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Research article

Low-dose chest computed tomography screening of subjects exposed to asbestos

Katsuya Kato[a], Kenichi Gemba[b], Kazuto Ashizawa[c], Hiroaki Arakawa[d], Satoshi Honda[e], Naomi Noguchi[f], Sumihisa Honda[c], Nobukazu Fujimoto[g,*], Takumi Kishimoto[h]

[a] Department of Diagnostic Radiology 2, Kawasaki Medical School, General Medical Center, 2-1-80 Nakasange, Okayama, 7008505, Japan
[b] Department of Respiratory Medicine, Chugoku-chuo Hospital, 148-13 Oazakamiiwanari, Miyukicho, Fukuyama, 7200001, Japan
[c] Department of Clinical Oncology, Nagasaki University Graduate School of Medicine, 1-7-1 Sakamoto, Nagasaki, 8528102, Japan
[d] Department of Radiology, Dokkyo Medical University, 880, Kita-Kobayashi, Mibu, Tochigi, 3210293, Japan
[e] Department of Radiology, Okayama Rosai Hospital, 1-10-25 Chikkomidorimachi, Okayama, 7028055, Japan
[f] Department of Radiology, Tamano Mitsui Hospital, 3-2-1 Tama, Tamano, 7060012, Japan
[g] Department of Medical Oncology, Okayama Rosai Hospital, 1-10-25 Chikkomidorimachi, Okayama, 7028055, Japan
[h] Department of Internal Medicine, Okayama Rosai Hospital, 1-10-25 Chikkomidorimachi, Okayama, 7028055, Japan

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ABSTRACT

Objectives: The primary aim was to reveal the prevalence of lung cancer (LC) and malignant pleural mesothelioma (MPM) in subjects with past asbestos exposure (AE). We also examined pulmonary or pleural changes correlated with the development of LC.

Materials and methods: This was a prospective, multicenter, cross-sectional study. There were 2132 subjects enrolled between 2010 and 2012. They included 96.2% men and 3.8% women, with a mean age of 76.1 years; 78.8% former or current smokers; and 21.2% never smokers. We screened subjects using low-dose computed tomography (CT). The CT images were taken with a CT dose Index of 2.7 mGy. The evaluated CT findings included subpleural curvilinear shadow/subpleural dots, ground glass opacity or interlobular reticular opacity, traction bronchiectasia, honeycombing change, parenchymal band, emphysema changes, pleural effusion, diffuse pleural thickening, rounded atelectasis, pleural plaques (PQs), and tumor formation.

Results: The PQs were detected in most of subjects (89.4%) and emphysema changes were seen in 46.0%. Fibrotic changes were detected in 565 cases (26.5%). A pathological diagnosis of LC was confirmed in 45 cases (2.1%) and MPM was confirmed in 7 cases (0.3%). The prevalence of LC was 2.5% in patients with a smoking history, which was significantly higher than that in never smokers (0.7%, $p = 0.027$). The prevalence of LC was 2.8% in subjects with emphysema changes, which was higher than that of subjects without those findings (1.6%); although, the difference was not statistically significant ($p = 0.056$). The prevalence of LC in subjects with both fibrotic plus emphysema changes was 4.0%, which was significantly higher than that of subjects with neither of those findings (1.8%, $p = 0.011$). Logistic regression analysis revealed smoking history, fibrotic plus emphysema changes, and pleural effusion as significant explanatory variables.

Conclusions: Smoking history, fibrotic plus emphysema changes, and pleural effusion were correlated with the prevalence of LC.

1. Introduction

Asbestos was commonly used during the 20th century and remains prevalent in many developing countries [1]. Asbestos causes pathological changes in the lung or the pleura including asbestosis, pleural plaques (PQs), benign asbestos pleural effusion [2], diffuse pleural thickening, and malignant neoplasms such as malignant pleural mesothelioma (MPM) and lung cancer (LC) [3,4]. According to the World Health Organization, > 107,000 people die each year from asbestos-related diseases due to occupational exposure [1]. These diseases usually develop after long latency periods of 40–50 years [5]. Thus, there will be more LC or MPM developing in the next few decades,

Abbreviations: AE, asbestos exposure; CT, computed tomography; LC, lung cancer; LDCT, low-dose computed tomography; MPM, malignant pleural mesothelioma; PQs, pleural plaques; SCLS/DOTS, subpleural curvilinear shadow/subpleural dots

* Corresponding author.
E-mail address: nobufujimot@gmail.com (N. Fujimoto).

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despite that asbestos use was banned in Japan in 2004. Subjects with histories of asbestos exposure (AE) in Japan are examined by annual chest X-ray; however, it is established that chest X-ray is not an efficient method forLC screening [6,7]. Thus, there is a need to establish a more useful screening strategy for subjects.

Mass screening of high-risk groups to detect LC could potentially be beneficial. Multidetector computed tomography (CT) has made high-resolution volumetric imaging possible during a single breath hold with acceptable levels of radiation exposure [8]. There were several reports that low-dose helical CT of the lung detected more nodules and LCs, including early-stage, than chest X-ray [9]. Recently, the National Lung Screening Trial, which recruited subjects at high-risk for LC, demonstrated that low-dose CT (LDCT) screening could decrease the death rate due to LC by about 20% compared with screening using chest X-ray [7]. In addition, there are some recent reports that LDCT screening is useful to detect LC at the earlier stages [10–12].

In the current study, we performed LDCT screening for subjects with histories of AE. The primary aim of the study was to reveal the prevalence of LC and MPM in the subjects. In addition, we focused on other pulmonary or pleural changes, such as fibrotic or emphysema changes and plaques, to determine what findings correlated with the prevalence of LC.

2. Materials and methods

2.1. Study approval

This study was conducted in compliance with the principles of the Declaration of Helsinki. This study was carried out according to The Ethical Guidelines for Epidemiological Research by the Japanese Ministry of Education, Culture, Sports, Science, and Technology, and the Ministry of Health, Labour, and Welfare. This study was approved by the Japan Health, Labour, and Welfare Organization and the institutional review boards of each institution. Patient confidentiality was strictly maintained and written informed consent was obtained from the subjects.

2.2. Subjects

This was a prospective, multicenter, cross-sectional study to reveal the prevalence of LC and MPM, and the prevalence of CT findings due to AE. The inclusion criteria of the subjects are 1) those who had engaged in asbestos-product manufacturing for more than 1 year, 2) those who had engaged in other industries related to AE for more than 10 years, or 3) those who had engaged in industries related to AE and demonstrated pleural plaques on chest X-ray or CT (regardless of the duration of AE). There were 2132 subjects enrolled in this study between 2010 and 2012. They included 2050 (96.2%) men and 82 (3.8%) women, with a mean (range) age of 76.1 (51–101) years. There were 502 subjects from Okayama Rosai Hospital, 392 from Chiba Rosai Hospital, 370 from Tamano Mitsui Hospital, 313 from Kinki Chuo Chest Medical Center, 214 from Kagawa Rosai Hospital, 196 from Toyama Rosai Hospital, 96 from Yamaguchi-Ube Medical Center, and 49 from Hokkaido Chuo Rosai Hospital. The occupational categories associated with AE are shown in Fig. 1. The main categories included 612 subjects (28.7%) in shipbuilding, 260 (12.2%) in chemical manufacturing, 259 (12.2%) in asbestos-product manufacturing, and 245 (11.5%) in construction. The smoking history was obtained from 2095 subjects and revealed 1651 (78.8%) former or current smokers and 444 (21.2%) never smokers.

2.3. CT acquisition and analysis

The CT images were taken in each institution with a median (range) CT dose Index of 2.7 (2.4–2.8) mGy. 2 mm thick images were obtained and stored in Digital Imaging and Communications in the Medicine format. The evaluated CT findings included pulmonary fibrotic changes, such as subpleural curvilinear shadow/subpleural dots (SCLS/DOTS), ground glass opacity or interlobular reticular opacity, traction bronchiectasia, honeycombing change, and parenchymal band (Fig. 2). Other evaluated findings were emphysema change, pleural effusion, diffuse pleural thickening, rounded atelectasis, PQs with or without calcification, and tumor formation. The CT images were taken with the subject in a prone position to differentiate slight pulmonary changes on the dorsal portion of the lungs from gravitational effects. Images were analyzed independently on the monitor, based on a quality standard, agreed on by two reference radiologists who were blinded to the clinical and demographic information of the subject and the results of one another's assessments. If there was a difference between the interpretations of the two radiologists, more rigorous interpretation was adopted with regard to emphysema changes, pleural effusion, diffuse pleural thickening, PQs, and tumor formation. For fibrotic changes, a third radiologist made the second-round interpretation and gave the final decision. When LC or MPM was suspected in subjects, further examinations such as bronchoscopy, needle biopsy, thoracentesis, and/or surgery were performed in the clinical practice.

This was a cross sectional study with only one CT performed in each subject. No follow up was performed for patients with a negative CT.

2.4. Statistical analysis

Comparisons between independent groups were performed using the chi-square test and the Mann-Whitney *U* test was used for non-parametric analysis. The average values were compared using the *t*-test. Overall survival of LC patients was obtained by using Kaplan-Meier methods. Logistic regression analysis was conducted as a multivariate analysis. Statistical calculations were performed using SPSS statistical package version 22.0 (IBM, Armonk, USA).

3. Results

3.1. CT findings

The CT findings of the 2132 subjects are summarized in Table 1. The PQs were detected in the majority of subjects (89.4%) and emphysema changes in about half of the subjects (46.0%). Fibrotic changes (at least one of: SCLS/DOTS, ground glass opacity or interlobular reticular opacity, traction bronchiectasia, honeycombing change, and parenchymal band) were detected in 565 cases (26.5%). There were 116 cases (5.4%) with suspected LC, including 101 with possible LC and 15 with definite LC.

The pathological diagnosis of LC was confirmed in 45 cases (2.1%), 44 men and 1 woman. Median (range) age at the diagnosis was 73 (60–87) years old. There were 31(68.9%) adenocarcinoma, 10(22.2%) squamous cell carcinoma, 3(6.7%) small cell carcinoma, and 1(2.2%) adenosquamous carcinoma. According to the International Association for the Study of Lung Cancer staging (7th Edition), there were 13 Stage IA, 14 Stage IB, 4 Stage IIA, 3 Stage IIB, 4 Stage IIIA, 2 Stage IIIB, and 1 Stage IV patients. Median overall survival (95% confidence interval) of these 13 patients was 26.8 (4.01–71.93) months.

Pleural effusion was detected in 45 subjects. Among them, LC was diagnosed in six cases including four adenocarcinomas and two squamous cell carcinomas. Pleural carcinomatosis was revealed in 2 of the 4 cases of adenocarcinoma. Another two subjects with adenocarcinoma and one of the 2 subjects with squamous cell carcinoma underwent thoracic surgery, suggesting they had post-operative pleural effusion. There were 16 subjects (0.8%) with suspected MPM and the pathological diagnosis was confirmed in seven cases (0.3%) including 4 cases of epithelioid, 2 cases of biphasic, and 1 case of sarcomatous subtype.

3.2. CT characteristics of LC cases

We examined the specific characteristics of patients in whom LC