# Prevalence of Chronic Obstructive Pulmonary Disease in Lung Cancer Patients in Dr. M Djamil General Hospital

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**KEYWORDS**

COPD, lung cancer, COPD, prevalence COPD, underdiagnosis COPD

**ABSTRACT**

**Background:** The prevalence of COPD is high in lung cancer patients ranging from 40-70%, but is often undiagnosed due to similar risk factors and chronic respiratory symptoms. Chronic obstructive pulmonary disease not only contributes to the occurrence of lung cancer but can also be an overlapping condition that affects prognosis and treatment options.

**Methods:** A descriptive-analytic study with a cross-sectional design was conducted on lung cancer patients who had known cell types at the polyclinic of Dr. M Djamil Padang Hospital and spirometry examination was performed.

**Results:** Total 49 subjects with 77.6% male, 40-59 years old (46.9%), former smokers (73.5%) with severe Brinkman index (IB) (78.9%). The most common type of lung cancer was squamous cell carcinoma (61.2%) and most subjects were at an advanced stage (83.6%) with ECOG clinical appearance 1 (79.6%). The location of lung cancer lesions was predominantly central (83.7%) with restriction lung function values (98%) and 37.5% of them with obstruction. The prevalence of COPD in lung cancer patients was 34.7% with patient characteristics mainly male (88.2%), 60-79 years (58.8%), former smokers (82.4%) with severe IB (86.7%). The types of lung cancer of subjects with COPD were mainly squamous cell carcinoma (52.9%), advanced stage (76.5%), ECOG 1 (70.6%) and centralized (94.1%). The degree of obstruction in the COPD group was mainly GOLD 2 (41.2%) with population group E (64.7%). There was no association between the type, staging, and location of lung cancer lesions with the degree of obstruction or with the COPD population group

**Conclusion:** Lung cancer patients with COPD are mainly male with an older age, the most common type is squamous cell carcinoma, advanced stage, with central lesion all lung cancer patients with COPD in the study were undiagnosed COPD cases.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and lung cancer are two lung diseases with high morbidity and mortality rates, closely associated with shared risk factors.[1] Exposure to harmful particles and gases, especially cigarette smoke and inhalation of other irritant particles and toxic gases such as biomass burning, air pollution, occupational exposure to hazardous chemicals and genetic factors are risk factors in COPD and lung cancer, so these two diseases can also be related in pathomechanism.[2,3] COPD is an independent risk factor for lung cancer, the incidence of lung cancer is 2 to 4 times higher than without COPD.[4]

Chronic obstructive pulmonary disease not only contributes to the occurrence of lung cancer but can also be an overlapping condition resulting in delayed diagnosis and therapy. COPD is often undiagnosed, data shows as many as 93% of patients are unaware of having COPD.[5,6] The prevalence of COPD is high in lung cancer patients and is often undiagnosed. Collar et al found that 60% of patients did not realise they had COPD until they were diagnosed with lung cancer. Undiagnosed COPD comorbidities in lung cancer patients are associated with advanced-stage lung cancer, high outpatient visit rates and mortality rates.[7]

Comorbid COPD can be a major contributor to treatment selection, survival and prognosis of lung cancer patients, so researchers are interested in conducting research on the prevalence of COPD in lung cancer and assessing the relationship between the type, stage, and location of lung cancer lesions with COPD classification in a population of lung cancer patients at the Polyclinic of Dr M Djamil Padang Hospital.

## METHOD

Descriptive analytical research with a cross-sectional design was conducted from March to June 2024 in lung cancer patients whose cell types were known and spirometry was performed. The sampling technique in this research was consecutive sampling.

## RESULT AND DISCUSSION

The study was conducted for 3 months from March 2024 to June 2024 involved 53 subjects of lung cancer patients who had known cancer cell types. A total of 4 subjects were excluded, 3 of which were due to failed spirometry maneuvers and 1 subject with unstable angina pectoris. A total of 49 subjects underwent spirometry, chest X-Ray, and chest CT. Flow chart of this research showed in Figure 1.

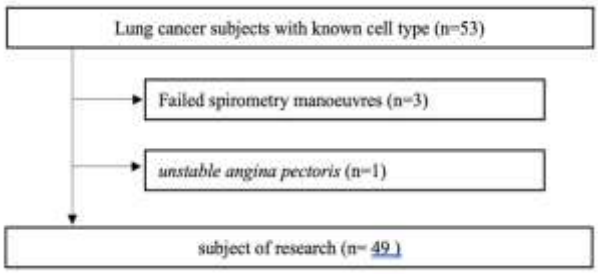


Figure 1. Flow of research subjects

The characteristics of lung cancer patients in this study were mostly in the age range of 40 - 59 years (46.9%) male (77.6%), former smokers (73.5%) with a heavy Brinkman index (78.9%). There was no large cell carcinoma cell type lung cancer in this study and 1 subject (2%) with small cell lung cancer (SCLC). The most common type of lung cancer was squamous cell carcinoma with 30 subjects (61.3%).

Table 5.1. Baseline characteristics of the study sample (n=49)

| | Total (n) | Percentage (%) |
|---|---|---|
| Gender | | |
| - Male | 38 | 77,6 |
| - Female | 11 | 22,4 |
| Age | | |
| - 20 - 39 years | 2 | 4,1 |
| - 40 – 59 years | 23 | 46,9 |
| - 60 – 79 years | 22 | 44,9 |
| - ≥ 80 years | 2 | 4,1 |

| | | |
|---|---|---|
| Smoking status | | |
| - Never smoker | 10 | 20,4 |
| - Former smoker | 36 | 73,5 |
| - Smoker | 3 | 6,1 |
| Brinkman Index | | |
| - Mild | 2 | 5,2 |
| - Moderate | 7 | 17,9 |
| - Severe | 30 | 78,9 |
| Lung cancer cell type | | |
| - SCC | 1 | 2,0 |
| - Adenocarsinoma | 13 | 26,5 |
| - Squamous cell carcinoma | 30 | 61,2 |
| - Adenosquamosa | 5 | 10,2 |
| *Staging* | | |
| - Early | 8 | 16,3 |
| - Advanced | 41 | 83,6 |
| Performance Status | | |
| - 1 | 39 | 79,6 |
| - 2 | 10 | 20,4 |
| Location | | |
| - Central | 41 | 83,7 |
| - Peripheral | 8 | 16,3 |
| Lung Function | | |
| - Normal | 1 | 2,0 |
| - KV < 80% | 48 | 98,0 |
| Mild | 6 | 12,5 |
| Moderat | 7 | 14,5 |
| Moderate-severe | 10 | 20,8 |
| Severe | 17 | 35,5 |
| Very severe | 8 | 16,7 |
| - VEP1/KVP < 75% | 18 | 37,5 |
| Mild | 1 | 5,5 |
| Moderate | 7 | 38,9 |
| Severe | 7 | 38,9 |
| Very severe | 3 | 16,7 |

Lung cancer patients in this study were mainly in advanced stage 41 subjects (83.6%) with ECOG 1 clinical appearance in 39 subjects (79.5%). The location of lung cancer lesions was mainly found in the centre of the lung in 41 subjects (83.7%). The results of spirometry examination in lung cancer patients found only 1 subject with normal lung function, 48 subjects with restriction (98%) and 37.5% of them were accompanied by obstruction (mixed type). The characteristics of lung cancer patients in this study can be seen in table 1.

Table 2. Prevalence of comorbid COPD in lung cancer patients based on spirometry examination (n=17)

| **Prevalence** | **Total (n)** | **Percentage (%)** |
|---|---|---|
| COPD | 17 | 34,7% |
| Non-COPD | 32 | 65,3% |

The prevalence of COPD obtained by spirometry examination in lung cancer patients in this study was 34%, the result can be seen in table 2. The characteristics of lung cancer patients with COPD in this study can be seen in table 3.

Table 3. Characteristics of lung cancer patients with COPD (n=17)

| | **Total (n)** | **Percentage (%)** |
|---|---|---|
| Gender | | |
| - Male | 15 | 88,2 |
| - Female | 2 | 11,8 |
| Age | | |
| - 20 - 39 years | 1 | 5,9 |
| - 40 – 59 years | 5 | 29,4 |
| - 60 – 79 years | 10 | 58,8 |
| - ≥ 80 years | 1 | 5,9 |
| Smoking status | | |
| - Never smoker | 2 | 11,8 |
| - Former smoker | 14 | 82,4 |
| - Perokok | 1 | 5,9 |
| Brinkman index | | |
| - Mild | 0 | 0 |
| - Moderate | 2 | 13,3 |
| - Severe | 13 | 86,7 |
| Lung cancer cell type | | |
| - SCLC | 1 | 5,9 |
| - Adenocarsinoma | 4 | 23,5 |
| - Squamous cell carcinoma | 9 | 52,9 |
| - Adenosquamous | 3 | 17,6 |
| *Staging* | | |
| - Awal | 4 | 23,5 |
| - Lanjut | 13 | 76,5 |
| Performance status | | |
| - 1 | 12 | 70,6 |
| - 2 | 5 | 29,4 |
| Location | | |
| - Central | 16 | 94,1 |
| - Peripheral | 1 | 5,9 |
| Obstruction severity | | |
| - GOLD 1 | 1 | 5,9 |
| - GOLD 2 | 7 | 41,2 |
| - GOLD 3 | 6 | 35,3 |
| - GOLD 4 | 3 | 17,6 |
| COPD group | | |
| - A | 2 | 11,8 |
| - B | 4 | 23,5 |
| - E | 11 | 64,7 |

Lung cancer patients with COPD in this study are male (88.2%), 60 - 79 years (58.8%), former smokers (82.4%) with a heavy Brinkman Index (IB) (86.7%). The most common cell type in lung cancer

with COPD is squamous cell carcinoma cell (52.9%) with advanced stage (76.5%). Performance status was ECOG 1 (70.6%) and there were no subjects with clinical appearance 0, 3, and 4. Lung cancer lesion location mainly in central of the lung (94.1%). COPD characteristics based on the severity of obstruction with GOLD 2 and GOLD 3 (41.2% and 35.3%) and COPD characteristics based on population group were mainly in group E with 11 subjects (64.7%).

The mean value of predicted FVC in lung cancer patients with COPD is 48.65% (severe restriction) with a range of values ranging from 21% to 83%. The mean post-bronchodilator FEV1/FVC ratio was 65.94% and based on the mean predicted FVC1 results showed severe obstruction (GOLD 3). The respondents pulmonary function values based on spirometry examination are shown in table 4.

Tabel 4. Lung function in lung cancer patients with COPD

| Variables | Minimal Value | Maximal Value | Mean | SD |
|---|---|---|---|---|
| - Actual FVC (ml) | 620 ml | 2820 ml | 1416,47 | 528,34 |
| - FVC Predicted (%) | 21% | 83% | 48,65 | 16,75 |
| - Actual FEV1(ml) | 410 ml | 1900 ml | 952,94 | 364,03 |
| - FEV1Predicted (%) | 19% | 80% | 46,76 | 17,31 |
| - FEV1/FVC | 57% | 69% | 65,94 | 3,05 |

Lung cancer patients with COPD with NSCLC cell type were mostly with GOLD 2 and 3 obstruction degrees, and SCLC with GOLD 4. There was no statistically significant difference in the fisher exact test between lung cancer type and obstruction degree (p = 0.69). Staging and location of lung cancer lesions were also not statistically significant (p = 0.57 and 0.58). The relationship between the type, staging and location of lung cancer lesions with the degree of obstruction can be seen in table 5.

Table 5. Relationship between the type, staging and location of lung cancer lesions with severity of obstruction

| | **Obstruction Stage (n=17)** | | | | **P** |
|---|---|---|---|---|---|
| | **GOLD 1** | **GOLD 2** | **GOLD3** | **GOLD 4** | |
| Lung cancer types | | | | | |
| - Adeno carcinoma | 0 | 3 | 1 | 0 | |
| - Adeno squamous | 0 | 1 | 2 | 0 | 0,69 |
| - Squamous cellcarcinoma | 1 | 3 | 3 | 2 | |
| - SCLC | 0 | 0 | 0 | 1 | |
| Staging | | | | | |
| - Early | 0 | 3 | 1 | 0 | 0,57 |
| - Adcanced | 1 | 4 | 5 | 3 | |
| Lesion | | | | | |
| - Central | 1 | 7 | 5 | 3 | 0,58 |
| - Peripheral | 0 | 0 | 1 | 0 | |

The relationship was found to be insignificant from the bivariate analysis between the type, staging, and location of lung cancer lesions and the COPD population group, as shown by the Fisher exact test results of 0.65, 0.78, and 1.00, respectively ($p > 0.05$). The relationship between type, staging, and location of lung cancer lesions and the COPD population group can be seen in Table 6.

Table 6. Relationship between type, staging, and location of lung cancer lesions and the COPD population group.

| | **COPD group (n=17)** | | | **P Value** |
|---|---|---|---|---|
| | **A (n=2)** | **B (n=4)** | **E (n=11)** | |
| Lung cancer types | | | | |
| - Adenocarsinoma | 0 | 1 | 3 | 0,65 |
| - Adenosquamos | 0 | 2 | 1 | |
| - Squamous cell carcinoma | 2 | 1 | 6 | |
| - SCLC | 0 | 0 | 1 | |
| Staging | | | | |
| - Early | 1 | 1 | 2 | 0,72 |
| - Advance | 1 | 3 | 9 | |
| Lesion | | | | |
| - central | 2 | 4 | 10 | 1 |
| - Peripheral | 0 | 0 | 1 | |

## DISCUSSION

There are 52 lung cancer patient subjects which cell types are known; 3 of these subjects were unable to perform spirometry manoeuvres, and 1 subject with unstable angina pectoris onset less than 7 days was excluded from the study. Subjects who are to undergo spirometry must be able to follow instructions and perform manoeuvres to meet the criteria of acceptable and reproducible results. Inadequate spirometry results can occur for various reasons, one of which is the patient's inability to understand and follow instructions.[8] Spirometry can be a challenge for lung cancer patients due to several factors, such as severe shortness of breath, general weakness after chemotherapy, cancer pain, reduced lung function, neurological impairments from metastasis to the brain, and psychological factors that limit the patient's capabilities.[9-11]

Shortness of breath in lung cancer patients can be caused by various causes such as effusion, endobronchial obstruction, infection, thrombosis, toxicity therapy and the presence of COPD can be one of the factors for shortness of breath in lung cancer patients, so not all patients can undergo spirometry examination for diagnosis. Corriveau et al in Canada found that 90.6% of 12,061 patients with early-stage lung cancer could undergo spirometry, while 31,314 patients with advanced lung cancer only 54.4% could be screened for spirometry.[9]

The basic characteristics of the study sample showed that the majority of the patients were male (77.6%). Patients in the age group of 40-59 years are the most (46.9%), followed by patients aged 60-79 years (44.9%). Smoking status from most patients (73.5%) are former smokers with severe IB (78.9%). A study by Ermayanti et al. at RSUP Dr. M Djamil Padang from 2004 to 2017 found that lung cancer patients were predominantly male (77.8%), with 95.4% of them being smokers or former smokers, and the most common type of lung cancer was squamous cell carcinoma.[12]

According to data from the Statistics, Epidemiology, and End Results (SEER) on 458,132 lung cancer cases over 8 years, 53% of cases were male, with an incidence rate of 73/100,000 compared to

females (47%) with an incidence rate of 51/100,000. Overall, the incidence of lung cancer was higher in males than females, both in early and advanced stages.[13]

Lung cancer was the most frequently diagnosed cancer in men in Indonesia in 2020, with 34,783 new cases, accounting for 14.1% of all cancers. [14] This finding aligns with the characteristics of lung cancer patients in this study, where the majority were male. The difference in gender distribution for lung cancer is often attributed to smoking habits, which are known to be a strong risk factor for both lung cancer and COPD.

The most common age group in this study was 40-59 years, which is similar to Ermayanti et al. study, which found an average age of lung cancer patients to be 57.81 ± 11.23 years for males and 52.97 ± 2.79 years for females. The 50–70 year age group is also the one with the highest incidence of lung cancer, according to cancer registry data from 2008 to 2012 at Cipto Mangunkusumo National General Hospital.[15] In the United States, the average age of lung cancer cases was found to be around 70 years for both males and females, with 53% of cases occurring in the 55 – 74 year age range and 37% occurring in those over 75 years. [21] In this study, the range of age for lung cancer patients was skewed toward younger ages compared to global epidemiological data, with the youngest patient being 30 years old. Lung cancer occurring in patients under 55 years old is estimated to account for about 10%, and the 20–46 year age group represents a younger population of lung cancer patients, more commonly female, with adeno carcinoma, non-smokers, and advanced stages.[16-17]

Primary lung cancer was previously known as a disease in the elderly which mainly affects patients in the age range of 50 to 80 years and is rarely found in patients under 40 years of age. The occurrence of lung cancer in young adults in Indonesia is linked to earlier smoking initiation, environmental exposure, asbestos use, and a family history of cancer. [18] The accumulation of genetic mutations from carcinogen exposure (such as tobacco smoke) and natural aging processes can lead to the transformation of normal cells into malignant cells. Aging is associated with a decrease in immune function, impairing the body's ability to eliminate cancer cells, thus leading to tumor progression.[19]

The most common types of lung cancer, according to the WHO 2015 classification, are adenocarcinoma (glandular cells), squamous cell carcinoma, and neuroendocrine cancers such as small cell carcinoma, large cell carcinoma, and carcinoid tumors.[20] Squamous cell carcinoma and small cell carcinoma are more commonly seen in males, with central lesions associated with a history of smoking, while adenocarcinoma is more common in females without a smoking history, and the lesions tend to be peripheral.[21] Squamous cell carcinoma was the most common type found in this study, accounting for 61.2% of cases, with the most frequent staging being advanced (75.5%) and the most common lesion location being central (83.7%). Squamous cell carcinoma accounts for 25-30% of all lung cancer cases, originating from the epithelium of the airway in the central bronchi, while adenocarcinoma accounts for 40% of cases, originating from the small airway epithelium and type II alveolar cells, often in peripheral lung areas and in both smokers and non-smokers.

Lung cancer is often diagnosed at an advanced stage, which may be attributed to a combination of factors related to symptoms, screening, early detection, and the biological characteristics of the disease. Global data shows that 65.1% of lung cancer patients are diagnosed at an advanced stage, with an even higher percentage found in this study, where 83.6% of patients were diagnosed at an advanced stage, similar to previous research by Ermayanti et al. (84.8%). The high number of advanced-stage lung cancer patients can be linked to the relatively recent implementation of more effective lung cancer screening programs in Indonesia.

Pulmonary function tests in nearly all lung cancer patients in this study showed restrictive patterns, with 48 out of 49 subjects demonstrating restriction, and 37.5% of them also showing obstruction (mixed type). Restrictive abnormalities indicate conditions where there is a reduction in lung expansion or lung volume, which can result from issues with lung parenchyma, extra-pulmonary causes, or both. Restriction in lung cancer patients may be influenced by factors such as tumor size, mediastinal lymph node enlargement, pleural effusion, pericardial effusion, bone metastasis in the thoracic area, and chest wall infiltration, all of which can affect lung function and expansion.[11,21]

Lung cancer patients with restrictive patterns in this study also had decreased FEV1% and FVC% values, which fall into the category of Preserved Ratio Impaired Spirometry (PRISm). The term PRISm refers to a group of patients with normal VEP1/KVP ratios but with decreased VEP1% or KVP%. Patients with PRISm are considered independent risk factors for the progression of COPD, and approximately 32.6% of patients with PRISm may develop COPD within 4-5 years. The PRISm group can be found in 7.1-20.3% of the smoking or former smoking population, which matches the characteristics of the subjects in this study, with 73.5% being former smokers. The pre-COPD group, marked by respiratory symptoms, emphysema, low VEP1, hyperinflation, decreased diffusion capacity, or rapid decline in VEP1, was not further investigated in this study.[22]

Obstructive abnormalities were also found in 18 subjects (37.5%) out of the 48 with restrictive patterns in this study. A study by Purdue et al. found a correlation between pulmonary function abnormalities and lung cancer incidence, with an increase in lung cancer incidence by 1.5 to 2 times in patients with both obstructive and restrictive abnormalities compared to subjects with normal lung function.[21] Obstructive abnormalities are typically associated with airway diseases, such as COPD, which is related to chronic inflammation, and this could explain the observed findings in this study.

Normal pulmonary function was only found in 1 subject (2%) in this study, who had undergone neoadjuvant therapy and radiotherapy. A study by Cerfolio reported an increase in FEV1 values in lung cancer patients who had received neoadjuvant chemotherapy or chemoradiation, though diffusion capacity was reduced. The increase in FEV1 has been reported in several case series and is suspected to be related to tumor regression following high-dose radiation therapy.[23,24]

Spirometry tests were performed on 49 study subjects, and the prevalence of COPD among lung cancer patients with known cell types was found in 17 subjects (34%). Similar studies conducted by Fathana in 2019 at Persahabatan Hospital and by Gurning at Arifin Achmad Hospital in Riau found higher prevalence rates of COPD in lung cancer patients, at 46.2% and 53.8%, respectively. [25,26] The prevalence of COPD in lung cancer patients varies considerably, ranging from 30% to 80% in various studies conducted previously.[4,9,27-2]

Studies by Corriveau et al., involving 146,787 new lung cancer patients, found that 34.9% of them were newly diagnosed with COPD after spirometry, and 6.8% were diagnosed with COPD within five years of being diagnosed with lung cancer. This suggests that pulmonary function testing should be done at the time of lung cancer diagnosis and regularly thereafter.[9]

No patients in this study had been previously diagnosed with COPD before the research was conducted, leading to a 100% underdiagnosis rate for COPD in lung cancer patients. Globally, the underdiagnosis rate for COPD in lung cancer patients ranges from 71% to 81%, which may be attributed to the lack of screening and pulmonary function tests for high-risk patients.[33-5] Underdiagnosis rate was reported as 81.4% in a study by Lamprecht et al In Latin America.[27,35] A study by Nguyen et al. on the prevalence of COPD among non-smokers in Vietnam and Indonesia found an underdiagnosis rate of 94%.[36]

A study by Bradley et al which conducted spirometry along with low-dose computed tomography (CT) as part of lung cancer screening, found that 1 out of 16 patients had undiagnosed COPD, with mild symptoms and mild functional impairment.[37] Inadequate routine spirometry screening in asymptomatic smokers and lung cancer patients can lead to missed COPD diagnoses. The high underdiagnosis rate of COPD in the general population may also occur in the lung cancer patient group. The focus on diagnosing lung cancer cell types, staging, and treatment can sometimes result in missed COPD diagnoses. Symptoms such as coughing or shortness of breath may be attributed solely to lung cancer, without considering the possibility of concurrent COPD.

Efforts to reduce the underdiagnosis rate of COPD in lung cancer patients require increased awareness, regular spirometry testing, and careful evaluation of respiratory symptoms and risk factors in all lung cancer patients. Early detection methods for COPD in primary healthcare settings in Indonesia, as outlined by the Ministry of Health Indonesia, can include the PUMA score. The use of the PUMA score is still relatively new in Indonesia and has not yet been implemented optimally, leading to insufficient spirometry testing in high-risk COPD patients. As a result, this contributes to the high

underdiagnosis rate of COPD. Spirometry is the standard diagnostic test for COPD, and its use has been widely reported to be beneficial in detecting COPD cases in lung cancer patients due to the overlap of symptoms and risk factors.[38,39]

In this study, lung cancer patients with COPD were mostly found in the older age group, particularly between 60 and 79 years old (58.8%), compared to the baseline age group of 40-59 years (46.9%). The incidence of lung cancer increases with age, while COPD generally affects smokers older than 40, with 2.5 fold increased risk in those above 60 years. Pulmonary function declines with age, and in COPD patients, this decline is accelerated due to inhalation exposures. Aging is mainly driven by the failure of organs to repair DNA damage caused by oxidative stress (non-programmed aging) and the shortening of telomeres (programmed aging).[40] The incidence of both lung cancer and COPD is expected to rise in those over 60 years of age. Fathana's study found the average age of lung cancer patients with COPD to be 60.3 years.[25]

The majority of lung cancer patients with COPD in this study were male (88.2%), a characteristic closely linked to smoking habits. The smoking status of the majority of lung cancer patients with COPD was former smokers (82.4%), with heavy index brinkman (86.7%). A large study by Park et al in Korea over a 9-year period found that male lung cancer patients with COPD were more likely to have comorbidities compared to those without COPD.[41]

Smoking plays an important role in the relationship between COPD and lung cancer, with 20% of smokers at risk of moderate COPD (GOLD 2), and 10% of smokers between the ages of 40-75 at risk for lung cancer.[28] Smoking increases the risk of lung cancer in COPD patients by 6.2 times, and 2.6 times in non-smokers with COPD.[42] A case-control study by Young found that the risk of COPD developing into lung cancer was around six times higher, regardless of smoking status.[28]

The most common cell type found in lung cancer with COPD in this study was squamous cell carcinoma (52.9%), followed by adenocarcinoma (23.5%), adenosquamous carcinoma (17.6%), and large cell neuroendocrine carcinoma (5.9%). The lesions were primarily located in the central regions of the lungs (94.1%). Papi et al. case-control study showed that COPD significantly increases the risk of squamous cell carcinoma by more than 4 times, while chronic bronchitis in COPD patients was associated with a 3.5 times higher risk of squamous cell carcinoma.[43] Similar findings were reported by Mourente-Roibas in a larger cohort of 602 lung cancer patients, where squamous cell carcinoma and large cell neuroendocrine carcinoma were more dominant in COPD patients (37% and 14%, respectively), compared to 15% and 8.7% in non-COPD lung cancer patients.[27]

However, other studies by Husebo et al. and Young et al. found that adenocarcinoma was the most common type of lung cancer in COPD patients (35.5% and 43%, respectively)[28,44]. Gurning's study also found a higher prevalence of COPD in adenocarcinoma lung cancer patients (61.5%) compared to squamous cell carcinoma (38.5%), while Fathana's study found equal proportions of squamous cell carcinoma and adenocarcinoma.[25,26] The prevalence of COPD in large cell neuroendocrine carcinoma (LCLC) was notably high in a study by Ju et al. (51.8%), though this study found only 5.9% of patients with LCLC had COPD.[45] Emphysema was identified as a significant risk factor for certain lung cancer subtypes, especially squamous cell carcinoma and LCLC, due to structural changes and immune responses in the lung parenchyma. However, emphysema was not specifically investigated in this study.[33]

Papi et al. also stated that COPD significantly increases the risk of squamous cell carcinoma by 4 times, while chronic bronchitis without COPD is a risk factor for adenocarcinoma.[43] The increased risk of adenocarcinoma in non-COPD patients is likely due to the absence of chronic airflow limitation, allowing tobacco smoke to reach more peripheral regions of the lung.

Squamous cell carcinoma consistently emerged as the most common type of lung cancer across all subjects in the study, as well as in the COPD subgroup. The proportion of COPD in squamous cell carcinoma was found in about one-third of all subjects (9 out of 30 subjects with squamous cell carcinoma), and a similar proportion was observed in adenocarcinoma (4 out of 13 subjects with adenocarcinoma). These findings suggest that there was no clear tendency for COPD to be higher in either squamous cell carcinoma or adenocarcinoma based on the data.

An interesting finding in this study was the higher rate of COPD in adenosquamous carcinoma (60% of cases). Adenosquamous carcinoma, a subtype of non-small cell carcinoma, consists of both adenocarcinoma and squamous cell carcinoma components and tends to appear in the peripheral lung, although it can also occur centrally.[46] To date, no studies have specifically addressed the prevalence of COPD in patients with adenosquamous carcinoma, so there is no comparison data available for this subtype.

The most common cancer stage in COPD patients was advanced stage (76.5%). Butler et al. in Ontario found that COPD patients with lung cancer were 30% less likely to be diagnosed at an advanced stage, as COPD was associated with earlier detection. In Indonesia, nearly half of lung cancer cases are diagnosed at an advanced stage (90%), and Cunningham et al. found that underdiagnosis of COPD was most common among patients with advanced lung cancer (72.8%).[31] High underdiagnosis rates of COPD and advanced lung cancer stages are intertwined health issues that can be addressed with earlier detection and screening. Lung cancer and COPD screening programs in primary healthcare facilities in Indonesia are still in the early stages, so they have not yet been fully implemented for high-risk individuals.

The functional status of patients in this study was assessed using the Eastern Cooperative Oncology Group (ECOG) performance status. Most lung cancer patients with COPD were found to have limitations in physical activities, but they were still able to perform light activities (ECOG 1) in 70.6% of cases. The remaining patients were classified as ECOG 2, and no subjects were classified as ECOG 0, 3, or 4. A study by Mohan et al. found no significant relationship between COPD and functional status in lung cancer patients.[47] The ECOG classification system is widely used to assess functional capacity, predict prognosis, and guide treatment decisions in cancer patients. Patients with COPD and lung cancer are often assigned higher ECOG scores due to activity limitations, but in this study, the ECOG scores were primarily 1 or 2. Factors that can contribute to the ECOG performance status of lung cancer patients was age, staging, comorbid, adverse event of the therapy, psychological and clinical manifestations. [48]

The degree of COPD obstruction, as classified by the GOLD system, was mainly in GOLD 2 (41.2%), followed by GOLD 3 (35.3%), GOLD 4 (17.6%), and GOLD 1 (5.9%). Wilson et al. found that most lung cancer patients with COPD had mild to moderate obstruction (GOLD 1 and 2), in 67% and 51% of cases, respectively.[49] Studies by Mannino and Purdue et al. reported that the risk of lung cancer increases by 2.8 times in patients with moderate-to-severe obstruction, and by 1.5 times in patients with mild COPD. The degree of obstruction in COPD appears to correlate with the incidence of lung cancer, with varying risk estimates depending on the severity of obstruction.[21,50,51]

In this study, the COPD population was predominantly classified into Group E (64.7%), followed by Group B (23.5%) and Group A (11.8%). These groups represent combined risk factors for exacerbations and clinical symptoms used to guide initial COPD therapy. The classification of COPD groups A, B, and E is a relatively new approach introduced in 2023, and no studies have previously focused on these categories in lung cancer patients.[52]

Group E patients had frequent exacerbations (more than two per year, or at least one requiring hospitalization in the past year). A study by Gagnat et al. found that COPD patients with a history of acute exacerbations were 2.7 times more likely to develop lung cancer. This finding is consistent with the results of this study, where the largest proportion of COPD patients in lung cancer cases were from Group E.[52].

Exacerbations in COPD increase the risk of future exacerbations, lead to more rapid declines in lung function (particularly in smokers), and cause significant reductions in FEV1 in severe exacerbations requiring hospitalization.[51] Pathogenic features of COPD that can initiate lung tumorigenesis include chronic inflammation and excessive oxidative stress leading to DNA damage. Inflammation in the airways is increased during each COPD excacerbations, marked by an influx of inflammatory cells, especially neutrophils, into the airways.[53]

In this study, mean FVC% predicted in lung cancer patients with COPD was found to be 48.65%, which indicates a severe restrictive pattern. Restriction is characterized by a reduction in the total lung

volume, primarily due to decreased lung elasticity or issues related to the ability of the chest wall to expand. This condition can be caused by intrinsic factors (affecting lung tissue) or extrinsic factors (external to the lungs, affecting the chest wall or respiratory muscles).[22]

The restrictive findings in lung cancer patients can be influenced by tumor size, enlarged mediastinal lymph nodes, pleural effusion, pericardial effusion, metastasis to the thoracic bones, and infiltration of the mass into the chest wall, all of which are related to the stage of lung cancer. Young et al. reported that only 12% of lung cancer patients with COPD showed restrictive findings on pulmonary function tests.[28] Study by Zhai et al. in the United States found that most early-stage lung cancer patients had obstructive patterns on pulmonary function tests, with an average FVC% of 86.4%.[55] Severe restriction, as observed in this study, could be linked to the advanced stage of lung cancer of the patients.

The average ratio of FEV1/FVC in this study was 65.94%, with a standard deviation of 3.05, and the mean of FEV1 predicted value was 46.76%, with a standard deviation of 17.31%. These findings suggest that the COPD patients in this cohort had severe airflow obstruction. A population study by Kang et al. in Korea found that low FEV1/FVC ratios (less than 70%) and low FEV1 values were associated with a higher incidence of lung cancer.[11] Other studies by Young et al. and Fathana, also noted that most lung cancer patients with COPD had moderate obstruction (GOLD 2), with proportions of 50% and 64%, respectively.[25,28] Sanchez et al and Wilson et al also found that lung cancer patients with COPD had obstruction especially on GOLD 1 and GOLD 2.[49,56]

COPD patients in the early stages tend to experience a more significant reduction in FEV1 compared to those in the late stages. Decline of FEV1 is related to the progression and severity of COPD and is associated with exacerbations. The more severe the obstruction, the more frequently COPD patients experience exacerbations. This may explain low FEV1 values and severe obstruction observed in the lung cancer patients with COPD in this study, particularly those in the COPD group E (frequent exacerbations). It is noted that for every exacerbation, there is a decrease in FEV1 by approximately 50 mL, and for more than two exacerbations, FEV1 decreases by about 80 mL.[57,58] Studies by Flencher and Peto on COPD populations found that the average annual decline of FEV1 in patients with GOLD 2 was between 47–79 mL/year, and between 56–59 mL/year for GOLD 3. [58]

Several studies have identified that COPD patients with GOLD 1 and 2 stages are at a significantly higher risk of lung cancer. Research by Husebo et al., Machida et al., Wilson et al., de Torres et al., and Mannino confirmed that these stages of COPD are statistically significant risk factors for lung cancer.[44,49,50,59,60] Young et al. also found that lung cancer patients with COPD had lower values of FEV1, predicted FEV1 %, and FEV1/FVC ratio compared to a control group.[28] Lung function decline in lung cancer patients can be influenced by several factors, including age, smoking history, environmental inhalational exposures, comorbid conditions, prior lung diseases, systemic inflammation, and a history of surgeries related to the cancer. Thus, it is important to recognize that varying pulmonary function test results may be seen in lung cancer patients with COPD depending on the individual characteristics of the patient.

In this study, squamous cell carcinoma (SCC) was the most common type of lung cancer found in patients with COPD, followed by adenocarcinoma, adenosquamous carcinoma, and small-cell lung cancer (SCLC). Among patients with lung cancer and COPD, those with adenocarcinoma and adenosquamous carcinoma predominantly exhibited moderate to severe obstruction (GOLD 2-3). Meanwhile, more severe obstruction (GOLD 4) was found exclusively in those with SCLC and SCC. However, the association between the type of lung cancer and the degree of COPD obstruction was not statistically significant in this study.

A study by de Torres et al. found that adenocarcinoma was the most common type of lung cancer in COPD patients with mild to moderate obstruction (GOLD 1–2), and that mild to moderate obstruction was an independent risk factor for lung cancer development.[60] In contrast, Young et al. found that lung cancer occurrence was associated with airway obstruction regardless of the severity, and the prevalence of COPD was slightly higher in patients with SCC and SCLC.[28] Research by Lim et al. also found a significant inverse relationship between the severity of airflow obstruction and EGFR mutations or ALK rearrangements in lung cancer ($p = 0{,}001$).[61]

Other studies, such as those by Papi et al., have explored the association between obstruction and SCC, although none have specifically linked the type of lung cancer to the degree of airflow obstruction.[43] Obstruction was less commonly observed in adenocarcinoma compared to SCC, which is often associated with central tumor lesions. Central lesions tend to cause more significant airway obstruction due to their location in the larger airways, slowing expiratory airflow and allowing harmful substances like cigarette smoke to linger longer in the airways, thereby increasing the risk of lung cancer.[25,43] Furthermore, patients with adenocarcinoma have been found to have a higher prevalence of emphysema.[25]

In this study, no significant relationship was found between lung cancer staging and the degree of airway obstruction, which is consistent with the findings of Mourente-Roibas et al., who also did not observe a significant association between cancer stage and severe or very severe obstruction ($p = 0.1$). Similarly, a study by Fathana did not find a significant correlation between the degree of obstruction and bronchial compression or mediastinal lymph node (KGB) enlargement—both of which are factors considered in lung cancer staging, echoing the findings of this study.

Spirometry results in lung cancer patients often show lower FEV1 values compared to controls.[28] Obstruction of the airways can lead to a reduced FEV1. Tumors located centrally in the lungs, closer to the larger airways, can cause obstruction that impedes airflow during expiration. Fathana's study found a significant association between the degree of obstruction and tumor location in the central airways.[25] The size and location of the tumor may also play a critical role in determining the level of airway obstruction. Larger tumors or those located centrally, such as in the mainstem bronchus, are more likely to obstruct the airflow, leading to a more significant reduction in FEV1 compared to peripheral tumors. However, this study did not assess the relationship between tumor size or central location and FEV1 values.

The analysis of the relationship between cancer cell types, staging, lesion location, and the COPD population group in this study did not reveal any statistically significant associations. A study by Gurning found a significant relationship between the cancer cell type and staging with the COPD group, but this study cannot be used for comparison due to differences in the classification of COPD populations.[26] Other studies directly assessing the relationship between cancer cell type, staging, lesion location, and COPD population groups (A, B, E) have not been identified by the researcher as comparative data.

Lung cancer is a group of tumors with heterogeneity that can be described histologically, cellularly, and molecularly/genetically. Tumor heterogeneity greatly influences the character, prognosis, and management of the disease. Histological heterogeneity in lung cancer can be seen in cancers that exhibit more than one type of differentiation, such as adenosquamous carcinoma. Adenosquamous carcinoma is a combination of adenocarcinoma and squamous cell carcinoma components, each contributing to the complexity of the tumor.[62] Lung cancer heterogeneity, such as that in adenosquamous carcinoma, may affect the analysis of the relationship between cancer cell type and COPD population.

Squamous cell carcinoma is one of the most common types of lung cancer found in COPD patients, typically seen in smokers, and located centrally in the airways, leading to obstructive symptoms and more severe complications related to COPD. The COPD population group can be identified by assessing the history of COPD exacerbations and the clinical symptoms of the patient using the CAT/mMRC score. A study by Mourente-Roibas et al. found a significant relationship between CAT scores and a history of more than two COPD exacerbations per year with advanced-stage lung cancer, with p-values of 0.001 and 0.05, respectively.[27] Two other studies by Czarnecka-Chrebelska and Yu found that respiratory symptoms such as cough, increased sputum production, and dyspnea were more severe and present in a greater number of patients with lung cancer and comorbid COPD compared to those without COPD.[1,2,62]

## CONCLUSION

The prevalence of COPD among lung cancer patients at RSUP Dr. M Djamil Padang is 34.7%. Most lung cancer patients in this study were male, aged 40-59, former heavy smokers, with squamous cell carcinoma, advanced staging, and central lung lesions. In patients with both lung cancer and COPD, the majority were male, aged 60-79, with moderate obstruction (GOLD 2) and severe restriction. No significant relationship was found between cancer cell type, staging, lesion location, and the degree of COPD obstruction or the COPD population groups. These findings suggest that while COPD is common in lung cancer patients, its impact on cancer characteristics is not statistically significant.

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**Conflict of Interest**

I declare that there is no conflict of interest regarding the research and the preparation of this thesis. All funding sources and affiliations have been disclosed, and no personal, professional, or financial relationships have influenced the outcomes or findings presented in this work

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