ONLINE FIRST

This is a provisional PDF only.

Nowotwory
Journal of Oncology

ISSN: 0029-540X

e-ISSN: 2300-2115

Lung cancer in the course of chronic obstructive pulmonary disease – clinical picture in the light of current diagnostic recommendations

Authors: Robert Uliński, Marta Dąbrowska, Joanna Domagała-Kulawik

DOI: 10.5603/njo.97112

Article type: Research paper (original)

Submitted: 2023-08-28

Accepted: 2023-10-17

Published online: 2023-11-14

How to cite:

Uliński R, Dąbrowska M, Domagała-Kulawik J. Lung cancer in the course of chronic obstructive pulmonary disease – clinical picture in the light of current diagnostic recommendations. NOWOTWORY J Oncol 2023; 73 (Ahead of print).

Lung cancer in the course of chronic obstructive pulmonary disease – clinical picture in the light of current diagnostic recommendations

Robert Uliński[1], Marta Dąbrowska[1], Joanna Domagała-Kulawik[2]

1. *Department of Internal Medicine, Pulmonary Diseases and Allergy, Medical University of Warsaw, Warsaw, Poland*
2. *Maria Skłodowska-Curie Medical Academy, Institute of Clinical Sciences, Warsaw, Poland*

Introduction. Lung cancer and chronic obstructive pulmonary disease (COPD) are one of the most important causes of death. The co-existence of COPD and lung cancer has a strong influence on treatment.

Material and methods. The data were collected retrospectively from the patients diagnosed with lung tumours between 2016 and 2022. Of 982 analysed cases, the 180 patients had co-existence of primary lung cancer and COPD.

Results. There were 46.1% of women in the study group. 99.0% of patients presented a history of smoking. 46.7% patients were diagnosed with COPD during lung tumor diagnosis. The 71.1% of patients suffered from non-small cell lung cancer (NSCLC). The majority of patients had locally or metastatic lung cancer.

Conclusions. High incidences of COPD as well as lung cancer among women is striking. Almost half of patients, were diagnosed with COPD while diagnosing lung tumors. A long history of smoking is still the main factor for developing these diseases.

Key words: lung cancer, chronic obstructive pulmonary disease, spirometry, emphysema, non-small cell lung cancer

Introduction

Lung cancer was the second most commonly diagnosed cancer in 2020, with 2,2 million new cases diagnosed yearly around the world (11.4% of all cancers) and remained the leading cause of cancer related death, with an estimated 1.8 million deaths (18%) [1].The prognosis in lung cancer is very poor – only 10 to 20% of patients survive 5 years after diagnosis in most countries [1]. Chronic

obstructive pulmonary disease (COPD) is the most commonly diagnosed chronic disease of the respiratory tract. Each year COPD is diagnosed in 17.98 million patients. COPD is the third leading cause of death worldwide, with around 3.324 million deaths, which accounts for 6% of all deaths in 2019 [2]. There is 4–6 fold greater risk of developing lung cancer in patients with coexistence of COPD in comparison with smokers with normal lung function. In patients with COPD the 10 year risk of developing lung cancer is about 8.8%, while in patients with normal respiratory function only 2% [3]. Nevertheless COPD will develop in only 20% and lung cancer in 15% of cigarette smokers though death from other smoking-related causes like stroke, heart disease and emphysema often occur in smokers [2, 3]. In patients with moderate COPD, lung cancer is the cause of death in around 30% of cases and it is the most common cause of death in COPD patients [2]. The co-existence of COPD and lung cancer has very important clinical consequences and has a strong impact on diagnostic procedures and treatment. The most powerful therapeutic approach for non-small-cell lung carcinoma is surgical resection. This treatment is possible mainly in stage I, II and IIIA [1]. However, this option is associated with higher morbidity and mortality in patients with low ventilatory reserve, which is a common limiting factor for lung cancer surgery in patients with COPD [4]. Coexistence of lung cancer with COPD was described in many previous studies[5, 8-20]. Thus, we aimed to analyze the clinical characteristics of patients with coexistence of lung cancer and COPD in many aspects, taking into account current rules of diagnosis of both diseases and possible specificity of the Polish population.

Material and methods

The demographic and clinical data were collected retrospectively from a medical histories of patients hospitalized and diagnosed with lung tumors between January 1, 2016 and June 30, 2022 in a single department of lung diseases. A total of 982 patients with lung tumors were diagnosed in the years 2016–2022. Lung cancer was pathologically confirmed in 524 patients. COPD was confirmed in 180

patients (34.4%) of this group. Patients with co-existence of primary lung cancer and COPD were included in further analysis (fig. 1). The following specifics were collected from medical records: age, sex, smoking status, lung cancer histological type, tumor size, disease stage, presence of metastases, treatment plan, co-existence of other diseases, results of pulmonary function tests, and presence of emphysema in computed tomography (CT) scans. The study was approved by the Committee of Research Ethics of the Medical University of Warsaw.

The diagnosis of lung cancer was confirmed pathologically in each case. The following subtypes of lung cancer were defined: small-cell lung cancer (SCLC) and NSCLC. NSCLC was further categorized as squamous-cell carcinoma (SCC), adenocarcinoma (ADC), large-cell carcinoma or not otherwise specified (NOS), or other [6]. Cancer stage was recorded using the TNM classification 8th edition [7].

COPD was diagnosed based on an irreversible obstruction in spirometry (the FEV1%FVC less than 5 percentile after bronchodilation) in correspondence with clinical data. Spirometry values were recorded using European reference values. FVC and FEV1 were presented in liters and as a percentage of predicted values. The GOLD (Global initiative for Chronic obstructive Lung Disease) criteria were used to assign a grade of clinical severity to COPD based on FEV1 [2]. Grade 1 was defined as having an FEV1 more or equal 80%; grade 2 as more or equal 50% FEV1 and less than 80%; grade 3 as more or equal 30% FEV1 and less than 50%; and grade 4 as FEV1 less than 30%. Patients were classified as having COPD at lung cancer diagnosis if they had a previous diagnosis of COPD in their medical records or if they fulfilled the spirometric criteria during current diagnostic procedures. Patients with bronchial asthma or an obvious explanation for abnormality in spirometry, such as a central tumor or atelectasis were excluded from the study.

Patients were classified into four groups (tab I): A,B,C, and D based on the level of symptoms (measured by modified Medical Research Council dyspnea scale (mMRC) or COPD Assessment Test (CAT), and the frequency of previous exacerbations [2].

Test

The presence of emphysema at lung cancer diagnosis was determined based on information from CT scans contained in medical records. All CT scans were reviewed at diagnosis by the radiologist experienced in pulmonary diseases. When emphysema was detected visually in the CT scan the patient was classified as having emphysema.

Apart from the whole group characteristic we performed a comparison of women with men, patients with emphysema and without emphysema, patients with different types of lung cancer. Unfortunately, not all data were available thus we present in each table the number of patients with completed results of records or results of investigations.

Statistical analysis

Statistical analysis was performed using STATISTICA 13.1, StatSoft software package. Descriptive statistics were used to describe the features of all participants. Proportions were expressed as percentages, continuous variables by mean if normally distributed or by median otherwise. For groups comparison divided in terms of sex, presence of emphysema, lung cancer histological type Mann–Whitney test for continuous variables and the Fisher's exact test for categorical variables were used. A p-value of >0.05 was used as the removal criterion.

Results

Clinical characteristics

The process of qualification of patients to the study group is presented in Figure 1. The general and clinical characteristics of the 180 patients finally enrolled in the study and comparison between male and female are presented in tables II and III. The mean age of the group was 70.4 years. The largest (45.0%) age group of patients was between 65 and 75 years. There were 97 males (53.9%) and 83 females (46.1%). Ninety-nine percent of all patients presented with a history of smoking, whereas

58.7% were still active smokers, and 40.6% were ex-smokers who ceased smoking at least 1 year ago. However 1.0% of non-smokers, were exposed to cigarette smoke as passive smokers; 77.7% of the group had a history of 20–60 pack years, while 13.5% had more than 60 pack-years in medical history. Males were exposed to significantly greater amounts of cigarette smoke than females ($p = 0.001$) in Fisher exact test.

COPD characteristics

Almost half of all patients (46.7%) were diagnosed with COPD during lung tumor diagnosis. Table II lists characteristics of COPD and comparison between male and female. The distribution of patients with COPD according to severity of the airway obstruction was as follows: grade 1 (FEV1 ≥ 80%) 12 patients (3.9%); grade 2 (50% ≤ FEV1 < 80%) 74 patients (56.9%); grade 3 (30% ≤ FEV1 < 50%) 41 patients (31.6%); and grade 4 (FEV1 < 30%) 2 patients (2.3%). Emphysema was found in 55.9% of patients by CT. In terms of comorbid diseases, the number of patients with one or higher number of comorbidities was 156 (86.7%) and 88 (48.9%) had three or more comorbid diseases. In particular, hypertension was the most common disease and occurred in 106 patients (58.9%) followed by heart failure – 39 (21.7%), diabetes type II – 34 (18.9%) and coronary heart disease – 31 (17.2%), followed by other diseases. There were no significant differences between males and females in age, sex, smoking status, COPD severity, presence of emphysema and number of comorbidities.

Lung cancer characteristics

In the study group there were 71.1% of patients with NSCLC, while in 28.9% of patients SCLC was diagnosed. Table 3 lists characteristics of lung cancer in the whole group and comparison between female and male. Of NSCLCs, squamous-cell carcinoma was the most dominant histological subtype of lung cancer – 41.4%, followed by adenocarcinoma – 36.7%, NOS -14.8% and large-cell carcinoma –

7.0%. Furthermore, in terms of cancer stage, stage III dominated in the group (52.5%), followed by stage IV (38.4%), stage I (5.7%), and stage II (3.4%). Substage IIIB was the most common in the group (28.8%), followed by IVA(23.7%). Potentially resectable cancers (stage I–IIIA) consisted of only 26.6%. Comparison of cancer stage between men and women is presented in figure 2. Cancer was mainly located centrally (60.2%), in the right lung (52.8%) and in the upper lobe (48.7%). Pleural effusion occurred in a minority of patients (38.8%). Additionally, metastases to the lung were most frequent (21.7% of all metastases), followed by metastases to liver (15.3%), adrenal glands (14.4%), bones (14.4%), central nervous system (7.69%) and lymph nodes (7.69%). There were no significant differences between men and women in histological type of cancer, tumor localization, presence of pleural effusion, lung cancer stage, number and localization of metastases.

Treatment and outcome

The records on treatment were available in 67 patients (37.2% of the whole group) and on outcome in 32 patients (17.8%). Of them only 10.9% of patients underwent surgical excision of the cancer even though 26.6% of patients were potentially resectable (stage I–IIIA). The most common treatment was palliative approach (29.7%) which consisted of palliative care and palliative radiotherapy. Chemoradiotherapy was administered in 21.9% of patients. Overall outcome was positive in only 6.25% of patients, while 93.75% of patients died. There were no significant differences between men and women in treatment and outcome.

Comparison of patients with and without emphysema

When comparing patients with and without emphysema, no significant differences in demographic data, lung cancer characteristics and COPD stage were found. There were slightly more men than women in the emphysema group (tab. IV).

Comparison of patients between NSCLC and SCLC, and SCC and non-SCC

Patients with COPD and SCLC were in significantly more advanced lung cancer stages than those with NSCLC ($p < 0.05$). The treatment was significantly different with chemotherapy as the most common in SCLC group (obvious situation) and chemoradiotherapy as the most common in NSCLC group ($p < 0.05$) (tab. V). There were no significant differences between groups in terms of age, sex, smoking status, COPD severity, number of metastases, treatment and outcome. The median pack-years in both groups was equal (45). There were no significant differences in patients with COPD between two main NSCLC types - SCC and non-SCC in age, sex, smoking status, COPD severity, lung cancer stage, number of metastases, treatment and outcome.

Discussion

The coexistence of COPD and lung cancer is a known clinical observation. However, previous studies are sometimes incomplete with only selective data or performed on a small number of patients (8–21). We present a large group patients with established COPD and lung cancer with precise characteristics of both diseases performed according to current guidelines [2]. The advantage of this study is the focus on the Polish population.

The main characteristics of patients with COPD and lung cancer from other studies was shown in Table 6. In our study we reported a similar mean age of patients as in other studies as well as sex distribution, which was almost equal in men and women. It is confirmed in a few studies [9, 11, 13], but most of them show a higher proportion of men[8, 10, 14–20]. Lung cancer and COPD are the diseases generally considered as attributed to men. Our results indicate the tendency of high incidence of COPD as well as lung cancer among women which was confirmed by epidemiological studies [22]. In our study the number of women and men was similar and the features of both serious

diseases unexpectedly didn't differ in statistical analysis. However smoking exposure was significantly higher in men than in women, as in other studies [22]. In women, cigarette smoke has greater influence on developing lung cancer because the differences in lung anatomy and lung development, and also other factors such as different hormonal effects due to estrogen play an important role [23]. Our observation indicates women need to be perceived on the same level in the context of careful early diagnosis and screening programs in lung cancer as well as COPD. The common opinion among physicians should be verified.

Cigarette smoke is the main risk factor for developing COPD and lung cancer [22, 24]. In our study group almost all patients were exposed to cigarette smoke. Interestingly most of the patients are still current smokers after establishing the diagnosis despite medical advice to quit smoking. COPD often remains undiagnosed for a long time [19, 25]. In our group of patients almost 50% were diagnosed with COPD during the diagnosis of lung cancer. It is a striking number and underlines the importance of active COPD diagnosing in smokers and the need for multiple pulmonary function tests in every smoking patient over years. COPD with predominance of emphysema are known to be a poor prognostic indicator in lung cancer patients [21, 26]. In our study, more than half of patients presented COPD phenotype with emphysema. However groups with and without emphysema didn't differ statistically in clinical characteristics. COPD with emphysema-predominant phenotype decreases the 5 year survival rate up to 5.4% [26] in stage III–IV, and to 65.2% in stage I-II [27]. In our study the survival rate is low due to the high proportion of advanced cancer stages (III and IV) (Fig.2). Stage III and IV are the most common and represent almost 70% of newly diagnosed lung cancer [28], in patients with coexistence of COPD even more: 68.5-88% [11, 13, 15, 17]. A similar observation was found in our study. Some explanation of more advanced stages in cases with coexistence of COPD than in lung cancer only could be a delayed diagnosis. Patients attribute symptoms like cough and dyspnea to COPD, and vigilance for lung cancer is lower [25].

Thanks to increasing cancer vigilance and modern diagnostic methods more lung cancers are diagnosed in the stages which are potentially resectable over the years. Surgery is the most powerful treatment approach but it can be used in patients with stages I–IIIA. 20.7% of lung cancer patients undergo surgery in USA [29], while in Poland it is about 20% [30]. In the majority of cases COPD is a serious and important contraindication for surgery, especially with severe and very severe obstruction. Because of that less patients are qualified to this radical treatment [4]. In our study FEV1% of less than 30% was reported in only 3% of patients, but FEV1% 30–50% in even 30% of patients, what had a serious influence on treatment choice. Finally only 10% of our patients underwent surgical excision of lung cancer, which is not a satisfactory rate, but common among COPD patients [27].

SCLC represents about 13-15% of lung cancers [27]. Our study reports almost twice the incidence of SCLC in COPD patients. There are a few recent studies which analyze COPD with SCLC and NSCLC patients together [13, 16, 18]. The proportion of SCLC patients in these studies is as follows: 7.4%, 9.0%, 2.2%. The difference depends on the method of the selection of the study group. The credibility of our study is underlined by the examination of the full available database of consecutive patients without selection of patients. High proportion of SCLC is undoubtedly connected with heavy smoking, also among women.

Similarly to high proportion of SCLC in our group we also noted predominance of SCC in patients with NSCLC, what probably resulted from high burden of smoking history. We also compared patients with SCC versus non-SCC as SCC is much more connected with smoking than ADC. The more immunological dysfunctions and destruction of tissue present in COPD patients, favor development of SCC, for this group immunotherapy could be promising treatment option [5]. SCC in our study group was no different from the others.

The important limitation of this study is its retrospective character. Thus some data were lacking in some patients. It especially concerns lung cancer molecular characteristics, programmed death ligand 1 (PD-L1) expression, qualifications to modern therapies and patients outcome.

Conclusion

In summary, COPD in patients with lung cancer is an important and growing clinical problem. High incidences of COPD as well as lung cancer among women is striking. The clinical pattern of lung cancer coexists with COPD. Lung cancer was considered as male disease, however frequency of lung cancer and COPD in women and men is similar. Almost half of patients, cigarette smokers were diagnosed with COPD while simultaneously diagnosing lung tumors. A long history of smoking is still the main factor for developing both of these diseases. More epidemiological studies on large groups of patients are needed for a full understanding of the correlation between COPD and lung cancer.

Article information and declarations

Data availability statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics statement

This study protocol was reviewed and approved by the Committee of Research Ethics of the Medical University of Warsaw.

Author contributions

Robert Uliński – was responsible for the concept and design of the study; involved in data collection; analyzed the data; was responsible for statistical analysis; wrote the manuscript.

Marta Dąbrowska – was responsible for the concept and design of the study.

Joanna Domagała-Kulawik - was responsible for the concept and design of the study; analyzed the data; wrote the manuscript.

All authors edited and approved the final version of the manuscript.

Acknowledgments

The authors thank Iwona Kwiecień for her supervision.

Conflict of interest

None declared

Robert Uliński

Medical University of Warsaw

Pulmonary Diseases and Allergy

Department of Internal Medicine

ul. Żwirki i Wigury 61a

02-091 Warszawa, Poland

e-mail: robert.ulinski@wp.pl

Received: 28 Aug 2023

Accepted: 17 Oct 2023

References

1. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;391(10125):1023-75.

2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease report; 2020 Available online: https://goldcopd.org/ (accessed on 20 June 2023).

3. Durham AL, Adcock IM. The relationship between COPD and lung cancer. Lung Cancer. 2015;90(2):121-7.

4. Hashimoto N, Matsuzaki A, Okada Y, et al. Clinical impact of prevalence and severity of COPD on the decision-making process for therapeutic management of lung cancer patients. BMC Pulm Med. 2014;14:14.

5. Ulinski R, Kwiecien I, Domagala-Kulawik J. Lung Cancer in the Course of COPD-Emerging Problems Today. Cancers (Basel). 2022;14(15).

6. https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Thoracic-Tumours-2021 (accessed on 20 June 2023)

7. Lim W, Ridge CA, Nicholson AG, Mirsadraee S. The 8(th) lung cancer TNM classification and clinical staging system: review of the changes and clinical implications. Quant Imaging Med Surg. 2018;8(7):709-18.

8. Dos Santos CF, Braz MG, de Arruda NM, et al. DNA damage and antioxidant capacity in COPD patients with and without lung cancer. PLoS One. 2022;17(11):e0275873.

9. Sandelin M, Mindus S, Thuresson M, et al. Factors associated with lung cancer in COPD patients. Int J Chron Obstruct Pulmon Dis. 2018;13:1833-9.

10. Yi YS, Ban WH, Sohng KY. Effect of COPD on symptoms, quality of life and prognosis in patients with advanced non-small cell lung cancer. BMC Cancer. 2018;18(1):1053.

11. Media AS, Persson M, Tajhizi N, Weinreich UM. Chronic obstructive pulmonary disease and comorbidities' influence on mortality in non-small cell lung cancer patients. Acta Oncol. 2019;58(8):1102-6.

12. Ju S, Lee HR, Kim JY, et al. Impact of coexistent chronic obstructive pulmonary disease on the survival of patients with small cell lung cancer receiving chemotherapy. Thorac Cancer. 2018;9(10):1271-8.

13. Lim JU, Yeo CD, Rhee CK, et al. Comparison of clinical characteristics and overall survival between spirometrically diagnosed chronic obstructive pulmonary disease (COPD) and non-COPD never-smoking stage I-IV non-small cell lung cancer patients. Int J Chron Obstruct Pulmon Dis. 2019;14:929-38.

14. Takegahara K, Usuda J, Inoue T, et al. Preoperative management using inhalation therapy for pulmonary complications in lung cancer patients with chronic obstructive pulmonary disease. Gen Thorac Cardiovasc Surg. 2017;65(7):388-91.

15. Omote N, Hashimoto N, Morise M, et al. Impact of mild to moderate COPD on feasibility and prognosis in non-small cell lung cancer patients who received chemotherapy. Int J Chron Obstruct Pulmon Dis. 2017;12:3541-7.

16. Wang W, Dou S, Dong W, et al. Impact of COPD on prognosis of lung cancer: from a perspective on disease heterogeneity. Int J Chron Obstruct Pulmon Dis. 2018;13:3767-76.

17. Yuan L, Guo T, Hu C, et al. Clinical characteristics and gene mutation profiles of chronic obstructive pulmonary disease in non-small cell lung cancer. Front Oncol. 2022;12:946881.

18. Suzuki Y, Kitaguchi Y, Ueno F, et al. Associations Between Morphological Phenotypes of COPD and Clinical Characteristics in Surgically Resected Patients with COPD and Concomitant Lung Cancer. Int J Chron Obstruct Pulmon Dis. 2022;17:1443-52.

19. Jo H, Park S, Kim NE, et al. Impact of COPD Treatment on Survival in Patients with Advanced Non-Small Cell Lung Cancer. J Clin Med. 2022;11(9).

20. Hu XL, Xu ST, Wang XC, et al. Status of coexisting chronic obstructive pulmonary disease and its clinicopathological features in patients undergoing lung cancer surgery: a cross-sectional study of 3,006 cases. J Thorac Dis. 2018;10(4):2403-11.

21. Gao YH, Guan WJ, Liu Q, et al. Impact of COPD and emphysema on survival of patients with lung cancer: A meta-analysis of observational studies. Respirology. 2016;21(2):269-79.

22. O'Keeffe LM, Taylor G, Huxley RR, et al. Smoking as a risk factor for lung cancer in women and men: a systematic review and meta-analysis. BMJ Open. 2018;8(10):e021611.

23. Orzolek I, Sobieraj J, Domagala-Kulawik J. Estrogens, Cancer and Immunity. Cancers (Basel). 2022;14(9).

24. Malhotra J, Malvezzi M, Negri E, et al. Risk factors for lung cancer worldwide. Eur Respir J. 2016;48(3):889-902.

25. Dai J, He Y, Maneenil K, Liu H, Liu M, Guo Q, et al. Timing of chronic obstructive pulmonary disease diagnosis in lung cancer prognosis: a clinical and genomic-based study. Transl Lung Cancer Res. 2021;10(3):1209-20.

26. Ajimizu H, Ozasa H, Sato S, et al. Survival impact of treatment for chronic obstructive pulmonary disease in patients with advanced non-small-cell lung cancer. Sci Rep. 2021;11(1):23677.

27. Wang Q, Gumus ZH, Colarossi C, et al. SCLC: Epidemiology, Risk Factors, Genetic Susceptibility, Molecular Pathology, Screening, and Early Detection. J Thorac Oncol. 2023;18(1):31-46.

28. Guibert N, Barlesi F, Descourt R, et al. Characteristics and Outcomes of Patients with Lung Cancer Harboring Multiple Molecular Alterations: Results from the IFCT Study Biomarkers France. J Thorac Oncol. 2017;12(6):963-73.

29. New Report: Lung Cancer Survival Has Increased, but Remains Significantly Lower for People of Color | American Lung Association https://www.lung.org/media/press-releases/solc-2021 (accessed on 20 June 2023).

30. Adamek M, Biernat W, Chorostowska-Wynimko J, et al. Lung Cancer in Poland. J Thorac Oncol. 2020;15(8):1271-6.

Table I. GOLD severity staging

Patients		**Symptoms**	
		CAT 0–9 **mMRC < 2**	**CAT 10–40** **mMRC ≥ 2**
exacerbations (in past 12 months)	no hospital admission or ⩽1 outpatient treatment	group A	group B
	≥1 hospital admission or ≥2 outpatient treatment	group C	group D

mMRC – measured by modified Medical Research Council dyspnea scale; CAT – COPD assessment

Table II. Demographic characteristics and features of COPD in investigated group. Comparison of female with male using Mann–Whittney test for continuous variables and the Fisher's exact test for categorical variables. Only significant differences were shown ($p < 0.05$). Data are given as number and percentages or mean ± standard deviation

Patients	**All**	**Female**	**Male**	**p-value**
number of patients	180	83 (46.1%)	97 (53.9%)	

age	70.4 (8.6)	70.0 (7.7)	70.7 (9.3)	
≤55 years old	7 (3.9%)	2 (2.4%)	5 (5.2%)	
56 ≥ 65	43 (23.9%)	19 (22.9%)	24 (24.7%)	
66 ≥ 75	83 (46.1%)	44 (53.0%)	39 (40.2%)	
76 ≥ 85	37 (20.6%)	17 (20.5%)	20 (20.6%)	
>85	10 (5.6%)	1 (1.2%)	9 (9.3%)	
smoking status (n = 155)				
active	91 (58.7%)	42 (57.5%)	49 (59.8%)	
former	63 (40.7%)	31 (42.5%)	32 (39.0%)	
never	1 (0.6%)	0 (0.0%)	1 (1.2%)	
no data (25: 16.1%)				
exposure – pack, years (n = 147)				
0 < 20	12 (8.2%)	10 (14.5%)	2 (2.6%)	p = 0.001
21 < 40	58 (39.5%)	33 (47.8%)	25 (32.1%)	
41 < 60	57 (38.8%)	22 (31.8%)	35 (44.9%)	
61 < 80	6 (4.0%)	3 (4.4%)	3 (3.8%)	
81 < 100	10 (6.8%)	0 (0.0%)	10 (12.8%)	
<100	4 (2.7%)	1 (1.5%)	3 (3.8%)	
no data (33: 18.3%)				
COPD diagnosed during investigation of lung tumor (n = 180)				
yes	84 (46.7%)	37 (44.6%)	47 (48.5%)	
no	96 (53.3%)	46 (55.4%)	50 (51.5%)	
COPD severity (Fev1 Range) n=130				
grade 1 (>80%)	13 (10.0%)	8 (12.9%)	5 (7.4%)	
grade 2 (50–80%)	73 (56.2%)	29 (46.8%)	44 (64.7%)	
grade 3 (30–50%)	41 (31.5%)	24 (38.7%)	17 (25.0%)	
grade 4 (<30%)	3 (2.3%)	1 (1.6%)	2 (2.9%)	
no data (30: 16.67%)				
emphysema (n = 138)				
yes	61 (44.2%)	35 (52.2%)	26 (36.6%)	p = 0.006
no	77 (55.8%)	32 (47.8%)	45 (63.4%)	
no data (42: 23.3%)				
GOLD (n = 59)				
A	20 (33.9%)	9 (32.1%)	11 (35.5%)	
B	27 (45.7%)	13 (46.4%)	14 (45.2%)	
C	3 (5.1%)	2 (7.1%)	1 (3.2%)	
D	9 (15.3%)	4 (14.3%)	5 (16.1%)	
no data (121: 67.2%)				
number of comorbidities (n = 180)				
0	24 (13.3%)	11 (13.3%)	13 (13.4%)	
1	38 (21.1%)	20 (24.1%)	18 (18.6%)	
2	30 (16.7%)	12(14.5%)	18 (18.6%)	
3	37 (20.6%)	21 (25.3%)	16 (16.4%)	

4	22 (12.2%)	8 (9.6%)	14 (14.4%)	
5	11 (6.1%)	5 (6.0%)	6 (6.2%)	
6	7 (3.9%)	1 (1.2%)	6 (6.2%)	
7	6 (3.3%)	4 (4.8%)	2 (2.0%)	
8	2 (1.1%)	0 (0.0%)	2(2.1%)	
9	2 (1.1%)	0 (0.0%)	2(2.1%)	
10	1 (0.6%)	1 (1.2%)	0(0.0%)	

p-values are given for differences between female and male groups; n – number

Table III. Lung cancer characteristics in investigated group. Comparison of female with male using Mann–Whittney test for continuous variables and the Fisher's exact test for categorical variables. Data are given as number and percentages

Lung cancer	**All patients**	**Female**	**Male**	**p-value**
histological types	n = 180	83 (46.1%)	97 (53.9%)	
NSCLC	128 (71,1%)	55 (66.3%)	73 (75.3%)	
SCLC	52 (28,9%)	28 (33.7%)	24 (24.7%)	
histological subtypes of NSCLC				
adenocarcinoma	47 (36.7%)	22 (40.0%)	25 (34.2%)	
squamous cell carcinoma	53 (41.4%)	20 (36.4%)	33 (45.2%)	
not otherwise specified (NOS) NSCLS	19 (14.9%)	7 (12.7%)	12 (16.5%)	
other	9 (7.0%)	6 (10.9%)	3 (4.1%)	
central/peripheral tumor (n = 176)				
central	106 (60,2%)	51 (63.0%)	55 (57.9%)	
peripheral	70 (39,8%)	30 (37.0%)	40 (42.1%)	
no data (4: 2.2%)				
lung right/left (n = 165)				
right	86 (52,1%)	36 (46.2%)	50 (57.5%)	
left	75 (45,5%)	40 (51.3%)	35 (40.2%)	
right and left	4 (2.4%)	2 (2.5%)	2 (2.3%)	
no data (25: 13.89%)				
lobe (n = 83)				
superior	40 (48.2%)	18 (48.7%)	22 (47.8%)	
inferior	35 (42.2%)	16 (43.2%)	19 (41.3%)	
middle	8 (9.6%)	3 (8.1%)	5 (10.9%)	
no data (97: 53.9%)				
pleural effusion (n = 124)				
yes	62 (50.0%)	29 (51.8%)	33 (48.5%)	
n	62 (50.0%)	27 (48.2%)	35 (51.5%)	
no data (31.1%)				

p-values are given for differences between female and male groups; n – number; NSCLC – non-small cell lung cancer; SCLC – small cell lung

Table IV. Lung cancer in patients with COPD- comparison of patients with emphysema with without emphysema using Mann–Whittney test for continuous variables and the Fisher's exact test for categorical variables. Data are given as number and percentages or mean ± standard deviation

Patients and lung cancer	**With emphysema**	**Without emphysema**	**p-value**
n = 138	77	61	
age	70.8 (8.2)	70.3 (7.9)	
female	32 (41.6%)	35 (57.4%)	p = 0.06
male	45 (58.4%)	26 (42.6%)	
smoking status (n = 122)			
active	39 (58.2%)	32 (58.2%)	
former	27 (40.3%)	23 (41.8%)	
never	1 (1.5%)	0 (0.0%)	
no data (16: 11.6%)			
COPD severity (Fev1 range) n = 99			
grade 1 (>80%)	8 (13.8%)	3 (7.3%)	
grade 2 (50–80%)	30 (51.7%)	25 (61.0%)	
grade 3 (30–50%)	19 (32.8%)	13 (31.7%)	
grade 4 (<30%)	1 (1.7%)	0 (0%)	
no data (39: 28.3%)			
histological types of lung cancer (n = 138)			
NSCLC	53 (68.8%)	43 (70.5%)	
SCLC	24 (31.2%)	18 (29.5%)	
histological subtypes of NSCLC			
adenocarcinoma	19 (35.8%)	13 (30.2%)	
squamous cell carcinoma	18 (34.0%)	22 (51.2%)	
not otherwise specified (NOS) NSCLS	10 (18.9%)	7 (16.3%)	
other	6 (11.3%)	1 (2.3%)	
stage (n = 136)	76 (55.9%)	60 (44.1%)	
1A	0 (0%)	5 (8.3%)	
1B	1 (1.3%)	1 (1.7%)	
2A	2 (2.7%)	0.(0%)	
2B	1 (1.3%)	1 (1.6%)	
3A	18 (23.7%)	6 (10.00%)	
3B	18 (23.7%)	15 (25.00%)	
3C	5 (6.6%)	3 (5.00%)	
4A	18 (23.7%)	20 (33.3%)	

4B	13 (17.1%)	9 (15.00%)	
no data (2: 1.5%)			
I–IIIA	19 (24.7%)	12 (19.7%)	
IIIB–IVB	58 (75.3%)	49 (80.3%)	

p-values are given for differences between with emphysema and without emphysema groups; n – number; NSCLC – non-small cell lung cancer; SCLC – small cell lung cancer

Table V. COPD in two main types of lung cancer- comparison of SCLC and NSCLC using Mann–Whittney test for continuous variables and the Fisher's exact test for categorical variables. Data are given as number and percentages or mean ± standard deviation

Patients	**SCLC**	**NSCLC**	**p-value**
n = 180	52	126	
age	70.6 (8.2)	70.2 (8.9)	
female	28 (53.8%)	54 (42.1%)	
male	24 (46.2%)	73 (57.9%)	
smoking status (n = 153)	45	108	
active	28 (62.2%)	63 (57.4%)	
former	17 (37.8%)	45 (41.7%)	
never	0 (0.0%)	1 (0.9%)	
no data (27: 15.0%)			
COPD severity – Fev1 range (n = 128)			
grade 1 (>80%)	2 (5.0%)	10 (11.4%)	
grade 2 (50–80%)	21 (52.5%)	51 (57.9%)	
grade 3 (30–50%)	16 (40.0%)	25 (28.4%)	
grade 4 (<30%)	1 (2.5%)	2 (2.3%)	
no data (52: 28.9%)			
stage (n = 172)			
1A	0 (0.0%)	7 (5.7%)	
1B	1 (2.0%)	1 (0.8%)	
2A	0 (0.0%)	3 (2.5%)	
2B	0 (0.0%)	3 (2.5%)	
3A	6 (12.0%)	24 (19.7%)	
3B	14 (28.0%)	36 (29.5%)	
3C	5 (10.0%)	6 (4.9%)	
4A	13 (26.0%)	30 (24.6%)	
4B	11 (22.0%)	12 (9.8%)	
no data (8: 4.4%)			
n = 175			
I–IIIA	7 (13.7%)	35 (28.2%)	p = 0.041
IIIB–IVC	44 (86.3%)	89 (71.7%)	

no data (5: 2.8%)			
number of metastases (n = 68)			
1	11 (44.0%)	26 (60.5%)	
2	7 (28.0%)	10 (23.2%)	
3	6 (24.0%)	3 (7.0%)	
4	1 (4.0%)	4 (9.3%)	
no data (112: 62.2%)			

p-values are given for differences between SCLC and NSCLC groups; n – number; NSCLC – non-small cell lung cancer; SCLC – small cell lung cancer

Table VI. Demographic data, lung cancer and COPD characteristics from articles published in years 2017–2023 focused on patients with coexistence of lung cancer and COPD. Data are given as number and percentages or mean ± standard deviation

Name, year	Patients number	M/F	Age [years]	Smoking history N/F/C (pack years)	SCLC/ NSCLC	ADC/ SCC/ other	STAGE I/II/III/IV	GOLD 1/2/3/4	Main finding
Dos Santos 2022[15]	18	12/6	70.2 ± 9.2	69 (50–106)	no data	no data	no data	4/7/7/0	COPD with lung cancer was associated with elevated DNA damage in peripheral lymphocytes
Sandelin 2018[16]	594	291/303	68.9 ± 8.5	no data	no data	no data	no data	no data	asthma diagnosis and use of inhaled corticosteroids were independently related to decreased risk of lung cancer in COPD patients, while the use of acetylsalicylic acid was associated with an increased risk
Yi 2018[17]	170	154/16	70.4 ± 8.9	ND/18/152 ND/10.6%/89.4%	0/100%	60/94	0/0/70/ 100	35/103/24/8	high prevalence of COPD among patients with advanced NSCLC, COPD patients complained about various symptoms had diminished quality of life
Schwan Media 2018[18]	329	191/138	69.4 ± 9.0	7/121/195 2.2%/37.5%/64.0% (40.6 ± 21.1)	0/100%	126/136	11.2%/20.5%/36.0%/32.5%	no data	COPD nor other common comorbidities are significantly associated with higher mortality in NSCLC patients
Sunmi 2018[19]	57	52/5	67.5 ± 7.4	4/22/31 7.0%/38.6%/54.4% (49.5 ± 24.2)	100%/0	-	24/33 LD/ED	19/21/16/4	although over half of the SCLC patients receiving chemotherapy had COPD, coexisting COPD had no impact on the survival of patients with SCLC
Lim 2019[20]	68	30/38	75.2 (48–89)	no data	7.4%/92.6%	no data	15/5/9/39	FEV1% 78.4% ± 20.2	never-smoker NSCLC patients with COPD had shorter OS times, compared to non-COPD never-smoker NSCLC patients
Takegahara	108	86/22	69.3 (46–84)	ND/63/45 ND/55.6%/44.	0/100%	53/38	73/23/12/0	no data	for lung cancer patients with COPD, preoperative management using LABA or LAMA bronchodilators and

ADC – adenocarcinoma; COPD – chronic obstructive pulmonary disease; CT – computed tomography; C – current; DNA – deoxyribonucleic acid; F – female; F – former; GOLD – Global Initiative for Chronic Obstructive Lung Disease; LABA – long-acting beta agonists; LAMA – long-acting muscarinic antagonist; M – male; N – never; ND – no data; NSCLC – non-small cell lung cancer; SCC – squamous cell carcinoma; SCLC – small cell lung cancer

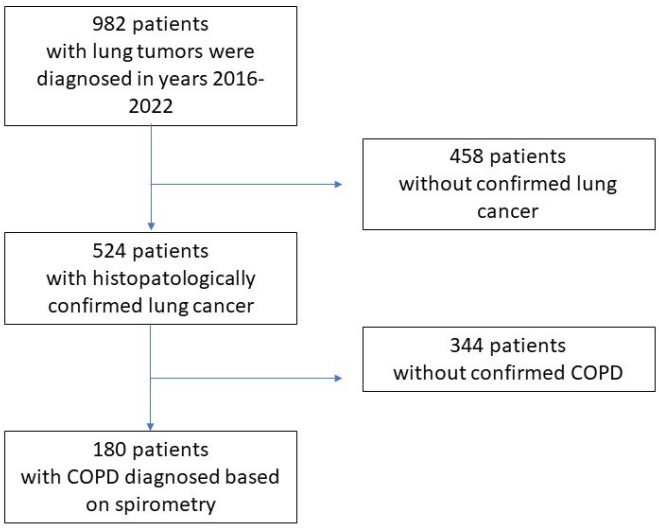

Figure 1. Patients selection to study group and reasons for patients exclusion

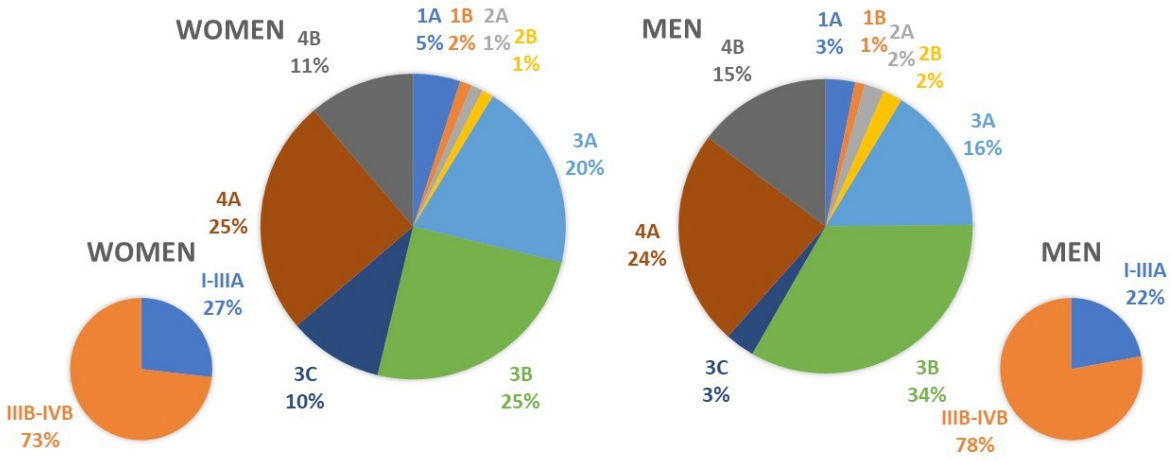

Figure 2. Lung cancer stages in patients with lung cancer in the course of COPD – comparison of men and women