УДК 616.24-006.6:616.23/.24-002.2]-036.8
https://doi.org/10.20538/1682-0363-2022-3-41-49

Lung cancer in patients with COPD and factors associated with reduced survival

Dobner S.Yu.[1], Fedosenko S.V.[2], Rodionov E.O.[1, 2], Yarovoy N.D.[3], Petrov V.A.[2], Tuzikov S.A.[1, 2], Starovoitova E.A.[2], Samykina I.A.[1]

[1] Cancer Research Institute, Tomsk National Research Medical Center (NRMC), Russian Academy of Sciences
5, Kooperativny Str., Tomsk, 634009, Russian Federation

[2] Siberian State Medical University
2, Moscow Trakt, Tomsk, 634050, Russian Federation

[3] Tomsk Regional Oncology Dispensary
115, Lenina Av., Tomsk, 634009, Russian Federation

ABSTRACT

Background. A combination of different types of lung cancer and chronic obstructive pulmonary disease (COPD) is very common. COPD, accompanied by ventilation disorders and, often, respiratory failure, is a significant additional risk factor for mortality in these patients. Identification of risk factors for mortality in patients with lung cancer and COPD can potentially be associated with better long-term outcomes.

Materials and methods. Using a Cox regression model based on information about the outcome of the disease and life expectancy after treatment initiation, a survival analysis was performed with an assessment of the contribution of various clinical and anamnestic factors for a group of 118 COPD patients with primary diagnosed lung cancer. These patients received treatment at the Cancer Research Institute in Tomsk in 2013–2019.

Results. The study included 118 patients (87.3% men and 12.7% women). Among them, 77.97% of patients were active or former smokers with smoking index (SI) ≥ 10 pack-years, and 22% of patients had never smoked or had SI < 10 pack-years but had other risk factors for COPD. Peripheral lung cancer was detected in 45.8% of cases. Squamous cell carcinoma was noted in 54.2% of cases, adenocarcinoma – in 34.7%, large cell carcinoma – in 1.7%, small cell carcinoma – in 5.9%, and carcinoid tumors – in 2.5% of cases. Patients were characterized by varying degrees of severity of ventilation disorders in accordance with the GOLD classification: stage 1 was observed in 44% of patients, stage 2 – in 38.1 % of patients, stage 3 – in 16.9 % of patients, and stage 4 – in one patient. Three-year mortality was 28.12%.

Conclusion. According to the results of the Cox regression analysis, factors that significantly reduced the survival rate of patients with lung cancer in combination with COPD were more severe stages in terms of the size of the primary tumor and its localization, the prevalence of metastasis (according to TNM classification), more severe dyspnea (mMRC scale), lower oxygen saturation values, atelectasis, and episodes of pneumonia, including paracancrotic pneumonia, over the previous 12 months. The presence of certain types of metastases, such as metastatic lesions of the pleura, adrenal glands, distant non-regional lymph nodes, and bones should also be noted as negative factors for survival. It is worth noting that surgical treatment of the primary tumor was associated with an increase in the survival rate in patients with lung cancer in combination with COPD.

Keywords: lung cancer, chronic obstructive pulmonary disease, COPD, patient survival

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The authors state that they received no funding for the study.

✉ *Dobner Svetlana Yu.,* dobnersv@gmail.com

Conformity with the principles of ethics. All patients signed an informed consent to participate in the study. The study was approved by the local Ethics Committee at the Cancer Research Institute of Tomsk NRMC (Protocol No. 10 of 26.09.2016).

For citation: Dobner S.Yu., Fedosenko S.V., Rodionov E.O., Yarovoy N.D., Petrov V.A., Tuzikov S.A., Starovoitova E.A., Samykina I.A. Lung cancer in patients with COPD and factors associated with reduced survival. *Bulletin of Siberian Medicine.* 2022;21(3):41–49. https://doi.org/10.20538/1682-0363-2022-3-41-49.

Рак легкого у больных ХОБЛ и факторы, ассоциированные со снижением их выживаемости

Добнер С.Ю.[1], Федосенко С.В.[2], Родионов Е.О.[1, 2], Яровой Н.Д.[3], Петров В.А.[2], Тузиков С.А.[1, 2], Старовойтова Е.А.[2], Самыкина И.А.[1]

[1] Научно-исследовательский институт (НИИ) онкологии, Томский национальный исследовательский медицинский центр (НИМЦ) Российской академии наук
Россия, 634009, Томск, пер. Кооперативный, 5

[2] Сибирский государственный медицинский университет (СибГМУ)
Россия, 634050, Томск, Московский тракт, 2

[3] Томский областной онкологический диспансер (ТООД)
Россия, 634009, Томск, пр. Ленина, 115

РЕЗЮМЕ

Актуальность. Сочетание различных форм рака легкого и хронической обструктивной болезни легких (ХОБЛ) встречается очень часто. ХОБЛ, сопровождающаяся вентиляционными нарушениями и нередко дыхательной недостаточностью, является существенным дополнительным фактором риска летальности у этих больных. Выявление факторов риска смертности у пациентов с раком легкого и ХОБЛ потенциально может быть связано с лучшими отдаленными результатами.

Материалы и методы. С помощью регрессии Кокса, основанной на информации об исходе заболевания и продолжительности жизни после начала лечения, проведен анализ выживаемости с оценкой вклада различных клинико-анамнестических факторов для группы из 118 больных ХОБЛ с первично диагностированным раком легкого. Эти больные получали лечение в НИИ онкологии в Томске в период с 2013 по 2019 г.

Результаты. В исследование включены 118 пациентов (87,3% мужчин и 12,7% женщин). Среди них 77,97% пациентов были активными или бывшими курильщиками с индексом курильщика (SPI) ≥ 10 пачек/год, а 22% никогда не курили или с SPI < 10 пачек/лет, но имели другие факторы риска развития ХОБЛ. Периферический рак легкого выявлен в 45,8% случаев. Плоскоклеточный рак отмечен в 54,2% случаев, аденокарцинома – у 34,7% больных, крупноклеточный рак – у 1,7%, нейроэндокринный мелкоклеточный рак – у 5,9%, карциноидные опухоли – у 2,5% пациентов. Больные характеризовались различной степенью выраженности вентиляционных нарушений по классификации GOLD: первая стадия ХОБЛ наблюдалась у 44% больных, вторая – у 38,1%, третья – у 16,9%, четвертая стадия – у одного из пациентов. Трехлетняя выживаемость составила 28,12%.

Заключение. По результатам анализа методом регрессии Кокса в качестве факторов, значительно снижающих выживаемость больных раком легкого в сочетании с ХОБЛ, необходимо выделить более распространенные стадии по размеру первичной опухоли и ее локализации, а также выраженность метастазирования (по классификации TNM), более значительную одышку (по шкале mMRC), более низкое значение сатурации кислорода, наличие ателектаза легкого, эпизодов пневмонии, в том числе параканкрозной, в предшествующие 12 мес. В качестве негативных факторов выживания следует также отметить наличие некоторых видов метастазов, таких как метастатическое поражение плевры, надпочечников, отдаленных нерегиональных лимфатических узлов, костей скелета. Отметим, что хирургическое лечение первичной опухоли было связано с увеличением выживаемости больных раком легкого в сочетании с ХОБЛ.

Ключевые слова: рак легкого, хроническая обструктивная болезнь легких, ХОБЛ, выживаемость больных

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты подписали информированное согласие на проведение исследования. Исследование одобрено локальным этическим комитетом НИИ онкологии Томского НИМЦ (протокол № 10 от 26.09.2016).

Для цитирования: Добнер С.Ю., Федосенко С.В., Родионов Е.О., Яровой Н.Д., Петров В.А., Тузиков С.А., Старовойтова Е.А., Самыкина И.А. Рак легкого у больных ХОБЛ и факторы, ассоциированные со снижением их выживаемости. *Бюллетень сибирской медицины.* 2022;21(3):41–49. https://doi.org/10.20538/1682-0363-2022-3-41-49.

INTRODUCTION

Lung cancer (LC) is a malignant neoplasm (MN) characterized by a high mortality rate. Every year in Russia, more than 60,000 people die from it, 80% of them are men. According to statistics, after the initial diagnosis, one-year mortality reaches more than 50%, and the average five-year survival rate, even with adequate treatment, is about 10–16% [1].

Survival in LC depends on many factors, such as the stage of the disease, tumor morphology, patient's age, concomitant chronic pathology, and treatment strategy [2].

Almost 2/3 of men and half of women with newly diagnosed primary LC have signs of airway obstruction [3]. J.P. De-Torres et al. examined outpatients in the United States and Spain (n = 2,125) and developed criteria to predict LC. These criteria include age over 60 years, body mass index < 25 kg / m^2, smoking index (SI) > 60 pack – years, emphysema on CT scan, and signs of chronic obstructive pulmonary disease (COPD) according to spirometry [3]. Thus, airflow limitation and emphysema, which are typical of COPD, should probably be considered as potential risk factors for the development of LC.

LC and COPD are comorbidities with a similar pathogenetic mechanism underlying the development of pathology in the bronchi and lung parenchyma, caused by systematic damaging effects of smoking, radon, asbestos, and pollutants, combined with genetic susceptibility [4–6].

Currently, COPD is considered an independent risk factor for LC [7]. According to epidemiological data, the incidence of LC in smokers with COPD is 4–5 times higher than in smokers without COPD [7, 8]. R. P. Young et al. showed that decreasing forced expiratory volume in 1 second (FEV1) in COPD increased the risk of LC by 4 times compared with smokers with normal lung function, regardless of their age and smoking history [9]. J. Murakami et al. noted that the cancer that occurs with emphysema is more aggressive and has a higher postoperative recurrence [9].

Understanding of the general mechanisms of LC and COPD development suggests that timely diagnosis and long-term effective treatment of chronic inflammation in the respiratory tract associated with bronchial obstruction in patients with COPD in combination with elimination of altering factors can probably prevent and reduce the risk of developing LC [6, 10].

It is COPD that typically leads to pulmonary function decline. It determines the frequency of complications and the risk of death in cancer patients. According to R. Kondo et al. (2011), the five-year survival rate in LC patients with and without COPD was 38% and 54 %, respectively. At the same time, the mortality rate in patients with and without COPD was 63% and 45%, respectively [7].

COPD is a significant perioperative mortality predictor and the most common cause of postoperative pulmonary complications and respiratory failure due to severe respiratory dysfunction. These concerns are the main reason for refusing radical surgery in some patients, since severe COPD and significant concomitant / comorbid pathology in aged patients make it very difficult to conduct mechanical ventilation and manage the early postoperative period, which is associated with an increased risk of mortality in this patient group [10, 11].

The aim of this retrospective study was to research the initial clinical and anamnestic data of patients with COPD and primary LC, assess the disease outcome and life expectancy during treatment, and establish factors associated with survival and mortality in this group of comorbid patients.

MATERIALS AND METHODS

We analyzed demographic, clinical, and anamnestic data from the health records of 118 patients with COPD who underwent examination and treatment (surgery, radiation therapy, chemotherapy or combined) for newly diagnosed MN in the bronchi and lung at the Cancer Research Institute (Tomsk National Research Medical Center, Russian Academy of Sciences) in 2013–2019.

Statistical processing of the obtained data was carried out using Statistica 10.0 and StatCalc 6.0 software packages. Qualitative data were presented as absolute or relative (%) frequencies, quantitative data were shown as $X \pm x$, where X is the arithmetic mean and x is the error of the mean. Results were considered statistically significant at $p < 0.05$. We conducted the survival analysis for these patients and assessed the contribution of various clinical and anamnestic factors using the Cox regression analysis based on information about the disease outcome and life expectancy after treatment initiation (within the assessment of one- and three-year survival).

RESULTS AND DISCUSSION

Currently, there are more men among patients with LC and / or COPD than women, and the incidence increases with age [2, 11]. According to our retrospective study, among 118 patients with COPD and newly diagnosed primary LC, 87.3 % of patients were male and 12.7 % were female. At the initiation of treatment, the age of patients was 63.63 ± 7.25 years, they were diagnosed with LC at the age of 61.92 ± 7.26 years.

It is known that in 90–95% of COPD cases, the cause of the disease is smoking. Smoking also has a carcinogenic effect on lung tissue in 85–95% of LC cases in men and in 65–80% of LC cases in women [6–8]. In the study group, 13 patients (11.1 %) used to smoke and 79 patients (66.9 %) smoked at the beginning of the follow-up period in the retrospective analysis with SI > 10 pack – years. In 26 patients (22 %), SI was < 10 pack – years, however, they had other COPD risk factors: exposure to occupational hazards (dust, chemical agents, acid, and alkali vapors) and industrial pollutants (SO_2, NO_2, furnace smoke, etc.). The average smoking history in the study group was 33.45 ± 13.58 years, and SI was 33.35 ± 14.53 pack – years. The longest smoking history was 55 years, and the maximum SI in the heaviest smokers was 60 pack – years. Peripheral LC was detected in 45.8 % of cases, central LC — in 44.2 % of cases.

We classified patients in accordance with the 7th edition of the International Classification of Malignant Neoplasms, TNM (2011) [12]. According to the spread of the primary tumor (TNM-T), T1, T2, T3, and T4 stages were diagnosed in 19%, 18.7%, 43.2%, and 22% of patients, respectively. Regional lymph node metastases were diagnosed in 67% of patients (N1, N2, and N3 in 22.9%, 34.7%, and 9.3%, respectively). Distant metastases (M1) were diagnosed in 22% of patients in the study.

Thus, metastatic pleurisy was diagnosed in 11.9 % of patients. Unilateral or contralateral pulmonary metastases were detected only in 5.9% of patients. Extrapulmonary metastases were detected in the bones (9.3% of patients), liver (5.9%), brain (3.4%), adrenal glands (6.8%), and non-regional lymph nodes (16%). Aggressive invasive tumor growth that invaded adjacent organs and tissues and great vessels was determined in 48% of patients.

The results obtained indicate that patients with neglected LC (locally advanced and metastatic) prevailed, which can be explained by the long-term low-symptom disease, masking its manifestations with symptoms and exacerbations of COPD in this group of patients, as well as a delay in seeking medical care. According to A.D.Kaprin et al., 68.7% of patients with LC were diagnosed at stages III-IV of the disease, of them, metastasis was determined in 40.8% of cases [1, 10, 13].

According to statistical data, LC most often develops in the right lung (56 %). Moreover, the upper lobe, the lower lobe, and the middle lobe of the lung are affected in 60%, 30%, and 10% of cases, respectively [1, 13]. We obtained similar results in the group of patients with combined COPD and LC. Thus, MN of the right lung was diagnosed in 64.4% of patients, and MN of the left lung – in 33.9% of patients. Only two patients (1.7%) were diagnosed with metachronous LC. Lesions of the upper lobe

were detected most often (in 57.6% of patients). An isolated lesion of the lower lobe was diagnosed in 24.6% of patients. The middle lobe of the right lung was affected in 8.5% of patients. Combined lesions located in two or three lobes were detected in 9.3% of patients.

According to the Russian and foreign literature, adenocarcinoma is the most common type of non-small cell lung cancer, which is diagnosed in about 40% of cases. Squamous cell lung carcinoma (epidermoid cancer) accounts for 25–30% of all LC cases and is detected more often in smokers [6, 7]. This may explain the fact that in the examined patients with combined LC and COPD, the vast majority of whom were heavy smokers, squamous cell LC was the dominant histologic pattern (identified in 54.4% of cases). Adenocarcinoma was detected in 35.5% of patients. Large cell LC (1.7%), small cell LC (5.9%), and carcinoid tumors (2.5%) were significantly less common.

It should be noted that patients with combined LC and COPD often have comorbidities that prevent from radical treatment (due to concomitant coronary artery disease, essential hypertension, cerebral atherosclerosis, peripheral arterial disease, gastric ulcer, and osteoporosis) [13, 14]. In addition to LC and COPD, concomitant pathology as a combination of several diseases was often noted in most of the patients examined. Arterial hypertension (66.9%), coronary artery disease (48.3%), gastric and / or duodenal ulcer (active disease or history in 28% of patients) were the most common. Obesity of varying severity was detected in 16.9% of patients, diabetes mellitus was revealed in 6.8% of cases. Concomitant chronic lung pathology other than COPD, but including asthma and bronchiectasis, was noted in 7.6% of patients. Some patients had history of myocardial infarction and stroke: 13.6% and 10.2%, respectively.

Based on the medical records, we noted variability in lung ventilation disorders caused by COPD in the patients. Mild and moderate bronchial obstruction were the most common, which could be due to the fact that patients without severe decompensated underlying diseases and concomitant pathology were primarily selected for treatment. Mild airflow limitation (FEV1 salbutamol challenge test [post-FEV1] > 80%) was detected in 44% of the patients, moderate (post-FEV1 50–80%) – in 38.1% of the patients, severe (post-FEV1 30–50%) – in 16.9% of the patients. Only one patient was diagnosed with very severe COPD (post-FEV1 < 30%). Baseline peripheral oxygen saturation in the blood in the patients was 96.86 ± 1.25%.

Based on the CT data, emphysema, chronic bronchitis, and a mixed phenotype of COPD were determined in 55.9%, 13.6%, and 30.5% of the cases, respectively. Within a year preceding the study, 72.9% of the patients had at least one episode of COPD exacerbation, and 53.4% of the patients had ≥ 1 episode of pneumonia, including paracancrotic pneumonia (in 29.7% of the patients). Antibiotic therapy (≥ 1 time in 12 months)for respiratory infections was required in 65.3% of the patients.

The absence of regular maintenance therapy for COPD remains a significant challenge in the efforts against the disease progression. It is especially typical of patients with mild symptoms [6, 11]. According to our study results, only 29.7 % of the patients received inhaled therapy for COPD routinely or episodically. Only 6.8% of the patients received long-acting bronchodilators which are the mainstay of modern COPD treatment (in combination with inhaled corticosteroids or without them).

Treatment strategy in non-small cell lung cancer (NSCLC) is ambiguous and depends on the stage of the disease, the histologic pattern of the tumor, differentiation of the tumor, regional and distant metastases, as well as somatic symptom pathology and functional reserves of vital organs and systems [16]. The most effective technique is surgery performed for resectable LC. Pneumonectomy or lobectomy with removal of all mediastinal lymph nodes on the side of the affected lung is considered standard surgical therapy. In addition to the lung resection, combined surgeries include resection of a neighboring organ invaded by the tumor (pericardium, chest wall, diaphragm, vagus or phrenic nerve, less often the superior vena cava, atrium, esophagus, and pulmonary artery). In patients with decreased pulmonary function (stage III–IV COPD) and severe cardiac pathology, a smaller extent of lung resection is acceptable, such as atypical resection and segmentectomy. However, it subsequently leads to a threefold increase in regional recurrence of LC [15].

Currently, patients with stage 0–IIIA NSCLC are considered operable, but patients with

stage IB, II, and IIIA and stage N1, N2 lymph node metastases are prescribed adjuvant chemotherapy to suppress the activity of the tumor cell and its effects on subclinical micrometastases in the lymph nodes and distant organs. At stage IV, a patient is prescribed palliative chemotherapy, immunotherapy, or their combination with radiation therapy [16]. In 2010, the Thoracic Cancer Department of Cancer Research Institute (Tomsk NRMC) developed a method for combination treatment of patients with stage III NSCLC, including two courses of neoadjuvant chemotherapy, radical surgery, and subsequent prescription of postoperative personalized adjuvant chemotherapy according to a scheme based on analysis of monoresistance gene expression. There was a decrease in the local recurrence rate and distant metastasis rate and an improvement in recurrence-free survival by 29.1% compared with the control group, which demonstrates the effectiveness of this approach in disease management [17].

According to the analysis performed, 76 (64.4%) patients underwent surgery: 42 (55.26%) patients underwent lobectomy, 9 (11.84%) patients – bilobectomy, 21 (27.63%) patients – pneumonectomy, 2 (2.63%) patients – atypical resection; one patient underwent diagnostic thoracotomy, and one patient – transbronchial endoscopic tumor resection. In 72 (94.74%) cases, radical surgery was performed in combination with ipsilateral mediastinal lymph node dissection. Reconstructive organ-preserving plastic surgery was performed in 23 (30.26%) patients. In accordance with modern guidelines [16], 95 (80.5%) patients received chemotherapy, 28 (23.7%) patients – external beam radiation therapy.

According to the literature, in most leading thoracic surgery clinics, where LC surgery is performed, the incidence of postoperative complications remains 15–25% [13, 18]. Complications can be surgical (bronchial anastomotic leakage, bronchial fistula, obstructive atelectasis, pleural empyema, bleeding) and non-surgical (pneumonia, acute cardiac failure, cardiac arrhythmia, myocardial infarction, pulmonary embolism, ischemic stroke). Pneumonia is more often observed after lung resection than after pneumonectomy (in 11.7% and 3% of the patients, respectively). It occurs due to impaired bronchial drainage, formation of atelectasis due to incomplete expansion of the remaining lobe or segment of the lung, circulatory disorders, and underlying chronic inflammation of the bronchi, especially in COPD. The most common cardiovascular complication is cardiac arrhythmia, namely atrial fibrillation and ventricular extrasystole [13, 18].

In our study, 44 (57.9%) of 76 operated patients developed surgical complications or a combination of them in the postoperative period. In particular, these complications included pneumonia (17.1%), pleurisy (17.1%), obstructive atelectasis (3.9%), cardiac arrhythmias (38.16%), acute myocardial infarction (2.63%), COPD exacerbation (34.21%), anastomotic leakage (10.53%), bronchopleural fistula (9.2%), pleural empyema (13.16%), and pulmonary hemorrhage (2.27%).

According to statistics, after the initial diagnosis, one-year mortality rate reaches more than 50%, and the average five-year survival rate, even with adequate treatment, is about 10–16% [1]. As part of our study, we assessed one- and three-year mortality of the patients. During the first year of the follow-up after the initiation of the treatment, 29 (24.58%) out of 118 patients died. Three-year mortality in the group of 96 patients was 71.88%; 69 patients died. The follow-up lasted less than 36 months for 22 patients from the study group. According to the literature analyzing 348 operated patients, the best survival in LC patients was observed in the absence of regional lymph node metastases, radical surgery, and squamous cell lung cancer [18].

The results of the Cox regression analysis showed that factors that significantly reduced the survival of patients with combined LC and COPD included more severe stages of the disease in terms of the size of the primary tumor and its localization, invasion into adjacent organs and tissues, severity of regional and distant metastasis (according to the TNM classification), and ventilation disorders, manifested through more severe dyspnea (according to the mMRC scale), reduced baseline values of peripheral blood oxygen saturation, pulmonary atelectasis, and episodes of pneumonia (including paracancrotic types) in the previous 12 months. The presence of metastases in the pleura (pleurisy), adrenal glands, and distant non-regional lymph nodes should also be considered as negative factors for survival. It should be noted that surgical removal of the primary tumor was associated with an increase in the survival rate of patients with combined LC and COPD (Table).

Table

Survival-associated factors in patients with combined LC and COPD

Factor	Beta*	OR	l_CI95	u_CI95	R^2	*p*
Tumor Spread (TNM-T)	0.4047	1.4988	1.1445	1.9628	0.078	0.0033
Distant metastases (TNM-M)	0.866	2.3775	1.4185	3.9847	0.081	0.001
mMRC	0.596	1.8149	1.279	2.5753	0.09	0.0008
Pronounced invasion into adjacent organs and tissues according to SCT (T3–T4 according to TNM classification)	0.429	1.5363	1.1132	2.1202	0.058	0.0089
Peripheral oxygen saturation	–0.2867	0.7507	0.6417	0.8783	0.088	0.00034
Pleural metastases	1.4122	4.1049	2.1791	7.7324	0.13	0.00012
Metastases in the adrenal glands	1.7178	5.5721	2.5707	12.0774	0.11	0.00013
Non-regional lymph node metastases	0.9620	2.6169	1.5176	4.5127	0.087	0.00054
Pneumonia in previous 12 months	0.8141	2.2571	1.3811	3.6888	0.094	0.0012
Pulmonary atelectasis	0.8648	2.3744	1.4746	3.8233	0.11	0.00037
Paracancrotic pneumonia in previous 12 months	0.8396	2.3156	1.4211	3.7732	0.089	0.00075
Surgical therapy for the primary tumor	–1.3606	0.2565	0.1594	0.4127	0.25	<0.00001

Note: beta is a coefficient indicating how much the units of standard deviation in the dependent variable changed to alter the unit of standard deviation in the independent variable of interest with all other controlled variables; OR – odds ratio; l(u)_CI95 is lower (upper) confidence interval; R^2 – the accuracy degree of the process description by the model; *p* – statistical significance of the differences; SCT – spiral computed tomography.

CONCLUSION

The combination of COPD and LC is still an important medical problem. On the one hand, COPD can be considered as an independent risk factor for LC. On the other hand, severe bronchial obstruction and emphysema often hinder radical LC treatment.

The study established that combined COPD and LC was more common among men (approximately 6.8 times more common than among women) with a long history and high intensity of smoking, which correlated with the predominance of squamous LC (54.4%) in the analyzed population.

The study highlighted the problem of late diagnosis of LC (at stage III–IV with the disseminated tumor and severe invasive tumor growth in adjacent organs and tissues), as well as the lack of adequate maintenance COPD therapy in most patients, despite of severe respiratory symptoms, significant obstructive ventilation disorders, and emphysema.

Factors associated with lower survival of patients with combined LC and COPD, besides advanced tumor stages, invasive tumor growth in adjacent organs and tissues, and severity of regional and distant metastasis (according to the TNM classification), included severity of ventilation disorders and dyspnea (according to the mMRC scale), reduced baseline peripheral oxygen saturation, pulmonary atelectasis, and episodes of pneumonia (including paracancrotic pneumonia) in the previous 12 months. Higher mortality was also associated with metastases in the pleura, adrenal glands, and distant non-regional lymph nodes.

REFERENCES

1. Kaprin A.D., Starinsky V.V., Shakhzadova A.O. Malignant neoplasms in Russia in 2019 (morbidity and mortality). Moscow: P. Hertsen Moscow Oncology Research Institute, branch of the National Medical Research Radiological Centre of the Ministry of Healthcare of the Russian Federation, 2020:239 (in Russ.).
2. Parshin V.D., Grigorieva S.P., Mirzoyan O.S., Ibragimova D.F., Nikoda V.V., Vizhigina M.A. et al. Surgery for lung cancer in elderly.*Pirogov Russian*. *Journal of Surgery.* 2010;(10):11–16 (in Russ.).
3. De-Torres J.P., Wilson D.O., Sanchez-Salcedo P., Weissfeld J.L., Berto J. et al. Lung cancer in patients with chronic obstructive pulmonary disease. Development and validation of the COPD Lung Cancer Screening Score. *American Journal of Respiratory and Critical Care Medicine*. 2015;191(3):285–291. DOI: 10.1164/rccm.201407-1210OC.
4. Leshchenko I.V., Baranova I.I. Chronic obstructive pulmonary disease: clinical issues, epidemiology, risk factors and basic therapy (review). *Consilium Medicum*. 2016;18(11):8–18 (in Russ.).
5. Tockman M.S., Anthonisen N.R., Wright N.C. et al. Airways obstruction and the risk of lung cancer. *Annals of Internal*

Medicine.1987;106(4):512–518. DOI: 10.7326/0003-4819-106-4-512.
6. Adcock I.M., Caramori G., Barnes P.J. Chronic obstructive pulmonary disease and lung cancer: new molecular insights. *Respiration.*2011;81(4):265–284. DOI: 10.1159/000324601.
7. Kondo R., Yoshida K., Eguchi T., Kobayashi N., Saito G., Hamanaka K. et al. Clinical features of lung cancer smokers with light and mind chronic obstructive pulmonary disease: a retrospective analysis of Japanese surgical cases. *European Journal of Cardio-thoracic Surgery.* 2011;40(6):1439–1443. DOI: 10.1016/j.ejcts.2011.03.017.
8. Young R.P., Hopkins R.J., Christmas T., Black P.N., Metcalf P., Gamble G.D. COPD prevalence is increased in lung cancer, independent of age, sex and smoking history. *Eur. Respir. Journal*. 2009;34(2):380–386. DOI: 10.1183/09031936.00144208.
9. Murakami J., Ueda K., Sano F., Hayashi M., Nishimoto A., Hamano K. Pulmonary emphysema and tumor microenvironment in primary lung cancer. *Journal of Surgical Research*. 2016;200(2):690–697. DOI: 10.1016/j.jss.2015.09.004.
10. Chissov V.I., Davydov M.I. Oncology: National guidelines. Moscow: GEOTAR-Media, 2008:1072 (in Russ.).
11. Mclntyre A., Ganti A.K. Lung cancer – a global perspective. *Journal of Surgical Oncology*. 2017;115(5):550–554. DOI: 10.1002/jso.24532.
12. Sobin L.H., Gospodarowicz M.K., Wittekind Ch.; translated from English by A.I. Shchegolev, E.A. Dubova, K.A. Pavlov. TNM. Classification of Malignant Tumors. Moscow: Logosfera, 2011:304 (in Russ.).
13. Trakhtenberg A.H., Kolbanov K.I. Lung cancer; edited by V.I. Chissov. Moscow: GEOTAR-Media, 2014:160 (in Russ.).
14. COPD. Clinical practice guidelines of the Ministry of Healthcare of the Russian Federation 2021. Moscow, 2021:94 (in Russ.).
15. Zhang L., Li M., Yin R., Zhang Q., Xu L. Comparison of the oncologic outcomes of anatomic segmentectomy and lobectomy for early-stage non- smoll cell lung cancer. *Ann. Thorac. Surg*. 2015;99(2):728–737. DOI: 10.1016/j.athoracsur.2014.08080.
16. Laktionov K.K., Artamonova E.V., Borisova T.N., Breder V.V., Bychkov Yu.M. et al. Malignant neoplasm of the bronchi and lung. *Journal of Modern Oncology*. 2021;23(3):369–402 (in Russ.). DOI: 10.26442/18151434.2021.3.201048.
17. Rodionov E.O., Miller S.V., Efteev L.A., Tuzikov S.A., Tsyganov M.M., Deryusheva I.V. et al. Combined treatment of patients with non-small cell lung cancer with personalized prescription of adjuvant chemotherapy. *Avicenna Bulletin*. 2019;21(3):420–425 (in Russ.). DOI: 10.25005/2074-0581-2019-21-3-420–425.
18. Trakhtenberg A.X, Kolbanov K.I., Sedykh S.A. Character features of diagnosis and treatment of lung carcinoma. *Pulmonologiya*. 2008;4:5–17 (in Russ.). DOI: 10.18093/0869-0189-2008-0-4-5-

Authors contribution

Dobner S.Yu., Fedosenko S.V. – conception and design; analysis and interpretation of the data; varying out of the research; justification of the manuscript and critical revision of the manuscript for important intellectual content; drafting of the manuscript. Tuzikov S.A. – analysis and interpretation of the data; final approval of the manuscript for publication. Yarovoy N.D., Petrov V. A. – analysis and interpretation of the data, editing of the manuscript. Rodionov E.O., Samykina I.A. – analysis and interpretation of the data, editing, critical revision of the manuscript for important intellectual content. Starovoitova E.A. – analysis and interpretation of the data.

Authors information

Dobner Svetlana Yu. – General Practitioner, Functional Diagnostics Doctor, Cardiologist, Head of the General Clinical Department, Cancer Research Institute, Tomsk NRMC, Tomsk, dobnersv@gmail.com, https://orcid.org/0000-0002-0338-3786

Fedosenko Sergey V. – Dr. Sci. (Med.), Associate Professor, Professor, General Medical Practice and Outpatient Therapy Division, Siberian State Medical University, Tomsk, s-fedosenko@mail.ru, https://orcid.org/0000-0001-6655-3300

Rodionov Evgeny O. – Cand. Sci. (Med.), Senior Researcher, Thoracic Cancer Department, Cancer Research Institute, Tomsk NRMC; Assistant, Oncology Division, Siberian State Medical University, Tomsk, rodionoveo@oncology.tomsk.ru, https://orcid.org/0000-0003-4980-8986

Yarovoy Nikolay D. – Medical Doctor and Statistician, Tomsk Regional Oncology Dispensary, Tomsk, koly-yarovoy@yandex.ru, https://orcid.org/0000-0003-3619-6095

Petrov Vyacheslav A. – Cand. Sci. (Med.), Junior Researcher, Center for Biological Research and Bioengineering, Siberian State Medical University, Tomsk, vyacheslav.a.petrov@mail.ru, https://orcid.org/0000-0002-5205-9739

Tuzikov Sergey A. – Dr. Sci. (Med.), Professor, Head of the Thoracic Cancer Department, Cancer Research Institute, Tomsk NRMC; Professor, Oncology Division, Siberian State Medical University, Tomsk, Tuzikovsa@oncology.tomsk.ru, https://orcid.org/0000-0002-0884-1838

Starovoitova Elena A. – Cand. Sci. (Med.), Associate Professor, Head of the General Medical Practice and Outpatient Therapy

Division, Siberian State Medical University, Tomsk, elena-starovoytova@yandex.ru, https://orcid.org/0000-0002-4281-1157

Samykina Irina A. – General Practitioner, Clinical Pharmacologist, Cancer Research Institute, Tomsk NRMC, Tomsk, irina.samykina@gmail.com, https://orcid.org/0000-0003-2681-7310

(✉) **Dobner Svetlana Yu.,** dobnersv@gmail.com

Received 07.02.2022;
approved after peer review 05.03.2022;
accepted 17.03.2022