. compared the abilities of MRI (Figure) alone and plain radiography plus MRI to discriminate benign and malignant bone tumors/tumor-like lesions in 51 patients and reported that the diagnostic sensitivity for malignant lesions showed no difference and was very satisfactory by both procedures, but that benign lesions tended to be overestimated as malignant tumors by MRI alone, and that the diagnostic specificity and accuracy were improved by 20 and 18%, respectively, when plain radiography and MRI were performed in combination.

There have been studies that compared the diagnostic ability of MRI with those of other modalities concerning the extent of bone tumors/tumor-like lesions. Hogeboom et al. compared the results of evaluation of invasion by MRI and CT in 25 patients with bone tumors/tumor-like lesions and reported that MRI was superior to CT in 25% concerning bone marrow invasion, 31% concerning soft tissue invasion, and 36.4% concerning joint invasion. As for the evaluation of destruction of bone cortex, CT was useful and superior to MRI in 13.6% of the same patients. Zimmer et al. also evaluated invasion in 52 patients with bone tumor/tumor-like lesions and reported that MRI was superior to CT in 33% of the patients for the diagnosis of bone marrow invasion and 38% for the diagnosis of soft tissue invasion. Bloem et al. compared the local staging ability of MRI with those of CT and angiography in 56 patients with malignant bone tumors and reported that the diagnostic sensitivity was 100, 33, and 83% by MRI, CT, and angiography and that the specificity was 98, 93, and 71%, respectively. They also reported that MRI was comparable to angiography in the evaluation of neurovascular invasion and recommended MRI for the local staging of malignant bone tumors.

Regarding the evaluation of internal properties, MRI with high contrast resolution has been reported to be useful in various diseases. It allows the evaluation of tissue constituents such as fat, hemorrhage/hemosiderin, cartilage matrix, myxoid matrix, collagen fibers, and cysts and contributes to the qualitative diagnosis of lesions. Mori et al. compared the diagnostic abilities of a combination of MRI and plain radiography and contrast-enhanced CT alone in 32 patients with bone tumors/tumor-like lesions and reported that CT was superior concerning the evaluation of destruction of bone cortex and calcification in lesions but that the combination between MRI and plain radiography was superior in 56% of the patients regarding analysis of histological properties of lesions.

In the diagnosis of bone tumors/tumor-like lesions, MRI is useful for the detection of lesions and evaluation of the disease state and is excellent particularly in the assessment of local invasion. However, CT is useful for the evaluation of bone cortex and calcification in lesions. Plain radiography is appropriate for screening, and MRI is recommended when a malignant tumor is suspected or the therapeutic strategy cannot be determined by plain radiography. For the assessment of MRI, plain radiography is recommended as a reference.

Index words and secondary materials used as references

A search of PubMed was performed using “bone tumor” and “MRI” as key words. The ACR Appropriateness Criteria and the Japanese Orthopaedic Association Committee on Musculoskeletal Tumors ed: General Rules for Clinical and Pathological Studies on Malignant Bone Tumors (3rd edition) 2000 were also used as references.
The Japanese imaging guideline 2013

Figure: Osteosarcoma
A  Frontal plain radiograph: Osteolytic lesions with indistinct margins are noted in the distal metaphysis of the right femur (→), and cloud-like calcifications are observed inside the lesions (▲). B  Coronal T1-weighted MRI: Eccentric hypointense lesions extending from the metaphysis to the epiphysis are observed (→). The extent of the lesion can be identified more clearly on MRI than on plain radiography.

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Is MRI appropriate for the diagnosis of soft tissue tumors/tumor-like lesions? Is contrast-enhanced MRI necessary?

<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Non-contrast MRI</th>
<th>Contrast-enhanced MRI</th>
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<tbody>
<tr>
<td>B</td>
<td>Non-contrast MRI is useful for the discrimination of benign and malignant lesions and qualitative diagnosis of benign masses. It should be performed in combination with clinical examinations and plain radiography.</td>
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<tr>
<td>C1</td>
<td>Contrast-enhanced MRI is occasionally useful for the discrimination of benign and malignant lesions, and its implementation may be considered.</td>
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Background/objective

MRI is an imaging modality that plays a central role in the diagnosis of soft tissue masses, but there is also the opinion that it is not necessarily useful. The usefulness of non-contrast MRI and necessity of contrast-enhanced MRI for the diagnosis of soft tissue tumors/tumor-like lesions were evaluated.

Comments

According to the ACR Appropriateness Criteria, when a soft tissue tumor is clinically suspected, plain radiography is recommended as first line. MRI is indicated for tumors with no clear calcification suggestive of benignancy when the possibility of malignancy cannot be clinically excluded. There have been a number of studies that evaluated the discrimination of benign and malignant soft tissue tumors/tumor-like lesions by non-contrast MRI. The sensitivity for various combinations of tumor size, morphology, site, findings of tumor margins, presence or absence of a reactive zone, homogeneity, signal intensity on T1- and T2-weighted imaging, and presence or absence of invasion to neurovascular bundles for the diagnosis of malignant lesions was high at 78-100%, but the specificity varied widely from 17-90%. The variation of the specificity is likely related to the number of patients evaluated and tumor types. According to the results of multivariate analysis concerning the discrimination of benign and malignant tumors, high signal intensity on T2-weighted imaging, a size of 3.3 cm or greater, and signal heterogeneity on T1-weighted imaging was the most sensitive combination of findings for the diagnosis of malignant tumors. Also, a combination of tumor necrosis, invasion to bones or neurovascular bundles, and a size of 6.6 cm or greater was the most specific. Non-contrast MRI is therefore useful for the discrimination of benign and malignant tumors.

Studies of the qualitative diagnosis have shown that 24-54% of benign tumors and 0-38% of malignant tumors could be qualitatively diagnosed, and the diagnostic ability was higher for benign than malignant lesions. The diagnosis of benign tumors has been reported to become more possible by the addition of plain radiography, age, and clinical symptoms such as pain. Moulton et al. evaluated 225 patients with soft tissue masses (benign in 179, malignant in 46) and reported that the specificity in the diagnosis of malignant tumors decreased from 89 to 76% by the exclusion of qualitatively diagnosable benign masses. Non-contrast MRI is more useful for the qualitative diagnosis of benign than malignant tumors, and it is recommended to be performed with clinical examinations and plain radiography.

Whether or not contrast-enhanced MRI, which prolongs the imaging time and increases the cost, should be performed on a routine basis remains controversial. The contrast-enhanced MRI has been reported not to contribute to the discrimination of benign and malignant lesions because most solid components of the lesions are enhanced similarly even though they are benign or malignant lesions. Rijswijk et al. evaluated 140 patients with soft tissue tumors (benign in 67, malignant in 73) and reported that the ability in the qualitative diagnosis of benign tumors and sensitivity in the diagnosis of malignant tumors were improved by the addition of contrast enhancement to T1- and T2-weighted imaging. Panzarella et al. observed that well-differentiated liposarcoma must be suspected if thick septa or nodules showing enhancement are noted in the interior of lipomatous tumor. Concerning dynamic contrast-enhanced MRI, the sensitivity was reported to be 66-91%, and the specificity to be 58-80%, when tumors showing early enhancement were judged to be malignant. There have also been reports that malignant tumors show periphery-dominant enhancement during early phase imaging, reflecting differences in the vascular architecture. However, among malignant tumors, sarcoma with mucus components tends to show gradual progression of contrast enhancement after injection of the contrast agent due to the slow blood flow. While the necessity of routine implementation of contrast-enhanced MRI is low, it is occasionally useful for the discrimination of benign and malignant tumors.
A search of PubMed was performed using “soft tissue tumor” and “MRI” as key words. The ACR Appropriateness Criteria and the Japanese Orthopaedic Association Committee on Musculoskeletal Tumors ed: General Rules for Clinical and Pathological Studies of Malignant Soft Tissue Tumors (3rd edition) 2002 were also used as references.

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