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The Effect of Preoperative Preparation with Helium-Oxygen Mixture on the Incidence of Pulmonary Complications in Patients with COPD and Lung Cancer

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Summary

Aim of the study. To study the effect of helium-oxygen mixture on predictors of postoperative pulmonary complications in cancer patients with chronic obstructive pulmonary disease (COPD).

Materials and methods. A single-center prospective clinical study with historical control included 208 patients, among them 104 patients received helium-oxygen mixture inhalations (70% helium and 30% oxygen) in the preoperative period (He group) and 104 patients were the historical control group (Ctrl group). Given the risk of bias associated with confounders, we conducted a one-to-one matching analysis based on pseudo-randomization to adjust for the unbalanced baseline characteristics of the groups. We used logistic regression to develop the pseudo-randomization estimates. We used the nearest neighbor matching 1:1 with a caliper of 0.1 to achieve better similarity among matched pairs. After pseudo-randomization, we included 87 patients in each group, ensuring adequate balance across all covariates. A multivariate logistic regression analysis was performed to identify factors associated with the risk of postoperative pulmonary complications.

Results. In the He group, there was a statistically significant improvement in a number of functional parameters compared to the Ctrl group. FEV_1, FVC, mod. Tiffeneau index values in the He group increased significantly (p=0.0009; p=0.0115; p=014, respectively), gas exchange parameters (PaO_2, $PaCO_2$, pH, SpO_2) improved (p=0.0006; p=0.004; p=0.0097; p=0.001, respectively). Hypoxia tolerance tests also showed significantly greater values in the He group (Stange test, p=0.016; Sabrazes (Hench) post-exhalation breath-holding test, p=0.024). Analysis of postoperative parameters showed significant advantage of the He group over the control group in terms of critically important clinical outcomes. At the final stage of stepwise selection, three independent predictors were included in the risk model for postoperative pulmonary complications: SpO_2, the breath-holding test, and the duration of postoperative mechanical ventilation. The quality of the model was high, with a correctly classified case rate of 92.2%, a Hosmer–Lemeshow goodness-of-fit statistic of p=0.933, and a total model significance of $p<0.000$.

Conclusion. We performed the first clinical study that showed the importance of preoperative preparation using a helium-oxygen mixture in cancer patients with chronic obstructive pulmonary disease and identified predictors of pulmonary complications after thoracic surgery.

Keywords: predictors of pulmonary complications; helium-oxygen mixture; Heliox; chronic obstructive pulmonary disease; lung cancer

Conflict of interest. The authors declare no conflict of interest.

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Introduction

Lung cancer is one of the most common causes of cancer-related morbidity and mortality, representing a significant challenge within healthcare systems. Worldwide over 2 million cases of various malignant lung tissue neoplasms, such as adenocarcinoma, squamous cell carcinoma, neuroendocrine carcinoma, and carcinoid, are reported annually [1].

Lobectomy and pulmonectomy are the main surgical options for lung cancer. According to most authors, it is advisable to consider reducing the scope of surgical intervention in patients with limited functional reserves, i.e., to reduce the volume of resected lung tissue and limit lymph node dissection. This approach is common in patients with metastatic lung disease, and also relevant in primary lung cancer, especially in patients with severe respiratory failure [2].

It's not uncommon that surgical access may require single-lung ventilation, which can increase dead space and intrapulmonary shunting, thereby causing hypoxemia in patients with low respiratory reserve. Traditional methods, including increasing PEEP, peak pressure, and plateau pressure, can worsen oxygenation and respiratory mechanics, especially in patients with COPD. In addition, thoracic surgeries are associated with postoperative complications such as alveolar-pleural fistula, pneumonia, and ARDS [3, 4]. According to some authors, the mortality rate after lung resection for cancer reaches 6% [5].

There are several factors that are directly and indirectly related to the risk of negative treatment outcomes. These include patient-related (ASA ⩾ III) and surgery-anesthesia related (ARISCAT ⩾ 26 scores) criteria. Quitting smoking provided a beneficial effect on patient's respiratory status during comprehensive preoperative preparation. According to the LAS VEGAS study, the number of pulmonary complications did not differ between smokers and non-smokers in the postoperative period, but the incidence of respiratory failure was statistically significantly higher in smokers (5.1% and 3.0%, respectively) [6].

Conventionally used predictors of postoperative pulmonary complications, such as age, volume of resected lung tissue, and baseline respiratory function, are well known. However, most existing models are static and do not take into account the potential for preoperative optimization of respiratory status. Berry et al. study has demonstrated that the predictive value of functional pulmonary tests in relation to postoperative pulmonary complications in patients with respiratory failure depends on the surgical access, as statistically significant correlation was found only in thoracotomy access, not in video-assisted thoracic surgery (VATS) [7]. D. Almqvist et al. have demonstrated in a recent study that FEV_1 and lung diffusion capacity did not have prognostic value in relation to survival rates in patients after surgical resection for early stage lung cancer. Meanwhile, the same functional tests significantly correlated with length of hospital stay [8].

The breath-holding test was introduced into practice in 1902 by Sabrazès Jean-Emile (1867–1943), who established that the normal duration of apnea is 20–25 seconds, and a reduction in time to 5–10 seconds is associated with various pathologies, such as mitral valve insufficiency. Later, V. A. Stange (1856–1918) recommended this test as «the best indicator of the patient's heart condition during operations under general anesthesia» [9].

Noble gases are a promising direction in therapy of critical conditions [10]. Xenon and argon possess organoprotective properties *in vitro* and *in vivo*, while studies of krypton are only at the beginning of the experimental path [11–13].

Helium is a monoatomic noble gas with a lower molecular mass compared to diatomic nitrogen (Mr He = 4.0 g/mol vs Mr N2 = 28.0 g/mol). Graham's law (Thomas Graham, 1805–1869), known as the law of relative rates of passage of substances through a membrane, states that the rate of gas flow is inversely proportional to the square root of its mass density [14]. Therefore, replacing nitrogen with helium in a breathing mixture will lead to a more active penetration of oxygen through the alveoli into the blood, which may be beneficial for patients with impaired gas exchange.

Heliox (a mixture of helium and oxygen) has been used for medical purposes since 1934, when Alvan Barach first described his own research on the use of the gas in patients with bronchial asthma and upper airway obstruction [15]. The dominant area of clinical application of Heliox is currently related to respiratory diseases, while its potential effects on other physiological systems (CNS, circulation, immunity) remain the subject of preclinical studies [15–21].

According to a systematic review and meta-analysis (Lakhin et al., 2022), adding of Heliox to conventional respiratory therapy for severe acute pneumonia improves oxygenation, reduces acute-phase proteins (APPs) levels, but does not reduce the length of ICU stay, rates of mechanically assisted ventilation, or in-hospital mortality rates [22].

Prevention of respiratory complications is a basic principle of perioperative management in thoracic anesthesiology. Finding the best strategy and tactics for managing patients can lead to a decrease in mortality, paving the way for a solution to this problem. To date, there are no studies on the impact of Heliox on the quality of prevention of pulmonary complications in the perioperative period.

The aim of the study is to investigate the effect of helium-oxygen mixture on predictors of postoperative pulmonary complications in cancer patients with chronic obstructive pulmonary disease.

Materials and Methods

A single-center prospective clinical study with historical control was conducted. The study protocol was approved by the local ethics committee of the Perm regional clinical hospital, No. 42 dated March 31, 2023.

The study analyzed two time-related cohorts. The retrospective part was formed from patients who met the inclusion criteria and received treatment between 01.11.2022 and 31.10.2023. The prospective cohort was recruited between 15.01.2024 and 15.06.2025. A buffer interval (November–December 2023) was set to exclude temporal overlap and potential data mixing between cohorts.

Taking into account the risk of systematic error associated with confounding bias, characteristic of retrospective studies, we used a propensity score matching (PSM) — a one-to-one matching analysis based on pseudo-randomization to adjust for the unbalanced baseline characteristics of the groups. Logistic regression was used to develop estimates of pseudorandomization. We used the nearest neighbor matching 1:1 with a caliper of 0.1 to achieve better similarity among matched pairs. This value of the caliper allowed to achieve a satisfactory balance between the SMD < 0.1 groups. Age, gender, Charlson comorbidity index, Stange post-inhalation breath-holding test, PaO_2, FEV_1, FVC, and COPD were included as covariates. The balance of covariates between groups was assessed by calculating and visualizing standardized mean differences (SMDs) using a love plot, using the threshold value of SMD ≤ 0.1 as a success criterion.

Criteria for the inclusion of patients in the study:

- verified diagnosis of lung cancer (non-small cell cancer);
- presence of chronic obstructive pulmonary disease (COPD stage I–III);
- age: 40–75 years old;
- elective surgery ((lobectomy, bilobectomy, pulmonectomy);
- consent to participate in the study.

Criteria for excluding patients from the study:

- severe concomitant somatic pathology (decompensated cardiovascular insufficiency, severe renal or hepatic dysfunction);
- acute infectious diseases in the preoperative period;
- absence of patient's informed consent;
- incomplete clinical and laboratory data that impede correct analysis (for example, absence of spirometry data (FEV_1, FVC), arterial blood gases, ABGs (PaO_2, $PaCO_2$, pH, SpO_2), breath holding tests — after deep inhalation and after full exhalation (Stange and Sabrazes (Hench) tests, respectively), or important demographic and clinical characteristics (age, COPD stage, Charlson comorbidity index, CCI) necessary for statistical analysis and comparison of the groups)

As part of the preoperative preparation, all patients underwent a comprehensive diagnostic examination. In cases of chronic respiratory failure, ventilation disorders were corrected under the dynamic supervision of a pulmonologist. During preparation for surgery, all patients were managed according to the current National clinical guidelines for patients with COPD and lung cancer that are prepared for thoracic surgery. The program included standard of care therapy (bronchodilators, inhaled glucocorticosteroids as indicated), breathing exercises, correction of nutritional status, and mastering coughing technique, if necessary.

Preoperative preparation in the He group. The breathing gas mixture of 70% helium and 30% oxygen «Heliox 70/30» was heated to 70°C and the inhalation procedure was performed for 10 minutes. After a short pause of 4 minutes, the procedure was repeated. After 6–8 hours, a second session of two inhalations was performed in the same mode. This inhalation regimen was carried out for 5–7 days during the preoperative period.

Preoperative preparation in the Ctrl group. Helium-oxygen mixture was not used in this group.

The results of preoperative preparation were assessed based on cardiovascular and respiratory system indicators, including ABGs analysis and spirometry, electrocardiography, and echocardiography data.

Criteria for the effectiveness of preoperative preparation:

- Improvement in the patient's well-being;
- Reduction in the severity of respiratory disorders (reduction in shortness of breath, dyspnea);
- Improvement in ABGs composition (increase in $pO_2 > 80$ mmHg, decrease in $pCO_2 < 45$ mmHg, P/F ratio > 300 mmHg);
- Improvement in spirometry indicators $FEV_1 > 70\%$, FVC, modif. Tiffeneau index;
- Improvement in functional test indicators (increase in Stange test > 30 sec, Sabarazes–Hench > 20 sec);

Patient's readiness for lung cancer surgery or the need for extended preoperative preparation was established by a consilium based on the dynamics in patient's condition evaluated by clinical data, results of laboratory and instrumental examinations.

All surgical interventions for lung cancer were performed under combined anesthesia: low-flow inhalation anesthesia based on desflurane and epidural anesthesia with ropivacaine [23, 24]. Ventilation with protective modes was performed using a Datex-Ohmeda Avance S/5 anesthesia and ventilation machine. Extended intraoperative monitoring included the following parameters: pulse, heart rate, noninvasive blood pressure, desflurane concentration, CO_2 and O_2 on inspiration and expiration, body temperature, depth of anesthesia (Conox, Fresenius Kabi). Before suturing the thoracotomy wound, anesthesia of the lung root and intercostal blockade were performed. Postoperative care was continued either in an intensive care or resuscitation unit, depending on patient's condition.

Statistical methods. The data were analyzed using Microsoft Office Excel 2019 spreadsheet software. Quantitative data were described as *Me* [*Q1; Q3*], where *Me* is the median value, *Q1* is the first quartile (25th percentile), and *Q3* is the third quartile (75th percentile). The Shapiro–Wilk test was used to assess the normality of the data. The distribution of most quantitative unrelated variables was significantly different from normal, therefore the nonparametric Mann–Whitney *U* test was used to assess intergroup differences. The Chi-square test or the Fisher's exact test was used to compare frequency of variables in unrelated groups (in cases where the frequency of the outcome was less than 10%).

To assess the degree of predictors' influence on the outcome of a particular event, the odds ratio (OR) was used. To assess the significance of predictors (of the development of a particular event, i. e., pneumonia, death), multivariate and univariate analyses based on logistic regression were used, as well as ROC analysis of the sensitivity and specificity of predictors. Multivariate analysis was performed using a stepwise method with inclusion criteria at $p < 0.05$ and exclusion criteria at $p > 0.1$. To determine the optimal cutoff point (related criterion) in ROC analysis, the Youden index was used. The critical two-tailed significance level p was set at 0.05. SPSS Statistics software (IBM SPSS Statistics for Windows, Version 27.0.1 Armonk, NY: IBM Corp) and MedCalc (MedCalc Software Ltd version 20.305, Ostend, Belgium; https://www.medcalc.org; 2023) were used for statistical data processing.

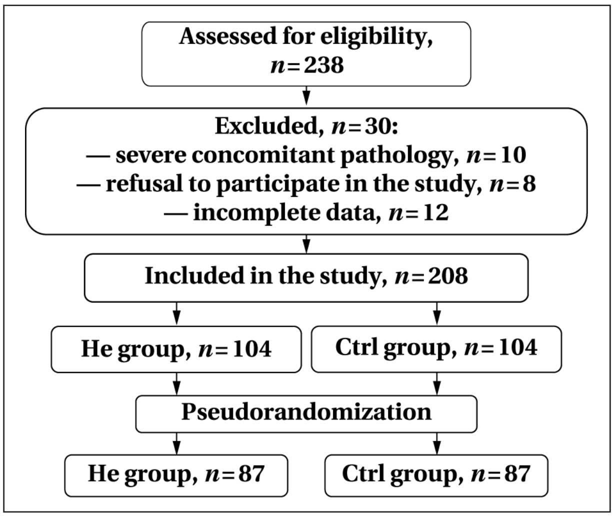

Fig. 1. Patient inclusion scheme.

Results

A total of 238 patients were evaluated. After screening for selection criteria, 30 patients were excluded from the study for the following reasons: presence of severe concomitant pathology ($n=10$), refusal to participate in the study ($n=8$) and incomplete data ($n=12$). As a result, 208 patients were included in the study, and divided into two groups: He group (receiving inhalations of a helium-oxygen mixture, $n=104$), and Ctrl group (historical control, $n=104$). After pseudo-randomization, 87 patients in each group with an adequate balance across all covariates were included in the final analysis (Fig. 1, Table 1).

After preoperative preparation, there was a statistically significant improvement of monitored functional parameters in He group compared with the Ctrl group (Table 2). FEV_1, FVC, and modified Tiffeneau index significantly improved in He group, as well as gas exchange parameters (PaO_2, $PaCO_2$, pH, SpO_2). Hypoxia tolerance tests values (Stange and Sabrazes (Hench) tests) also showed a statistically significant increase in He group.

Analysis of postoperative parameters demonstrated the advantage of the He group in terms of a number of critically important clinical outcomes (Table 3). In the He group, compared with the Ctrl group, the duration of mechanical ventilation was shorter: 4 [0–7] hours vs. 5 [0–9] hours ($p=0.032$); lactate 12 hours after surgery was lower: 1.9 [0.5–2.3] vs. 2.3 [0.5–3.1] mmol/L ($p=0.002$); the P/F ratio was higher at 6 hours (395 [395–395] vs. 373 [327–385] mmHg, $p < 0.0001$) and at 12 hours (398 [398–400] vs. 381 [357–397] mmHg, $p < 0.0001$), reflecting improved lung oxygenation. The ICU stay was shorter in the He group compared to the Ctrl group: 1 [0–2] vs. 2 [1–4] days ($p < 0.0001$). The total length of hospital stay was also shorter in the He group than in the Ctrl group: 21 [18–25] vs. 23 [19–28] days ($p=0.006$). The incidence of pulmonary complica-

Table 1. Patient characteristics.

Parameters	Values in the groups		p
	He, $n=87$	Ctrl, $n=87$	
Age, years	56 [47–64]	56 [44.5–67.5]	0.720
Gender (male), %	90	90	NA
Body weight, kg	65 [62–71.5]	68 [63–73]	0.053
BMI	22 [21–23]	22 [20–23]	0.669
COPD stage I, %	32	29	0.674
COPD stage II, %	54	54	1.000
COPD stage III, %	14	17	0.592
Charlson Comorbidity Index, score	9 [6–10]	8 [6–10]	0.804
FEV_1, % of predicted	71 [27–82]	67 [30–83]	0.618
FVC, L	4.24 [3.46–4.66]	4.28 [3.65–4.68]	0.851
Mod Tiffeneau–Pinelli (Hensler) index	0.62 [0.58–0.71]	0.6 [0.57–0.71]	0.263
Stange test, sec	34 [25–45]	33 [25–45.5]	0.777
Sabrazes (Hench) test, sek	20 [13–24]	19 [12–25]	0.647
PaO_2, mmHg	78 [73.5–80]	77 [74–80]	0.655
$PaCO_2$, mmHg	43 [40–47]	44 [40–48]	0.434
pH	7.39 [7.38–7.41]	7.39 [7.37–7.41]	0.789
SpO_2, %	95 [93–96]	96 [93–96]	0.603

tions in the He group was significantly lower than in the Ctrl group: respiratory failure — 3 vs. 13 cases (p=0.019), atelectasis — 1 vs. 4 (p=0.029), total number of pulmonary complications — 9 vs. 23 (p=0.006). Extrapulmonary complications and mortality did not differ statistically significantly between the groups (p>0.05).

Next, we conducted a univariate analysis of risk factors for pulmonary complications using univariate logistic regression. We identified a number of statistically significant predictors (Table 4, white rows).

Thus, both preoperative (especially pulmonary function tests, gas exchange parameters, and oxygen saturation) and early postoperative parameters served as significant risk factors for the development of pulmonary complications.

Multivariate logistic regression analysis was performed to identify factors associated with an increased risk of postoperative pulmonary complications (Table 5).

At the final stage of stepwise selection, two preoperative prognostic parameters (SpO_2 and Sabrazes (Hench) test) and one early postoperative marker/risk factor (duration of mechanical ventilation) were included in the model:

- SpO_2 after preparation: increased blood oxygen saturation was associated with a reduced risk of complications (coefficient=–0,09; p=0,0004; OR=0,41; 95% CI: 0,27–0,63);
- Sabrazes (Hench) test after preparation: a decrease in the duration of post-exhalation breath holding increased the risk of complications (coefficient=0,2; p=0,0001; OR=1,22; 95% CI: 1,09–1,36);

Table 2. Pulmonary function tests and gas exchange parameters after preoperative preparation of patients in the study groups.

Parameters	Values in the groups				p
	He, n=87		Ctrl, n=87		
	Me [*Q1*; *Q3*]	95% CI	*Me* [*Q1*; *Q3*]	95% CI	
FEV_1, % of predicted	81 [33–89]	77–87	69 [30–85]	62–73	0.0009
FVC, L	4.65 [3.78–5]	4.55–4.72	4.34 [3.7–4]	4.08–4.50	0.0115
modified Tiffeneau index	0.67 [0.64–0]	0.65–0.68	0.63 [0.59–0]	0.61–0.64	0.014
Stange test, sek	40 [30–54.5]	35–45	35 [26–48]	33–38	0.016
Sabrazes (Hench) test, sek	24 [15–29]	19–24	19 [12.5–25]	16–22	0.024
PaO_2, mmHg	84 [80–84]	84–84	80 [80–84]	80–84	0.0006
$PaCO_2$, mmHg	40 [38–43]	39–41	42 [38–46]	40–43	0.004
pH	7.42 [7.41–7.44]	7.41–7.43	7.41 [7.39–7.43]	7.40–7.42	0.0097
SpO_2, %	97 [91–97]	97–97	96 [91–97]	95–97	0.001

Table 3. Postoperative parameters and complications in patients in the study groups.

Parameters	Values in the groups		p
	He	Ctrl	
Frequency of pneumonectomy	9%	8%	0.817
Frequency of bilobectomy	3%	4%	0.725
Frequency of lobectomy	37%	38%	0.894
Risk scale post-op RF	39 [22–39]	34 [22–39]	0.387
Duration of post-op mechanical ventilation	4 [0–7]	5 [0–9]	0.032
Lactate 6 hours post-op, mmol/L	2.5 [0.7–3.3]	2.7 [0.7–3.2]	0.871
Lactate 12 hours post-op, mmol/L	1.9 [0.5–2.3]	2.3 [0.5–3.1]	0.002
PaO_2/FiO_2 = P/F ratio, mmHg after 1 hour	330 [279–370]	331 [281–360]	0.508
P/F ratio (after 3 hours)	344 [321–380]	341 [315–361]	0.323
P/F ratio (after 6 hours)	395 [395–395]	373 [327–385]	<0.0001
P/F ratio (after 12 hours)	398 [398–400]	381 [357–397]	<0.0001
Length of stay in the ICU, days	1 [0–2]	2 [1–4]	<0.0001
Length of hospital stay, days	21 [18–25]	23 [19–28]	0.006
Pneumonia, cases	1	3	0.060
Respiratory failure, sl.	3	13	0.019
Atelectasis, cases.	1	4	0.029
Bronchospasm, cases	1	0	0.500
ARDS, cases.	1	3	0.060
All pulmonary complications, cases	9	23	0.006
ACS, cases	1	2	0.123
PE, cases	1	2	0.123
Cerebral stroke, cases.	0	0	н/п
Severe arrhythmia, cases	4	6	0.001
Acute circulatory failure, cases.	1	2	0.123
All extrapulmonary complications, cases	7	12	0.226
In-hospital mortality, %	1.15	2.30	0.123

Table 4. Significance of risk factors for pulmonary complications.

Parameters	OR	95% CI	*p*
Baseline			
Age	0.98	0.94–1.23	0.320
Gender (male)	1.11	0.23–5.33	0.898
BMI	0.92	0.61–1.38	0.696
Charlson Comorbidity Index	0.98	0.78–1.38	0.681
FEV_1, % of predicted	0.95	0.92–0.98	0.0007
FVC, L	0.48	0.27–0.86	0.014
Stange test	0.95	0.91–0.99	0.029
Sabrazes (Hench) test	1.0	0.94–1.08	0.787
PaO_2	0.88	0.82–0.93	0.004
$PaCO_2$	1.19	1.08–1.33	0.0006
pH	1.38E-9	1.48E-14–0.0001	0.0016
SpO_2	0.65	0.52–0.82	0.0002
After preoperative preparation			
He group	2.74	0.92–8.17	0.058
FEV_1, % of predicted	0.93	0.91–0.97	0.0001
FVC, L	0.48	0.27–0.86	0.014
Modif Tiffeneau index	1.38E-9	1.48E-14–0.0001	< 0.0001
Stange test	0.95	0.91–0.99	0.02
Sabrazes (Hench) test	1.01	0.95–1.06	0.79
PaO_2	0.89	0.80–0.98	0.02
$PaCO_2$	1.24	1.12–1.38	0.0003
pH	1.38E-9	1.48E-14–0.0001	0.013
SpO_2	0.59	0.46–0.76	< 0.0001
Post-operative			
Pulmonectomy	2.0	0.59–6.74	0.28
Bilobectomy	4.82	1.30–17.82	0.03
Lobectomy	3.71	1.32–10.44	0.016
Risk scale post-op RF	1.07	0.99–1.16	0.054
Post-op mechanical ventilation	1.33	1.14–1.56	0.0001
Lactate 6 hours post-op	1.61	0.89–2.91	0.095
Lactate 12 hours post-op	2.55	1.35–4.82	0.002

- Duration of postoperative mechanical ventilation: prolongation of mechanical ventilation increased the likelihood of developing pulmonary complications (coefficient = 0,35; p = 0,0005; OR = 1,41; 95% CI: 1,16–1,72).

The quality of the final model was high: the percentage of correctly categorized cases was 92.2%, Hosmer–Lemeshow goodness-of-fit test was p = 0.933, and the overall significance of the model was p < 0.0001.

It should be noted that variables such as age, gender, type of surgery, Charlson comorbidity index, FEV_1, PaO_2, $PaCO_2$ after preparation, were not included in the final model, which confirms the independence of the identified factors from important clinical and demographic characteristics.

To assess the discriminatory ability of the factors, we performed ROC analysis of significant predictors of pulmonary complications (Table 6).

Factors with satisfactory and good model quality:

- FEV_1 after preparation: AUC = 0.813 (95% CI: 0.753–0.863), sensitivity 74.07%, specificity 77.35%%;
- SpO_2 after preparation: AUC = 0,814 (95% CI: 0,747–0,870), sensitivity 88,24%, specificity 68,00%;
- modified Tiffeneau index after preparation: AUC = 0,803; sensitivity 94,12%, specificity 59,33%;
- duration of post-op mechanical ventilation: AUC = 0,750; sensitivity 76,47%, specificity 83,33%.

Discussion

Reducing cardiorespiratory complications in patients with combined pathology (lung cancer and COPD) during surgery is an extremely pressing issue that requires development of appropriate treatment standards [25, 26]. Several factors contribute to the significant risks of postoperative respiratory failure, such as the duration of surgery exceeding 3 hours, urgency, tumor location in the chest, and trauma of major surgery (FAR guidelines, 2022). The negative effects of mechanical ventilation and intraoperative factors can lead to serious changes in respiratory biomechanics at all stages of anesthetic care [27].

Helium, due to its low density, reduces airway resistance, improving ventilation and gas exchange. A statistically significant improvement in functional parameters was reported in patients treated with helium-oxygen mixture: FEV_1 increased to 81% (versus 69% in the control group, p = 0.0009), SpO_2 reached 97% (p = 0.001), and the Tiffeneau index improved to 0.67 (p = 0.014). This confirms the effectiveness of using helium to optimize respiratory function in patients with obstructive pulmonary disease in the preoperative period. In our opinion, these indicators can be a useful tool in risk stratification.

The data obtained are comparable to the study by P. Jolliet et al., where a multicenter randomized controlled trial evaluating the effectiveness of Heliox in patients with COPD showed that the helium-

Table 5. Results of multivariate regression analysis.

Parameters	Coefficient	P	OR corr.	95% CI
SpO_2 after preparation	–0.09	0.0004	0.41	0.27–0.63
Sabrazes (Hench) test after preparation	0.2	0.0001	1.22	1.09–1.36
Duration of post-op mechanical ventilation	0.35	0.0005	1.41	1.16–1.72
Constant	75.06	0.0001		
Overall model quality assessment		<0.0001		
Percentage of correctly categorized cases 92.2%				
Hosmer–Lemeshow goodness-of-fit test, p = 0.933				

Note. Here and in the Table 6: AUC > 0.9 — excellent model quality; AUC > 0.8 — good model quality; AUC > 0.7 — satisfactory model quality.

Table 6. ROC analysis of significant predictors of pulmonary complications.

Parameters	AUC	95% CI	Related criterion	Sensitivity	95% CI	Specificity	95% CI
Baseline							
FEV_1, % of predicted	0.767	0.695–0.829	⩽47	47.06	23.0–72.2	92.00	86.4–95.8
FVC, L	0.677	0.600–0.747	⩽4.04	70.59	44.0–89.7	68.00	59.9–75.4
Stange test	0.649	0.572–0.722	⩽46	100.00	80.5–100.0	26.67	19.8–34.5
PaO_2	0.672	0.596–0.743	⩽72	47.06	23.0–72.2	85.33	78.6–90.6
$PaCO_2$	0.711	0.636–0.778	>46	58.82	32.9–81.6	74.00	66.2–80.8
pH	0.751	0.678–0.814	⩽7.38	76.47	50.1–93.2	64.67	56.5–72.3
SpO_2	0.767	0.696–0.829	⩽93	70.59	44.0–89.7	76.67	69.1–83.2
After preoperative preparation							
FEV_1, % of predicted	0.813	0.753–0.863	⩽61	70.59	44.0–89.7	78.00	70.5–84.3
FVC, L	0.680	0.603–0.750	⩽4.08	70.59	44.0–89.7	71.33	63.4–78.4
Mod Tiffeneau index	0.803	0.734–0.860	⩽0.64	94.12	71.3–99.9	59.33	51.0–67.3
Stange test	0.667	0.589–0.737	⩽36	76.47	50.1–93.2	54.67	46.3–62.8
PaO_2	0.627	0.549–0.701	⩽80	58.82	32.9–81.6	65.33	57.1–72.9
$PaCO_2$	0.715	0.640–0.782	>39	82.35	56.6–96.2	47.33	39.1–55.6
pH	0.701	0.626–0.770	⩽7.4	58.82	32.9–81.6	73.33	65.5–80.2
SpO_2	0.814	0.747–0.870	⩽95	88.24	63.6–98.5	68.00	59.9–75.4
Postoperative							
Duration of post-op mechanical ventilation	0.750	0.677–0.813	>8	76.47	50.1–93.2	83.33	76.4–88.9
Lactate 12 hours post-op	0.698	0.623–0.767	>2.3	52.94	27.8–77.0	70.67	62.7–77.8

oxygen mixture reduced respiratory acidosis, decreased shortness of breath, and reduced the severity of encephalopathy [28].

ABGs analysis remains the gold standard in assessing gas exchange in patients with COPD in the acute stage. The use of Helioxs led to an improvement in parameters such as PaO_2, $PaCO_2$, and pH, indicating a significant correction of ventilation-perfusion mismatch in the He group. Improved oxygenation and tissue perfusion parameters reduced the risk of multiple organ dysfunction and the frequency of pulmonary complications. This inevitably led to a reduction in duration of mechanical ventilation and ICU stay among patients in the He group. According to a study by L.V. Shogenova, the use of a helium-oxygen mixture in combination with nitric oxide and molecular hydrogen also led to a reduction in hypercapnia and hypoxemia, an increase in exercise tolerance, and an improvement in the clinical condition of patients with COPD [29].

According to a study by P. Singh et al., preoperative assessment of the risk of respiratory disorders can be performed using the Sabrazes (Hench) test. This method allowed predicting the likelihood of hypoxia in the early postoperative period in patients after surgery on the paranasal sinuses [30]. Multivariate analysis demonstrated a statistically significant correlation between shortened Sabrazes (Hench) breath-holding test and an increased risk of pulmonary complications.

Therefore, SpO_2 value and the Sabrazes (Hench) test are clinically significant parameters for preoperative prediction. The duration of mechanical ventilation is an important postoperative risk factor and essential target indicator for the prevention of secondary complications during treatment.

It should be emphasized that inclusion of helium-oxygen therapy in comprehensive preoperative preparation led to an improvement in functional parameters and laboratory indicators, contributing to a reduction in postoperative respiratory risks in cancer patients.

Conclusion

The use of a helium-oxygen mixture as part of preoperative preparation in cancer patients with COPD undergoing lung resection leads to a statistically significant improvement in functional respiratory parameters and a reduction in the incidence of postoperative pulmonary complications. Low saturation after preoperative preparation may be associated with an increased risk of complications, confirming the importance of oxygenation in prevention of respiratory dysfunction. In our opinion, the results of Sabrazes (Hench) breath-holding test correlates with the risk of complications, which may imply a decrease in breathing reserve (BR). An increase in the duration of mechanical ventilation is associated with an increased likelihood of complications, which is explained by the risk of barotrauma, atelectasis, and ventilator-associated lung injury.

The study confirms that preoperative optimization of respiratory function reduces the incidence of postoperative pulmonary complications in patients with COPD. The identified predictors can be used for individual risk prediction and the development of personalized management protocols.

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