Repeat lung cancer screenings reveal less CXR abnormalities with different variations than first-time screening

Tatsuo Kimura*, Shinya Fukumoto1, Akemi Nakano1, Hideki Fujii1, Yuji Nadatani1, Yukie Tauchi1, Shingo Takashima1, Yuko Nishii1, Koji, Otani2, Naomi Ageshio3, Tomohiro Suzumura2 and Norifumi Kawada1,5

1Department of Premier Preventive Medicine, Graduate School of Medicine, Osaka City University, Osaka, Japan
2Department of Gastroenterology, Graduate School of Medicine, Osaka City University, Osaka, Japan
3Department of Diagnostic and Interventional Radiology, Graduate School of Medicine, Osaka City University, Osaka, Japan
4Department of Clinical Oncology, Graduate School of Medicine, Osaka City University, Osaka, Japan
5Department of Hepatology, Graduate School of Medicine, Osaka City University, Osaka, Japan

Abstract

Objectives: Chest radiography (CXR) is the most common screening procedure for the detection of lung cancer. A comparative CXR review can help to detect new shadows. Participants (pts) who undergo repeated screening at the same facility as the health check-up can receive a comparative review of the CXR. It has been hypothesized that the diagnosis of CXR abnormalities in screening would be different when compared to previous CXR and when not.

Methods: We retrospectively analyzed one-year cohort derived from the ongoing MedCity21 health check-up registry. The pts with abnormalities requiring medication in CXR were invited to our clinic for chest computed tomography (CT). We compared the varieties of abnormalities on CXR between repeated and first-visit pts using chi-square tests.

Results: A total of 13,690 repeated / first visits of 7872 / 5818 (57.5 / 42.5%) pts were enrolled. The CXR abnormalities included 324 of 143 / 191 pts and 234 of 108 / 126 pts who underwent chest CT, respectively. Repeated pts had a significantly lower proportion of abnormalities in CXR that required medication than the first-visit pts (p < 0.01). CT confirmation revealed that CXR abnormalities in repeated pts were diagnosed with different variations compared to those of first-visit pts. Repeated pts had a significantly lower proportion of old inflammatory changes (p=0.02) and a higher proportion of acute inflammatory shadow (p=0.02) than first-visit pts.

Conclusions: Immediate confirmation by CT revealed that CXR abnormalities in repeated pts were diagnosed with different variations compared to those of first-time pts. A comparative review of previous CXR may be highly effective in ruling out lung cancer.

Abbreviations: CXR: Chest X-ray; pts: participants, CT: computed tomography; LDCT: low dose CT; GGO: Ground glass opacity; MLP: Mayo Lung Project

Introduction

Lung cancer is the third most common form of cancer and the leading cause of cancer-related deaths in both men and women in Japan. Smoking, exposure to secondhand smoke, a family history of lung cancer, procedures leading to exposure to radiation such as imaging tests, environmental exposure to air pollution, and workplace exposure to asbestos and arsenic can all increase the risk of lung cancer [1]. Although avoiding risk factors may lower patient risk, it does not mean that all lung cancers can be prevented. As people age, they spend more time exposed to environmental factors, and their chances of developing cancer increase accordingly. Therefore, routine health check-ups are important. Early diagnosis improves cancer outcomes by providing care at the earliest possible stage.

The American Cancer Society recommends yearly lung cancer screening with a low-dose CT (LDCT) for certain people at higher risk of lung cancer who meet the following conditions: aged 55 to 74 years and in good health, currently smoking or having quit smoking in the past 15 years and have at least a 30 pack-year smoking history [2]. However, people who are not at higher risk of lung cancer, lung cancer must be screened using chest X-ray (CXR) in residential or workplace health examinations. When previous CXR had old inflammatory shadows such as tuberculosis, calcification, and fibrotic change, it would become increasingly difficult to detect newly occurring lung cancer.

A comparative review of the CXR with the previous one helps in the detection of a new shadow. Pts who undergo repeat health check-ups at the same facility can receive a comparative review of the CXR. It has been hypothesized that the diagnosis of CXR abnormalities in screening would be different when compared to previous CXR and when not. To clarify this, we conducted a retrospective cohort study in a large Japanese population to clarify the merits of comparative review in CXR, as well as a variety of chest abnormalities in CXR screening.

*Correspondence to: Tatsuo Kimura, M.D. Ph.D., Department of Premier Preventive Medicine, Graduate School of Medicine, Osaka City University, 1-1-43 AbenoHARUKAS 21F, Abenosuji, Abeno-ku Osaka 545-6090, Japan, Tel: 81-6-6624-4041; Fax: 81-6-6624-8212; E-mail: kimutats@med.osaka-cu.ac.jp

Key words: health check-up, lung cancer screening, CXR abnormalities, repeater

Received: April 17, 2021; Accepted: April 26, 2021; Published: April 29, 2021
Participants and methods

Study population

We analyzed one-year cohort derived from the ongoing MedCity21 health examination registry from January 1 to December 31, 2019. Participants aged 20 years or older who were receiving a course including CXR were enrolled. Our clinic, “MedCity21,” is a university outpatient clinic which performs complete health check-up. Pts with abnormalities that require medical care detected on CXR were immediately announced by call for recommendation for further examination and encouraged to visit our facility to undergo further examination by chest CT scan. The pts who previously visited MedCity21 to undergo a health check-up with CXR were called “repeat pts,” and pts who visited MedCity21 for the first time were called “first-visit pts.” This study was conducted in accordance with the tenets of the Declaration of Helsinki. The registry protocol of the MedCity21 health examination and this retrospective observational study protocol was approved by the Ethics Committee of Osaka City University Graduate School of Medicine (approval No. 2927 and No. 2020-087, respectively). We performed an opt-out option, as explained in the instructions posted on the website of our facility.

Clinical assessment

CXR was performed using a direct radiography system (Radnext 50; Hitachi Healthcare Systems Inc., Tokyo, Japan) in the posterior-anterior (120 kV, 200 mA) and lateral positions (120 kV, 320 mA). Two doctors, board-certified in internal medicine specialty, respiratory medicine, and oncology, reviewed the CXR results using 3M monochrome monitor (RadiForce GX340, EIZO Corporation, Ishikawa, Japan). For baseline screening, the results of the initial CXR were categorized into five categories according to the criteria of the Japan Society of Ningen Dock [3]: A: Normal. B: Slightly abnormal. Nothing to worry about at present, or merely a deviation from normal that is not detrimental to your health. C: Require follow-up. There is a slight problem, but it is not serious now, and if you make the necessary changes, it is easily treated. D: Medical care needed. and E: On treatment. The abnormal shadows of category D in lung fields were classified into eight items, and those outside the lung field were classified into two categories. The items included nodular shadow 5 mm in diameter, ground glass opacity (GGO), granular shadow, reticular or interstitial shadow, cystic shadow, linear shadow including atelectasis, infiltration shadow, and pleural sign (pleural thickening, effusion, and pneumothorax), mediastinum abnormality, and cardiovascular system.

CT images were reviewed by two doctors certified as radiologists or oncologists. A CT device (Supria, Hitachi Healthcare Systems Inc., Tokyo, Japan) was used at 120 kV, 30-250 mA of normal dose, scan time 0.75 s/rot, 1.25 times 16 collimation, table pitch of 1.3125, slice/interval 5 / 5 mm, and the same monitor as described above. The abnormalities in CXR were diagnosed by CT and classified into 10 items and others: old inflammatory change, nodules including GGO, granular shadow, acute inflammatory change, interstitial lung disease, pleural disease, nipples, bone shadow including bone island in the rib and spine of vertebrae, cardiovascular system, and soft tissue (fat, muscle, etc.). If an abnormality was noted on CXR but not on CT, it was classified as “no abnormality”.

Patients with small nodules should undergo tailored follow-up according to guidelines [4]. Briefly, in the CT scans, if all solid or partly solid noncalcified pulmonary nodules or GGOs were less than 10.0 mm in diameter, a follow-up CT examination was performed 3 months later. On CT, none of the nodules grew over 10.0 mm in diameter, and CT was repeated 6 months later. In principle, a patient with a nodule 10 mm in diameter or larger, or a pleural sign, was referred to a specialized outpatient at Osaka City University Hospital or another equivalent hospital for further examinations. In the case of other diseases, we referred pts to the appropriate hospitals. In each case, doctors conferred with patients to decide on a course of action. Follow-up data were retrieved from the MedCity21 health examination registry and referral letters from other hospitals at approximately 1 year of complete follow-up.

Statistical analysis

The baseline characteristics of the repeated and first-visit patients were compared using a chi-square test. We also compared the varieties of shadows on CT scans between repeat and first-visit pts using chi-square tests. Statistical significance was set at p <0.05. Statistical analyses were conducted using GraphPad PRISM for Windows version 5.0.1 software (GraphPad Software, San Diego, CA, USA).

Results

Participant characteristics

A total of 13,690 pts was enrolled, including 6,622 men (48.4%) and 7,068 women (51.6%) (Table 1). Pts ages ranged from 20 to 90 years, with a median age of 51 years, and the 25-75 percentile was 43-60 years. Four lung cancer cases were found. One was male and three were female. One of them was a smoker. The detection rate was 29.2 / 100,000. All cases were resected and revealed stage I adenocarcinoma. There were 7481 (57.1%) non-smokers, 3821 (27.9%) ex-smokers, 1281 (13.3%) smoked pts less than 20 cigarettes per day, and 232 (1.7%) smoked pts more than 21 cigarettes per day (15.0%). Smoking was significantly less common among women than among men (p<0.01).

The numbers of repeated and first-visit pts were 7,872 (57.5%) and 5,818 (42.5%), respectively (Figure 1). Category D in CXR included a total of 334 (2.4%) of 143 repeated pts and 191 first-visit pts. Repeated pts had a low proportion of abnormalities requiring further examination (p<0.01). After the announcement by call for recommendation for further examination, a total of 234 pts (70.1%) of 108 / 126 patients received chest CT scans in our facility.

Abnormalities detected by chest X ray

Figure 2a shows the classification of CXR abnormalities by repeated and first-visit pts. A total of 234 of 108 repeated and 126 first-visit pts who underwent chest CT scans in our clinic were analyzed for abnormalities. Nodular shadows were the most frequently noted shadows on CXR in both repeated (70.4%) and first-visit (71.4%) pts. The second most frequently noted shadow was a GGO in both repeated (12.0%) and first-visit (8.7%) pts. The following were granular

| Table 1. Participant’s characteristics | All | Male | Female | p |
|---|---|---|---|---|
| N | 13690 | 6622 | 7068 |  |
| Age | median (range) | 51 (20-90) | 52 | 50 | N.S. |
| <65 | 6297 | 3054 | 3243 | 0.01* |
| >65 | 7713 | 4568 | 3145 |  |
| Tobacco use | Never smoked | 7816 | 3788 | 4028 | <0.01* |
| Past smoker | 3821 | 1883 | 1938 | 1093 |
| Current smoker | 1-20/day | 1821 | 1337 | 484(1) |
| 21/day | 232 | 216 | 16 |  |

*Smoking was significantly less common among women than among men (p<0.01)
Repeat lung cancer screenings reveal less CXR abnormalities with different variations than first-time screening

Kimura T (2021) Repeat lung cancer screenings reveal less CXR abnormalities with different variations than first-time screening

Volume 5: 3-5
Health Prim Car, 2021 doi: 10.15761/HPC.1000210

2.8 / 6.3%, reticular 0.0 / 4.0%, cystic 0.0 / 2.4%, linear 1.9 / 0.8%, infiltration 11.1 / 0.8%, pleural 0.9 / 2.4%, mediastinum 0.9 / 1.6%, and cardiovascular 0.0 / 1.6%, respectively. There was no significant difference in the distributions between the repeated and first-visit pts.

Diagnoses by chest CT

CT revealed CXR abnormalities (Figure 2b). CT scan revealed that the most frequently noted shadow was a bone shadow in both sets of pts. The second most frequently noted shadow was a granular shadow in repeated pts and old inflammatory changes in first-visit pts. The third most frequently noted shadow was acute inflammatory change in repeated pts and nodules, including GGO in first-visit pts. Repeated pts had a significantly lower proportion of old inflammatory changes (p = 0.02), and a higher proportion of acute inflammatory shadow than first-visit pts (p = 0.02). The percentages of diagnosis of repeated/first-visit pts on chest CT were as follows: old inflammatory 11.2 /
22.2%, nodules including GGO 8.3 / 11.1%, granular 15.7 / 7.9%, acute inflammatory 14.8 / 4.8%, interstitial lung disease 0.0 / 3.2%, pleural 8.3 / 7.9%, nipple 6.5 / 1.6%, bone 19.4 / 23.0%, cardiovascular 2.8 / 7.9%, soft tissue 4.6 / 1.6%, others 2.8 / 4.0%, and no abnormality 3.7 / 6.3%, respectively.

Discussion
Repeate pts had a significantly lower proportion of abnormalities requiring further examination in CXR than the first-visit pts. Immediate confirmation by CT revealed that CXR abnormalities in repeated pts were diagnosed with different variations compared to those of first-visit pts. On CXR as category D, the repeated pts had a significantly lower proportion of old inflammatory changes and a higher proportion of acute inflammatory shadows than first-visit pts. This means that the repeated pts may benefit from a decrease in false-positives and an increase in true-positives.

For a comparative review of the previous CXR, annual visits to health check-ups are recommended. A visit interval may be estimated by the speed of tumor growth based on tumor doubling time. In a review of the natural history of lung cancer over time, the mean tumor volume doubling time is approximately 135 days for patients diagnosed during routine medical care, 150 days in screening studies involving CXR, and 480 days in screening studies involving CT [5]. Most reports show doubling times in the range of 100 to 300 days for lung cancer [6,7]. In fact, in our study, all lung cancer cases were resected and revealed differences in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR. A granular shadow due to old tuberculosis may not change over many years. Indeed, the prostate, lung, colorectal, and ovarian cancer screening trial revealed the most common difference in body position for CXR.

In conclusion, immediate confirmation by CT revealed a difference in the proportion of CXR abnormalities between repeated and first-visit patients. We believe that regular physical examinations performed at the same facility are highly effective in ruling out lung cancer. A comparative review of previous CXR may be highly effective in avoiding unnecessary further examination. This will help improve lung cancer screening.

Author Contributions
Conceptualization: Tatsuo Kimura,

Data curation: Tatsuo Kimura, Shinya Fukumoto, Akemi Nakano, Hideki Fujii, Yuji Nadatani, Yukie Tauchi, Shingo Takashima, Yuko Nishii, Koji Otani, Naomi Aegeshio

Supervision: Shinya Fukumoto, Yuji Nadatani, Norifumi Kawada,

Formal analysis: Naomi Aegeshio, Tomohiro Suzumura,

Methodology: Tatsuo Kimura

Writing original draft: Tatsuo Kimura

Writing-review and editing: Tatsuo Kimura, Shinya Fukumoto, Akemi Nakano, Hideki Fujii, Yuji Nadatani, Yukie Tauchi, Shingo Takashima, Yuko Nishii, Koji Otani, Tomohiro Suzumura

Project administration: Tatsuo Kimura

Acknowledgements
The authors thank Mrs. Utsunomiya, Mr. Kusumi, and Mr. Miyao for help in data collection and Mrs. Sakama for secretary work.

Financial support statement
This work was supported by a Grant-in-Aid for Scientific Research (C) from JSPS KAKENHI 19K10579.

Conflict of interest statement
The authors declare that they have no financial conflicts of interest.

References
1. https://www.cancer.gov/types/lung/patient/lung-prevention-pdq
2. Wender R, Fontham ET, Barrera E, Colditz GA, Church TR, et al. (2013) American Cancer Society lung cancer screening guidelines. CA Cancer J Clin 63: 107-117. [Crossref]
3. https://www.ningen-dock.jp/en/other/inspection
4. Wood DE, Kazerooni EA, Baum SL, Eapen GA, Ettinger DS, et al. (2018) Lung Cancer Screening, Version 3.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 16: 412-441. [Crossref]
5. Deterbeck FC, Gibson CJ (2008) Turning gray: the natural history of lung cancer over time. J Thorac Oncol 3: 781-792. [Crossref]
6. Usuda K, Saito Y, Sagawa M, Sato M, Kanma K, et al. (1994) Tumor doubling time and prognostic assessment of patients with primary lung cancer. Cancer 74: 2239-2244. [Crossref]
Kimura T (2021) Repeat lung cancer screenings reveal less CXR abnormalities with different variations than first-time screening

7. Yankelevitz DF, Kostis WJ, Henschke CI, Heelan RT, Libby DM, et al. (2003) Overdiagnosis in chest radiographic screening for lung carcinoma: frequency. Cancer 97: 1271-1275. [Crossref]

8. Hammer MM, Palazzo LL, Kong CY, Hunsaker AR (2019) Cancer Risk in Subsolid Nodules in the National Lung Screening Trial. Radiology 293: 441-448. [Crossref]

9. Marcus PM, Bergstralh EJ, Fagerstrom RM, Williams DE, Fontana R, et al. (2000) Lung cancer mortality in the Mayo Lung Project: Impact of extended follow-up. J Natl Cancer I 92: 1308-1316. [Crossref]

10. Pinsky PF, Freedman M, Kvale P, Oken M, Caporaso N, et al. (2006) Abnormalities on chest radiograph reported in subjects in a cancer screening trial. Chest 130: 688-693. [Crossref]

11. https://ganjoho.jp/reg_stat/statistics/dl/index.html#mortality

12. Kimura T, Fukumoto S, Nakano A, Fujii H, Nadatani Y, et al. (2020) Repeat lung cancer screenings by chest X ray have a profit for the avoidance of further examinations (abstract number: OOP-5-1). In: The 27th International Health Evaluation and Promotion Association and The 4th World Congress on Ningen Dock, Yokohama, Japan.

Copyright: ©2021 Kimura T. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.