Estimation of mortality reduction of lung cancer in Japan by chest X-ray and low-dose CT screening using prevalence model

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Abstract：We estimated mortality reduction of lung cancer by chest X-ray(CXR) and low-dose CT(LDCT) screening performed in Japan. In this study, the prevalence model and observed data from Anti-Lung Cancer Association(ALCA) are used for calculation. Both screenings are assumed to be annual screening and are performed to be steady state in order to eliminate the effect of base-line screening. Results are as follows: using 2005 data of lung cancer incidence of Japan, lung cancer deaths are calculated to be 65427 persons/year which is good agreement with 2009 data of lung cancer deaths. With CXR screening, the deaths are 58221 persons/year and relative risk(RR) is 0.89. With LDCT screening, the deaths are 42009 persons/year and RR is 0.64. Thus LDCT screening is more effective than CXR screening. We recommend that the lung cancer screening with CXR should to be replaced by that with LDCT.
Key words: Lung cancer, Screening, Chest X-ray, Low Dose CT, Mortality Reduction

1. Introduction

Since the NLST reported 20% mortality reduction of lung cancer by means of randomized controlled trial(RCT)1), we try to estimate similar mortality reduction for lung cancer screening in Japan using a prevalence model and observed data2). We use incidence number of lung cancer in Japan and stage distribution of detected lung cancer. Finally, the relative risk(RR) and number of lives saved from lung cancer are calculated for Japanese population.

2. Methods and materials

Lung cancer screening by chest X-ray and low dose CT is assumed to be performed annually for a long time and steady state is achieved so that effect of baseline screening is not present. Then, a mathematical model of calculating number of deaths due to lung cancer are presented: 1) unscreened population for whole Japanese, 2) unscreened population for Japanese of 50 to 79 years old, 3)screened population by chest X-ray for whole Japanese, 4)screened population by chest X-ray for Japanese of 50 to 79 years old, 5) screened population by low dose CT for whole Japanese, 6) screened population by low dose CT for Japanese of 50 to 79 years old. The unscreened and screened populations are assumed to be completely identical and number of lung cancer is constant for 3 years.

2.1.Number of lung cancer deaths for unscreened whole Japanese:(Uall)

Following equation represents number of deaths per year for whole Japanese.

Uall=Incidence of lung cancer of whole Japanese/year(Fraction of early lung cancer in unscreened population＊Death rate of early lung cancer＋Fraction of late lung cancer in unscreened population＊Death rate of late lung cancer).

Here, the early lung cancer means clinical stage 1 lung cancer and the late lung cancer means clinical stage 2-4 lung cancers. Fraction of early lung cancer + that of late lung cancer =1.0.

2.2. Number of lung cancer deaths for unscreened Japanese of 50 to 79 years old:(U50-79)

U50-79=Incidence of lung cancer for 50 to 79 y.o. Japanese/year＊(Fraction of early lung cancer in unscreened population＊Death rate of early lung cancer＋Fraction of late lung cancer in unscreened population＊Death rate of late lung cancer).

2.3. Number of lung cancer deaths for whole Japanese with chest X-ray(CXR) screening: (CXR all)

The CXR screening is performed for several years and is in the stable condition which means no effect from baseline screening present. The screened population is all Japanese aged from 50-79 years old. Following equation gives the number of deaths per year.

CXR all=Incidence of lung cancer for 50 to 79 y.o. Japanese/year＊(Fraction of early lung cancer in CXR screened population＊Death rate of early lung cancer＋Fraction of late lung cancer in CXR screened population＊Death rate of late lung cancer) +Incidence of lung cancer for Japanese other than 50-79 y.o.＊(Fraction of early lung cancer in unscreened population＊Death rate of early lung cancer＋Fraction of late lung cancer in unscreened population＊Death rate of late lung cancer).

2.4. Number of lung cancer deaths for Japanese of 50 to 79 years old with chest X-ray(CXR) screening:(CXR50-79)

Here, number of lung cancer deaths are calculated for the screened population only.

CXR50-79=Incidence of lung cancer for 50 to 79 y.o. Japanese/year＊(Fraction of early lung cancer in CXR screened population＊Death rate of early lung cancer＋Fraction of late lung cancer in CXR screened population＊Death rate of late lung cancer)

2.5. Number of lung cancer deaths for whole Japanese with low-dose CT(CT) screening:(CT all)

The CT screening is performed for several years and is in the stable condition which means no effect from baseline screening present. The screened population is all Japanese aged from 50-79 years old. Following equation gives the number of deaths per year.

CT all= Incidence of lung cancer for 50 to 79 y.o. Japanese/year＊(Fraction of early lung cancer in CT screened population＊Death rate of early lung cancer＋Fraction of late lung cancer in CT screened population＊Death rate of late lung cancer) +Incidence of lung cancer for Japanese other than 50-79 y.o.＊(Fraction of early lung cancer in unscreened population＊Death rate of early lung cancer＋Fraction of late lung cancer in unscreened population＊Death rate of late lung cancer).

2.6. Number of lung cancer deaths for Japanese of 50 to 79 years old with low-dose CT Screening:(CT50-79)

Here, number of lung cancer deaths are calculated for the screened population only.

CT50-79=Incidence of lung cancer for 50 to 79 y.o. Japanese/year＊(Fraction of early lung cancer in CT screened population＊Death rate of early lung cancer＋Fraction of late lung cancer in CT screened population＊Death rate of late lung cancer)

2.7. Relative risk(RR) and number of lives saved from lung cancer death(NLS)

As the final results, the relative risk and number of lives saved from lung cancer death are calculated by the following equations;

a)RR for whole Japanese with CXR vs Unscreened=CXR all/U all

b)RR for Japanese of 50-79 with CXR vs Unscreened=CXR50-79/U50-79

c)RR for whole Japanese with CT vs Unscreened=CT all/U all

d)RR for Japanese of 50-79 with CT vs Unscreened=CT50-79/U50-79

e)NLS for whole Japanese with CXR vs Unscreened=U all－CXR all

f)NLS for Japanese of 50-79 with CXR vs Unscreened= U50-79－CXR50-79

g)NLS for whole Japanese with CT vs Unscreened= U all－CT all

h)NLS for Japanese of 50-79 with CT vs Unscreened= U50-79－CT50-79

3.Numerical variables introduced in the equations

Various parameters are estimated in order to introduce in the above equations.

1)Incidence of lung cancer for whole Japanese(2005):3)

Male(M):58264 persons Female(F):25617 persons total(T):83881 persons

2)Incidence of lung cancer for Japanese of 50-79 y.o.(2005):

M:43144 persons F:16901 persons T:60045 persons

3)Incidence of lung cancer for Japanese of other than 50-79 y.o.(2005):

M:15120 persons F:8716 persons T:23836 persons

4)Death rate of early lung cancer: 30%

5)Death rate of late lung cancer: 90%

6)Fraction of early lung cancer in unscreened population: 20%

7)Fraction of late lung cancer in unscreened population: 80%

8)Interval of screening: 1 year , 2 years and 3 years

9)Fraction of early lung cancer in CXR screened population:

40%(1 year) 30%(2 years) 20%(3 years)

10)Fraction of late lung cancer in CXR screened population:

60%(1 year) 70%(2 years) 80%(3 years)

11)Fraction of early lung cancer in CT screened population:

85%(1 year) 80%(2 years) 75%(3 years)

12)Fraction of late lung cancer in CT screened population:

15%(1 year) 20%(2 years) 25%(3 years)

13)Number of lung cancer deaths for whole Japanese(2007)

M:47685 persons F:17923 persons T:65608 persons

Among these numerical values, 4) and 5) are the death rates of stage Ⅰ and stage Ⅱ to Ⅳ combined. Fraction of early lung cancer(stage Ⅰ) and that of late lung cancer (stage Ⅱ to Ⅳ combined) are varied with the interval of screening which are the most important values to be investigated.

4.Results

Using the above equations and numerical variables, the following results are obtained.

4.1. Number of lung cancer deaths for unscreened whole Japanese:(Uall)

83881*0.2*0.3+83881*0.8*0.90=5033+60394=65427 persons/year

4.2. Number of lung cancer deaths for unscreened Japanese of 50 to 79 years old:(U50-79)

60045*0.2*0.3+60045*0.8*0.9=3603+43232=46835 persons/year

4.3. Number of lung cancer deaths for whole Japanese with chest X-ray(CXR) screening: (CXR all)

4.3.1. Screening interval of 1 year

60045*0.40*0.3+60045*0.60*0.90+23836*0.2*0.3+23836*0.8*0.90=

7205+32424+1430+17162=58221 persons/year

RR:58221/65427=0.89 NLS：65427－58221=7206 persons/year

4.3.2. Screening interval of 2 years

60045*0.30*0.3+60045*0.70*0.90+23836*0.2*0.3+23836*0.8*0.90=

5404+37828+1430+17162=61824 persons/year

RR:61824/65427=0.94 NLS：65427－61824=3603 persons/year

4.3.3. Screening interval of 3 years

60045*0.20*0.3+60045*0.80*0.90+23836*0.2*0.3+23836*0.8*0.90=

3603+43232+1430+17162=65427 persons/year

RR:65427/65427=1.0 NLS：65427－65427=0 person/year

4.4. Number of lung cancer deaths for Japanese of 50 to 79 years old with chest X-ray(CXR) screening:(CXR50-79)

4.4.1. Screening interval of 1 year

60045*0.40*0.30+60045*0.60*0.9=7205+32424=39629 persons/year

RR：39629/46835=0.85 NLS：46835□39629=7206 persons/year

4.4.2. Screening interval of 2 years

60045*0.30*0.3+60045*0.70*0.90=5404+37828=43232 persons/year

RR:43232/46835=0.92 NLS：46835－43232=3603 persons/year

4.4.3. Screening interval of 3 years

60045*0.20*0.3+60045*0.80*0.90=3603+43232=46835 persons/year

RR:46835/46835=1.0 NLS：46835－46835=0 persons/year

4.5. Number of lung cancer deaths for whole Japanese with low-dose CT(CT) screening: (CT all)

4.5.1. Screening interval of 1 year

60045*0.85*0.3+60045*0.15 *0.90+23836*0.2*0.3+23836*0.8*0.90=

15311+8106+1430+17162=42009 persons/year

RR:42009/65427=0.64 NLS：65427－42009=23418 persons/year

4.5.2. Screening interval of 2 years

60045*0.80*0.3+60045*0.20*0.90+23836*0.2*0.3+23836*0.8*0.90=

14411+10808+1430+17162=43811 persons/year

RR:43811/65427=0.67 NLS：65427－43811=21616 persons/year

4.5.3. Screening interval of 3 years

60045*0.75*0.3+60045*0.25*0.90+23836*0.2*0.3+23836*0.8*0.90=

13510+13510+1430+17162=45612 persons/year

RR:45612/65427=0.70　NLS：65427−45612=19815 persons/year

4.6. Number of lung cancer deaths for Japanese of 50 to 79 years old with low-dose CT Screening:(CT50-79)

4.6.1. Screening interval of 1 year

60045*0.85*0.30+60045*0.15*0.9=15311+8106=23417 persons/year

RR：23417/46835=0.50　NLS：46835 - 23417=23418 persons/year

4.6.2. Screening interval of 2 years

60045*0.80*0.3+60045*0.20*0.90=14411+10808=25219 persons/year

RR:25219/46835=0.54　NLS：46835−25219=21616 persons/year

4.6.3. Screening interval of 3 years

60045*0.75*0.3+60045*0.25*0.90=13510+13510=27020 persons/year

RR:27020/46835=0.58　NLS：46835−27020=19815 persons/year

5. Discussions

Since NLST showed mortality reduction of lung cancer with LDCT by RCT, we try to estimate the similar mortality reduction of lung cancer in Japan with LDCT. Although we could not perform the RCT in Japan, there are many observational results of LDCT screening showing reduced lung cancer deaths. We proposed the prevalence model in which change in clinical stage distribution of lung cancer between unscreened and CT-screened population are used to calculate the difference of lung cancer deaths between the two populations. The early stage is assumed to be clinical stage 1 and the late stage is clinical stages of 2 to 4 combined.

First, the stage distribution for the unscreened is assumed to be 20% for early stage and 80% for late stage and fatality rates of early stage and late stage are assumed to be 30% and 90%. Using these values and incidence of lung cancer of 2005 in Japan, the calculated number of lung cancer deaths is 65427 persons which is almost equal to actual number of deaths of 65698 persons in 2007.

Then we assume that ratio between early stage and late stage(E/L ratio) changes with interval of screening. The E/L ratios are 85/15 for CT and 40/60 for CXR with 1 year interval, 80/20 for CT and 30/70 for CXR with 2 year interval and 75/25 for CT and 20/80 for CXR with 3 year interval. We assume that all Japanese of 50-79 years old will join the screening, and number of lung cancer deaths is calculated. For 1 year interval, number of lung cancer deaths are 58221 persons for CXR and 42009 persons for CT. For 2 year interval, number of lung cancer deaths are 61824 persons for CXR and 43811 persons for CT. For 3 year interval, number of lung cancer deaths are 65427 persons for CXR and 45612 persons for CT, while number of lung cancer deaths are 65427 persons for unscreened whole Japanese in 2005. Thus CT screening is clearly better than CXR screening.

Main problems of this study are 1) the appropriateness of prevalence model and 2) numeric variables used in the model. The model is the static model in which the screening is performed for long period and steady state is attained. Most critical variables are E/L ratio of detected lung cancer with changing screening intervals. We must wait more exact values from future studies. Another points are age and sex dependence of variables in the model which need further studies. Problem of overdiagnosis can be avoided by estimating proper E/L ratio.

This study employed lung cancer incidence of Japanese in 2005 and so number of lung cancer deaths will change with time. We continue to calculate the new values and estimate the cost/effectiveness ratio of CT screening in order to pave the road to organized screening.

6.Conclusions

We estimate the mortality reduction of lung cancer for Japanese by CT and CXR screening. We find that the CT screening is superior to the CXR screening which is same as the results of NLST. In the future, we try to estimate more accurate values of E/L ratios with screening intervals of CT screening. Finally CT screening for lung cancer may be established as an organized screening system in Japan and World.

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