

# Incidence of Lung Cancer in COPD Patients in Western Yokohama Managed by Primary Care Physicians with Hospital Collaboration

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**Purpose:** Chronic obstructive pulmonary disease (COPD) is a common condition with respiratory obstructive impairment, and is often treated by primary care physicians. Because COPD is a high-risk factor for lung cancer, chest computed tomography (CT) is used to screen for early cancer detection. However, it is difficult for primary care physicians to conduct regular CT examinations. In the western Yokohama area, we have established a system of collaboration between primary care physicians and our hospital to manage COPD patients. We hypothesized that routine standard-dose CT examinations could detect lung cancer at early stage in COPD patients managed by primary care physicians via COPD coordinated system.

**Patients and Methods:** From 114 COPD patients who visited Yokohama Seibu Hospital between January 2013 and March 2020 for the purpose of COPD consultation, we selected the 70 in whom either abnormal shadows had been detected or negative imaging findings confirmed on chest CT over a 5-year period.

**Results:** Nodules were detected in 15 patients (21.4%) during the course of the study, with six of these founded to have lung cancer. Five of the six had were operable as early-stage cancer, and one had advanced small cell lung cancer and received chemotherapy. Detection of operable cases was difficult with chest X-rays.

**Conclusion:** Routine chest CT may contribute to the early-stage detection of cancer in patients with COPD managed by primary care physicians in collaboration with hospitals.

**Keywords:** chronic obstructive pulmonary disease, computed tomography, lung cancer, primary care

## Introduction

Chronic obstructive pulmonary disease (COPD) is a common pulmonary disease. Clinically, COPD causes irreversible obstructive respiratory failure in spirometry, resulting in symptoms such as dyspnea, sputum, and chronic cough.<sup>1,2</sup> In Global Initiative for COPD (GOLD) 2024 report,<sup>1</sup> COPD is classified by cause; genetical determined (COPD-G), due to abnormal lung development (COPD-D), cigarette smoking (COPD-C), biomass and pollution expose (COPD-P), due to infection (COPD-I) COPD and childhood asthma (COPD-A). In Japan, most COPD patients were COPD-C.<sup>2</sup> The prevalence is high, and many COPD patients are managed by primary care physicians. A particular problem for primary care physicians managing COPD patients is comorbidity such as cardiovascular disease or lung cancer.<sup>1-4</sup>

One of important complications of COPD-C is lung cancer. COPD patients have a threefold higher risk of developing the disease than those without COPD.<sup>5,6</sup> Early detection and treatment of lung cancer is essential to improving the prognosis of COPD patients. In Japan, two cohort studies have shown that the incidence of lung cancer in COPD patients



is about 1.85% or 2.3%/year.<sup>7,8</sup> In addition, COPD patients with lung cancer are at high risk for severe emphysematous changes, interstitial pulmonary fibrosis, and smoking, so special attention should be paid to COPD patients with these risk factors.<sup>7,8</sup>

As of 2025, chest X-ray was main method lung cancer screening in Japan, but there were limitations to early cancer detection. The screening using chest computed tomography (CT) was useful because of high sensitivity. Van Ierselet al showed that the standard-dose CT were more effective in detecting lung cancer in patients with a history of heavy smoking.<sup>9</sup> Moreover, low-dose CT, which reduces radiation exposure for use in screening, is attracting attention.<sup>10,11</sup> The national lung screening trial (NLST) showed that low-dose chest CT had significantly greater detection power and resulted in lower mortality rates, indicating that CT is useful for lung cancer screening.<sup>11</sup> These results suggested that chest CT was effective for early detection of lung cancer, but there are some problems. First, false-positive results were presented.<sup>9,11</sup> Second, considering cost and radiation exposure, it should be limited to subjects at higher risk of developing lung cancer.<sup>9,10</sup> Third, it was difficult to detect at early stage in small cell lung cancer.<sup>11</sup> Therefore, COPD-C patients should undergo routine screening with chest CT, but even if a chest CT detects a new abnormal shadow, the diagnosis of lung cancer should be made with caution. As of 2025 in Japan, only applicants were able to undergo lung cancer screening using low-dose CT.<sup>12</sup>

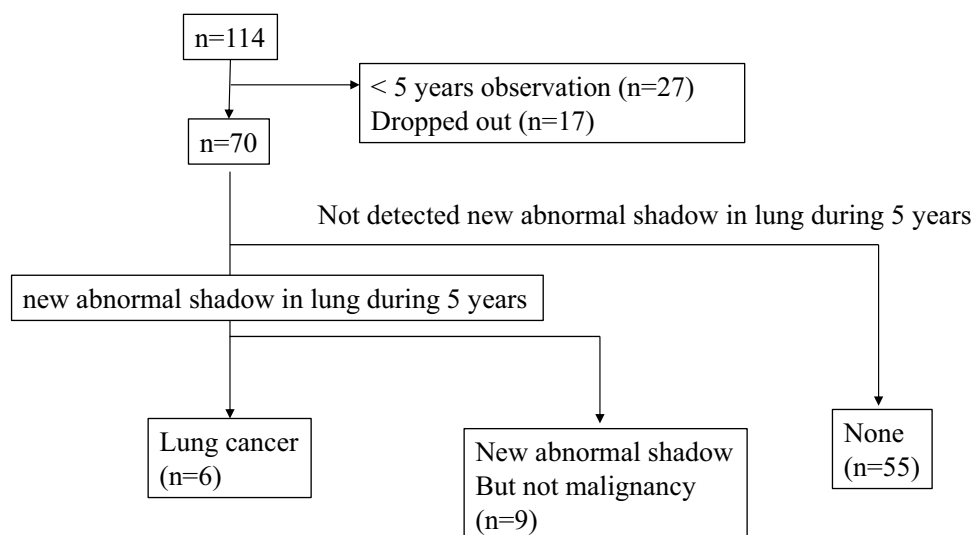
In western Yokohama, primary care physicians are entrusted with the management of COPD patients for the sake of efficient medical care, but each primary care physician and our hospital, which is the core facility, collaborate in a circular-type hospital-diagnosis collaboration that includes annual chest CT and periodic reevaluation to deal with complications and exacerbations.<sup>13</sup> Standard-dose chest CT is considered useful not only for detecting lung cancer but also for detecting complications such as pulmonary fibrosis or pulmonary vascular abnormalities in COPD patients. Therefore, our coordinated system uses standard-dose CT in order to detect complications of COPD. The patients managed via our system reflect the optimal management of COPD by primary care physicians in Japan. However, there is a lack of knowledge in this area.

We hypothesized that routine standard-dose CT examinations could detect lung cancer at early stage in COPD patients managed via COPD coordinated system. We investigated the complications and details of lung cancer in patients with COPD managed by primary care physicians in a circular collaboration with our hospital in western Yokohama, including the value of annual standard-dose chest CT evaluation.

## Materials and Methods

This was a retrospective observational study. It was conducted at St. Marianna University Yokohama Seibu Hospital from January 2013 to March 2020. From 114 patients who visited the hospital for COPD consultation, we excluded those in whom respiratory diseases other than COPD were considered to be the main health problem, patients whose full histories were unknown because of the destruction of medical records, and patients with observation periods of less than 5 years with no indications of lung cancer on chest CT. Seventy patients observation periods of at least 5 years without abnormal findings were selected (Figure 1). Twenty-seven patients were excluded because their follow-up period was less than 5 years, and 17 patients were excluded because they no longer attended the hospital. The reasons for the dropped-out patients' withdrawal were unclear, but previous report showed that these patients were elderly and had relatively mild COPD.<sup>13</sup> The diagnosis of COPD was confirmed in these patients, who were at least 40 years of age, had a smoking history of at least 20 pack-years, and  $FEV_1/FVC < 70\%$  after bronchodilator administration.<sup>1,2</sup> Severity classification and treatment selection were made by a respiratory specialist based on the basis of guideline according to symptoms and respiratory function. The severity of illness was classified as follows: stage I:  $\%FEV_1 \geq 80\%$ , stage II:  $50\% \leq \%FEV_1 < 80\%$ , stage III:  $30\% \leq \%FEV_1 < 50\%$ , stage IV:  $\%FEV_1 < 30\%$ .<sup>1,2</sup> In addition, we detected other complications of patients from medical records. All patients had quit smoking during observation period.

All subjects underwent chest CT before the start of observation. Standard-dose chest CT was performed with an Aquilion CX TSX-101A (Toshiba Medical Systems; now Canon Medical Systems, Tochigi, Japan). Several physicians from the hospital's Department of Respiratory Medicine and Department of Radiology read the images and confirmed the findings. Observation of any existing abnormal shadows was started after confirmation at least 12 months that they were not lung cancer. Patients in whom new abnormal shadows that were suspicious for lung cancer, such as nodules or ground



**Figure 1** Flowchart of patient selection.

glass opacities, appeared were defined as having new abnormal shadows; those in whom these abnormal shadows spontaneously shrunk or disappeared and were not considered to be lung cancer were defined as no malignancy, and those whom lung cancer cells were detected in obtained specimens from the newly or enlarging abnormal shaded areas seen on chest CT by bronchoscopy or Video-Assisted Thoracic Surgery (VATS), were defined as having lung cancer. The staging was based on the Japanese Lung Cancer Society Guideline<sup>14</sup> after confirmation of the metastatic status by imaging.

Spirometry was performed using the CHESTAC-8800 (Chest, Tokyo, Japan). Measurements were performed according to American Thoracic Society / European Respiratory Society guideline.<sup>15</sup> FVC, FEV<sub>1</sub>, and flow volume curves were evaluated from maximum inspiration to maximum expiration, with values measured when sufficient expiration was achieved.

Statistical analysis was performed by using JMP Pro ver. 16 (SAS Institute, Tokyo, Japan). Each indicator was expressed a frequency or mean and standard deviation (normal distribution) or a median and quartiles (non-normal distribution) according to the presence or absence of normal distribution, and the Mann Whitney *U*-test was performed for differences between groups, with  $p < 0.05$  being considered a significant difference. For the association between the frequencies of each indicator, a  $\chi^2$  test was performed and  $p < 0.05$  was considered to indicate a significant difference. When significance was discovered,  $\chi^2$  values and deviations were calculated for each category, and elements with high  $\chi^2$  values were considered to have a significant relationship.

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of St. Marianna University School of Medicine (No.6918). It was a survey of routine clinical examinations, so that patients' consent to review their medical records was not required by the Ethics Committee of St. Marianna University School of Medicine. After collecting the patients' data, our information manager anonymized it. Therefore, the personal information of the patients in this study cannot be identified from published data. This study plan was posted on the St. Marianna University Medical School website and in the outpatient consultation room by using the put-out method to accumulate clinical indicators of usual care, and the subjects were given free access to the study plan. A system was set up to respond immediately to any questions or requests.

## Results

We applied disease diagnosis system to the 114 subjects (Figure 1). All patients were classified as COPD-C, because none had a history of childhood asthma or air pollution exposure, no patients had a history of developmental disorders or genetic disorders, 3 patients with a history of tuberculosis had only mild chest deformation, and also all patients had

a history of heavy smoking and lung emphysematous changes. Seventy patients were included, with the exclusion of 27 who had been under observation for less than 5 years without shadowing and 17 who dropped out during the course of the study. The backgrounds of the 70 patients are shown in Table 1. The mean age of the patients was  $75.7 \pm 7.64$  years, and 63 of them were male. Mild COPD (stage I or II) was found in 60 (85.7%). There were no patients who worsed their complications during the course of the observation. Details of COPD medications are shown in Table e1. Nodules were detected in 15 (21.4%) during the observation period. Lung cancer was diagnosed in six of the 70 patients (8.6%, 40% of all patients in whom nodules were detected) (Table 2, Figure 2). The background factors for each group at the beginning of observation are shown in Table 2. There were significantly more patients without medication for COPD in the lung cancer group ( $p = 0.027$ ), and no significant differences between group in other background factors. The median number of observation days until lung cancer detection was 885, which was not significantly different from the median of 1103 days for detection of nonmalignant abnormal shadows. Lung fibrosis tended to be more frequent in the lung cancer group (16.6%, one patients) compared with other groups, but the difference was not statistically significant. The frequency of COPD exacerbations was higher in the no-shadow group, but with no significant difference. The localization of abnormal shadows is shown in Table 3. Figure 2 shows the details of the follow-up procedure after routine CT screening. Lung

**Table 1** Background Characteristics of Subjects

No. of Patients Enrolled	70
Sex (M / F)	63 / 7
Age	$75.7 \pm 7.64$
BMI	$22.1 \pm 2.56$
GOLD stage (1 / 2 / 3 / 4)	40 / 20 / 7 / 3
Smoking history (pack-year)	50 (40, 64.3)
Duration of COPD (year)	3 (1.75, 7)
Comorbidity	
Asthma-COPD overlap	44
Colon cancer	3
Gastric cancer	2
Old tuberculosis	3
Cardiovascular disease	9
Diabetes	2
Therapy	
LAMA/LABA/ICS	25
LAMA/LABA	1
LAMA/ICS	5
LABA/ICS	29
LAMA	3
LABA	0
ICS	1
No medication	6
FVC (L)	$3.23 \pm 0.28$
FVC (% of predicted)	$104.6 \pm 20.6$
FEV1 (L)	$1.77 \pm 0.72$
%FEV1 (% of predicted)	$82.8 \pm 27.1$
FEV1/FVC (%)	$54.1 \pm 15.1$

**Notes:** Data are presented as median (interquartile range) or mean  $\pm$  SD.

**Abbreviations:** BMI, body mass index; LAMA, long-acting muscarinic antagonist; LABA, long acting beta2 agonist; ICS, inhaled corticosteroid; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s.

**Table 2** Comparison of Lung Cancer Group, New Abnormal Shadow but No Malignancy Group, and None of New Shadow Group

	Lung Cancer	New Abnormal Shadow but No Malignancy	None	p
No. of patients (%)	6 (8.57%)	9 (12.8%)	55 (78.5%)	***
Sex (M/F)	4/2	8/1	51/4	0.1
Age	71.5 ± 8.41	73.4 ± 2.22	75.7±1.06	0.287
BMI	23.4 ± 2.45	20.7 ± 0.72	22.3 ± 0.33	0.109
GOLD stage (1 / 2 / 3 / 4)	4 / 2 / 0 / 0	5 / 3 / 1 / 0	31 / 15 / 6 / 3	0.773
Smoking history (pack-years)	61.5 (39.2, 150)	55 (45, 60)	50 (40, 65)	0.438
Duration of COPD (years)	3 (1, 11)	5 (2, 11)	3 (1, 6)	0.42
No. of days until detection	885 (621, 1645)	1103 (922, 1599)	***	0.262
Interstitial pulmonary Fibrosis (+/-)	1/5	1/8	3 / 52	0.52
COPD exacerbation (+/-)	1/5	1/8	16 / 39	0.4
Asthma COPD Overlap (+/-)	3/3	5/4	36 / 19	0.743
<b>Medication for COPD (+/-)</b>	<b>4/2 *</b>	<b>8/1</b>	<b>52/3</b>	<b>0.027</b>

**Notes:** Data are presented as median (interquartile range) or mean ± SEM. P values were analyzed by Wilcoxon test (age, BMI, smoking history, duration, no. of days until detection) or  $\chi^2$  square test (sex, GOLD stage, interstitial pulmonary fibrosis, COPD exacerbation). \*: There were significantly more untreated patients in the lung cancer group. The bold text indicates statistically significant differences. \*\*\*: There is no data corresponding to this item.

**Abbreviations:** BMI, body mass index; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

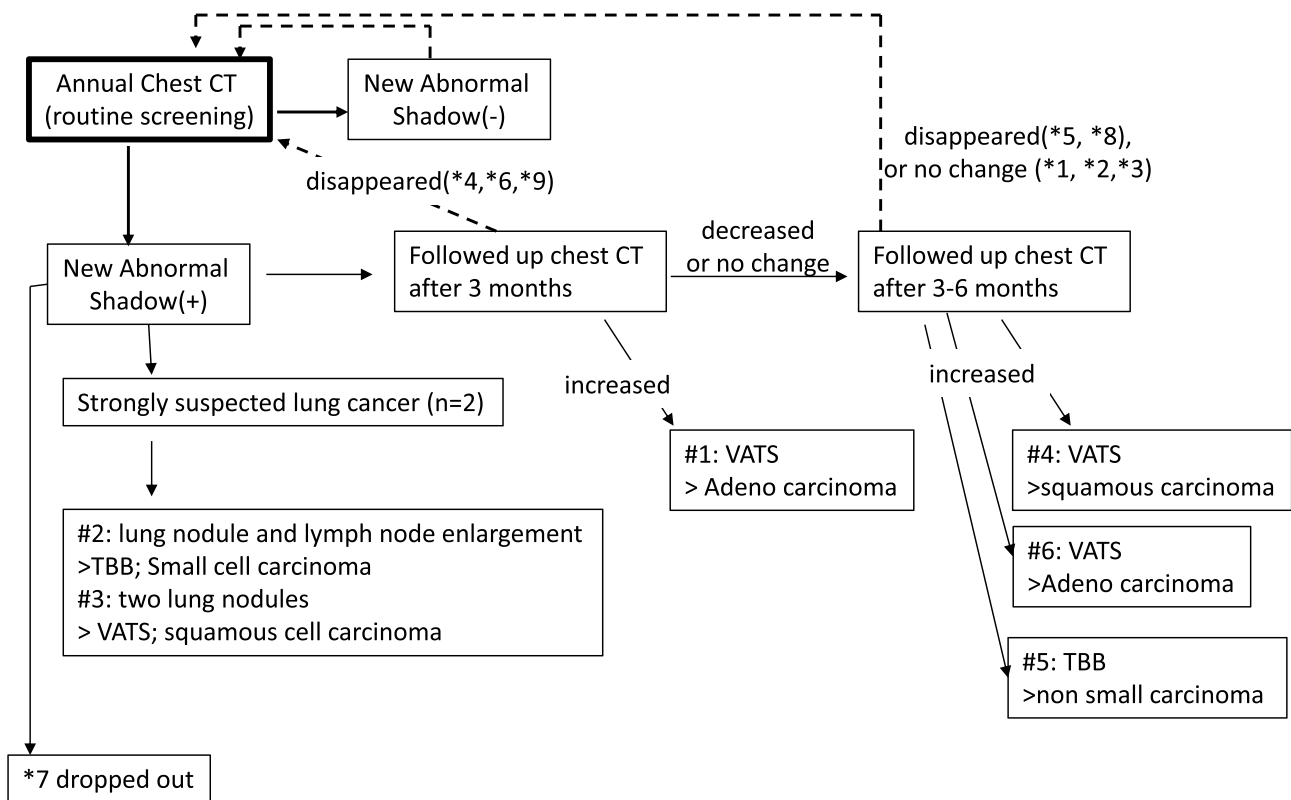
cancer was found in the right upper lobe in three and in the right lower lobe in the other three. Five patients were early-stage carcinomas. Nine patients had non-malignant abnormal shadows. Five of the six lung cancer cases were operable as early-stage cancer, and four patients underwent surgery, and one patient avoided surgery and opted for radiation therapy instead. One case of advanced small cell lung cancer was treated with chemotherapy and radiotherapy (Table 3 and Table 4). Detection of the lesions in all of the operable patients was difficult on chest X-ray.

Details of the lung cancer group are shown in Table 4 and chest CT images are shown in Figure 3. The small cell carcinoma in patient (#2) was judged to be stage IVb because it was accompanied by mediastinal lymph node, supraclavicular lymph node, and intraperitoneal metastasis. All other non-small cell carcinoma patients were in early stage. In patients #5, cytology confirmed malignant cells of non-small cell carcinoma but did not identify the histological type. Treatment consisted of surgery in patients #1, #3, #4, and #6, and radical radiation therapy in patient #5. Chemotherapy and radiotherapy was given for #2. The outcome was death in patient #2, and at least 2-year survival (lost to follow up) in patient #5. All other patients survived and were considered cured.

Table 5 shows the details of patients with new abnormal shadows but no malignancy. The abnormalities disappeared in five patients (\*4, \*5, \*6, \*8, \*9), remained in three patients (\*1, \*2, \*3) but did not worsen; one of the patients dropped out, with unknown results (\*7) (Table 3, Table 5, Figure 2). No additional medications were administered after nodule detection.

## Discussion

Lung cancer screening by using standard-dose chest CT was performed in patients with COPD managed by primary care physicians registered in a circular management system with our hospital. Annual chest CT was followed up for 5 years or until abnormal shadows were detected. Fifteen of the 70 patients had abnormal shadows, and 6 of these 15 patients had lung cancer. Five of the lung cancers were non-small cell carcinomas and one was a small cell carcinoma. The incidence of lung cancer was 1.71%/year. Our hypothesis that “routine standard-dose CT examinations could detect lung cancer at early stage in COPD patients managed via COPD coordinated system”, was considered plausible.



**Figure 2** Details of the CT screening process.

**Notes:** #lung cancer; \*new abnormal shadow but no malignancy.

**Abbreviations:** TBB, transbronchial biopsy, VATS, Video-Assisted Thoracic Surgery.

Although the study focused mainly on patients with mild COPD, the incidence of lung cancer was relatively high. Previous reports in the same Japanese population as used in this study have shown that the incidence of lung cancer in Japanese patients with COPD is 1.85% or 2.3%/year, and that risk factors for lung cancer include a large area of emphysematous change (LAA%), concomitant interstitial pulmonary fibrosis, current smoking history, and stage IV severe COPD.<sup>7,8</sup> These two previous reports were on patients managed by university hospital outpatient departments,

**Table 3** Localization and Outcome of Lesions in Lung Cancer and New Abnormal Shadow but No Malignancy Groups

	Lung Cancer	New Abnormal Shadow but No Malignancy
No. of patients (%)	6 (8.57%)	9 (12.8%)
Lesion		
Left Lung		
Upper lobe	0	2
Lower lobe	0	0
Right lung		
Upper lobe	3	6
Middle lobe	0	0
Lower lobe	3	1

(Continued)

**Table 3** (Continued).

	Lung Cancer	New Abnormal Shadow but No Malignancy
Type of carcinoma		
(adeno/squamous/small/ large /unknown*)	2 / 2 / 1 / 0 / 1	***
Stage	IA 4, IIA1, IVb1	
Outcome of abnormal shadow		
Disappeared	***	5
Remained with no change on follow up	***	3
Unknown (lost to follow up)	***	1
Therapy for carcinoma		
Surgery	5	***
Chemotherapy + radiation therapy	1	***
Radiation therapy	1	***

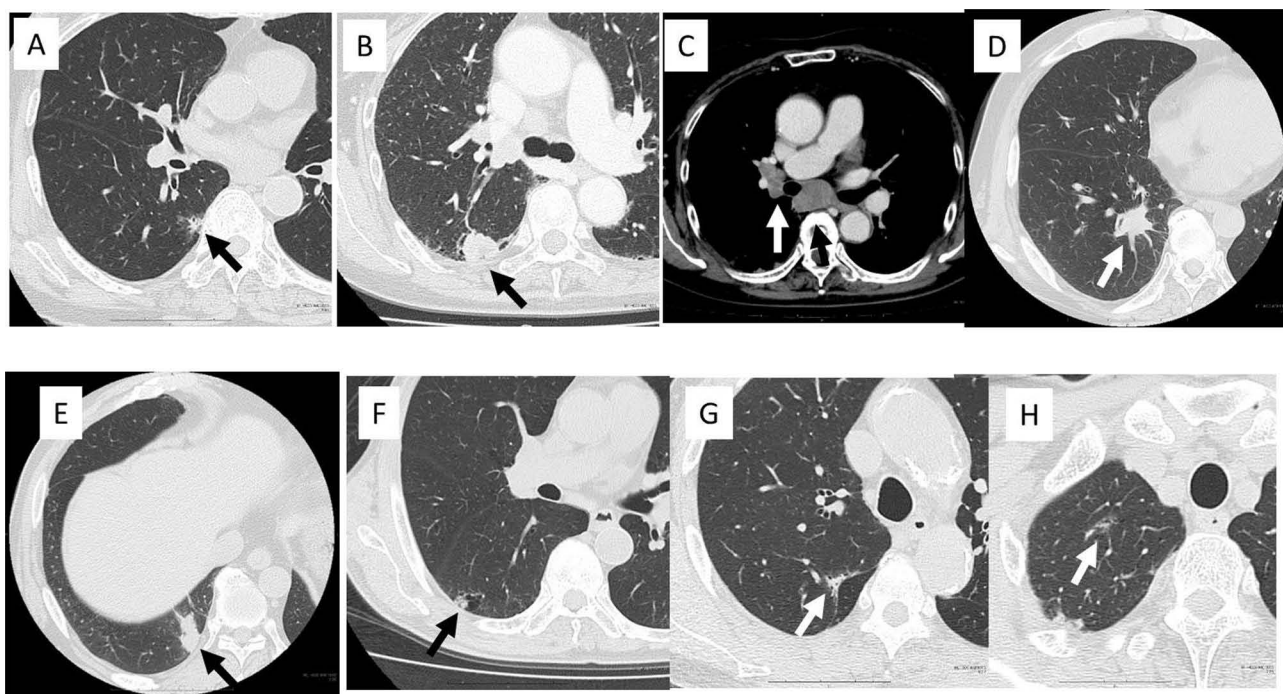
**Notes:** \*: This patient had non-small cell carcinoma, but the histology could not be determined. \*\*\*: There is no data corresponding to this item.

**Table 4** Details of Patients Diagnosed with Lung Cancer

Number	Age	Sex	Duration of COPD (Year)	COPD Stage	Histology	TMN	Stage	Days Before Onset	Therapy	Outcome	Lesion
#1	80	F	1	1	Adeno	T1aN0M0	IA	2121	Operation	Survival	rt lower
#2	72	F	3	1	Small	T3N2M1b	IV b	1487	Chemotherapy	Death	rt upper
#3	72	M	3	2	Squamous	T1bN1M0	IIA	828	Operation	Survival	rt lower
#4	75	M	20	1	Squamous	T1N0M0	IA	878	Operation	Survival	rt lower
#5	67	M	8	2	Non-small	T1N0M0	IA	892	Radiation	Unknown (survival 2years)	rt upper
#6	63	M	1	1	Adeno	T1N0M0	IA	90	Operation	Survival	rt upper

**Abbreviations:** TMN, tumor, node, metastasis; rt, right.

whereas ours was a follow-up study of a group of patients, mainly with stage I or stage II mild COPD managed by primary care physicians. The percentage of patients with interstitial pulmonary fibrosis was higher in the lung cancer group compared with other groups. This may have been a risk factor, but no statistically significant difference was observed, probably because of the small number of patients. In addition to a high LAA%, airflow obstruction and COPD exacerbations have been reported as possible risks for lung cancer development.<sup>16,17</sup> Although the cause of relationship between lung cancer development and COPD exacerbation is not clear. The possible mechanisms include a history of heavy smoking as a common risk factor for both COPD exacerbations and lung cancer, and chronic inflammation of COPD increasing the risk of lung cancer or lung inflammatory nodule.<sup>17,18</sup> We found no between group difference in exacerbation frequency or COPD severity (Table 2). This study mainly included patients with mild and stable COPD managed by primary care physicians and had a small sample size, so that exacerbation frequency and COPD severity may have had little effect on the development of lung cancer. Additionally, there were significantly more untreated



**Figure 3** Chest CT images of lung cancer patients (A) #1, (B) and (C) #2, (D) and (E) #3, (F) #4, (G) #5. G. (H)#6. Arrows indicate areas where tumor was detected.

patients for COPD in the lung cancer group. One study of COPD patients managed by primary care showed that patients with asthma and those using inhaled steroids had a significantly lower risk of lung cancer.<sup>19</sup> There was no significant difference in the frequency of Asthma COPD overlap between groups, and treatment for COPD was determined based on the status of COPD. Although the number of these risk factors was small in the study population, the annual incidence of lung cancer was 1.71% per year, suggesting that screening for early detection of lung cancer is necessary even in patients with COPD managed by a primary care physician.

**Table 5** Details of Patients Diagnosed with Abnormal Shadow but No Malignancy

Number	Age	Sex	Type of Lesion	Duration of COPD (Year)	No. of Days Before Onset	Outcome	Lesion Location (Lobe)	COPD Stage
*1	75	F	Nodule (5mm)	10	1703	No change	rt lower	2
*2	80	M	Nodule (15mm) calcification	5	2442	No change	rt upper	2
*3	62	M	Nodule (15mm)	4	373	No change	rt upper	2
*4	87	M	Nodule (5mm)	20	1261	Disappeared after 3mth	rt upper	1
*5	75	M	Nodule (5mm) fibrosis	1	790	Disappeared after 9mth	lt upper	1
*6	75	M	Nodule (5mm) GGO (10mm)	1	1103	Disappeared after 3mth	rt upper	1
*7	82	M	Nodule (5mm)	12	899	Unknown	rt upper	3

(Continued)

**Table 5** (Continued).

Number	Age	Sex	Type of Lesion	Duration of COPD (Year)	No. of Days Before Onset	Outcome	Lesion Location (Lobe)	COPD Stage
*8	77	M	Nodule (13mm)	2	1825	Disappeared after 9mth	lt upper	I
*9	75	M	Nodule (17mm)	9	1257	Disappeared after 3mth	rt upper	I

**Abbreviations:** GGO, ground glass opacity; lt, left; rt, right.

Evidence had shown that there were several problems when using chest CT (standard-dose or low-dose) for lung cancer screening.<sup>9,11</sup> Previous report suggested that standard-dose chest CT were useful for people with a history of smoking.<sup>9</sup> When used for screening of lung cancer in wide population, low-dose CT are recommended to avoid radiation exposure.<sup>12</sup> The NLST study of this screening method reduced mortality rates not only in COPD but also in subjects with a history of heavy smoking.<sup>11</sup> Moreover, in that study, more than 90% of the positive screening results were false positives, and also early detection was difficult in small-cell lung cancer. On the point of false positive, our false-positive rate was lower (60%) than that for low-dose CT in the abovementioned previous report (94.5%).<sup>11</sup> This may have been due to the fact that in our study chest standard-dose CT had already been performed before the start of observation, so existing abnormalities had already been evaluated; the study was therefore started in the absence of any abnormalities that would have raised suspicion of lung cancer. In addition, because standard-dose CT clearly depict shadows, potentially making diagnosis more accurate. Two patients who were strongly suspected of having lung cancer, were immediately evaluated, and both were diagnosed with lung cancer (Figure 2). On the point of small cell carcinoma, of the 6 patients of lung cancer, five were detected in the early stages, suggesting that screening with chest CT was effective for early detection at our institution. The only case of advanced lung cancer was one of small-cell lung cancer, this is in agreement with the above-mentioned finding that early detection of small-cell lung cancer is difficult.<sup>11</sup> This may be because small cell lung cancer progresses quickly and 1-year follow-up interval is too long. On the other hand, frequent CT examinations increase radiation exposure, costs, and effort, and one study using low-dose CT have shown no difference between annual and biennial examinations,<sup>20</sup> making it difficult to determine the appropriate frequency of examinations.

In this study, it was difficult to predict results of prognosis and histology based on the background information and the location of the shadow. Table 3 and Figure 2 shows the localization of the abnormal shadows and the outcome. All cancers were in the right lung. The reason for this is unknown, although it may be because the right lung is larger than the left. Chest CT followed up the nine patients with abnormal shadows but no malignancy revealed disappearance of the shadows in five patients and no change in three. When new abnormal shadows were detected on routine chest CT of our subjects, a short follow-up of 3 months was implemented (Figure 2). Maci et al reported that inflammatory nodules in COPD patients shrink after a short period of smoking cessation.<sup>18</sup> This result of no malignancy shadow may be due to the fact that all subjects had quit smoking. On the point of lung cancer, histologically, higher proportion of squamous cell carcinoma has been reported in lung cancer in COPD patients than in non-COPD patients.<sup>21–23</sup> We found two patients of adenocarcinoma, two patients of squamous cell carcinoma, one patient of small cell carcinoma, and one patient of unknown classification (non-small cell carcinoma). This is consistent with a higher proportion of squamous cell carcinoma compared to epidemiological studies of lung cancer overall.<sup>21–23</sup> This may have been due to our COPD patients' history of heavy smoking. Further studies will be needed to prove causation.

The study had a number of limitations. First, because it was a retrospective observational study, the causal relationship of whether annual standard-dose chest CT as a collaborative COPD assessment contributed to the early detection of lung cancer was unknown. Second, because the study was conducted at a single institution, the number of patients was small and was likely influenced by institutional and regional characteristics. In addition, the number of patients made statistical evaluation difficult, and risk assessment of lung cancer incidence on the basis of interstitial pulmonary fibrosis and the exacerbation frequency was not possible. Third, the degree of emphysema, which has been presented as a risk factor in previous reports,

could not be directly compared with those in previous reports because we did not quantify the LAA%.<sup>7</sup> Fourth, the outcomes of those patients who dropped out were unknown. Fifth, in this study, we used standard-dose CT. Now that low-dose CT are now recommended for screening of lung cancer, whether or not to switch to a low-dose scan must be considered in relation to screening for other complications. Sixth, there was no information available regarding passive smoking, so this point cannot be considered. Prospective, multicenter, observational studies are needed to answer these questions.

## Conclusion

In conclusion, we observed new lung cancer patients in COPD managed by primary care physicians by standard-dose chest CT over a 5-year period. CT findings suspicious for lung cancer were observed in 15 patients (21.4%), of which six (8.5%, 40% of patients with abnormal shadows) were confirmed to have lung cancer; five of six were detected at an early stage, indicating the usefulness of annual chest standard-dose CT evaluation. However, small-cell carcinoma is likely to progress rapidly and further efforts are needed to detect lung cancer early in COPD patients managed by primary care physicians, through active cooperation between the hospital medical and diagnostic departments.

## Declaration

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of St. Marianna University School of Medicine (No. 6918). It was a survey of routine clinical examinations, so that patients' consent to review their medical records was not required by the Ethics Committee of St. Marianna University School of Medicine. The study plan was posted on the St. Marianna University Medical School website and in the outpatient consultation room by using the put-out method to accumulate clinical indicators of usual care, and the subjects were given free access to the study plan. A system was set up to respond immediately to any questions or requests.

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## Author Contributions

All authors made substantial contributions to the reported work in terms of conception, study design, conduct, acquisition, analysis, and/or interpretation of data, participated in drafting, revising, or critical review of the paper, gave final approval of the version to be published, agreed to the journal to which the paper will be submitted, and agree to be accountable for all aspects of the work.

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## Disclosure

Authors other than MM have no conflicts of interest to disclose.

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