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Estimation of the Prevalence of Latent Abnormalities in the Lung and the Accuracy of Indirect Chest X-ray Examination among Japanese Workers of Different Age Groups

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Abstract: It is considered that annual chest x-ray (CXR) examination can be restricted to workers by age; however, adequate epidemiological evidence is needed regarding the difference in the effectiveness of CXR examination between younger and older age groups. This study attempted to estimate the prevalence of latent abnormalities (*P*) in the lung and the false negative rate (*F*) and false positive rate (*G*) of examinations among workers of different age groups. 112,482 subjects who were screened for three consecutive years with no findings at the first screening, were selected. The proportion of positive findings at the second screening and the proportion of negative findings at the third screening were incorporated into a stochastic model, and 5-yr-age-specific *P*, *F*, and *G* were estimated. *P* tended to increase with increasing age. *F* was 40–45% in <45-yr-old subjects and was only 10% in the older age groups. *G* showed a steady increase with increasing age. This study indicates that the nature of findings differs between younger and older age groups, and this difference affects the accuracy of examination. In Japan, the age of workers should be considered when a CXR examination is performed.

Key words: Age groups, Epidemiology, Mass chest x-ray examination, Mass screening, Occupational health, Stochastic model

Introduction

In Japan, the Industrial Safety and Health Law (enacted in 1972) requires employers to provide annual medical screening examinations for their workers. Annual chest x-ray examination is a mandatory item according to the Ordinance on Industrial Safety and Health (enacted in 1972). The primary purpose of chest x-ray examination was to identify workers with latent tuberculosis, since this law aimed at securing the safety and health of workers. In Japan, the prevalence of tuberculosis has continued to decline since the 1950s[1]. Moreover, 80% of the newly diagnosed tuberculosis cases were reported in patients aged above 60 yr, most of whom were already retired from work[1]. Thus, the criteria and need for annual chest x-ray examination has changed among Japanese workers, and the Amended Tuberculosis Prevention Law stated that annual chest x-ray examination in workers should be restricted to those placed in a high-priority group, which was based on high-risk occupations or age groups with a higher risk.

In response to a nationwide debate regarding this issue, the role of annual chest x-ray examination in the

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Industrial Safety and Health Law was reconsidered in 2005 and an advisory report[2] to the Minister of Health, Labour and Welfare issued a statement that chest x-ray examination for workers under 40 yr of age could be omitted at the discretion of physicians. To examine the validity of this modification, we conducted an epidemiological survey of 2,611,675 chest x-ray examinations (indirect radiography) in workers between the ages of 20 and 64 yr old in 5 yr, from 2002 to 2006. The prevalence of positive findings, i.e., findings indicating a need for further diagnostic procedures, in the lung and pleural region was estimated to be significantly higher among workers over 40 yr of age as compared to those under 40 yr of age; it was 9.2 per 1,000 examinees for workers aged ≥ 40 yr versus 3.1 per 1,000 examinees for workers aged < 40 yr[3].

Generally, the purpose of a mass screening program is to identify persons with latent pathological changes requiring medical attention (hereafter "latent abnormalities"). A mass screening program usually consists of two sequential examinations—a screening test to identify a positive finding and a secondary test to make a final diagnosis for the positive finding[4]. The rationale is that those with positive findings include true positives as well as false positives, whereas those without positive findings include true negatives as well as false negatives. Thus, to estimate the prevalence of latent abnormalities —i.e., the sum of true positives and false negatives— reliable estimates of the false negative rate, i.e., the proportion of false negatives among the screenees with latent abnormalities, and the false positive rate, i.e., the proportion of false positives among the screenees without latent abnormalities, in the screening test should be taken into account. In this context, the observed difference in the prevalence of positive findings between two age groups[3] might merely reflect a difference in the false negative rate or false positive rate of abnormalities noted in chest x-ray examinations.

In the present study, we attempted to estimate the prevalence of latent abnormalities in the lung and pleural region among workers of different ages. A stochastic model was applied to longitudinal observation by annual chest x-ray examinations to simultaneously estimate the prevalence of latent abnormalities and the false negative and false positive rates of such abnormalities in chest x-ray examinations.

Subjects and Methods

The results of the annual chest x-ray examinations conducted between 2002 and 2006 were obtained for 68,4302 workers (418,188 men and 266,114 women) who were aged between 20 and 64 yr and were examined by 2 organizations belonging to the National Federation of Labor Standards Association. One organization is located in Tokyo and the other in Gifu; the procedures followed in both the organizations are accredited by the National Federation of Labor Standards Association. The study population did not represent all the workers of the nation, but in the light of the high participation rate of screening programs, it is not likely that the study population was a biased sample with regard to the prevalence of lung abnormalities. The information included in the dataset was as follows: date of birth, sex, date of examination, method of examination, site of findings, name of findings, and diagnostic classification of findings. No data regarding job categories or business establishment size were available. The analysis was restricted to the findings by indirect radiography. The dataset was anonymized; however, longitudinal observation was possible by the unique personal identification number assigned to each subject.

Since the diagnostic classification differed in the two organizations, the findings were reclassified into common criteria as follows: S0, no abnormal findings; S1, a trivial finding indicating no need for prospective annual follow-up; S2, a finding indicating a need for prospective annual follow-up; S3, a finding indicating a need for further diagnostic procedures; and S4, a finding indicating a need for continuing medical treatment. In this study, we mainly focused on the findings from the lung and pleural regions and excluded those from cardiac or musculoskeletal regions. Those classified to S4 were excluded from our study, and the prevalence of positive findings was estimated by the formula S3 / (S0 + S1 + S2 + S3).

To simultaneously estimate the prevalence of latent abnormalities (P) and the false negative rate (F) and false positive rate (G) for the findings of the chest x-ray examination, we selected the subjects who were screened for 3 consecutive years, i.e., 2002–2004, 2003–2005, and 2004–2006. These 3 parameters were estimated for the screening results of the second year. As the first step, those with any findings —i.e., S1, S2, S3, or S4— noted in the first year's screening were excluded to avoid the effect of past findings. Since positive findings included both true positives and false positives, the cumulative incidence rate of positive findings at the second year's screening could be formulated using the following equation.

$$P \times (1 - F) + (1 - P) \times G \text{ -----Equation 1}$$

Further, the results of the third year's screening were used to differentiate true positives and false positives from the results of the second year's screening. The rationale was that a true positive finding from the second year's results would not result in no abnormal findings (S0) or a trivial finding without the need for further follow-up (S1) at the third year's screening. True positive findings defined as above may possibly include findings that did not need therapeutic intervention. Nevertheless, we adopted this criterion because it reflects findings requiring continuous medical attention for at least one year. Taking into account the possibility of false negative findings at the third year's screening, the proportion of both S0 and S1 in the third year's results among those with S3 findings in the second year's results can be formulated using the following equation.

$$[P \times (1 - F) \times F + (1 - P) \times G \times (1 - G)] \, / \, [P \times (1 - F) + (1 - P) \times G] \text{ -----Equation 2}$$

Using Equations 1 and 2, the parameters P, F, and G were estimated by fitting these two equations to the observed dataset by dividing the subjects into 5-yr age groups. The data used for parameter estimation were not the number of diseases but the number of findings identified by the chest x-ray examination. Since only two equations were available for determining three unknown parameters, the data observed for adjacent two 5-yr age groups were used for parameter estimation. Denoting the parameters P, F, and G for age x as P_x, F_x, and G_x, the observed data for ages 20–24 and ages 25–29 were used to estimate P_{25}, F_{25}, and G_{25}; then, the observed data for ages 25–29 and ages 30–34 were used to estimate P_{30}, F_{30}, and G_{30}; and this was repeated. The MODEL procedure of SAS system® Windows version 9.1 (the SAS Institute, Cary, North Carolina, USA) was used for parameter estimation[5].

Results

The prevalence of positive findings in a single year in the 5-yr period between 2002 and 2006 is shown according to gender and 5-yr age groups along with the number of chest x-ray examinations in Table 1. The prevalence of positive findings increased with age in both men and women; a slightly higher prevalence was observed for men than women in the age group of 20–54 and 60–64 yr; however, in the age group of 55–59 yr, the prevalence was slightly higher among women than in men.

The dataset used for parameter estimation is shown in Table 2. A total of 112,482 subjects comprising 69,312 men and 43,170 women who underwent consecutive

Table 1. Number of chest X-ray examinations in a 5-yr period (2002–2006) that were included in the analysis with the prevalence in a single year's examination

Age group (yr)	Number of chest x-ray examinations in 5 yr: Men	Women	Prevalence* per 1000: Men	Women
20–24	33,186	54,539	5.2	4.2
25–29	61,940	46,083	6.0	5.3
30–34	71,472	35,076	7.9	7.8
35–39	59,403	25,436	9.0	8.9
40–44	48,015	23,091	10.9	9.7
45–49	39,932	22,292	13.3	13.2
50–54	43,871	25,344	19.1	18.6
55–59	39,075	22,303	24.2	24.9
60–64	21,294	11,950	32.7	31.7
All ages	418,188	266,114		

*Proportion of examinees with findings indicating a need for a further medical procedure.

Table 2. Data set used for analysis based on the stochastic model

	Men			Women		
Age group (yr)	Number of examinees followed up for 3 yr	Number of observed persons: Total*	S0/S1**	Number of examinees followed up for 3 yr	Number of observed persons: Total*	S0/S1**
20–24	7,722	51	46	11,971	55	53
25–29	11,375	118	107	6,396	40	35
30–34	11,537	100	90	4,733	31	27
35–39	9,492	120	105	3,620	41	39
40–44	7,517	119	108	3,668	35	32
45–49	6,411	100	90	3,751	52	41
50–54	7,663	168	126	4,629	83	64
55–59	4,991	113	85	3,126	71	54
60–64	2,604	75	56	1,276	39	30
All ages	69,312	964	813	43,170	448	375

*Number of persons whose second year examination showed S3 findings.
**Number of persons whose third year examination showed S0 or S1 findings.
Key:
S0: no abnormal findings, S1: finding indicating no need for annual follow up or medical procedure, and S3:finding indicating a need for a further medical procedure.

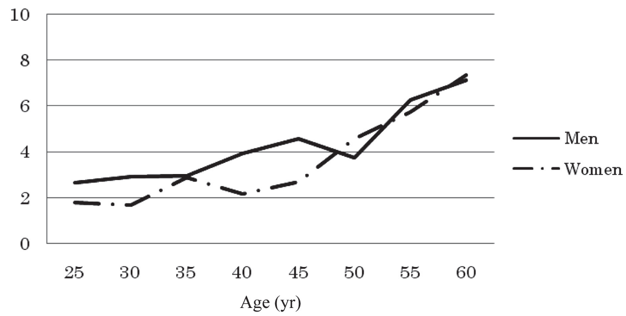

Fig. 1-i. The estimated prevalence of latent abnormalities (per 1,000)

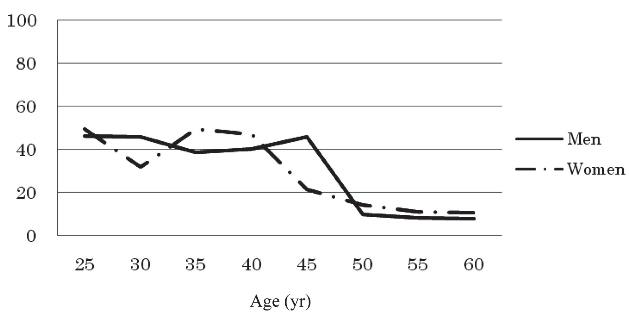

Fig. 1-ii. The false negative rate (%)

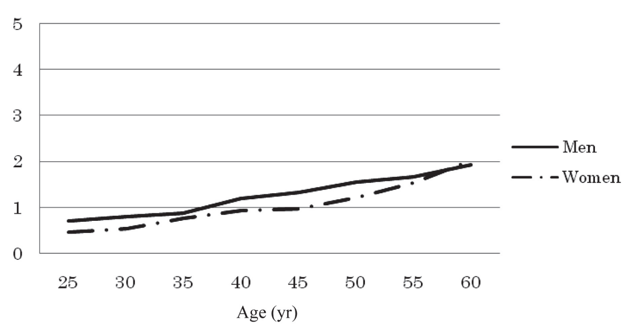

Fig. 1-iii. The false positive rate (%)

Fig. 1. Estimated values of prevalence of latent abnormalities, the false negative rate, and the false positive rate.

3-yr examinations with S0 findings at the first year's screening were included in the analysis. Among them, 964 men (1.4%) and 448 women (1.0%) were classified to S3 at the second year's screening; further, among these, 813 men (84.3%) and 375 women (83.7%) were classified to S0 or S1 at the third year's screening.

The estimates of the three parameters are shown according to gender and age in Fig. 1. The estimated prevalence (per 1,000) of latent abnormalities showed a tendency to increase with age in both women and men, i.e., from 2.64 to 7.13 in men and from 1.69 to 7.37 in women, respectively. The false negative rate showed a higher value in younger age groups (40–45% between ages 25 and 45 yr in men and 25–40% in women, respectively), and then showed a sharp downward change to ~10% in older age groups. The false positive rate showed a tendency to increase with age in both men and women, i.e., from 0.7 to 1.9% in men and from 0.5 to 2.0% in women, respectively.

The observed prevalence of positive findings at the second year's screening was compared with the expected prevalence calculated by Equation 1 with the estimated *P*, *F*, and *G* values. Further, the observed proportion of S0+S1 at the third year's screening among those with S3 findings at the second year's screening was compared with the expected value calculated by Equation 2 with the estimated *P*, *F*, and *G* values, as displayed in Fig. 2. The expected values showed good fits with the observed values in the whole range of age groups in both comparisons.

Discussion

The present study is, to our knowledge, the first study that successfully estimated the age-specific prevalence of latent abnormalities, together with age-specific false negative and false positive rates of findings of chest x-ray examination in Japanese workers. The prevalence of latent abnormalities in the lung and pleural region was found to be lower in all the age groups in both men and women as compared to the prevalence of positive findings as shown in Table 1. This difference possibly reflects the influence of false positives in the prevalence of positive findings. Moreover, noteworthy is the fact that the increase with age in the prevalence of latent abnormalities was lower than that in the prevalence of positive findings. Since the estimated false positive rate increased with age, as shown in Fig. 1, a part of the increase in the prevalence of positive findings can therefore be attributed to the increase in false positive results with increasing age. The estimated false negative rate showed a sharp decrease in older age groups; thus, a proportion of the increase in the prevalence of positive findings can also be attributed to the decrease in false negatives in the older age group.

The estimated false positive rate showed a steady tendency to increase with age. A false positive finding is, by our definition, a positive finding (S2, S3 or S4) that was classified as no finding (S0) or a trivial finding (S1) at the next year's screening. Therefore, the increase in the false positive rate with age might reflect an accumulation of shadows that attracted the attention of the reading radiologists but were found to be clinically nonsignificant. The estimated false negative rate, on the other hand, differed from the false positive rate —i.e., it remained within a range of 40 to 45% in the younger age groups (<40 yr) and then sharply decreased in the

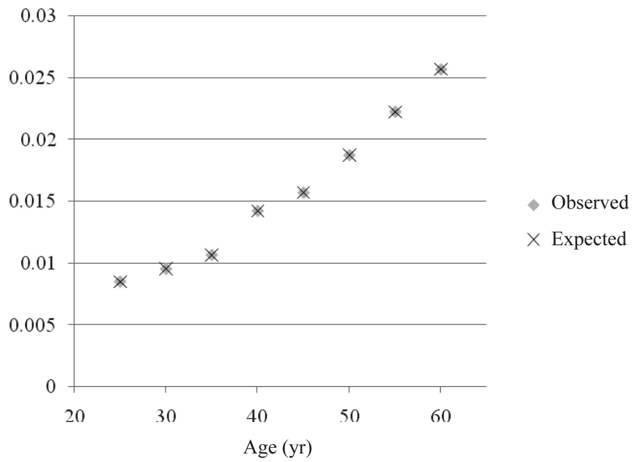

Fig. 2-i. The observed prevalence of positive findings at the second year's screening* among men.

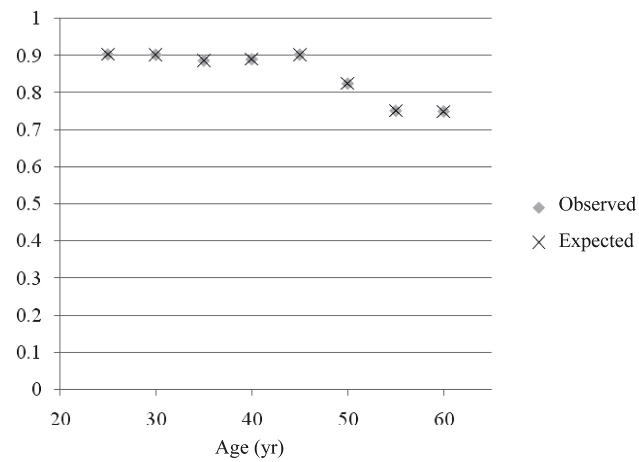

Fig. 2-iii. The observed proportions of S0+S1 at the third year's screening among those with S3 findings at the second year's screening** among men.

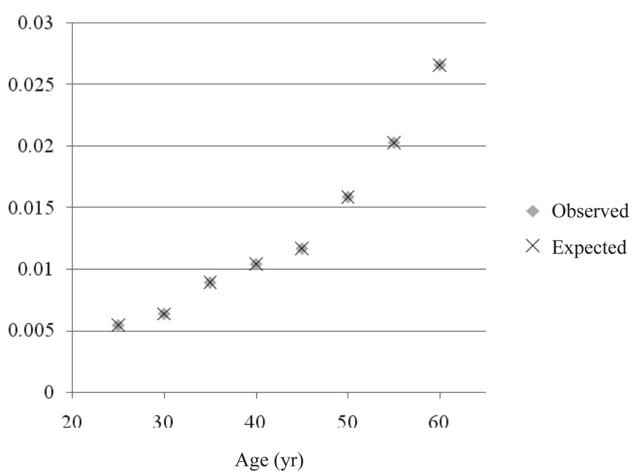

Fig. 2-ii. The observed prevalence of positive findings at the second year's screening* among women.

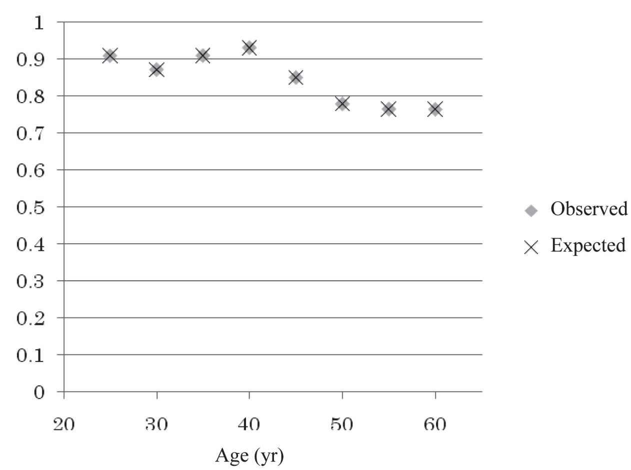

Fig. 2-iv. The observed proportions of S0+S1 at the third year's screening among those with S3 findings at the second year's screening** among women.

Fig. 2. The fit between the observed numbers and the expected numbers that were caluculated from the stochastic model.

*The prevalence is denoted as Equation 1 in the text.

**These proportions are denoted as Equation 2 in the text.

40–45 yr age group to the level of 10%. This might reflect a difference between the younger and older age groups in the nature of the latent abnormal changes; a latent abnormal change in a young individual might tend to be transient in nature, as exemplified by pneumonia and other acute inflammatory changes, whereas that in an older individual might tend to be persistent in nature, as exemplified by tuberculosis and lung cancer.

To accurately estimate the false negative rate and false positive rate of findings of chest x-ray examinations, a prospective follow up of all the screened subjects with and without positive findings is necessary. In this scenario, however, only a single or limited number of diseases are usually targeted for the purpose of screening, and only clinically identified cases are taken into consideration. According to the Patients' Survey of the Ministry of Health, Labour and Welfare, the prevalence (per 100,000 hospitalized patients) of lung tuberculosis, lung cancer, and other respiratory diseases was reported to be 4, 1, and 40, for individuals aged 20–39 yr and 16, 64, and 82, for individuals aged 40–64 yr, respectively[6]. Thus, the target of chest X-ray examination has shifted from lung tuberculosis to various lung abnormalities in recent decades. In this regard, chest X-ray examination should be evaluated for its ability to detect various lung abnormalities. As already mentioned, it would be best to conduct a prospective follow-up study to evaluate the effectiveness of chest X-ray examination as a screening method, but this would need to be a large-scale study because of the low prevalence of abnormalities. Our method might be less accurate with regard to such estimation, but its advantage is that we could obtain age-specific estimates for false negative and false positive rates. Another advantage is that our method could take into account latent abnormal changes that were not actually identified in the clinical setting, since a latent abnormality was defined as a pathological change that required medical attention, regardless of the actual diagnosis.

In conclusion, the prevalence of latent pathological changes in the lung and pleural region that require medical attention was found to increase with age. The false negative rate and false positive rate of findings in chest x-ray examinations were also found to change with age; the false negative rate was higher in younger age groups than in older age group, whereas the false positive rate increased steadily with age. These results indicate that the age of workers should be taken into account when performing chest x-ray examinations as a mass screening test among workers in Japan.

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