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Research Article

Actual Situation on Low-dose Computed Tomography Screening for Thoracic Diseases at Health Checkup

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Abstract

Background: The usefulness of low-dose computed tomography (LDCT) for early detection of lung cancer has been widely reported. In addition to the early detection of lung cancer, many improved cases and false-positive scans by LDCT screening have also been reported. Therefore, the actual situation of LDCT screening for lung cancer and other thoracic diseases remains unclear. The aim of this study was to investigate the detailed clinical course of cases detected by LDCT and evaluate the usefulness of LDCT for lung cancer and other thoracic diseases during health checkups.

Materials and Methods: Among 6,402 (4,444 men and 1,958 women) individuals who had received LDCT at health checkups over a recent 12-year period, we investigated the number of cases who have abnormal opacity on LDCT and warrant detailed examination. We also investigated the final outcomes of these patients after a detailed examination.

Results: Totally, 206 cases were detected for detailed examination by LDCT and 50 out of 206 cases (24%) were finally taken medical treatment. Among them, the most commonly encountered lesion was pulmonary infection, and 22 patients were treated with antibiotics. Eleven patients with lung cancer and 4 patients with mediastinal tumors were also detected, which could lead to early surgical treatment. Early signs of chronic obstructive pulmonary disease (COPD) was also found and among them, smoking cessation could be performed in 10 patients. Other pulmonary diseases were occasionally detected using LDCT, including 1 case of lymphangioleiomyomatosis (LAM), 1 case of idiopathic pulmonary fibrosis (IPF), and 1 case of pulmonary sequestration. In contrast, 156 other cases (76%) were determined to continue follow-up or improve spontaneously at the time of the outpatient clinic.

Conclusions: LDCT found various thoracic diseases including lung cancer, mediastinal tumors and COPD which could lead to early treatment. However, we also found that more than three-quarters of untreated cases were present after a detailed examination.

Keywords: Lung Cancer; Mediastinal Tumor; Chronic Obstructive Pulmonary Disease; Pulmonary Infection; Low-Dose; Computed Tomography

Introduction

Chest radiography (CR) is a commonly used modality [1] for annual health checkups in Japan. It is widely available, involves less radiation exposure, and is less expensive than computed tomography (CT). However, CR has a low sensitivity [2] and is usually considered an ineffective modality for the detection of lung nodules less than 10 mm [3]. Hence, lung cancers detected using this method are often at an advanced stage at the time of diagnosis [4]. In contrast, low-dose computed tomography (LDCT) enables the detection of small lesions located in the lung and mediastinum. Several studies have shown that LDCT contributes to the early detection of lung cancer and improves outcomes when compared to CR [5-8]. LDCT has recently become available in many healthcare facilities, and some people who undergo medical health checkups undergo LDCT examinations. In our facility, approximately 500 individuals undergo LDCT examination as well as CR in every year of health checkups, and we sometimes experience various thoracic diseases by using LDCT alone, which was overlooked by CR. However, we also experienced many improved cases at outpatient clinics and false-positive scans on LDCT. Therefore, the actual status of LDCT screening in the clinical setting remains unclear. Therefore, this study aimed to investigate the final clinical course of these cases detected for detailed examination by LDCT and to evaluate the actual utility of LDCT screening at health checkups.

Materials and Methods

Subjects

Approximately one million individuals who underwent health checkups in our facilities during the last 12 years (Healthcare Center, 7th floor Shinjuku Oiwake Clinic and 6th floor Shinjuku Oiwake Clinic Ladies Branch, Seikokai, Shinjuku-ku, Tokyo) from April 1, 2012, to March 31, 2024, individuals who underwent LDCT as an option were eligible. A total of 6,402 people consisting of 4,444 men (aged 14 — 75 years, mean ± standard deviation [SD] = 48.2 ± 10.3 years) and 1,958 women (aged 24—75 years, mean ± SD = 49.0 ± 10.1 years) were evaluated. Among the 6,402 individuals, 6,396 individuals also underwent CR examination.

Measurement of LDCT examination

CT examinations were performed using a 4-row helical CT scanner (ROBSTO; Hitachi, Tokyo, Japan) from April 2012 to April 2018 and a 64-row helical CT scanner (SUPRIA GRANDE; Hitachi) from May 2018 to March 2024 under the same conditions of 50 mA at 120 kV and without contrast medium, and 5 mm-axial images were acquired.

Interpretation and Evaluation of LDCT image

Interpretation of LDCT was performed independently with double or triple-checking where appropriate by at least one pulmonologist, radiologist, or internal medicine specialist. If there were discrepancies between the interpretations, the final decision was made by a pulmonologist or a radiologist. In these studies, we investigated the number of cases of abnormal opacity that warrant detailed examination on LDCT and investigated the final outcome of these cases, whether they received treatment.

Ethical approval

The present study was conducted in accordance with the Declaration of Helsinki, and the Seikokai Group Ethics Committee approved the study protocol. Informed consent was obtained during the health checkups at our facilities and from the case reporting the LDCT.

Results

Characteristics of cases detected for detailed examination by LDCT

Among 6,402 individuals, 206 (3.2%) on LDCT examination had abnormal lesions and were determined to need detailed examination. The detection rate of LDCT was almost equivalent to that previously reported in Japan [9]. Seventy-one of 206 cases were also detected for detailed examination by CR, and 135 remaining cases were detected only by LDCT. The detection rate of CR (1.1%; 71/6,396) was also equivalent to that previously reported in Japan [9]. Details of the 206 cases detected by LDCT are presented in Table 1. Pulmonary infiltrative changes, such as segmental ground-glass opacity (GGO) or airspace consolidation, were most frequently observed, and 80 cases (41 men and 39 women) were detected. Pulmonary nodule or mass, low attenuation area (LAA), mediastinal nodule or mass, and local solitary GGO were often recognized in 37 (26 men and 11 women), 35 (29 men and 6 women), 22 (14 men and 8 women), and 21 (15 men and 6 women) cases, respectively. Three cases of vascular abnormality and reticular change and 2 cases of tracheal polypoid lesions were also detected. The remaining cases included 1 case of pulmonary cavity, 1 case of pleural thickening, and 1 case of arteriosclerosis.

Abnormal findings	n	M / W
Pulmonary infiltrative change	80	41 / 39
Pulmonary nodule or mass	37	26 / 11
LAA	35	29 / 6
Mediastinal nodule or mass	22	14 / 8
Solitary GGO lesion	21	15 / 6
Vascular abnormality	3	3 / 0
Reticular change	3	2 / 1
Tracheal polypoid lesion	2	2 / 0
Pulmonary cavity	1	1 / 0
Pleural thickening	1	0 / 1
Arteriosclerosis	1	1 / 0
	206	134 / 72

Table 1: Characteristics of 206 cases detected for detailed examination by LDCT.

M, men; W, women; LAA, Low attenuation area; GGO, ground-glass opacity.

After detailed examination in collaborating hospitals or our clinic, 50 of 206 cases (24%) were finally treated medically treatment. The final diagnose of the 50 patients are presented in Table 2. The most commonly treated thoracic disease after further examination was pulmonary infection (22 patients). Next, 11 patients with lung cancer and 10 with initial signs of COPD were treated. In addition, four patients with mediastinal tumors, one with lymphangioleiomyomatosis (LAM), one with idiopathic pulmonary fibrosis (IPF), and one with pulmonary sequestration were also found and received medical treatment.

Clinical diagnosis	n	M / W
Pulmonary infection (n = 22)		
CAP	17	9 / 8
Tuberculosis, NTM	4	2 / 2
Pneumomycosis	1	1 / 0
Lung cancer	11	9 / 2
Incipient sign of COPD	10	9 / 1
Mediastinal tumors	4	3 / 1
LAM	1	0 / 1
IPF	1	0 / 1
Pulmonary sequestration	1	1 / 0
	50	34 / 16

Table 2: Characteristics of 50 patients who were taken medical treatment detected by LDCT.

M, men; W, women; CAP, community-acquired pneumonia;

NTM, non-tuberculous mycobacterium; COPD, chronic obstructive pulmonary disease;

LAM, lymphangioleiomyomatosis; IPF, idiopathic pulmonary fibrosis.

On the other hand, 156 out of 206 (76%) were either follow-up, positive scans, spontaneous improvement, and no treatment was administered.

Actual detection of pulmonary infections by LDCT

The most commonly encountered were pulmonary infiltrative lesions, and 80 cases were detected by LDCT. Among them, 22 patients were finally treated with antibiotics, consisting of 17 with community-acquired pneumonia (CAP), 4 with mycobacterial infections, 2 with tuberculosis and 2 with non-tuberculous mycobacterium (NTM) infections, and one with pneumomycosis. An LDCT image of a pulmonary infection is shown as an example in Figure 1. LDCT revealed a small nodular lesion with a cavity in the right lower lung field. After detailed examination, the patient was diagnosed with Cryptococcus disease. Including this patient, the early detection of various pulmonary infections using LDCT could lead to early antibiotic, antitubercular and antifungal treatment.

Figure 1: LDCT image of 38 years old man taken at health checkup. LDCT revealed a small nodular lesion with a cavity in the right lower lung field (white arrow). The patient was diagnosed with Cryptococcus disease. An antifungal agent was administered after diagnosis.

In contrast, many cases (n=58) of infiltrative change had already improved spontaneously or had no evidence of exacerbation at a time of diagnosis, and no treatment was needed. We demonstrate one of these cases as an example (Figure 2A and 2B).

Figure 2: A: LDCT image of 28 years old man taken at health checkup. LDCT showing inflammatory change in the left lower lung field (white arrow). B: LDCT in this case 1 year after the first examination. The lesion improved spontaneously without any medication (white arrow).

Actual detection of lung cancer by LDCT

In total, 37 cases of pulmonary nodules or masses, and 21 solitary GGO-like lesions suspicious for lung cancer were detected for detailed examination by LDCT. Among these, 11 patients with lung cancer were identified. An example of a patient with lung cancer is shown in Figure 3A and 3B. The LDCT image of this patient (Figure 3A) shows a small solitary nodular lesion in the left upper lung field. However, the CR image of the patient obtained on the same day showed an abnormal shadow (Figure 3B). The patient was finally diagnosed with stage IA lung cancer. Including this patient, 10 patients were diagnosed at an early stage and could be successfully treated with thoracoscopic surgery. One remaining patient was diagnosed with small cell lung cancer that had already progressed to an advanced stage. In this study, we also found that 9 out of 11 lung cancer patients were over the aged ≥ 50 years men who have smoking habit.

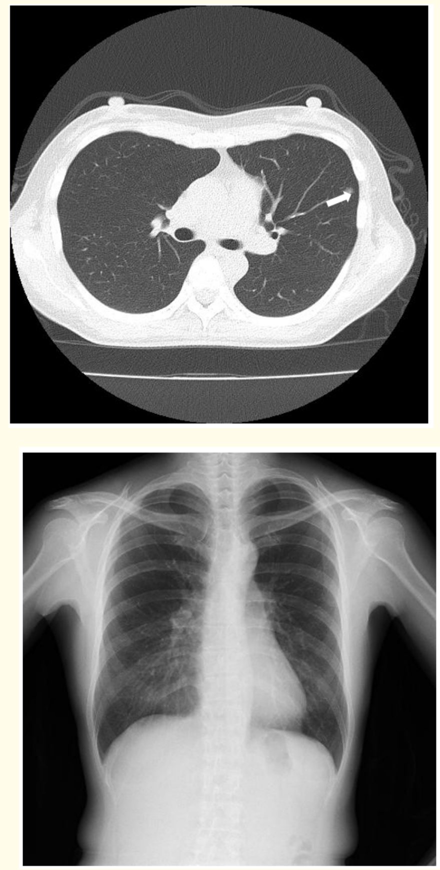

Figure 3: A: LDCT image of 50 years old woman taken at health checkup. LDCT shows a local solitary nodular lesion in the left upper lung field (white arrow). This patient was diagnosed with stage IA lung cancer. Tumor was successfully resected within the early stage. B: A CR image of the patient taken on the same day reveals no abnormal opacity.

On the other hand, many other cases of nodular or local solitary GGO lesion (47 cases) detected by LDCT continued to be followed-up periodically owing to possible malignancy, and these cases have to be followed-up for a long period. Most of these lesions showed no growth (Figure 4A and 4B) or improvement during the follow-up period.

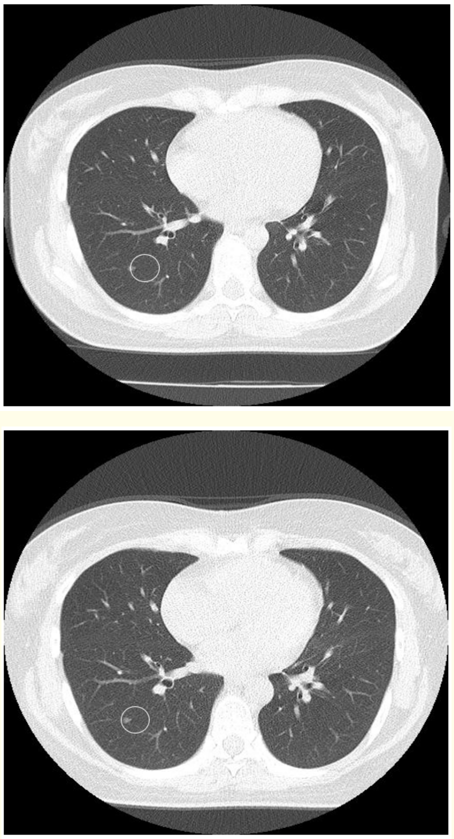

Figure 4: A: LDCT image of 40 years old woman taken at health checkup. LDCT showing a small nodule located in the right lower lung field (circled). B: LDCT image obtained in this case 1 year after the first examination. The nodular lesion showed no growth (circled) compared with that at the first examination.

Actual detection of initial COPD sign by LDCT

We detected 35 cases of LAA, which is an incipient sign of COPD [10], for detailed examination using LDCT. Most of these changes were spread under 25% of lung field (Goddard classification; Score 1) [11], and the level of forced expiratory volume in one second to forced expiratory vital capacity (FEV_1/FVC) using a spirometer did not decrease below 70% except one patient with COPD. An LDCT image of a case is shown as an example in Figure 5. We led to early implementation of smoking cessation in 10 patients. However, 25 other patients did not undergo any detailed examinations or smoking cessation.

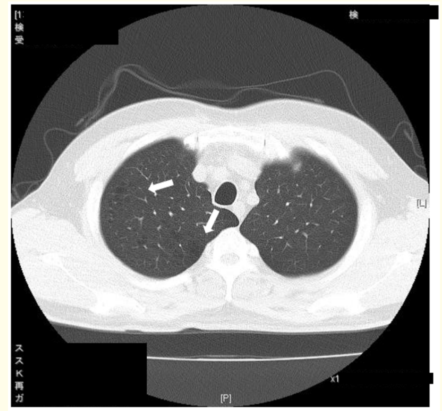

Figure 5: LDCT image of 47 years old man taken at health checkup. LDCT shows some LAA in the right upper lung fields (white arrows).

Actual detection of mediastinal tumors by LDCT

We detected 22 cases of mediastinal masses or nodules using LDCT, and 4 patients were finally diagnosed with mediastinal tumors: 1 thymoma, 1 teratoma, 1 bronchogenic cyst, and 1 liposarcoma. A patient with teratoma is shown in Figure 6A and 6B. The LDCT image of this patient showed a heterogeneous tumor mass in anterior mediastinum (Figure 6A), whereas the CR image showed no abnormal opacity (Figure 6B). Finally, all mediastinal tumors were successfully resected. In contrast, 18 other cases of mediastinal nodular lesions need to be followed-up periodically. After several years of observation, no enlargement has been observed to date.

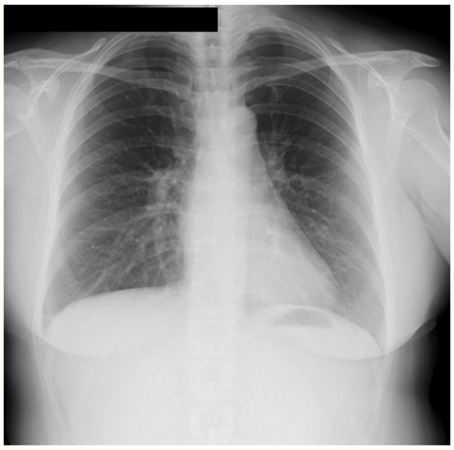

Figure 6: A: LDCT image of 40 years old woman taken at health checkup. LDCT shows a mass lesion with calcification on anterior mediastinum (white arrow). This patient was diagnosed with mediastinal teratoma. Tumor was successfully resected. B: The CR image of the patient obtained on the same day revealed no abnormal opacity.

Actual detection of other thoracic diseases by LDCT

We found some other thoracic diseases using LDCT during this period. For example, one IPF case (Figure 7) and one LAM case were detected by LDCT, which could lead to early diagnosis and subsequent treatment. In addition, we also detected a few cases of vascular changes, such as arterial dilatation and arteriosclerosis, and tracheal polypoid lesions and pleural thickening determined for further examination by LDCT. Among them, one patient had pulmonary sequestration (Figure 8) which led to surgical treatment.

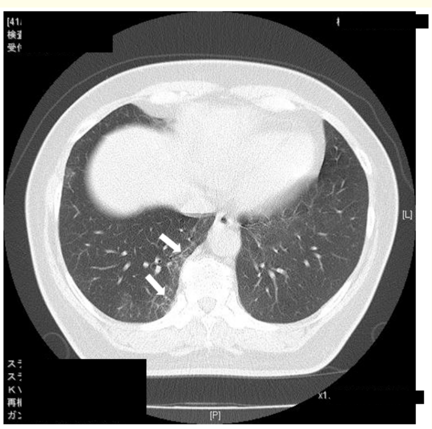

Figure 7: LDCT image of 58 years old woman taken at health checkup. LDCT shows reticular changes located on the subpleural area of right lower lung field (white arrows). This patient was finally diagnosed with IPF.

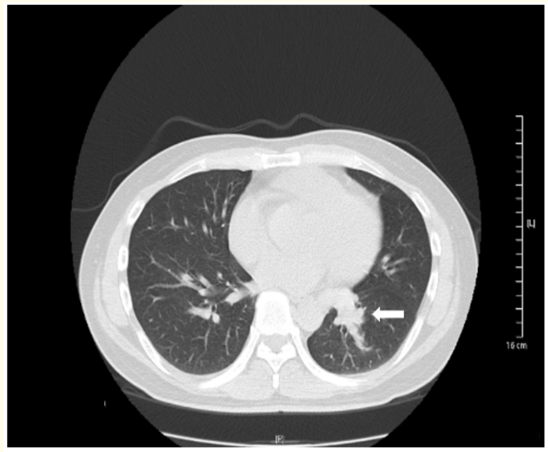

Figure 8: LDCT image of 46 years old man taken at health checkup. LDCT reveals a vascular abnormality which branched from descending aorta directly (white arrow). This patient was diagnosed with intralobar pulmonary sequestration.

Discussion

Japan has its own medical checkup system, and most people in the working-age generation undergo CR examinations annually, whereas only a portion of people also undergo CT. Among 6,402 people who underwent LDCT during a health checkup in the past 12 years which record remained, we found 15 cases of thoracic tumors, including 11 lung cancers, using LDCT. These findings (15/6,402; 0.23%) were much higher than those of CR screening (5/6,396; 0.08%). Lung cancer is now the leading cause of cancer-related deaths worldwide because of its heterogeneity, aggressive nature, and poor prognosis [12-14], despite its lower incidence than that of other major cancers, such as gastric, colorectal, and prostate cancer in men and breast cancer in women [15]. Therefore, we consider that early stage detection of lung cancer is very important for prompt surgical resection and may contribute to reducing cancer-related deaths [5-7]. The utility of LDCT in detecting lung cancer has long been debated. In Japan, a combination of CR and sputum cytology is routinely recommended for initial assessment in lung cancer screening in patients over the age of 40 years [16]. CR has been used as a common imaging modality, and a recently developed automated analysis of CR can help with interpretation during health checkups. It can assist pulmonologists and radiologists in interpreting and triaging, thereby easing their workload [17-19]. However, a recent randomized controlled trial on lung cancer screening by CR did not show a reduction in mortality compared to usual care [20]. In contrast, several studies have shown that screening using LDCT contributes to the early detection of lung cancer and improves outcomes compared to screening using CR [5-7]. Recently, a large randomized study by the National Lung Screening Trial reported in 2011 that adherence to a protocol of annual LDCT lung cancer screening and follow-up also showed reduced lung cancer mortality by 20% compared with that following CR screening in smokers [21]. However, a recent population-based study identified a key problem in implementing LDCT screening in every day practice as used in trial settings [22]. The prevalence of CT screening among eligible people in the United States has remained virtually stagnant over the past few years: 3.3% in 2010 and 3.9% in 2015, and the majority of cigarette smokers continue to undergo screening with CR rather than LDCT [22,23]. The acceptance rate of LDCT for lung cancer screening is much lower than that of other disease screening tests; for example, in many countries, the majority of eligible women undergo screening mammography [24]. The primary reason for the low prevalence of CT may be its high cost. LDCT examinations cost approximately US$ 100 per test and are much more expensive than CR examinations. This cost versus benefit is an important aspect to consider when implementing it as a population-based screening tool [25]. Regarding this matter, our previous report and current study showed [8] that the detection rate of lung cancer (0.19%) by LDCT was also high as other major cancers, and when we focused it on individuals aged ≥ 50 years men smokers, the detection rate (0.32%) was higher rather than other major cancers such as gastric (0.13%), colorectal (0.27%), and breast cancers (0.29%) [9]. Our current data (0.23%) also supports the previous data and we found lung cancer constantly by LDCT alone in this period especially among the people who are aged ≥ 50 years men smokers. Therefore, in our facility, we have enlightened the use of LDCT examination for individuals who undergo medical health checkups among male smokers aged ≥ 50 years.

In this study, we encountered 4 cases of mediastinal tumors detected by LDCT, which could lead to early surgical treatment. Mediastinal tumors have a lower frequency than lung cancer but also a heterogeneous nature and various tumor features [26-28]. Although approximately 80% of tumors are benign histological types [29,30], even the benign tumors have been indicated for aggressive surgical intervention because they are anatomically important parts of the human body [31]. However, early detection of mediastinal tumors by CR is difficult because of the location of their occurrence [8]. In fact, four mediastinal tumors detected by LDCT were overlooked in CR at our health checkups. Fortunately, we found one liposarcoma using only LDCT (data not shown), which is known to be a rare tumor with poor prognosis [32-34]. Currently, there is no evidence regarding adjuvant therapy for this tumor [35,36], and surgical resection at an early phase is the only way to expect a complete cure for this disease.

In addition to the early detection of thoracic tumors by LDCT, many pulmonary and mediastinal mass lesions suspicious for malignancy have not been diagnosed. This false-positive finding is often recognized in benign lesions such as consolidation of old inflammation, and clinicians often encounter cases during LDCT examination [37,38]. Cases have to be followed up periodically, and patients are often distressed during the follow-up period. We consider that this is not a matter that can be ignored, especially in LDCT examinations.

In this study, the most commonly detected abnormal lesion on LDCT was a pulmonary infection, and 22 cases were finally treated with antibiotics. Lung cancer and COPD are usually found in older individuals [39], whereas pulmonary infection often occurs during the working-age generation; therefore, we encountered it frequently during health checkups rather than lung cancer and COPD. Among these, the most frequently identified cause of pulmonary infection is CAP caused by *Streptococcus pneumoniae*, *Staphylococcus aureus*, or *Mycoplasma* [40], which usually improves spontaneously. In our study, 58 other cases of infiltrative lesions detected by LDCT also improved spontaneously or showed no exacerbation at the time of diagnosis, and any treatment was needed. Even the infiltrative shadow detected by CR sometimes improves spontaneously; therefore, the tiny infiltrative change detected by LDCT often improves spontaneously [41]. However, we found some important infections that require specific treatment with antibiotics, such as tuberculosis, NTM infections, and Cryptococcus disease, using LDCT and could lead to specific antibiotic treatment. In addition, an important factor for clinicians is that the recently prevalent SARS-CoV-2 often causes pneumonia [42-44]. Although these cases have now reduced [45-47] after the omicron variant outbreak, if the shadow is suspicious for COVID-19, it could still worsen, and even if it did not worsen, we could alert the patient to avoid spreading the infection [48].

In this study, we also detected many cases of LAA using LDCT within the early phase, some of which could be successfully treated with smoking cessation. Although various etiologies of COPD have been reported [49,50], the established risk factors for the pathogenesis of COPD are cigarette smoking [51-54] and severe α_1-antitrypsin deficiency [55]. Of these two, α_1-antitrypsin deficiency is mainly related to Caucasians, and cigarette smoking is the most important risk factor for other ethnic groups. For the most part, this disease is characterized by irreversible airflow limitation, and also have systemic affection such as skeletal muscle dysfunction, nutritional disorders, and osteoporosis. For this reason, early initiation of smoking cessation is important to prevent the exacerbation of COPD [56,57].

Essentially, the diagnosis of COPD is based on the presence of clinical symptoms and the ratio of post-bronchodilator forced expiratory volume in one second to forced expiratory vital capacity (FEV_1/FVC) using a spirometer being less than 70%. CT and CR imaging did not provide a definitive diagnosis of COPD. In fact, there is a relatively poor correlation between autopsy-proven emphysema, pulmonary function test abnormalities, and CT with some pathology-proven cases not being evident on CT, and some patients with abnormal CT have no pulmonary dysfunction [58,59]. However, CR and CT imaging play subsidiary roles in the detection of COPD. CR shows some distinctive features of COPD, such as radiolucency of the lung field, depression and flattening of the diaphragm, a tear-drop heart, and the absence of vasculature [60]. However, these findings are recognized mainly in moderate and severe phases of the disease. Individuals who show these CR findings usually have clinical symptoms and visit a hospital for further examination. Therefore, we consider that there are high expectations regarding early detection and implementation of smoking cessation treatments for the incipient signs of COPD resulting from LDCT [8].

Besides being a successful treatment, we also experienced many patients with LAA who continued smoking despite our repeated guidance and education. Unfortunately, such cases are often encountered in the clinical setting. A major problem is that COPD and its clinical importance have not been well recognized in Japan compared to lung cancer, which has led to a delay in implementing smoking cessation measures. COPD has become a major cause of morbidity and mortality worldwide; it also has a high incidence [61,62] and an estimated prevalence of 5.3 million in Japan [63]. Therefore, we are going to continue to advocate the clinical importance of quitting smoking habits during health checkups.

Additionally, a case of IPF, pulmonary sequestration, and LAM were detected by LDCT in this study. These diseases have a relatively lower incidence than other diseases, as mentioned above. Among these, we detected some other cases of IPF during this period, but these were also detected by CR. We also detected 1 case of pulmonary sequestration using LDCT. CR is nearly always obtained in the management of suspected CVD and provides an important means to appreciate morphological changes in the heart, such as cardiomegaly [64]. LDCT can also detect abnormal vascular runs and arteriovenous malformations with higher accuracy, and LDCT is considered a more effective tool for detecting aortic sclerosis and dissection with higher accuracy than CR [65,66].

Radiation exposure should be considered when evaluating CT examinations. The average dose for conventional standard chest CT is approximately 7 – 8 mSv, resulting in high exposure to radiation [67]. The average dose for LDCT imaging is approximately 1.5 mSv, which is half the natural ambient exposure dose of approximately 3 mSv per year [68]. In addition, the average dose of radiation exposure with LDCT is less than that for the upper gastrointestinal series (UGI) [69], which is performed annually during health checkups in Japan. Even if LDCT examination is repeated every 3 months, the radiation exposure per year is less than that with standard CT. Therefore, we believe that LDCT examination may not result in an undue increase in radiation exposure.

Finally, while it may be argued that the utility of LDCT for thoracic diseases in health checkups is not sufficient for a veridical method in Japan, we submit that our current data are sufficiently compelling to elicit further examination by investigators with access to similar studies. As such, the present data may shed light on the path by which further insight into these intriguing studies might be gained.

As a limitation of this study, we could not obtain some cases of final outcomes; therefore, we could not evaluate it sufficiently in several cases despite close collaboration with other hospitals.

Conclusions

We investigated the clinical course of the cases detected by LDCT examination during health checkup. Among 6,402 individuals who underwent LDCT screening, 206 cases (3.2%) were detected to have abnormal findings. This detection was much higher than that of CR screening (1.1%). Among them, 50 out of 206 cases (24%) were finally taken medical treatment. However, 156 remaining cases (76%) were followed up periodically or showed improvement in the outpatient clinic. We conclude that LDCT screening is an effective method for detecting various thoracic diseases at an early stage. However, we also found that more than three-quarters of the cases were not treated with LDCT screening after detailed examination.

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Author Contribution

- Methodology: This study was designed and conducted by Ikuma Kasuga.
- Investigation: Main research was performed by Ikuma Kasuga.
- Original draft writing and data curation was performed by Ikuma Kasuga.
- This study was supervised by Osamu Ohtsubo.
- This Study was resourced by Osamu Ohtsubo.
- All authors scrutinized and confirmed the final version of this manuscript.

Conflict of Interest

The authors declare that they have no conflicts of interest regarding this manuscript.

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