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Changes in the ventilation function of the lungs during the formation of chronic obstructive pulmonary disease and its combination with lung cancer

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ABSTRACT

Aim. To study the ventilation function of the lungs in patients with varying degrees of severity of chronic obstructive pulmonary disease (COPD) and in patients with COPD combined with lung cancer (LC), as well as to establish the features of its disorders using spirography and body plethysmography.

Materials and methods. A clinical and functional study of 57 individuals was carried out with 10 healthy patients (control group), 30 patients with COPD and 17 patients in whom LC was combined with COPD using the Masterlab Pro diagnostic complex (Erich Jaeger, Germany).

Results. In patients with early COPD, a decrease in MEF_{75} (a ventilation parameter characterizing small airway patency) is the most informative. With the progression of bronchial obstruction, both restrictive and obstructive disorders, characterized by a decrease in FEV_1, VC, a change in the structure of the total lung capacity in the form of an increase in the RV/TLC ratio such as an increase in the RV/TLC ratio and an increase in bronchial resistance were recorded. In patients with LC and mild COPD, pulmonary volumes, capacities, flow-volume loop and bronchial resistance parameters did not differ from patients with COPD with a similar bronchial obstruction. In patients with LC and more severe COPD, in contrast to patients suffering from a similar severity of COPD, a decrease in the patency of large, medium and small diameter bronchi (PEF, MEF_{25}, MEF_{50}, MEF_{75}) was detected, which indicated development of generalized bronchial obstruction.

Conclusion. Modern diagnostics of pulmonary ventilation disorders in patients with LC and COPD should be aimed at identifying the disease, and drug therapy should target maximum leveling of reversible components of bronchial obstruction in order to increase the functional reserve of the respiratory system and reduce the risk of postoperative complications caused by COPD.

Key words: chronic obstructive pulmonary disease, lung cancer, pulmonary ventilation function, spirography, bodyplethysmography.

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Изменение вентиляционной функции легких в процессе формирования хронической обструктивной болезни легких и при ее сочетании с раком легкого

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РЕЗЮМЕ

Цель. Изучение вентиляционной функции легких у пациентов с различной степенью тяжести хронической обструктивной болезни легких (ХОБЛ) и при ее сочетании с раком легкого (РЛ), а также установление особенностей респираторных нарушений с помощью спирографии и бодиплетизмографии.

Материалы и методы. Проведено клинико-функциональное исследование 57 лиц (10 здоровых (группа контроля), 30 больных с ХОБЛ и 17 больных, у которых РЛ сочетался с ХОБЛ) при помощи диагностического комплекса Masterlab Pro (Erich Jaeger, Германия).

Результаты. При начальной стадии ХОБЛ наиболее информативно снижение максимального объема скорости на уровне 75% от форсированной жизненной емкости легких ($МОС_{75}$) – вентиляционного показателя, характеризующего проходимость мелких дыхательных путей. При прогрессировании бронхиальной обструкции отмечались как обструктивные, так и рестриктивные нарушения, характеризующиеся снижением объема форсированного выдоха за первую секунду, жизненной емкости легких, изменением структуры общей емкости легких в виде увеличения отношения остаточного объема легких к общей емкости легких и повышения бронхиального сопротивления. У пациентов, страдающих РЛ в сочетании с нетяжелой ХОБЛ, показатели вентиляции легких и бронхиальное сопротивление не отличались от пациентов с ХОБЛ, имеющих аналогичную степень бронхиальной обструкции. При РЛ в сочетании с более тяжелой ХОБЛ, в отличие от пациентов, страдающих аналогичной тяжестью ХОБЛ, установлено снижение проходимости бронхов крупного, среднего и мелкого диаметра (пиковая объемная скорость, $МОС_{25}$, $МОС_{50}$, $МОС_{75}$), свидетельствующее о развитии генерализованной бронхиальной обструкции.

Заключение. Современная диагностика нарушений вентиляции легких у больных РЛ в сочетании с ХОБЛ должна быть направлена на выявление, а медикаментозная терапия – на максимальное нивелирование обратимых компонентов бронхиальной обструкции с целью повышения функционального резерва системы дыхания и снижения риска послеоперационных осложнений, вызванных ХОБЛ.

Ключевые слова: хроническая обструктивная болезнь легких, рак легкого, вентиляционная функция легких, спирография, бодиплетизмография.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and lung cancer (LC) usually coexist and represent a row of clinical problems [1–3]. At the same time, COPD more often leads to a decrease in the external respiration function and is a factor determining the frequency of complications and the risk of death in some patients with LC [4, 5].

The diagnosis of COPD is largely functional. Characteristics of the pulmonary ventilation function (PVF), namely, the forced expiratory volume during the first second of the test (FEV_1), vital capacity (VC), and the Tiffno index are the "gold standard" for diagnosing COPD [1]. However, often at the onset of the disease, obstructive disorders developing in the distal parts of the bronchial tree are more effectively diagnosed using parameters of maximal expiratory flow (MEF) of the forced expiratory flow and body plethysmography [6, 8]. Body plethysmography additionally allows to determine bronchial resistance (Raw), to diagnose manifestations of lung hyperinflation, which are used in pulmonology as reliable signs of bronchial obstruction and changes in the lung tissue elastance [7, 8]. Identification of abnormality of these parameters helps early diagnosis of COPD and more effective treatment of this common lung pathology [8].

Annually, 63–65 thousand people fall ill with LC in Russia, and 1.04 million people in the world, which makes up 12.8% of all recorded neoplasm cases [9]. A characteristic feature of everyday clinical practice is an increase in the number of patients operated on in older age groups and a high percentage of postoperative complications [2, 4]. Soon, a further increase in demographic aging of the population and an increase in the number of patients with comorbid pathology are expected [10, 11].

In this regard, the increased interest in assessing COPD as a factor that can lead to complications in the perioperative period in patients with LC is understandable [4, 5]. The use of existing effective methods for diagnosing PVF disorders in this group of patients is an important task for modern scientific research.

The purpose of the study was to study PVF in patients with varying COPD severity and in patients with LC and COPD, as well as to identify the characteristics of PVF disorders using spirography and body plethysmography.

MATERIALS AND METHODS

To meet the aim of the research, clinical and functional study of 57 patients was carried out with 10 healthy patients (control group), 30 patients with COPD and 17 patients with LC and COPD. The sample of subjects included in the study was formed from patients being treated at the therapeutic clinic of Siberian State Medical University and the Department of Thoracic Oncology of Cancer Research Institute, Tomsk NRMC.

According to the PVF study, 8 patients with COPD had clinical signs of bronchitis and small bronchi obstruction, but FEV_1 was normal (group 0). The remaining 22 patients were diagnosed with COPD according to the COPD diagnostic criteria [1]: in group 1 (10 subjects) – $FEV_1 \geq 80\%$ of the proper values; in group 2 (12 subjects) $FEV_1 < 80\%$ of the proper values – 7 patients had $50\% \leq FEV_1 < 80\%$, and 5 patients – $30\% \leq FEV_1 < 50\%$ of the proper values. In 6 patients with LC + COPD, FEV_1 was $\geq 80\%$ of the proper values (group 3), in the remaining 11 patients (group 4), FEV_1 was $< 80\%$ of the proper values, in 9 of them – $50\% \leq FEV_1 < 80\%$, and in 2 – $30\% \leq FEV_1 < 50\%$ of the proper values.

PVF was evaluated on a Masterlab Pro diagnostic complex (Erich Jaeger, Germany). The test was conducted in the morning on an empty stomach in conditions of relative rest in the orthostatic position of a patient. None of the patients in study groups received any bronchoactive agents for COPD. Spirography and pneumotachography methods analyzed respiratory minute volume (RMV), vital capacity (VC), forced expiratory volume during the first second of the test (FEV_1), Tiffno index (FEV_1/VC), flow-volume loop parameters (FVL) – peak expiratory flow (PEF), maximum expiratory flow occurring at the point that is 25% of FVC from the beginning of the exhalation (MEF_{25}), maximum expiratory flow occurring at the point that is 50% of FVC from the beginning of the exhalation (MEF_{50}), maximum expiratory flow occurring at the point that is 75% of FVC from the beginning of the exhalation (MEF_{75}). Body plethysmography determined the structure of total lung capacity (TLC): residual lung volume (RV), residual lung volume to total lung capacity ratio (RV/TLC), as well as bronchial resistance (Raw).

The average age of patients with COPD (group 2) was 59.7 ± 3.0 years, they were older than the subjects in the control group, patients of group 0 and group 1 (52.6 ± 2.7; 48.2 ± 3.0; 49.0 ± 2.2, respectively). The average age of patients with LC and COPD (group 3) was 56.7 ± 2.0, while of patients in group 4 is was 60.8 ± 2.0. Patients of group 3 were older than patients of group 1. There were no statistical differences in age between patients of groups 2 and 4.

COPD confirmation was carried out by collecting complaints, medical history, physical examination and the questionnaire for the COPD diagnosis (CAT and mMRC scales) [1, 12]. Groups of patients with LC and COPD (groups 3 and 4) included patients with IIA – n IIIB stages of LC. Group 3 included 6 patients, 3 patients of them had stage II, another 3 patients had stage IIIA. Group 4 included 3 patients with IIA–B stage of non-small cell lung cancer, 7 patients with IIIA stage and 1 patient with IIIB stage. Central LC was diagnosed in 12 (70.6%) patients and peripheral LC in 5 patients (29.4%).

The study inclusion criteria were the following: smoking; absence of other lung and severe somatic pathology, which could affect the parameters of external respiratory function at the moment of inclusion in the study; absence of regular baseline and symptomatic COPD therapy, and consent to participate in the study.

Statistical analysis of the obtained data was carried out on a personal computer using the statistical software package Statistica 10. The normal distribution was checked by the Shapiro – Wilk method. Due to the lack of normal distribution, when comparing group averages for quantitative characters, the Mann – Whitney test was used. Quantitative data are presented as the median *Me*, the 25th and 75th percentiles *(LQ; UQ)*. The differences were considered statistically significant at $p \leq 0.05$.

RESULTS AND DISCUSSION

When analyzing the PVF parameters presented in the Table, it was found that in patients with COPD (group 0), bronchial patency at the level of MEF_{75} was on average lower than in healthy subjects in the absence of differences in FEV_1, as well as other flow and volume ventilation characteristics. In group 1, there was a decrease in the average values of FEV_1, Tiffno index, VC, and FVL (MEF_{25}, MEF_{50}, MEF_{75}) compared with the average values of the control group and a decrease in FEV_1, MEF_{25}, MEF_{50}, MEF_{75} with an increase in RV, RV/TLC in comparison with group 0. In addition, with an increase in obstruction, the patients of group 2 demonstrated an additional decrease in VC, an increase in RV, RV/TLC compared with the healthy subjects of group 0, as well as a pronounced tendency (85.2%) to increase RV/TLC compared with group 1.

The restructuring in the TLC structure, detected in patients with COPD in the form of an increase in RV/TLC with a progressive decrease in FEV_1, indicated the development of pulmonary hyperinflation (PHI), the formation of "air trapping", an increase in lung volumes at the end of spontaneous expiration by the valve obstruction mechanism at the level of small airways [7, 13, 14] Studies show that PHI leads to unfavorable functional effects: respiratory muscle weakness, limited respiratory volume increase during exercise stress, positive end-expiratory pressure, and alveolar hypoventilation [8, 14].

Raw in patients with COPD in group 0 and group 1 was in the reference range and did not differ from the control group (Table). In contrast, Raw in group 2 averaged 153.6%, and was significantly higher than in the control group and in patients of group 0 and group 1.

When analyzing the PVF parameters of patients with LC and COPD presented in the table below, it was found that in patients with degree 1 of obstruction (group 3), the average bronchial patency was reduced in comparison with control subjects and patients of group 0, in the absence of differences in parameters with COPD patients of group 1, who had a similar degree of reduction in FEV_1. When comparing the PVF of patients with LC and COPD of group 4 and patients with COPD with a similar reduction in FEV_1 (group 2), the studied pulmonary volumes and capacities did not differ, however, in patients of group 4, PEF, MEF_{25}, MEF_{50}, MEF_{75} were decreased, which testified to widespread, generalized obstruction. Moreover, between the analyzed groups there were no differences in the magnitude of bronchial resistance (Raw).

It can be assumed that in this case, local stenosis or complete obturation of the bronchial lumen (dystelectasis, atelectasis) by a neoplasm, limited in length, leads to impaired ventilation of the lung tissue. At the same time, the Euler – Liliestrand mechanism restricts blood flow through the hypoventilated area, thereby preventing venous blood bypass, and the unaffected areas of the lungs can compensate for the loss of ventilation.

Despite the positive results achieved in the technique of surgical treatment for LC combined with COPD, the final effects of the treatment remain not entirely satisfactory, primarily due to the significant number of postoperative complications caused by COPD [15].

Studies have shown that tobacco smoking, and in a lesser extent exposure to other pathogenic particles or gases, is a major risk factor for developing COPD. These factors cause an inflammatory process in the lungs, progression of which leads to typical pathophysiological disorders: mucus hypersecretion and ciliary dysfunction, airflow limitation and hyperinflation, pulmonary hypertension and systemic effects, forming reversible and irreversible components of bronchial obstruction [6]. It can be expected that modern functional diagnostics and effective drug therapy of the reversible component of bronchial obstruction will open prospects for improving the perioperative results in patients with LC and COPD.

Table

Results of comparison (p) of PVF parameters in the control group, in patients with COPD and in patients with LC combined with COPD, *Me (LQ; UQ)*

Parameter	Healthy (c) (n = 10)	COPD			COPD + LC		*p*				
		0 (n = 8)	1 (n = 10)	2 (n = 12)	3 (n = 6)	4 (n = 11)	0-c	1-c 1-0	2-c 2-0 2-1	3-c 3-0 3-1	4-2 4-3
VC	117.6 (107.7; 129.6)	106.4 (98.5; 112.5)	104.2 (97.0; 108.7)	93.3 (87.6; 100.3)	106.9 (106.2; 108.7)	91.8 (85.7; 93.1)	0.062	0.023 0.824	<0.001 0.037 0.013	0.074 0.846 0.415	0.406 0.001
FEV$_1$	109.1 (102.0; 117.0)	107.8 (104.3; 117.7)	94.5 (85.7; 104.0)	44.4 (38.0; 65.3)	91.5 (86.9; 98.2)	73.9 (65.9; 80.9)	1.0	0.013 0.037	<0.001 <0.001 <0.001	0.004 0.008 0.745	0.056 <0.001
PEF	127.3 (113.7; 145.2)	127.4 (106.2; 145.7)	105.1 (94.1; 116.8)	44.6 (40.6; 74.3)	106.7 (97.5; 115.0)	78.4 (55.5; 101.8)	0.859	0.028 0.051	<0.001 <0.001 <0.001	0.057 0.175 0.828	0.023 0.087
MEF$_{25}$	122.1 (100.0; 141.6)	123.3 (101.2; 142.2)	77.6 (65.2; 86.7)	15.4 (11.7; 34.3)	60.4 (50.9; 75.8)	37.6 (31.3; 72.5)	0.657	0.003 0.001	<0.001 <0.001 <0.001	0.003 0.002 0.158	0.031 0.070
MEF$_{50}$	83.9 (76.0; 102.6)	95.7 (80.1; 110.6)	47.2 (39.2; 57.3)	11.5 (7.5; 17.1)	54.1 (46.7; 66.2)	36.6 (24.1; 46.9)	0.656	<0.001 0.001	<0.001 <0.001 <0.001	0.003 0.012 0.278	0.018 0.035
MEF$_{75}$	85.0 (60.8; 110.6)	50.0 (35.6; 62.4)	25.9 (21.9; 37.1)	9.2 (5.6; 19.8)	37.9 (30.7; 44.6)	26.4 (14.0; 33.4)	0.033	0.007 <0.001	<0.001 <0.001 <0.001	0.004 0.272 0.083	0.006 0.009
RV	99.7 (93.1; 110.0)	79.2 (63.7; 102.3)	105.2 (92.8; 129.9)	141.3 (132.1; 150.5)	127.0 (92.5; 136.4)	120.8 (110.2; 142.2)	0.083	0.496 0.045	0.003 0.001 0.044	0.175 0.045 0.405	0.218 0.763
RV/TLC	90.5 (87.3; 94.6)	74.6 (70.6; 95.5)	104.6 (83.7; 120.0)	121.6 (115.1; 130.6)	102.1 (81.1; 105.4)	116.4 (107.1; 124.1)	0.109	0.121 0.016	0.001 <0.001 0.056	0.481 0.272 0.329	0.295 0.003
Raw	73.7 (42.7; 94.0)	67.1 (51.5; 80.2)	65.3 (52.3; 126.0)	139.5 (101.9; 197.8)	98.3 (86.4; 119.2)	132.4 (94.5; 174.4)	0.859	0.405 0.789	0.002 0.004 0.011	0.074 0.081 0.447	0.622 0.269

Note: c – control group.

CONCLUSION

1. In patients with early COPD, a decrease in MEF$_{75}$ (ventilation parameter characterizing small airway patency) is the most informative. With the progression of bronchial obstruction, obstructive and restrictive disorders develop, which are characterized by a decrease in FEV$_1$, VC, a change in the structure of the total lung capacity in the form of an increase in the RV/TLC ratio, indicating the development of pulmonary hyperinflation. It was found that a high degree of obstructive disorders leads to increased bronchial resistance.

2. In patients with LC and mild COPD, pulmonary volumes, capacities, flow-volume loop and bronchial resistance parameters did not differ from patients with COPD with a similar degree of bronchial obstruction.

3. In patients with LC and COPD with a greater degree of obstructive disorders, in contrast to COPD with the same degree of reduction in FEV$_1$, the development of generalized bronchial obstruction at the level of bronchi of large, medium and small diameter (PEF, MEF$_{25}$, MEF$_{50}$, MEF$_{75}$) was determined in the absence of differences in static and dynamic pulmonary volumes, and bronchial resistance.

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Authors contribution

Dobner S.Yu. – conception and design, analysis and interpretation of data, substantiation of the manuscript. Dubakov A.V. – conception and design, analysis and interpretation of data, substantiation of the manuscript. Porovskiy Ya.V. – conception and design, analysis and interpretation of data, substantiation of the manuscript, critical revision for important intellectual content. Tuzikov S.A. – conception and design, analysis and interpretation of data, substantiation of the manuscript, critical revision for important intellectual content, final approval of the manuscript for publication. Miller S.V. – analysis and interpretation of data. Rodionov E.O. – analysis and interpretation of data.

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