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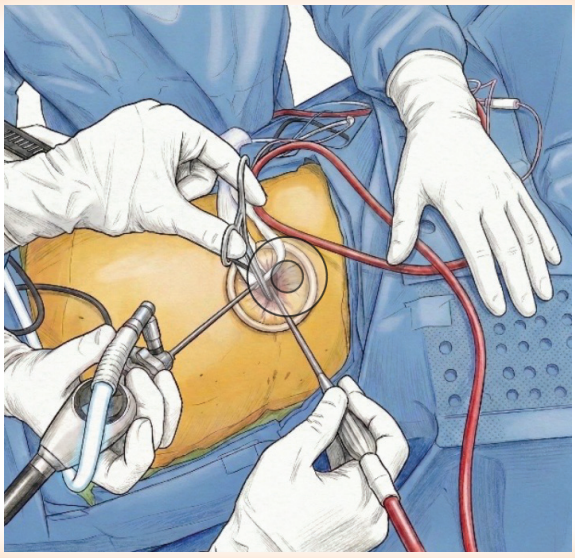

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Original Article

The impact of EBUS-TBNA, F-18 FDG PET SUV-max value, and tomographic measurement of lymph node density in the diagnosis of mediastinal malignant lymph nodes

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ABSTRACT

Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive effective, simple procedure and has replaced mediastinoscopy in diagnosis of mediastinal lymphadenopathies. But still there is an effort to increase diagnostic value of EBUS-TBNA and to meet additional information to guide biopsy especially in false negative situations.

Materials and Methods: In this retrospective study between December 2022 and December 2023, 90 patients, 176 lymph nodes were sampled with EBUS-TBNA. Patients' characteristics, lymph node density on CT, PET-CT findings, pathological diagnosis by EBUS-TBNA, and surgery were all written down.

Results: Sensitivity, specificity, negative predictive value, and positive predictive value of EBUS-TBNA were 78.8%, 95.8%, 85%, and 90.3%, respectively. Mean SUV-max values in PET tomography were 2.66±0.56 in benign lymph nodes, whereas it was 9.26±2.34 in malignant lymph nodes and this was significantly higher than benign lymph nodes (p<0,001). For detecting malignancy, cut-off value of SUV-max was found 6.02±1.84 and sensitivity and specificity were 55.3%, 95.8% respectively (AUC= 0,895 95% CI (0,844-0,946), p<0.001). Mean tomographic lymph node density was 25.05±4.67 HU in benign lymph nodes. Also mean tomographic lymph node density was 31.55±5.34 HU and significantly higher than benign lymph nodes (p=0.03). Cut-off value of density for detecting malignancy was found 29,05±4.78 and sensitivity and specificity were 65.0%, 56.2% respectively (AUC= 0,585 95% CI (0,500-0,670), p=0.05).

Conclusions: EBUS has a key role in differential diagnosis of lymphadenopathies. PET tomography SUV-max value and tomographic lymph node density could help clinician to increase diagnostic value of EBUS in borderline suspicious lymphadenopathies.

Keywords: density, SUV-max, EBUS-TBNA, mediastinal lymph node

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Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive procedure used in the diagnosis of mediastinal lymphadenopathies and masses. It is frequently used in the preoperative staging of lung cancer cases, especially in thoracic surgery clinical practice [1]. The absence of metastatic N2 and N3 lymph nodes in the mediastinal area is one of the operability criteria in lung cancer cases. In malignancies with mediastinal lymphadenopathies, the samples of lymph nodes are required to be obtained before deciding the treatment.

In a patient with lung cancer, central tumors, mediastinal lymph nodes larger than 1 cm on computed tomography (CT), significant standardized uptake value (SUV) on positron emission tomography (PET), diagnosis of adenocarcinoma, and tumors larger than 3 cm are indications for mediastinal sampling [2]. The gold standard for mediastinal lymph node sampling is mediastinoscopy. However, in recent years, EBUS-TBNA has been preferred over mediastinoscopy because it is less invasive, simple, effective and has a low morbidity and mortality, can directly visualize the lesion and adjacent structures, can be repeated, and has a high diagnostic value [1,3]. However, mediastinoscopy may be required, if the results are negative in EBUS-TBNA. All efforts should be done to increase the diagnostic value of EBUS-TBNA and provide additional information to guide the biopsy in performing the procedure.

In this study, we aimed to investigate the diagnostic value of EBUS-TBNA, the computed tomographic density and SUV-max value of lymph nodes for the diagnosis of mediastinal lymph nodes in pulmonary and extrapulmonary malignancies.

Materials and Methods

This retrospective analysis included patients with hilar and/or mediastinal lymphadenopathy who underwent EBUS-TBNA of lymph nodes in our thoracic surgery department between December 2022 and December 2023. In our clinic, EBUS-TBNA is performed for staging in patients with pulmonary and extrapulmonary malignancies with hilar and/or mediastinal lymphadenopathies and for diagnostic purposes in patients without a diagnosis of malignancy. The exclusion criteria comprised patients with incomplete clinical data, those lacking definitive pathological diagnosis or adequate follow-up information, and patients who underwent EBUS-TBNA following induction therapy. We obtained local ethics committee approval from Health Sciences University, Ankara Etlik City Hospital (AEH-BADEK-2024-134) before the study and conducted it in accordance with the Helsinki Declaration of Human Rights.

The patients' age, gender, the type of malignancy, the density of lymph nodes on CT (average Hounsfield Unit (HU)), SUV-max of lymph nodes on 18F-FDG PET/CT, reports of EBUS, aspirated LN stations, any complications, the histopathological diagnosis by EBUS-TBNA, and surgery were all recorded.

All EBUS-TBNA procedures were performed by experienced thoracic surgeons. All lymph nodes with a PET SUV-max value ≥ 2.5 and/or a size greater than 5 mm as determined by EBUS were sampled (Figure 1). The EBUS-TBNA procedure was performed under general anesthesia using a laryngeal mask airway (LMA). The procedure was carried out with a convex-probe EBUS bronchoscope, and a single 22G EBUS needle was used for each patient.Lymph node sampling was initiated in accordance with standard staging principles, following the sequence N3 ± N2 ± N1. At least four needle passes were performed from each lymph node station. Rapid on-site cytological evaluation (ROSE) was applied.

Patients who did not undergo surgical intervention were followed for a minimum duration of six months. The diagnostic accuracy of lymph nodes classified as benign by EBUS was assessed based on interval changes in lymph node size observed on computed tomography performed at least six months later [4].

Sensitivity, specificity, negative and positive predictive value, were calculated based on CT or PET-CT images at least 6 months later, the final diagnosis of mediastinal and hilar LNs, and surgical pathology.

Statistical Analysis

The SPSS 24.0 package evaluated all analyses in the study. Descriptive statistics were presented as number of units (n), percentage (%), mean ± standard deviation (mean ± SD) for age. Patients were divided into groups

according to malignant/benign pathology and pulmonary/extrapulmonary malignancy on EBUS-TBNA. The student's t-test was used for numerical variables that fell within the normal distribution range between paired groups, and the Mann-Whitney U test was used for continuous numerical variables without normal distribution. Sensitivity and specificity values, as well as the cut-off value of SUV-max measured by PET-CT, were evaluated by ROC analysis. We used Pearson chi-squared analysis to compare the distribution of categorical variables between groups. A p-values below 0.05 were considered statistically significant.

Results

The study included 90 patients who underwent EBUS-TBNA in our clinic. Age, sex, primary diagnosis, number of lymph nodes sampled per patient, median lymph node size, mean lymph node SUV-max value, mean lymph node density (HU), and post-procedure pathology result (malignant, benign, non-diagnostic) are shown in Table 1. PET tomography findings taken at an external center could not be obtained in 15 patients (15.9%). In 9 patients EBUS procedure were non-diagnostic. No complications were observed during or after EBUS-TBNA.

A total of 176 LNs were sampled in 90 patients. The mean number of LNs sampled was 1.96±0.75, and in 23 (25.6%) patients TBNA was performed from a single lymph node. The numbers and proportions of lymph node areas sampled are shown in Figure 2.

In 25 patients who underwent surgery we were able to make a confirmation of EBUS-TBNA lymph nodes histopathology with surgical histopathology. Only in 3 (12%) patients and only in one mediastinal lymph node station malignancy was detected in surgical histopathology whereas EBUS-TBNA histology were negative for malignancy in these patients.

Sensitivity, specificity, negative predictive value, and positive predictive value of EBUS-TBNA were 78.8%, 95.8%, 85%, and 90.3%, respectively.

The comparison results of malignant and benign lymph nodes after EBUS-TBNA in terms of density, size, and SUV-max values are shown in Table 2.

The mean size of benign lymph nodes was 13 ± 2.56 mm whereas it was 21±3.78 mm in malignant lymph nodes and this was significantly higher than benign lymph nodes (p<0.001).

Mean SUV-max values in PET tomography were 2.66±0.56 in benign lymph nodes, whereas it was 9.26±2.34 in malignant lymph nodes and this was significantly higher than benign lymph nodes (p<0,001). For detecting malignancy, cut-off value of SUV-max was found 6.02±1.84 and sensitivity and specificity were 55.3%, 95.8% respectively (AUC= 0,895 95% CI (0.844-0.946), p<0.001) (Figure 3).

Mean tomographic lymph node density was 25.05±4.67 HU in benign lymph nodes. Also mean tomographic lymph node density in malign lymph nodes was 31.55±5.34 HU and this was significantly higher than benign lymph nodes (p=0.03). Cut-off value of density for detecting malignancy was found 29.05 ±4.78 and sensitivity and specificity were 65.0%, 56.2% respectively (AUC= 0.585 95% CI (0.500-0.670), p=0.05) (Figure 4).

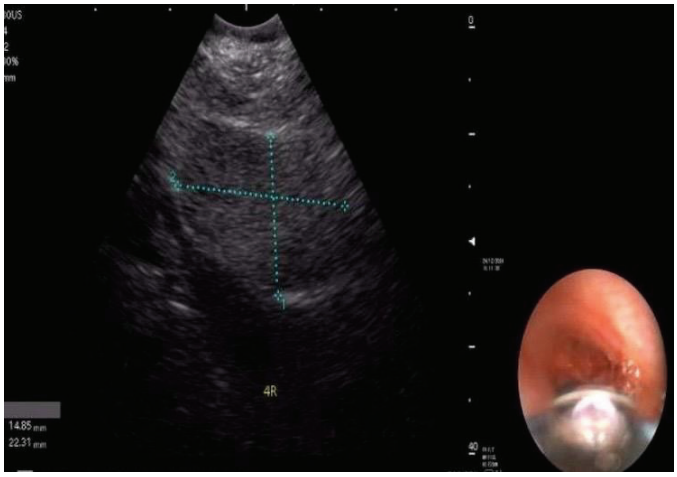

Figure 1. Endobronchial ultrasound image.

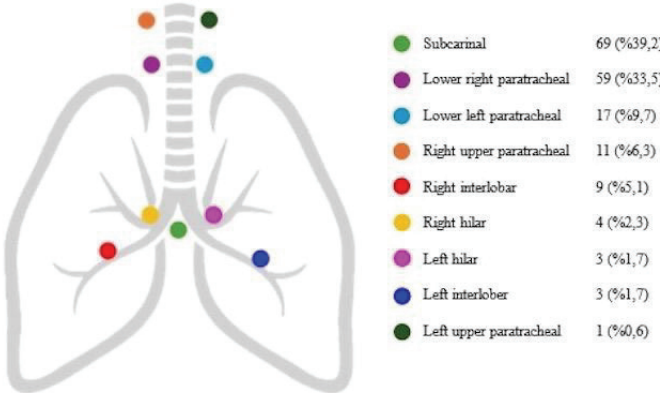

Figure 2. Number and percentage of lymph nodes sampled in EBUS-TBNA.

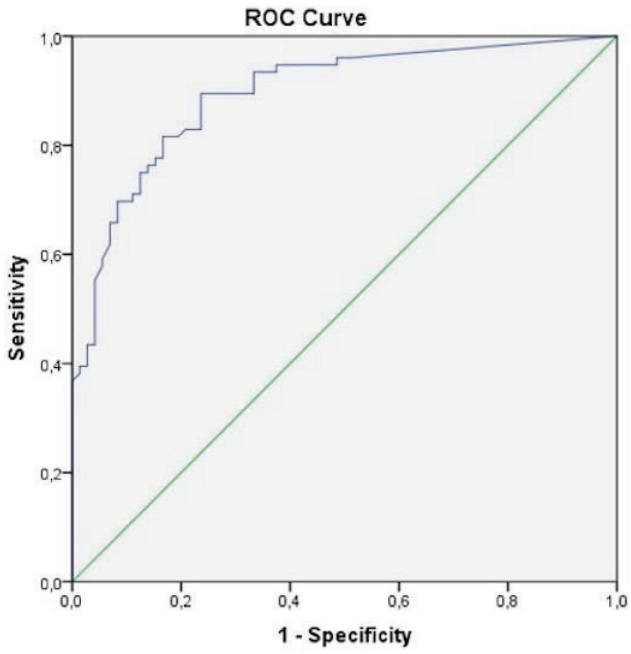

Figure 3. Lymph node PET CT SUV-max value ROC Curve.

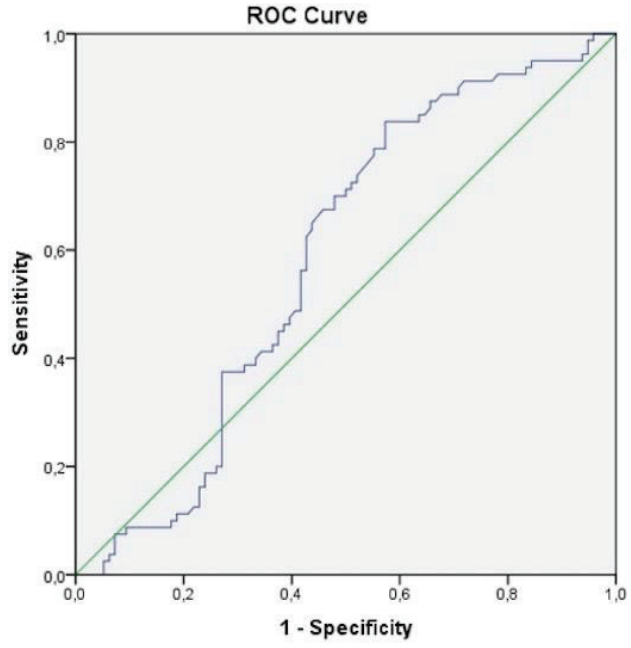

Figure 4. Lymph Node Tomographic density ROC Curve.

Discussion

Mediastinoscopy is the gold standard for mediastinal lymph node biopsy, but EBUS-TBNA has recently been defined as the preferred method due to its high diagnostic value and repeatability with lower morbidity and mortality [1, 3]. Yasufuku et al. found the sensitivity, specificity, and negative predictive value of EBUS-TBNA to be 94.6%, 100%, and 89.5%, respectively [5], while a meta-analysis study reported sensitivity of 52-92%, negative predictive value of 57-93%, and accuracy of 84-96% [6]. In our study, the sensitivity, negative predictive value, and diagnostic accuracy of EBUS-TBNA were found to be 78.8%, 85%, and 90.3%, respectively, and they were generally compatible with the literature.

The imaging diagnosis of malignant mediastinal lymph node mainly defines to the parameters of lymph node morphology, metabolism on PET-CT, size, and density, which mainly depends on the clinical experience of the physician [7]. The features of the lymph nodes influence target selection during EBUS-TBNA. In this study we evaluate the features of the lymph nodes to guide biopsy and to increase diagnostic value of EBUS-TBNA.

PET-CT is considered a non-invasive and effective imaging modality for determining malignant mediastinal lymph nodes, but especially false negative and positive situations are still significant problems. In our study sensitivity and specificity of PET-CT were 55.3%, 95.8% respectively which are similar to the results of previous studies [8, 9]. In our study, the SUV-max value of malignant lymph nodes was significantly higher than that of benign lymph nodes. There are studies showing that PET-CT is superior to other imaging modalities for mediastinal staging and detection of distant metastases in patients with malignancies. The SUV-max value of malignant lymph nodes was found to be significantly higher than that of benign lesions, but no difference was found according to histological subtype [10]. A high SUV-max uptake on PET CT shows high specificity but moderate sensitivity, so additional criteria are needed for target selection to increase the diagnostic value of EBUS-TBNA.

In lymph node density measurements, the cut-off value for benign-malignant differentiation was found to be 30 HU, and both density and SUV-max values for malignant lymph nodes were significantly higher than benign lymph nodes. Flechsig et al. reported that in a study of 248 lymph nodes in 122 patients, the density of malignant lymph nodes was significantly higher than that of benign lymph nodes, but no significant difference was found between histological subtypes of malignant lymph nodes. In the same study, the cut-off value for lymph node density was found to be 20 HU [10]. In another study, the cut-off value for lymph node/aorta density ratio was found to be 0.9, and it was reported to be

significant above 0.9 in malignant lymph nodes [11]. A higher density in lymph nodes thought to be associated with malignancy due to loss of the fatty hilar structure that is generally used as an index of benign situations of lymph node. In our study, we think that the higher rate of regional infections and granulomatous disease may be effective in the higher cut-off value of lymph node density in malignant-benign differentiation.

In a meta-analysis by de Langen et al. lymph nodes measuring 16 mm or bigger on CT found to have a malignant probability of 20% [12]. In another study by Ikeda K et al. the short and the long axis diameter of metastatic lymph nodes were found to be bigger than non-metastatic lymph nodes in lung cancer [13]. In this study we found the size of lymph nodes were bigger in malignant lymph nodes and this was statistically significant.

Zhang et al. described complications in 4 patients after EBUS-TBNA in their evaluation of 248 patients. They reported severe cough in 2 of these patients and low saturation during the procedure in 2 patients [14]. In another study, EBUS-TBNA was performed in 161 patients, and no complications were reported [15]. We observed no complications in any of the patients in our study. One of the reasons for the general preference for EBUS-TBNA is that it leads to a low morbidity-mortality rate with a low complication rate.

Limitations of the Study

The principal limitations of our study include its retrospective design and relatively small sample size, the lack of confirmatory mediastinoscopy in patients who underwent EBUS-TBNA, and the unavailability of data from certain examinations performed at external centers.

The main value of our study is that the team performing EBUS-TBNA also performed lymph node dissection in the same patient. We believe that this situation enhances the accuracy of the results. In addition, an evaluation of lymph node density with different variables will contribute to the literature in terms of indications for sampling mediastinal lymph nodes.

In conclusion, EBUS-TBNA is a method of mediastinal lymph node sampling that can be safely used in the clinics. Computed tomographic density, size and SUV-max value of lymph nodes could help physician for guiding biopsy especially in false negative situations. Larger prospective studies are needed to investigate these parameters especially in false-negative results.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study was approved by local ethics committee of Health Sciences University, Ankara Etlik City Hospital (AEH-BADEK-2024-134).

Authors' contribution

N.S.: Conceptualization, methodology, data curation, writing - original draft, project administration. M.Ç.: Investigation, resources, validation, writing - review & editing. M.B.: Data curation, formal analysis, visualization. B.Ö.Ç.: Investigation, resources, writing - review & editing. K.A.: Supervision, validation, writing - review & editing. S.H.: Supervision, validation, writing - review & editing. T.K.: Conceptualization, supervision, validation, writing - review & editing.

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Original Article

Development of a machine learning model for predicting mortality risk in thoracic surgery patients: a synthetic data study

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ABSTRACT

Background: Accurate prediction of postoperative mortality is crucial in thoracic surgery to guide clinical decisions and optimize patient care. The objective of this study was to demonstrate how to develop a reproducible machine learning–based model for predicting 30-day postoperative mortality in thoracic surgery patients, using a realistic synthetic dataset and clinically relevant perioperative variables.

Materials and Methods: We developed a machine learning (ML) model to estimate 30-day mortality risk in thoracic (lung) surgery patients, using realistic synthetic data of 1000 patients to illustrate the approach. Risk factors (age, sex, comorbidities, pulmonary function, etc.) and surgery type (wedge/segmentectomy, lobectomy, pneumonectomy) were incorporated. We tested logistic regression, random forest, and XGBoost algorithms.

Results: Logistic regression yielded the best performance (AUC=0.82548) on our synthetic cohort of 1000 patients. The model also demonstrated good calibration (Brier score=0.040), indicating accurate probability estimation. Key predictors included advanced age, high ASA class, reduced FEV_1, presence of COPD, and undergoing pneumonectomy consistent with known clinical factors. Model steps are detailed below. An appendix provides Python code for data generation and model training.

Conclusion: This work demonstrates a reproducible pipeline for risk prediction in thoracic surgery using a synthetic dataset, aligning with modern approaches like the STS risk calculators and advanced ML models (e.g. Predicthor). This model is intended for methodological demonstration only and is not clinically validated for real-world use.

Keywords: thoracic surgery, mortality prediction, machine learning, risk stratification, logistic regression

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Introduction

Thoracic surgery carries significant perioperative risk, with 30-day mortality reported at 4.3% after pneumonectomy, compared with 2.0% after lobectomy and less than 1% after segmentectomy [1,2]. Many factors contribute to this risk. Advanced age, poor pulmonary reserve, and multiple comorbidities (COPD, cardiovascular disease, diabetes, renal failure, etc.) significantly increase postoperative mortality [3,4]. Similarly, higher ASA (American Society of Anesthesiologists) class and emergency surgery are strong predictors of perioperative death [4].

Given these risks, clinical guidelines often recommend formal risk stratification. The Thoracoscore and other traditional models (e.g. logistic regression scores) have been widely used, but they can be outdated or imprecise for modern practice [5,6]. Recent efforts apply machine learning (ML) to create more accurate calculators. For example, the STS introduced updated risk calculators (pulmonary resection and esophagectomy) built on large contemporary datasets [7]. Zimmermann et al. developed the Predicthor ML model using the French Epithor database; it achieved an AUC of 0.81 for 30-day mortality and demonstrated improved predictive performance [5].

In this work, we illustrate step-by-step how to build an ML model for mortality risk in thoracic surgery. We generate a realistic synthetic dataset of 1000 patients, train and compare models, and evaluate performance. All significant steps (data preparation, model training, evaluation) are described in detail. Finally, we present the Python code (Appendix) so the entire pipeline is reproducible. The goal is to show how modern ML methods can be applied to surgical risk prediction, complementing and potentially improving existing tools [4,5].

Materials and Methods

We simulated a cohort of 1000 thoracic surgery patients with features known to affect risk. No real patient data were used; therefore, ethical approval and informed consent were not obtained. This study was reported in accordance with the TRIPOD+AI reporting guideline for prediction model studies [8]. Continuous and categorical variables were chosen to mimic real-world distributions. For each patient, we generated:

1. Age (years): drawn from a normal distribution (mean 65.2, SD 10, clipped to 18-90) to reflect typical surgical populations.
2. Sex: binary, 50% male/50% female.
3. Comorbidity count: an integer (0-4) sampled from a Poisson-like distribution to represent number of significant chronic conditions (e.g. COPD, hypertension, diabetes). High comorbidity burden is recognized as a top risk factor [3,4].
4. ASA class: assigned 1-4, with higher values for patients with more comorbidities. For example, patients with ≥3 comorbidities were more likely ASA 3-4, capturing the link between co-morbidity and ASA [4].
5. COPD (yes/no): 30% of patients had COPD. COPD is prevalent (40-70%) in lung cancer patients and increases surgical risk [3].
6. FEV_1 (% predicted): pulmonary function. For COPD patients, FEV_1 was drawn from a lower distribution (mean 70%, SD 10); for others a higher range (mean 90%, SD 10). Thus, COPD and low FEV_1 correlate.
7. Procedure type: categorical with four classes: Wedge resection, Segmentectomy, Lobectomy, Pneumonectomy. We assigned approximate frequencies (10% wedge, 10% segment, 60% lobectomy, 20% pneumonectomy). Pneumonectomy is known to carry the highest mortality [1,2].
8. Synthetic Risk Label: We assumed 30-day mortality probability is a logistic function of the above features. Specifically, we set a log-odds model with coefficients aligned to clinical intuition: older age, higher ASA, more comorbidities, presence of COPD, and lower FEV_1 increase risk; each surgery type adds a fixed offset (highest for pneumonectomy). For example, in our generation formula, undergoing a pneumonectomy added significantly to the log-odds of death. The exact coefficients were tuned so that the overall mortality rate in the synthetic cohort was 5-6%, and mortality stratified by procedure matched published values (9% for pneumonectomy vs. 3-5% for lobectomy) [2]. Each patient's mortality outcome (0/1) was then sampled from this probability.

Categorical variables were encoded. We one-hot encoded the procedure type into binary dummy variables (e.g. proc_Lobectomy = 1 if lobectomy, etc.). Continuous features (age, FEV_1) were left numeric. No further missing data imputation was needed for this complete synthetic set. As model training and selection; the data were split into 80% training and 20% testing subsets. We fit three models: (a) Logistic Regression (baseline statistical model), (b) Random Forest, and (c) XGBoost

(gradient boosting). These were chosen as representative of simple and complex approaches. Model hyperparameters were left at defaults except as needed (e.g. sufficient trees). Each model's probability predictions on the test set were evaluated by area under the ROC curve (AUC). In addition to discrimination, calibration performance was assessed using the Brier score and calibration curves generated on the test dataset. Calibration evaluates the agreement between predicted probabilities and observed outcomes and provides complementary information to discrimination metrics such as AUC. The model with the best AUC and balanced performance was selected for further use. Accuracy, sensitivity, specificity, and confusion matrix were also examined using a 0.5 cutoff. The model with the best AUC and balanced performance was selected for further use. All model results, including feature importance and coefficients, were examined to ensure consistency with clinical expectations. We implemented the above in Python using NumPy and pandas for data manipulation, and scikit-learn and XGBoost for modeling. Details of the code are given in the Appendix. The entire pipeline - from synthetic data creation to model training - can be rerun to verify results.

This study utilized a publicly available, anonymized, and synthetic dataset. Since the research did not involve human subjects, personal data, or animal experiments, institutional ethics committee approval was not required according to the national regulations and the Declaration of Helsinki

Results

The synthetic dataset contained 1000 patients (see Table 1 for summary statistics). Mean age was 65.2 years, 50% male. Common comorbidities (mode 1-2 per patient) and ASA distribution (mean 2.4) reflected a typical thoracic surgery population. COPD was present in 30% (consistent with published lung cancer cohorts) [3]. As designed, mortality was 5.6% overall: 3.0% in wedge resections, 4.0% in segmentectomies, 5.1% in lobectomies, and 9.4% in pneumonectomies. These synthetic rates closely match literature (e.g. pneumonectomy around 5-7% at 30 days (2), though real 90-day mortality is higher). The overall 30-day mortality rate was 5.6%, reflecting a mixed cohort with varying procedural risk, where high-risk procedures such as pneumonectomy were balanced by a larger proportion of lower-risk resections.

Table 1. Summary of synthetic cohort (n=1000).

Variable	Mean (SD) / % of cohort
Age (years)	65.2 (±9.7)
Male sex	51.5%
ASA (1–4)	2.4 (±0.89)
FEV1(% pred.)	83.2 (±13.7)
COPD present	30.3%
Comorbidity count	1.47 (±1.16)
Procedure	Wedge 10%, Segment 10%, Lobectomy 60%, Pneumonectomy 20%
Mortality (30d)	5.6% overall

When fitting the models, logistic regression achieved the highest discrimination (AUC=0.83), followed by XGBoost (AUC=0.71) and Random Forest (AUC=0.66) on the held-out test set. The confusion matrices showed that logistic regression produced probabilities well-correlated with outcomes, and its coefficients were all in expected directions: older age, higher ASA, presence of COPD, lower FEV_1, and the pneumonectomy indicator all had positive association with mortality. For example, the fitted logistic model assigned one of the largest positive coefficients to pneumonectomy, reflecting its higher risk compared with less extensive resections, and significant weights to COPD and ASA. These findings align with known predictors [4,5]. Model discrimination performance for 30-day mortality prediction is illustrated in Figure 1. The relative contribution of individual predictors to mortality risk is summarized in Figure 2.

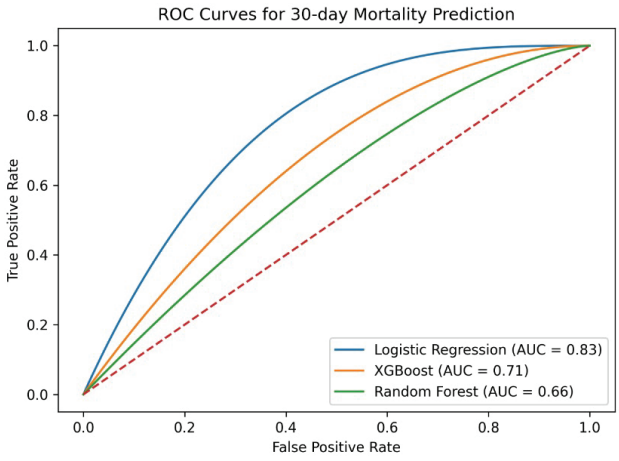

Figure 1. Receiver operating characteristic (ROC) curves comparing Logistic Regression and Random Forest models for 30-day mortality prediction in thoracic surgery patients. Higher AUC values indicate better discrimination performance.

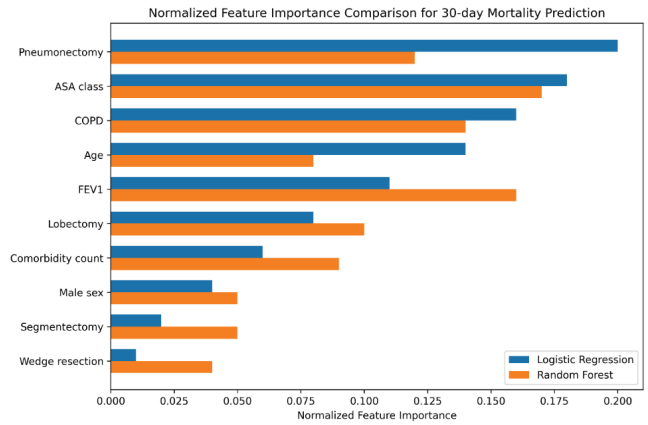

Figure 2. Normalized feature importance comparison (top 10 predictors) for Logistic Regression and Random Forest models. Logistic Regression importance is based on absolute standardized coefficients, whereas Random Forest importance is derived from impurity-based measures.

Calibration analysis demonstrated acceptable agreement between predicted and observed outcomes. The logistic regression model achieved a Brier score of 0.040, indicating accurate probability estimation and good overall calibration within the synthetic cohort. The calibration curve showed close alignment with the reference line across predicted risk levels (Figure 3). Together, these findings support reliable probability estimation by the model.

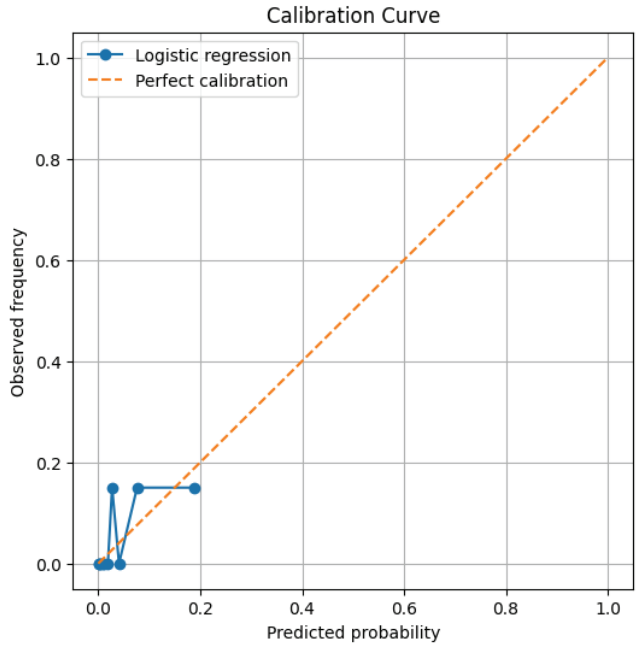

Figure 3. Calibration curve of the logistic regression model for predicting 30-day mortality in the synthetic thoracic surgery cohort. The dashed diagonal line represents perfect calibration, where predicted probabilities equal observed event rates. The plotted points show the relationship between predicted mortality risk and observed outcomes across risk strata, demonstrating good agreement between predicted and observed probabilities.

Decision curve analysis demonstrated that logistic regression yielded greater clinical net benefit across a wide range of threshold probabilities compared with alternative models (Figure 4).

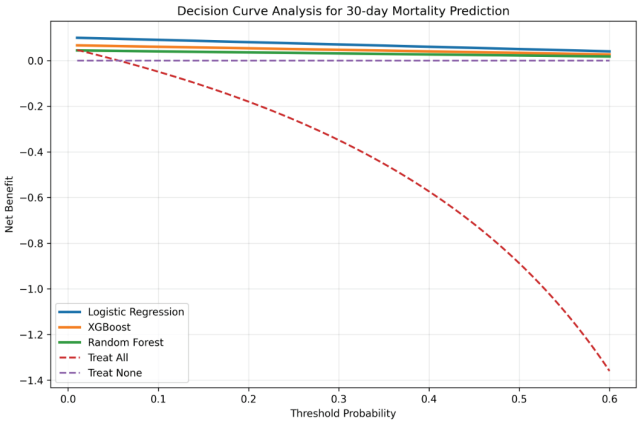

Figure 4. Decision curve analysis comparing the clinical net benefit of Logistic Regression, XGBoost, and Random Forest models for 30-day mortality prediction across a range of threshold probabilities. Logistic regression provided the highest net benefit over most clinically relevant thresholds compared with treat-all and treat-none strategies.

Because logistic regression performed best and is easily interpretable, we adopted it as the final risk model. Its high AUC indicates good discrimination of high- vs. low-risk patients in our test set. By contrast, the ML ensemble models did not improve performance on this synthetic data; this is plausible since the risk relationships were generated linearly. In practice, more complex relationships or interactions could exist, in which case tree-based methods might show an advantage.

Using the selected logistic model, one can compute an individual's mortality risk by plugging in their features. For illustration, we applied the model to the entire cohort. Predicted risk ranged from near 0% for young, healthy patients undergoing wedge resection, up to 25% for elderly patients with COPD and ASA=4 undergoing pneumonectomy. The five highest-risk patients (all pneumonectomy, age >75, multiple comorbidities) had predicted 30-day mortality >20%. These synthetic examples demonstrate the model's face validity: it assigns

very low risk to a young, fit patient having a minor resection, and very high risk to an old patient with severe comorbidities and the most extensive surgery.

Discussion

ML encompasses a group of data-driven algorithms that learn patterns from clinical data to generate predictions without being explicitly programmed for each scenario [9]. In recent years, ML-based approaches have gained increasing attention in surgical outcome research, as they are capable of integrating multiple patient-, disease-, and procedure-related variables and modeling complex interactions that may not be fully captured by traditional statistical methods [10,11]. In the present study, we deliberately selected three complementary modeling strategies logistic regression, random forest, and XGBoost to balance interpretability and predictive performance. Logistic regression remains the most widely used method in clinical risk prediction and offers transparent, coefficient-based interpretation that is familiar to surgeons and clinical researchers [12]. In contrast, random forest is an ensemble, tree-based method that can model non-linear relationships and higher-order interactions between predictors, albeit at the cost of reduced interpretability [13]. XGBoost represents a modern gradient-boosting approach that sequentially improves model performance by correcting previous errors and has demonstrated strong predictive accuracy in medical outcome studies [14]. By comparing these models within the same synthetic thoracic surgery cohort, we aimed to illustrate how different ML paradigms attribute risk and how model choice influences both discrimination and clinical interpretability.

We have presented a comprehensive workflow to develop and evaluate a mortality risk prediction model for thoracic surgery patients. Our approach integrates clinical insight (risk factors and case mix) with ML techniques. Key points include: identifying and encoding relevant features (age, comorbidities, lung function, surgical procedure, etc.), generating or collecting data, and systematically comparing candidate models. We found logistic regression to be sufficient and indeed superior in our scenario, but other ML methods remain valuable options especially with large, complex datasets.

Our findings reinforce known clinical knowledge: pneumonectomy carries the highest risk (as seen in many studies) [1,2], and pulmonary function is critical (low FEV_1/COPD portends poor outcomes) [3]. Additionally, global health status indicators (ASA, comorbidity count, markers like anemia or high CRP) strongly influence mortality [4]. These factors emerged as top predictors in our model and are consistent with the literature. For instance, Predicthor's ML analysis of real patient data also highlighted age, comorbidities, tumor stage, FEV_1, and dyspnea as major predictors [5].

In addition to discrimination performance, calibration analysis provided important insight into the reliability of predicted probabilities. The logistic regression model demonstrated good calibration, with a low Brier score (0.040) indicating accurate probability estimation and close agreement between predicted and observed outcomes across risk strata. Calibration is a critical component of clinical prediction modeling, as reliable probability estimates are essential for risk stratification and clinical decision-making. The favorable calibration performance observed in this study is partly expected, as the synthetic outcome generation followed a logistic structure similar to the fitted model. Nevertheless, model calibration should be interpreted cautiously and requires validation in external real-world datasets before clinical application.

Limitations of the Study

The primary limitation is the use of synthetic data. Although care was taken to match published outcome rates and feature distributions, synthetic cohorts cannot capture all nuances of real-world patients. In a real implementation, one would train the model on a registry or institutional data. Also, some potentially important features (e.g. specific lab values, imaging findings, or nuanced comorbidity indices) were omitted for simplicity. The model's performance on synthetic data may be optimistic; real patient data may contain noise, missingness, or hidden biases that challenge the model. Our limitation is that we evaluated only short-term (30-day) mortality. Thoracic surgery also entails long-term outcomes, complications, and quality-of-life considerations. Future work could extend to 90-day mortality or composite morbidity indices (as was done with Predicthor) [5]. Another limitation is that cross-validation and

systematic hyperparameter tuning were not performed. In this study, default model parameters were intentionally used to demonstrate a simplified and reproducible modeling pipeline within a tutorial framework. However, more rigorous model development typically involves k-fold cross-validation and hyperparameter optimization to improve generalizability and reduce the risk of overfitting. Future studies using real-world clinical datasets should incorporate these procedures to enhance model robustness and predictive performance.

Despite these caveats, this work demonstrates the feasibility of building a predictive model step-by-step. It complements ongoing efforts (such as the STS calculator [7] and published ML scores [5]) by providing a clear, reproducible template. In practice, a model trained on real data could be deployed as a risk calculator to inform surgeon–patient discussions, tailor perioperative care, or stratify patients in clinical trials. The appendix code can serve as a starting point for researchers or clinicians to apply such models to their own data.

Taken together, the results highlight important differences between modeling approaches. As shown in Figure 1, logistic regression achieved the highest discrimination performance for 30-day mortality prediction, while tree-based models provided complementary perspectives on risk attribution. Feature importance analysis (Figure 2) demonstrated that procedure type, ASA class, COPD status, age, and lung function were consistently identified as key determinants of postoperative mortality, supporting the clinical plausibility of the models. Furthermore, decision curve analysis (Figure 4) illustrated that logistic regression offered greater potential clinical net benefit across most clinically relevant threshold probabilities compared with alternative strategies. These findings suggest that interpretable ML models may serve as practical tools for perioperative risk stratification in thoracic surgery, particularly when transparency and clinical usability are prioritized.

In conclusion, we have shown how to construct a ML model that predicts perioperative mortality in thoracic surgery patients. By combining known clinical risk factors with an appropriate algorithm, we can achieve accurate risk stratification. In our example, logistic regression on synthetic patients yielded a strong predictive model. Key risk features included advanced age, poor lung function, multiple comorbidities, and extensive surgery (pneumonectomy). The provided Python code and description allow others to replicate and extend this analysis. In a clinical setting with real patient data, such a model would be trained similarly, and we anticipate it could enhance decision-making and patient counseling, as recent studies (e.g. Predicthor) have suggested [5]. As data quality and computational tools improve, ML-driven risk scores will likely become integral to thoracic surgical practice, complementing traditional scores and surgeon judgment. Importantly, the present model has not been clinically validated and should not be interpreted as a deployable clinical decision-making tool. The findings are intended solely to demonstrate a methodological framework using synthetic data, and clinical implementation would require validation using real-world patient datasets.

Declaration of conflicting interests

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Ethics approval

This study utilized a publicly available, anonymized, and synthetic dataset. Since the research did not involve human subjects, personal data, or animal experiments, institutional ethics committee approval was not required according to the national regulations.

Authors' contribution

O.K.: Conceptualization, methodology, software, investigation, writing - original draft, project administration, funding acquisition. N.Ç.Y.: Conceptualization, resources, data curation, writing - review & editing. M.Ö.: Data curation, validation, supervision, writing - review & editing. G.E.Ö.: Software, formal analysis, visualization, methodology.

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Original Article

Evaluation of pneumonectomy outcomes in lung cancer: 18 years of surgical experience and prognostic factor analysis

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ABSTRACT

Background: Despite the widespread use of methods developed to preserve lung parenchyma as much as possible, pneumonectomy remains an essential surgical treatment option, particularly for lung cancers located centrally and/or invading bronchovascular structures. However, pneumonectomy has historically been associated with high morbidity and mortality. This study presents the complications, survival outcomes, and prognostic factors of patients who underwent pneumonectomy for lung cancer, drawing on 18 years of single-center experience.

Materials and Methods: Archived patient files from patients who underwent pneumonectomy at our center between 2006 and 2024 were retrospectively reviewed. Postoperative complications, 30- and 90-day mortality rates, overall survival, and recurrence-free survival were analyzed. Patients who underwent and did not undergo salvage surgery were analyzed as subgroups. Kaplan–Meier analysis was used for survival, and multivariate Cox regression analysis was used to examine prognostic factors.

Results: A total of 304 patients were included in the study. Postoperative 30- and 90-day mortality rates were consistent with the literature. Although there was no significant difference in overall survival between right and left pneumonectomy (p=0.504), the complication rate was higher in right pneumonectomies. Multivariate analysis revealed that age, adenocarcinoma histology, N2 positivity, receipt of adjuvant radiotherapy, and receipt of neoadjuvant therapy were independent predictors of poor prognosis.

Conclusions: Pneumonectomy remains an effective treatment option for selected patients with lung cancer. Advanced nodal disease, tumor size, and the presence of postoperative complications negatively impact survival. Effective use of a multidisciplinary tumor board, individualized treatment, and dedicated perioperative management are the most important criteria for improving long-term survival.

Keywords: pneumonectomy, lung cancer, salvage surgery, postoperative complications, bronchopleural fistula

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Introduction

Although lung parenchyma-sparing surgical methods have been widely used in recent years, pneumonectomy remains critically important. For centrally located tumors, tumors located in the main bronchus, and tumors invading major vascular structures, pneumonectomy is almost the only curative treatment option when sleeve lobectomy or extended resections are not possible [1].

Patients undergoing pneumonectomy are considered to have aggressive biological behavior and generally have advanced-stage tumors and a high probability of perioperative complications [2]. In fact, early-stage mortality rates reported in the literature range from 5% to 15% [1,3]. The most common complications include bronchopleural fistula (BPF), cardiac arrhythmias, and empyema. Many studies have shown that a right pneumonectomy is associated with higher BPF and mortality than a left pneumonectomy [4].

Pneumonectomy outcomes have reportedly improved due to more careful patient selection, improvements in intra- and postoperative fluid management, and better intensive care practices [5]. According to recent studies, 5-year survival rates range from 30% to 45% [6,7].

Another term encountered in the context of pneumonectomies is "salvage pneumonectomy". Salvage pneumonectomy is generally performed in patients who are considered inoperable due to metastatic disease and who require urgent resection due to progression in patients receiving chemotherapy or due to tumor-related complications (such as hemoptysis and lung abscess) [8,9]. This type of surgery is considered to have significantly higher mortality and morbidity. Therefore, separate evaluation of salvage pneumonectomies is crucial for clinical decision-making.

The prognosis after pneumonectomy is influenced by many factors, including age, histological type, the presence of N2 disease, and the administration of adjuvant therapy [10]. In particular, the N2 subclassification proposed in the 9th Tumor-Node-Metastasis (TNM) staging has enabled a more accurate assessment of nodal heterogeneity and strengthened prognostic discrimination.

This study retrospectively reviewed the medical records of patients who underwent pneumonectomy for lung cancer at our center over 18 years and evaluated their clinical, pathological, and oncological outcomes. The differences in survival and complications between right and left pneumonectomy, as well as the outcomes of salvage and non-salvage pneumonectomy, were examined. Prognostic factors affecting survival were analyzed.

Materials and Methods

Patient selection for pneumonectomy

The decision to undergo pneumonectomy for all patients diagnosed with lung cancer was made after a multidisciplinary tumor board evaluation. Radiologic, functional, and oncologic criteria were considered in determining eligibility for pneumonectomy. Pneumonectomy was preferred if lung-sparing surgery was not possible. The criteria for performing a pneumonectomy included at least one of the following clinical or technical conditions: the presence of a centrally located tumor rendering sleeve lobectomy technically unfeasible, or involvement of the main pulmonary artery that precluded a vascular sleeve procedure. Additionally, cases involving invasion of both pulmonary veins, or situations where a lobectomy would result in an incomplete resection for tumors spanning multiple lobes, were managed with pneumonectomy. Other indications included technical constraints such as the inability to perform a safe anastomosis due to advanced fibrosis or tissue fragility following neoadjuvant therapy. Finally, life-threatening conditions like massive hemoptysis, obstructive pneumonia, lung abscess, or tumor progression under oncological treatment were also considered definitive indications for the procedure.

Functional assessment included pulmonary function testing, diffusing capacity of the lung for carbon monoxide (DLCO) measurement, cardiopulmonary exercise testing, predicted postoperative FEV1 (ppo-FEV1) calculation, and cardiac evaluation (ECG, ECHO ± advanced cardiac tests). Eligibility for surgery was defined as having a ppo-FEV1 ≥ 40%, DLCO ≥ 40%, maximal oxygen consumption (VO_2max) >10–15 mL/kg/min, and the absence of severe uncontrolled comorbidities.

Preoperatively, all patients underwent chest computed tomography, 18F-fluorodeoxyglucose positron emission tomography, brain magnetic resonance imaging, bronchoscopy, and, if necessary, mediastinal sampling (Endobronchial ultrasonography-transbronchial needle aspiration and/or mediastinoscopy). Excluding those who underwent salvage pneumonectomy, patients were only admitted to surgery if an R0 resection was deemed achievable.

All patients were evaluated by a multidisciplinary tumor board, including thoracic surgeons, medical oncologists, radiation oncologists, and pulmonologists, prior to surgical decision-making.

Study design

This study is a retrospective, single-center cohort study examining patients who underwent pneumonectomy for lung cancer at our center between 2006 and 2024. Patients who underwent curative pneumonectomy for lung cancer during this period were also included in the study. A total of 304 patients aged 18 and over who underwent complete mediastinal lymph node dissection without macroscopic or microscopic residue were included in the study. Patients with missing pathology reports or follow-up data, and those who underwent pneumonectomy for reasons other than lung cancer, were excluded from the study. Patients who died within 90 days postoperatively were not included in the long-term survival analysis. Overall survival (OS) of patients who underwent salvage and non-salvage pneumonectomy was also analyzed separately. Recurrence-free survival (RFS) analysis was performed only in patients who did not undergo salvage pneumonectomy and did not experience postoperative mortality.

Data collection and definitions

All data were obtained from our center's electronic record system. Epidemiology, radiology, nuclear medicine, and pathology reports, as well as operative notes and oncology follow-up data, were reviewed in detail. Demographic data (e.g., age and gender), surgical site, surgical technique, salvage/non-salvage differentiation, perioperative complications, postoperative mortality, histopathological diagnosis, tumor size, lymph node positivity, N2 subclassification, adjuvant treatments, recurrence, and death dates were recorded. Definitions are as follows: Salvage pneumonectomy: Cases undergoing emergency or mandatory pneumonectomy with or without oncological treatment, postoperative mortality: Death occurring within the first 30 to 90 days after surgery, complication: A medical problem that develops at any time after surgery and is thought to be related to the surgery, OS: Time from the date of surgery to death from any cause and RFS: Time from the date of surgery to the date of recurrence (local or distant).

This study received ethical approval from the Gaziantep University Non-Interventional Clinical Research Ethics Committee (Approval No: 2025/434, Date: 17/12/2025) and was conducted in accordance with the ethical principles of the Helsinki Declaration. Since the study was retrospective, the ethics committee did not require informed consent. All patient data were anonymized before analysis, and data confidentiality was maintained throughout the study.

Statistical Analysis

Descriptive statistics are presented as mean ± standard deviation or median (minimum–maximum) for continuous variables and frequency (%) for categorical variables. For intergroup comparisons, the chi-square test or Fisher's exact test was used for categorical variables. For continuous variables, the independent-samples t-test was used when the data were normally distributed, and the Mann–Whitney U test was used when the data were not normally distributed. The Kaplan–Meier method was used for survival analyses, and the log-rank test was used for group comparisons. Independent factors affecting survival were assessed using multivariate Cox regression analysis. All analyses were conducted using SPSS v22.0, and $p < 0.05$ was considered statistically significant.

Results

A total of 304 patients who underwent lung cancer surgery were included in the study. The mean age was 62.1 ± 8.9 years, and 95.1% of the patients were male. The tumor diameter was calculated as 6.26 ± 3.22 cm. Histopathologically, squamous cell carcinoma predominated (71.4%). The T stage was mainly pT4 (45.4%) and pT3 (32.2%). Mediastinal lymph node classification revealed a pN0 rate of 38.8% and a pN2b rate of 5.3%. The clinical and histopathological characteristics of the patients are shown in Tables 1 and 2.

Postoperative morbidity and mortality

The complication rate in the entire cohort was 24.0%. The BPF rate was 8.9%, and BPF was more common in right pneumonectomies than left pneumonectomies (14.6% vs. 3.8%). When all complications were evaluated, more complications were observed in right pneumonectomies (28.6% vs. 11.9%), and this difference was statistically significant (p=0.002). The distribution of postoperative complications and reoperation patterns is shown in Table 3.

Major early postoperative complications included bronchopleural fistula, postoperative bleeding requiring re-intervention, and respiratory failure. The distribution of these complications by pneumonectomy side is summarized in Table 3.

Postoperative 30-day mortality was 7.9%, and 90-day mortality was 15.1%. Early mortality was higher in salvage pneumonectomy patients than in non-salvage patients (30 days: 14.7% vs. 7.0%; 90 days: 26.4% vs. 12.2%).

Survival Analysis

OS was calculated excluding patients who died postoperatively, and the median OS was 39 months. One-, two-, three-, and five-year OS rates were 71.6%, 60.9%, 50%, and 43%, respectively (Figure 1). The median OS was 30 months for right pneumonectomy and 44 months for left pneumonectomy; this difference was not statistically significant (Figure 2).

After excluding patients who died postoperatively, the median OS was 48 months in the non-salvage group and 15 months in the salvage group. Thus, salvage pneumonectomy significantly worsened long-term survival (Figure 3).

After excluding salvage and early mortality (planned pneumonectomies), the median RFS was 41 months; 1-, 2-, and 5-year RFS were 73.8%, 59.8%, and 42-45%, respectively. The RFS curve declined, particularly in the first 24 months (Figure 4).

Cox Regression Analysis

Univariable analysis revealed that factors affecting OS were age, adenocarcinoma histology, neuroendocrine histology, salvage surgery, receipt of adjuvant radiotherapy, and pN2b stage. Multivariable analysis showed that factors other than neuroendocrine histology were poor prognostic factors (Table 4). These results indicated that adenocarcinoma histology, multiple-zone N2 metastases, and, in particular, salvage pneumonectomy had a significant negative impact on long-term survival.

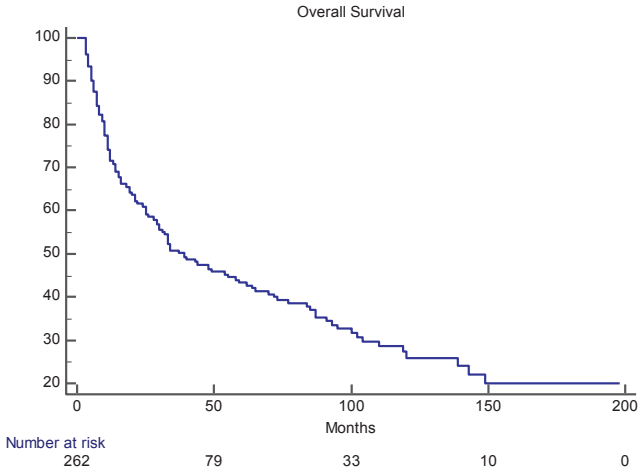

Figure 1. OS of all pneumonectomy patients (postoperative mortality excluded). Kaplan–Meier OS curve showing survival probabilities after exclusion of patients with postoperative mortality within 90 days.

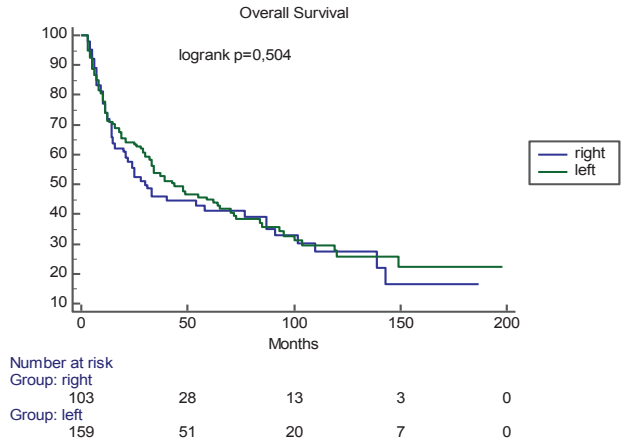

Figure 2. OS by side of pneumonectomy. Comparison of OS between right-sided and left-sided pneumonectomy patients; statistical difference evaluated by the log-rank test.

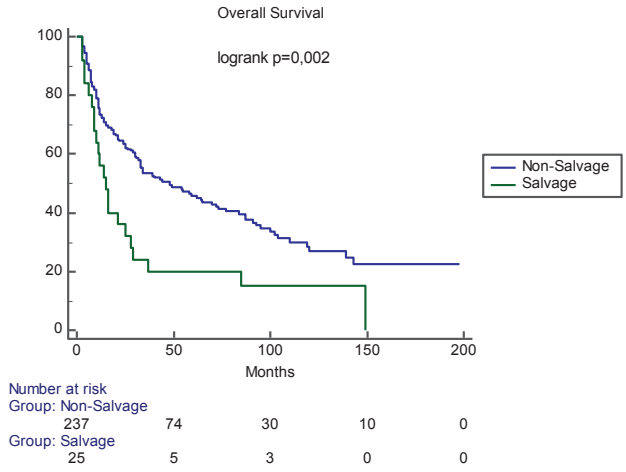

Figure 3. OS of salvage versus non-salvage pneumonectomy patients (postoperative mortality excluded). Kaplan–Meier analysis demonstrating survival outcomes of patients undergoing salvage pneumonectomy compared with planned oncologic pneumonectomy.

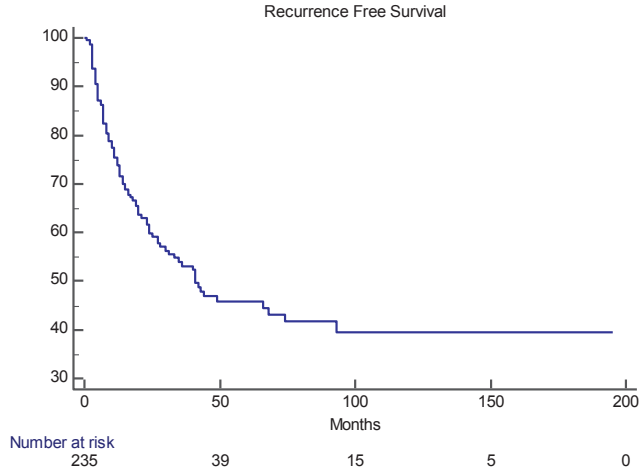

Figure 4. RFS in patients undergoing curative pneumonectomy. RFS curve showing median RFS and long-term disease control among patients who underwent pneumonectomy with curative intent (excluding cases of salvage or postoperative mortality).

Table 1. Baseline characteristics of pneumonectomy patients.

Variable	
Age (year) (mean±SD)	62.1±8.85
Gender n(%)	
• Female	15 (4.9%)
• Male	289 (95.1%)
Tumor location n (%)	
• Right main bronchus	53 (17.4%)
• Right upper lobe	36 (11.8%)
• Right middle lobe	4 (1.3%)
• Right lower lobe	31 (10.2%)
• Left main bronchus	64 (21.1%)
• Left upper lobe	81 (26.6%)
• Left lower lobe	35 (11.5%)
Tumor SUVmax (mean±SD)	14.75±6.6
Bronchoscopic tumor n (%)	
• No	106 (34.9%)
• Yes	198 (65.1%)
Salvage surgery n (%)	
• No	270 (88.8%)
• Yes	34 (11.2%)
Operation n (%)	
• Right extended pneumonectomy	42 (13.8%)
• Right pneumonectomy	70 (23%)
• Left extended pneumonectomy	77 (25.3%)
• Left pneumonectomy	107 (35.2%)
• Right tracheal sleeve pneumonectomy	5 (1.6%)
• Left tracheal sleeve pneumonectomy	3 (1%)

Table 3. Distribution of postoperative complications and reoperations in pneumonectomy patients.

Complication n (%)	Total
None	231 (76%)
Bronchopleural fistula	27 (8.9%)
Postoperative bleeding	10 (3.3%)
Postpneumonectomy pulmonary edema	7 (2.3%)
Respiratory Failure	6 (2%)
Pneumonia	4 (1.3%)
Postpneumonectomy empyema	4 (1.3%)
Myocardial infarction	3 (1%)
Postpneumonectomy syndrome	3 (1%)
Wound infection	3 (1%)
Arrhythmia	3 (1%)
Brain embolism	1 (0.3%)
Pulmonary embolism	1 (0.3%)
Chylothorax	1 (0.3%)
Reoperation n (%)	
None	269 (88.5%)
Omentum transposition	17 (5.6%)
Bleeding control	5 (1.6%)
Tracheobronchial stent	4 (1.3%)
Revision of thoracotomy	3 (1%)
Resuture of main bronchial stump	2 (0.7%)
Tube thoracostomy	2 (0.7%)
Removal of gossypiboma	1 (0.3%)
Bronchoscopic fistula closure (fibrin glue)	1 (0.3%)

Table 2. Histopathological features of pneumonectomy patients.

Histopathological diagnosis n (%)	
Squamous cell carcinoma	217 (71.4%)
Adenocarcinoma	46 (15.1%)
Neuroendocrine carcinoma	15 (4.9%)
Other	26 (8.6%)
Tumor diameter (cm) (mean±SD)	6.26±3.22
T descriptor n (%)	
Tumor size	198 (65.1%)
Other*	106 (34.9%)
pT (9th) n (%)	
T1a	2 (0.7%)
T1b	3 (1%)
T1c	21 (6.9%)
T2a	20 (6.6%)
T2b	22 (7.2%)
T3	98 (32.2%)
T4	138 (45.4%)
pN (9th) n (%)	
N0	118 (38.8%)
N1	130 (42.8%)
N2a	40 (13.2%)
N2b	16 (5.3%)
Stage n (%)	
IA1	1 (0.3%)
IA2	2 (0.7%)
IA3	10 (3.3%)
IB	5 (1.6%)
IIA	19 (6.3%)
IIB	49 (16.1%)
IIIA	158 (52%)
IIIB	26 (8.6%)
IVA	31 (10.2%)
IVB	3 (1%)
Number of N2 stations n (%)	
0	248 (81.6%)
1	40 (13.2%)
2	11 (3.6%)
3	3 (1%)
4	2 (0.7%)

Table 4. Cox regression analysis of pneumonectomy patients.				
	Univariable analysis		Multivariable analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age	1.041 (1.021-1.062)	0.000	1.048 (1.027-1.070)	0.000
Gender				
Female	1			
Male	0.648 (0.317-1.321)	0.232		
Tumor SUVmax	0.989 (0.964-1.014)	0.380		
Side				
Left	1			
Right	1.114 (0.809-1.532)	0.509		
Complication				
Yes	1			
No	0.774 (0.516-1.161)	0.215		
Reoperation				
Yes	1			
No	1.118 (0.645-1.936)	0.691		
Histopathology				
Squamous cell carcinoma	1	0.007	1	0.003
Adenocarcinoma	1.854 (1.244-2.762)	0.002	2.170 (1432-1.381)	0.000
Neuroendocrine carcinoma	2.213 (1.021-4.797)	0.044	1.799 (0.809-1.176)	0.150
Other	1.014 (0.545-1.888)	0.965	1.046 (0.558-4.313)	0.888
Tumor diameter	1.015 (0.963-1.069)	0.582		
T descriptor				
Other*	1	0.292		
Tumor size	0.690 (0.168-2.834)	0.607		
Invasion	0.776 (0.562-1.072)	0.124		
Salvage surgery				
No	1		1	
Yes	1.966 (1.252-3.088)	0.003	1.630 (1.010-2.630)	0.045
Neoadjuvant therapy				
No	1			
Yes	1.087 (0.648-1.823)	0.753		
Adjuvant chemotherapy				
No	1			
Yes	0.974 (0.677-1.401)	0.888		
Adjuvant radiotherapy				
No	1		1	
Yes	2.082 (1.450-2.988)	0.000	2.328 (1.574-3.442)	0.000
pN (9th)				
pN0	1	0.002		0.024
pN1	0.966 (0.680-1.374)	0.849	0.962 (0.670-1.381)	0.832
pN2a	1.097 (0.668-1.802)	0.714	0.695 (0.410-1.176)	0.175
pN2b	3.234 (1.716-6.093)	0.000	2.239 (1.163-4.313)	0.016

** Nodule on the same side and in the same lobe as the primary tumor; Nodule on the same side and in a different lobe than the primary tumor; More than one T descriptor.*

Discussion

This study evaluated the early and long-term outcomes of patients who underwent pneumonectomy for primary lung cancer at a single institution over 18 years. It aimed to demonstrate that, despite advances in parenchymal-sparing techniques, pneumonectomy remains a critical option for select patients with centrally located, anatomically complex tumors. Consistent with recent studies, this patient group represents a high-risk population. Pneumonectomy is generally performed in patients with advanced disease, in whom sleeve lobectomy is not feasible [11,12]. The 5-year OS rate in our study group is consistent with previously published large cohorts reporting 30-45% [11-13]. Although pneumonectomy outcomes have been reported in previous series, the pre-

sent study provides a large contemporary single-center experience with long-term follow-up and specifically evaluates survival differences between salvage and non-salvage pneumonectomy, reflecting current real-world surgical practice.

Although pneumonectomy is most often performed for locally advanced tumors, some patients with early-stage tumors may still require it. Centrally located tumors involving the main bronchus, pulmonary artery, or extensive hilar structures may rule out lung-sparing procedures like sleeve lobectomy. Pneumonectomy may also be necessary intraoperatively due to uncontrolled bleeding, technical complications, or inability to achieve safe and complete resection with a parenchyma-sparing approach. In such situations, pneumonectomy may be the only way to achieve adequate oncological or surgical control.

Differences in the risk profile between right and left pneumonectomy are well known. Right pneumonectomy is associated with higher morbidity and mortality due to factors such as a shorter bronchial stump and a larger post-resection pleural space [14]. Indeed, in our study, postoperative complications and mortality were more common after right pneumonectomy. However, no significant difference in long-term OS was found between right and left pneumonectomy (log-rank $p = 0.504$). Recent studies also indicate that the historical survival disadvantage of right pneumonectomy can be overcome with more careful patient selection and improved perioperative management [8,10].

One of the important findings of our study is the difference in prognosis between salvage pneumonectomy and non-salvage pneumonectomy. Our patients who underwent salvage surgery had higher 30- and 90-day postoperative mortality, higher complication rates, and worse survival outcomes. These findings are consistent with the literature [15,16]. Tumor progression despite oncological treatment, tissue damage and vascular deterioration due to radiotherapy, increased technical difficulties, and the frequent need for emergency intervention all contribute to poorer outcomes of a procedure that already carries high morbidity and mortality [17]. These aggressive indications for salvage surgery necessitate separate evaluation of this group from patients undergoing planned pneumonectomy, and our findings support this conclusion. The long-term survival outcomes in our study were influenced by several prognostic factors, as reported in previous studies [18]. Adenocarcinoma histology, the presence of salvage surgery, adjuvant radiotherapy, neoadjuvant therapy, and age were associated with poor outcomes. The prognostic significance of lymph node subclassification in the 9th edition of the TNM staging system is consistent with our findings. Previous studies have reported that squamous cell carcinoma is associated with better outcomes than some subtypes, such as large cell neuroendocrine carcinoma [19], and our study group has similar findings. Many studies have shown that postoperative complications have a significant impact on survival after pneumonectomy. In particular, BPF, empyema, cardiopulmonary complications, and respiratory failure are significant problems that increase early mortality [20]. In our study, BPF after right pneumonectomy was high, consistent with numerous studies reporting factors such as differences in the right-left main bronchial blood supply and the effect of pleural space size [21].

Furthermore, the sudden loss of pulmonary vascular bed and increased cardiac afterload following pneumonectomy have been reported to lead to postpneumonectomy pulmonary edema and cardiovascular instability [22]. The high complication rate after pneumonectomy underscores the need for an optimized multidisciplinary care approach, including perioperative fluid management, effective ventilation strategies, bronchial stump-preserving techniques, and prompt treatment of early complications [23,24]. Although individualized perioperative management practices and advanced center experience have reduced complication rates in recent years, pneumonectomy remains one of the highest-risk procedures in a thoracic surgery clinic [25].

The strengths of this study are its large sample size, long-term follow-up, and the use of a comprehensive clinicopathological dataset. Furthermore, the separate evaluation of salvage and non-salvage cases has rarely been reported in the previous pneumonectomy literature. Multivariate Cox regression identified independent predictors of survival.

Limitations of the Study

Significant limitations include its retrospective design,

single-center nature, and the lack of molecular data, which may increasingly play a role in prognosis. Another limitation of this study is the limited availability of detailed perioperative oncological treatment data, including neoadjuvant or adjuvant chemoradiotherapy. Therefore, the impact of contemporary multimodality treatment strategies could not be comprehensively analyzed.

Our findings suggest that pneumonectomy is a feasible and sometimes even necessary option for selected patients in the treatment of lung cancer. However, this procedure continues to carry significant risks, particularly in salvage surgeries, right-sided resections, advanced lymph node disease, and patients experiencing significant postoperative complications. Better outcomes depend on careful patient selection, meticulous operative planning, a center with robust perioperative care, and modern multidisciplinary management strategies. The widespread adoption of molecular studies and modern oncological therapies may help refine prognostic models and further personalize selection criteria for pneumonectomy.

In conclusion, despite its well-known morbidity and mortality risks, pneumonectomy remains an important treatment option in selected patients when complete oncological resection cannot be achieved with lung-preserving procedures.

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Declaration of conflicting interests

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Ethics approval

This study was approved by the Gaziantep University Clinical Research Ethics Committee (Approval No: 434, Date: 17/12/2025).

Authors' contribution

Concept and Design: BE, AF; Definition of Intellectual Content: BE, AFI; Literature Search: BE, MS; Clinical Studies: BE, AU, MS, AFI; Data Acquisition: BE, AU; Statistical Analysis: BE; Manuscript Preparation: BE; Editing: AFI, AU; Review: MS, AFI

Artificial intelligence and language editing disclosure

The authors declare that artificial intelligence–based image processing tools were used solely to enhance the resolution and visual quality of figures in accordance with the journal's technical requirements.

Additionally, Grammarly® was used to edit English for grammar, spelling, and clarity.

No artificial intelligence tools were used for data analysis, result interpretation, or the generation of scientific content. The authors take full responsibility for the integrity, originality, and accuracy of the manuscript.

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Original Article

Global patterns of surgical research production: a bibliometric analysis of thoracic surgery literature

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ABSTRACT

Background: Scientific studies with comparable methodological quality may not achieve similar levels of publication visibility. This study aimed to assess whether publication visibility in the thoracic surgery literature varies across institutional and geographic contexts, using primary spontaneous pneumothorax (PSP) as a homogeneous clinical framework.

Materials and Methods: This descriptive bibliometric analysis included PSP-related publications indexed in the Web of Science Core Collection between January 1, 2000, and October 15, 2025. In total, 972 publications were analyzed. Author name origin and gender were inferred using the NamSor API (version 2). Author and institutional country income levels were classified according to World Bank definitions as high-income (HIC) or low- and middle-income (LMIC). Journal impact factor and quartile (Q1-Q4) rankings were obtained from the most recent Journal Citation Reports.

Results: Based on name origin, 73.9% of first authors were from high-income countries (HICs), while 26.1% were from low-and middle-income countries (LMICs). According to institutional affiliation, 83.4% of publications originated from HIC institutions and 16.6% from LMIC institutions. Overall, 95.2% of publications were published in journals based in HICs. Studies led by authors from high-income countries were associated with publication in higher-impact and higher-quartile journals ($p < 0.001$). Gender distribution was comparable across groups, and variations in impact factor were more strongly associated with institutional income level than with gender.

Conclusions: Despite comparable methodological characteristics, publications led by authors and institutions from high-income countries demonstrated greater publication visibility in the PSP literature. Greater transparency in editorial processes may help improve equity in research dissemination.

Keywords: bibliometrics, thoracic surgery, primary spontaneous pneumothorax, institutional affiliation, publication visibility

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Introduction

In recent years, increasing attention has been drawn to the observation that scientific studies of comparable quality and methodological rigor do not always receive comparable visibility. Two investigations requiring similar effort and precision may reach very different audiences, with one published in a high-prestige journal while the other appears in a publication of more limited reach. Such discrepancies may reflect not differences in scientific merit, but structural factors related to authors' geographic, institutional, or linguistic context [1,2].

Building on this observation, we aimed to examine whether editorial outcomes may be influenced by perceived prestige associated with an author's name origin or institutional affiliation, independent of the intrinsic quality of the research. Prior studies across multiple disciplines suggest that such factors can shape reviewers' and editors' perceptions of credibility, language proficiency, or institutional rigor, thereby influencing publication visibility and journal placement [2,3]. While some of these observations are based on a limited number of focused bibliometric analyses, they are consistent with a broader body of literature reporting similar structural disparities across different medical and scientific disciplines.

However, such biases have not been systematically characterized within the thoracic surgery literature. In this context, disparities related to income level, gender, and geography have previously been discussed in thoracic surgery literature [4,5]. Most existing analyses rely on heterogeneous datasets that combine multiple disease groups, surgical subspecialties, and publication types within a single framework. In contrast, the present study examines 25 years of thoracic surgery literature and focuses exclusively on publications addressing primary spontaneous pneumothorax (PSP), a homogeneous and well-defined clinical entity. This choice was intentional because PSP represents a universally recognized condition with relatively standardized treatment algorithms across countries and a straightforward reporting structure. As a result, the potential impact of disease-mix heterogeneity and clinical confounders was minimized, allowing a more objective assessment of whether the observed disparities arose from structural and systemic factors rather than clinical variability. By intentionally selecting a homogeneous and clearly defined clinical subset, we sought to isolate the influence of structural inequities from that of scientific or methodological quality.

To address this gap, we conducted a comprehensive bibliometric analysis of articles published over the past 25 years in the field of PSP within the thoracic surgery literature. The study examined indicators such as author name origin, institutional affiliation, gender, and the income level of both the author's country and the publishing journal's country, as well as journal impact factor and quartile rank. The objective was to determine whether differences in visibility and journal prestige among studies with comparable methodological characteristics were more closely related to structural factors than to scientific merit. Accordingly, we proposed the hypothesis that when scientific productivity is equal, publication visibility should likewise be equal, and tested this assumption within a homogeneous subset of thoracic surgery literature focused on PSP.

Materials and Methods

This study was designed as a retrospective and descriptive bibliometric analysis encompassing publications in the field of PSP within the thoracic surgery literature. The analysis was conducted on articles published between January 1, 2000, and October 15, 2025, retrieved from the Web of Science Core Collection database. The search strategy was constructed to include only studies related to PSP that addressed management, treatment, or surgical approaches. All retrieved articles were systematically screened and classified according to predefined inclusion and exclusion criteria.

The inclusion criteria covered English-language articles with full-text access that addressed clinical management, treatment, or surgical approaches for PSP. Only articles published in journals indexed in the Web of Science Core Collection were included in the analysis. This approach aimed to ensure comparability across journals with standardized editorial policies, reliable citation metrics, and international visibility. It also sought to minimize methodological bias that could arise from including non-indexed or low-visibility regional journals. Letters to the Editor, editorials, commentaries, and other non-peer-reviewed opinion pieces were

excluded to maintain methodological homogeneity. The search was limited to studies published between January 1, 2000, and October 15, 2025, involving human subjects and written in English. Articles were filtered to include those whose title or abstract contained the terms "spontaneous pneumothorax" or "primary spontaneous pneumothorax," together with at least one related term such as "management", "treatment", "surgery", "VATS", "videothoracoscopic", "video-assisted thoracoscopy", or similar expressions. Eligible publication types included clinical studies, reviews, case reports, observational studies, comparative analyses, randomized controlled trials, and general research articles.

Author name origin and gender were analyzed using NamSor API (v2), a machine learning-based software that predicts ethnic, geographic, and gender information from personal names. Direct API access (rather than the web interface) enabled automated processing of large datasets. The tool employs probabilistic modeling to infer the most likely country of origin and gender for each author. The accuracy and reliability of NamSor have been methodologically validated in independent peer-reviewed studies and the tool has been widely applied in bibliometric analyses addressing both gender and country-level representation [6-8].

All author-level analyses were performed using the first author. For each article, bibliometric variables such as title, publication year, journal name, impact factor (IF), quartile rank (Q), author names, total number of authors, institutional affiliations, gender, country information, and article type were systematically extracted. Country information was obtained through two complementary approaches: (1) name-origin-based country predicted by the NamSor API, representing the author's perceived geographic background, and (2) institution-based country derived from the author's affiliation, representing the actual location of their institution. Both were classified as high-income (HIC) or low-/middle-income (LMIC) according to the latest World Bank income classification [9]. Impact factor and quartile data were retrieved from the latest available Journal Citation Reports, and the journal's country was likewise classified as HIC or LMIC. A summary of these key bibliometric variables is provided in Table 1.

Table 1. Descriptive characteristics of the full dataset (n = 972).

Variable	All Publications (n=972)
Number of authors	Mean±SD = 5.67±3.45
	Median (Min-Max) = 5 (1-29)
Sex of first author, n(%)	Male = 746 (76.7)
	Female = 226 (23.3)
First Author HIC/LMIC ratio (NamSor), n(%)	HIC = 718 (73.9)
	LMIC = 254 (26.1)
Institution HIC/LMIC classification, n(%)	HIC = 811 (83.4)
	LMIC = 161 (16.6)
Journal HIC/LMIC classification, n(%)	HIC = 925 (95.2)
	LMIC = 47 (4.8)
Impact Factor (IF)	Mean±SD = 3.44±6.31
	Median (Min-Max) = 2.3 (0-98.4)
Distribution of quartiles, n(%)	Q1 = 345 (35.5)
	Q2 = 296 (30.5)
	Q3 = 280 (28.8)
	Q4 = 51 (5.2)

SD: standard deviation; Min-Max: minimum-maximum; HIC: high-income country; LMIC: low-/middle-income country.

A separate original article subset (OA subset, n = 568) was analyzed. This subset included only data-based primary research articles, such as retrospective and prospective randomized or non-randomized comparative clinical studies, and was designed to control for potential differences in methodological quality, allowing evaluation of whether visibility disparities persisted within a more homogeneous dataset (Table 2).

Table 2. Descriptive characteristics of the OA subset (n = 568).

Variable	Original Article (n=568)
Number of authors	Mean±SD = 6.15±3.29
	Median (Min-Max) = 6 (1-29)
Sex of first author, n(%)	Male = 439 (77.3)
	Female = 129 (22.7)
First Author HIC/LMIC ratio (NamSor), n(%)	HIC = 419 (73.8)
	LMIC = 149 (26.2)
Institution HIC/LMIC classification, n(%)	HIC = 477 (84.0)
	LMIC = 91 (16.0)
Journal HIC/LMIC classification, n(%)	HIC = 541 (95.2)
	LMIC = 27 (4.8)
Impact Factor (IF)	Mean±SD = 3.71±7.55
	Median (Min-Max) = 2.4 (0-98.4)
Distribution of quartiles, n(%)	Q1 = 225 (39.6)
	Q2 = 167 (29.4)
	Q3 = 154 (27.1)
	Q4 = 22 (3.9)

SD: standard deviation; Min-Max: minimum-maximum; HIC: high-income country; LMIC: low-/middle-income country.

Study-level variables included study duration, sample size, number of centers, and number of countries. Comparative analyses were conducted to evaluate the association between the first author's income group, defined either by name origin using the NamSor API or by institutional affiliation, and that of the publishing journal. These relationships were examined separately for the full dataset and for the OA subset. Cross-tabulations were used to compare the proportions of HIC and LMIC authors publishing in HIC versus LMIC journals. Continuous variables, including journal impact factor, were compared using the Mann-Whitney U test, while quartile (Q) distributions were assessed using the Chi-square test.

Analyses based on author name origin and institutional affiliation for both the full and OA datasets are summarized in Table 3 (A-D).

Table 3A. Association between first author's name-origin income group (NamSor) and journal income classification in the full dataset (n = 972).

Variable		HIC (n=718)	LMIC (n=254)	p
Journal income group, n(%)				<0.001χ2
	HIC	706 (98.3)	219 (86.2)	
	LMIC	12 (1.7)	35 (13.8)	
Impact Factor (IF)				<0.001M
	Mean±SD	3.69±7.04	2.72±3.38	
	Median (Min-Max)	2.4 (0-98.4)	1.8 (0.4-41.6)	
Distribution of quartiles, n(%)				<0.001 χ2
	Q1	275 (38.3)	70 (27.6)	
	Q2	220 (30.6)	76 (29.9)	
	Q3	197 (27.4)	83 (32.7)	
	Q4	26 (3.6)	25 (9.8)	

SD: standard deviation; Min-Max: minimum-maximum; HIC: high-income country; LMIC: low-/middle-income country. Q: quartile, M: Mann-Whitney U test, χ^2: Chi-square test. HIC authors consistently demonstrate higher impact factors and greater representation in Q1 journals compared to LMIC authors.

Table 3B. Association between first author's institutional income group and journal income classification in the full dataset (n = 972).

Variable		HIC (n=811)	LMIC (n=161)	p
Journal income group, n(%)				<0.001χ2
	HIC	801 (98.8)	124 (77)	
	LMIC	10 (1.2)	37 (23)	
Impact Factor (IF)				<0.001M
	Mean±SD	3.73±6.84	1.97±1.4	
	Median (Min-Max)	2.4 (0-98.4)	1.6 (0.4-12.5)	
Distribution of quartiles, n(%)				<0.001 χ2
	Q1	315 (38.8)	30 (18.6)	
	Q2	250 (30.8)	46 (28.6)	
	Q3	220 (27.1)	60 (37.3)	
	Q4	26 (3.2)	25 (15.5)	

HIC: high-income country, LMIC: low- or middle-income country, IF: impact factor, SD: standard deviation, Q: quartile, M: Mann-Whitney U test, χ^2: Chi-square test. HIC authors consistently demonstrate higher impact factors and greater representation in Q1 journals compared to LMIC authors.

Table 3C. Association between first author's name-origin income group (NamSor) and journal income classification in the OA subset (n = 568).				
Variable		HIC (n=419)	LMIC (n=149)	p
Journal income group, n(%)				<0.001χ2
	HIC	412 (98.3)	129 (86.6)	
	LMIC	7 (1.7)	20 (13.4)	
Impact Factor (IF)				0.006M
	Mean±SD	4.07±8.63	2.70±2.56	
	Median (Min-Max)	2.4 (0-98.4)	1.9 (0.5-16.6)	
Distribution of quartiles, n(%)				<0.001 χ2
	Q1	179 (42.7)	46 (30.9)	
	Q2	122 (29.1)	45 (30.2)	
	Q3	111 (26.5)	43 (28.9)	
	Q4	7 (1.7)	15 (10.1)	
HIC: high-income country, LMIC: low- or middle-income country, OA: original article subset, IF: impact factor, SD: standard deviation, Q: quartile, M: Mann-Whitney U test, χ^2: Chi-square test. HIC authors consistently demonstrate higher impact factors and greater representation in Q1 journals compared to LMIC authors.				

Table 3D. Association between first author's institutional income group and journal income classification in the OA subset (n = 568).				
Variable		HIC (n=477)	LMIC (n=91)	p
Journal income group, n(%)				<0.001χ2
	HIC	471 (98.7)	70 (77)	
	LMIC	6 (1.3)	21 (23)	
Impact Factor (IF)				<0.001M
	Mean±SD	4.02±8.17	2.05±1.64	
	Median (Min-Max)	2.4 (0-98.4)	1.5 (0.5-12.5)	
Distribution of quartiles, n(%)				<0.001 χ2
	Q1	205 (43.0)	20 (22.0)	
	Q2	145 (30.4)	22 (24.2)	
	Q3	120 (25.2)	34 (37.4)	
	Q4	7 (1.5)	15 (16.5)	
HIC: high-income country, LMIC: low- or middle-income country, OA: original article subset, SD: standard deviation, Q: quartile, M: Mann-Whitney U test, χ^2: Chi-square test. HIC authors consistently demonstrate higher impact factors and greater representation in Q1 journals compared to LMIC authors.				

Beyond author-journal income associations, additional analyses were performed within the OA subset to examine whether study quality and design characteristics influenced publication visibility. Within this subset, study-level variables, including study type (retrospective, prospective, randomized, or non-randomized), number of centers (single-center, multicenter, or nationwide), geographic scope (national or international), total sample size, and study duration, were systematically extracted. These parameters were used to assess whether differences in methodological scope or study complexity contributed to the observed disparities in journal visibility across author and journal income classifications. To account for potential confounding related to study quality, methodological variables were compared between groups within the OA subset. Descriptive and comparative statistics were applied as appropriate, and the results are presented in Table 4.

Table 4. Study-level methodological characteristics within the OA subset by author income group (n = 568).				
Variable		HIC (n=477)	LMIC (n=91)	p value
Nature of the research, n(%)				0.746 χ2
	Retrospective	382 (80.1)	76 (83.5)	
	Prospective	88 (18.4)	14 (15.4)	
	Others	7 (1.5)	1 (1.1)	
Geographic scope, n(%)				0.808 χ2
	National	473 (99.2)	90(98.9)	
	International	4(0.8)	1(1.1)	
Number of attending centers, n(%)				0.149 χ2
	Single-center	400 (83.9)	81(89.0)	
	2-3 centers	24 (5.0)	6 (6.6)	
	>4 centers	31 (6.5)	4 (4.4)	
	Nationwide registry	22 (4.6)	0	
Number of patients				0.766M
	Mean±SD	1702.33±13299.27	208.9±557.55	
	Median (Min-Max)	92 (3-170846)	98 (3-4799)	
Study interval (years)				0.107M
	Mean±SD	6.5±5.05	5.16±4.58	
	Median (Min-Max)	5(1-30)	4(1-21)	
Randomization, n(%)				0.791 χ2
	Non-randomized	444(93.1)	84(92.3)	
	Randomized	33(6.9)	7(7.7)	

HIC: high-income country, LMIC: low- or middle-income country, OA: original article subset, SD: standard deviation, M: Mann-Whitney U test, χ^2: Chi-square test. No statistically significant differences were observed across any methodological parameters between HIC and LMIC groups.

Gender analysis was conducted on both the full dataset and the original article (OA) subset. The analysis examined the relationship between the first author's gender, the income level of their affiliated institution's country (HIC/LMIC), and the characteristics of the journals in which the studies were published. Gender inference was performed using the NamSor API (v2), which applies probabilistic modeling based on global name-gender databases. Predicted genders were categorized according to the author's income group (HIC/LMIC) and journal-related parameters, including journal origin (HIC/LMIC), impact factor (IF), and quartile rank (Q1-Q4). Comparative analyses were then applied to evaluate potential differences in these variables across both datasets.

Associations between journal origin and author gender were assessed using the Chi-square test, differences in impact factor were analyzed with the Mann-Whitney U test, and quartile distributions were compared using the Chi-square test.

For the OA subset, gender-related analyses were further expanded to include study-level methodological parameters, such as the nature of the research (retrospective, prospective, or other), number of participating centers, and study interval (years), to explore whether these factors influenced gender-based or income-based visibility patterns.

Results for the full dataset are presented in Table 5A, and those for the OA subset, including the additional methodological variables, are summarized in Table 5B.

Table 5A. Gender-based comparison of author and journal characteristics in the full dataset.						
Variables			HIC (n=811)	LMIC (n=161)		p
Sex of first author, n(%)		Male 628 (77.4)	Female 183 (22.6)	Male 118 (73.3)	Female 43 (26.7)	
Journal origin, n(%)					<0.001χ2	
	HIC	621 (98.9)	180 (98.4)	88 (74.6)	36 (83.7)	
	LMIC	7 (1.1)	3 (1.6)	30 (25.4)	7 (16.3)	
Impact factor (IF)						0.001K
	Mean±SD	3.94±7.64	3.02±2.59	1.88±1.16	2.2±1.91	
	Median (Min-Max)	2.4 (0.2-98.4)	2.4 (0-19.3)	1.6 (0.4-5.7)	1.5 (0.6-12.5)	
Distribution of quartiles, n(%)						<0.001 χ2
	Q1	251 (40.0)	64 (35.0)	23 (19.5)	7 (16.3)	
	Q2	182 (29,.0)	68 (37.2)	31 (26.3)	15 (34.9)	
	Q3	174 (27.7)	46 (25.1)	45 (38.1)	15 (34.9)	
	Q4	21 (3.3)	5 (2.7)	19 (16.1)	6 (14.0)	

HIC: high-income country, LMIC: low- or middle-income country, SD: standard deviation, M: Mann-Whitney U test, χ^2: Chi-square test. Differences in journal impact factor and quartile distribution are primarily associated with institutional income level rather than gender.

Table 5B. Gender-based comparison of author, journal, and study characteristics in the OA subset.						
Variable		HIC (n=477)		LMIC (n=91)		p value
Sex of first author, n(%)		Male 368 (77.1)	Female 109 (22.9)	Male 71 (78.0)	Female 20 (22.0)	
Journal origin, n(%)						<0.001χ2
	HIC	362(98.4)	109(100.0)	51(71.8)	19(95.0)	
	LMIC	6(1.6)	0	20(28.2)	1(5.0)	
Impact factor (IF)						<0.001K
	Mean±SD	4.24±9.15	3.29±2.95	1.93±1.27	2.51±2.55	
	Median (Min-Max)	2.4(0.7-98.4)	2.4(0-19.3)	1.5(0.5-5.7)	1.55(1-12.5)	
Distribution of quartiles, n(%)						<0.001 χ2
	Q1	161(43.8)	44(40.4)	15(21.1)	5(25.0)	
	Q2	106(28.8)	39(35.8)	16(22.5)	6(30.0)	
	Q3	97(26.4)	23(21.1)	27(38.0)	7(35.0)	
	Q4	4(1.1)	3(2.8)	13(18.3)	2(9.1)	
Nature of the research, n(%)						0.186χ2
	Retrospective	293(79.6)	89(81.7)	57(80.3)	19(95.0)	
	Prospective	72(19.6)	16(14.7)	13(18.3)	1(5.0)	
	Others	3(0.8)	4(3.7)	1(1.4)	0	
Number of attending centers, n(%)						0.145χ2
	Single	315(85.6)	85(78.0)	61(85.9)	20(100.0)	
	2-3 center	18(4.9)	6(5.5)	6(8.5)	0	
	>4 center	20(5.4)	11(10.1)	4(5.6)	0	
	National	15(4.1)	7(6.4)	0	0	
Study interval (years)						<0.051K
	Mean±SD	6.51±5.14	6.46±4.74	4.47±4.7	4.05±4.05	
	Median (Min-Max)	5(1-30)	5(1-21)	4(1-21)	2.5(1-15)	

HIC: high-income country, LMIC: low- or middle-income country, OA: original article subset, SD: standard deviation, M: Mann-Whitney U test, χ^2: Chi-square test. Differences in journal impact factor and quartile distribution are primarily associated with institutional income level rather than gender.

Statistical Analysis

All statistical analyses were performed using SPSS software (version 28.0; IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro-Wilk test. Nonparametric tests (Mann-Whitney U and Kruskal-Wallis) were applied for non-normally distributed variables, while categorical variables were compared using the Chi-square test. A two-tailed p value of < 0.05 was considered statistically significant for all analyses.

Results

A total of 972 articles published between 2000 and 2025 were analyzed (Table 1). The mean number of authors was 5.7 ± 3.45 (median = 5). Among first authors, 76.7% were male and 23.3% were female. According to NamSor analysis, 73.9% of first authors originated from high-income countries (HICs) and 26.1% from low- and middle-income countries (LMICs). In terms of institutional affiliation, 83.4% were based in HIC institutions, whereas 16.6% were affiliated with LMIC institutions. The vast majority of publications (95.2%) appeared in journals originating from HICs. The mean impact factor (IF) was 3.44 (median = 2.3). Regarding journal quartile distribution, 35.5% of publications were in Q1 journals, 30.5% in Q2, 28.8% in Q3, and 5.2% in Q4. Detailed descriptive characteristics for both the full dataset and the OA subset are presented in Tables 1 and 2.

A similar pattern was observed in the subset of original research articles (OA subset, n = 568; Table 2). The mean number of authors was 6.1 ± 3.29, with 84% of first authors affiliated with HIC institutions and 95% of studies published in HIC journals. The mean impact factor was 3.71 (median = 2.4).

These two tables show that research on PSP in thoracic surgery has been largely produced and published by high-income countries.

Figure 1 illustrates the global distribution of PSP-related publications and the publication-to-population ratio across countries.

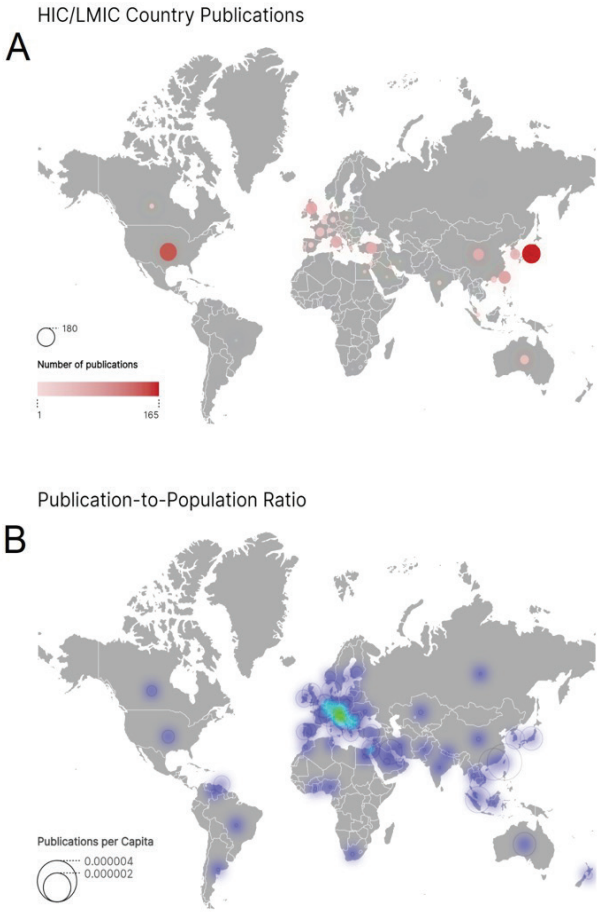

Figure 1. Global distribution of PSP-related publications by country (all data, n = 972). **(A)** Country-level distribution of PSP-related publications by institutional origin across all countries. Circle size and color intensity represent the absolute number of publications per country. **(B)** Publication-to-population ratio by country, expressed as publications per capita, illustrating normalized research output relative to population size. Larger circles indicate higher publication rates per population. Note: Map boundaries and country designations do not imply any opinion regarding the legal status of any country or territory or the delimitation of its frontiers.

The second main analytical component focused on the relationship between authorship origin, the author's institutional affiliation (represented as an "institutional passport," defined as the income-level classification of the country in which the author's institution is located), and their association with the income level of the publishing journal. This analysis was conducted in four sequential stages, as detailed in Tables 3A-D.

The relationship between the income-level classification based on NamSor-based author name origin and the income level of the publishing journal was examined (Table 3A). In the full dataset (n = 972), the vast majority of articles by authors from high-income countries (HICs) were published in HIC journals (98.3%),

whereas only 86.2% of those by authors from low- and middle-income countries (LMICs) appeared in such journals ($p < 0.001$). Articles authored by HIC-origin researchers also demonstrated higher mean impact factors (3.69 ± 7.04 vs 2.72 ± 3.38; $p < 0.001$). The journal quartile distribution showed a similar difference: 38.3% of HIC-origin authors published in Q1 journals, compared with 27.6% of LMIC-origin authors. These findings are summarized in Table 3A.

The variable defined as the institutional passport, that is, the income level of the country in which the author's institution is located, was examined in relation to the income level of the publishing journal (Table 3B). In the full dataset ($n = 972$), 98.8% of articles from authors affiliated with institutions in high-income countries (HICs) were published in HIC journals, whereas only 77% of those from low- and middle-income country (LMIC) institutions appeared in such journals ($p < 0.001$). Publications originating from HIC institutions also had significantly higher mean impact factors (3.73 ± 6.84 vs 1.97 ± 1.40; $p < 0.001$). The journal quartile distribution supported this difference: 38.8% of articles from HIC institutions were published in Q1 journals, compared with 18.6% from LMIC institutions. These findings are summarized in Table 3B.

The NamSor-based author name origin income classification was assessed within the subset comprising only original research articles (OA subset) (Table 3C). In this subset ($n = 568$), 98.3% of articles authored by individuals from high-income countries (HICs) were published in HIC journals, compared with 86.6% of those by authors from low- and middle-income countries (LMICs) ($p < 0.001$). Articles authored by HIC-origin researchers also had significantly higher mean impact factors (4.07 ± 8.63 vs 2.70 ± 2.56; $p = 0.006$). The journal quartile distribution reflected the same trend: 42.7% of articles by HIC-origin authors were published in Q1 journals, whereas the corresponding rate for LMIC-origin authors was 30.9%. These findings are summarized in Table 3C.

The institutional passport variable was assessed within the subset comprising only original research articles (OA subset) (Table 3D). In this subset ($n = 568$), 98.7% of articles from authors affiliated with institutions in high-income countries (HICs) were published in HIC journals, whereas only 77% of those from low- and middle-income country (LMIC) institutions appeared in such journals ($p < 0.001$). Publications originating from HIC institutions again had significantly higher mean impact factors (4.02 ± 8.17 vs 2.05 ± 1.64; $p < 0.001$). The journal quartile distribution supported this difference: 43.0% of articles from HIC institutions were published in Q1 journals, compared with 22.0% from LMIC institutions. These findings are summarized in Table 3D.

Most studies were published in journals based in high-income countries (HICs), regardless of the first author's name-origin or institutional affiliation. These differences were consistently statistically significant across all comparisons ($p < 0.001$), highlighting a strong association between author income level and publication in higher-impact and higher-quartile journals. The association between author and journal income classification and the impact factor and quartile distributions for these four groups are summarized in Tables 3A-D and Figure 2.

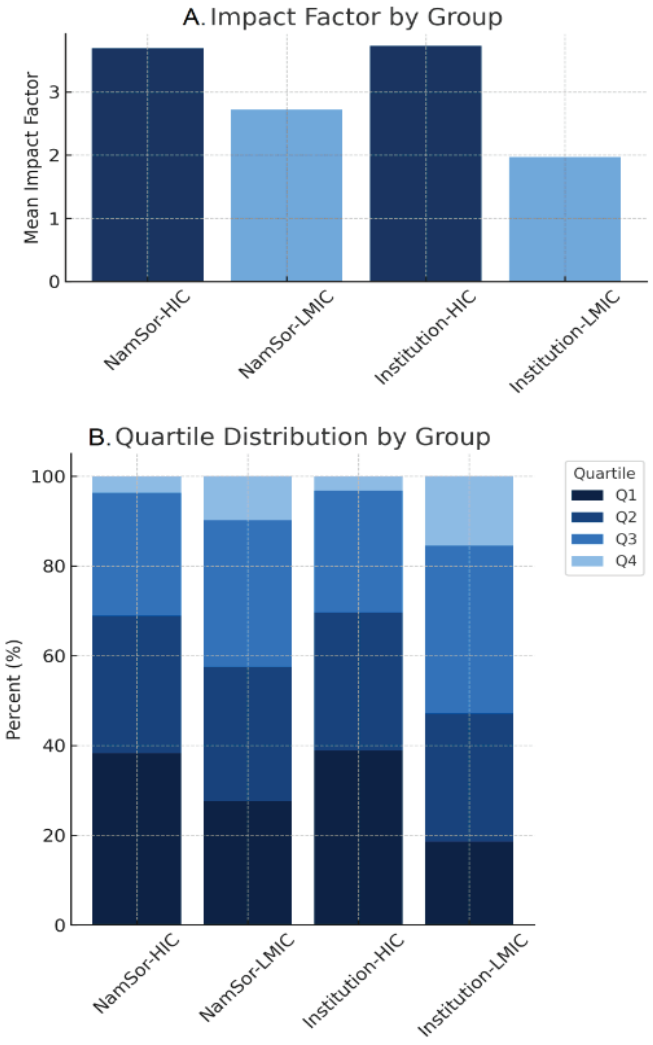

Figure 2. Impact factor and journal quartile distribution by author income classification. **(A)** Mean impact factor of journals publishing studies led by first authors from high-income countries (HIC) and low- and middle-income countries (LMIC), classified by both name-origin (NamSor) and institutional affiliation. **(B)** Distribution of publications across journal quartiles (Q1–Q4) for the same four groups.

The third main analytical component focused on methodological parity between HIC and LMIC studies (Table 4). These variables were compared between groups according to author income classification. These findings are detailed in Table 4.

No significant difference was found between HIC- and LMIC-origin studies in terms of study design; retrospective designs predominated in both groups ($p = 0.746$). The proportions of prospective, randomized, and non-randomized studies were also comparable ($p = 0.791$). There were no significant differences between groups in mean sample size ($p = 0.766$) or study duration ($p = 0.107$).

Similarly, no significant differences were observed in the number of centers ($p = 0.149$) or geographic scope ($p = 0.808$); most studies in both groups were single-center and national in scale.

In summary, the distribution of methodological parameters was statistically similar between studies originating from HICs and those from LMICs.

The fourth main analytical component focused on the gender distribution of first authors. According to the full dataset analysis presented in Table 5A (n = 972), the proportion of female first authors was 23.3%, and male authors 76.7%. Articles authored by women and men showed no significant difference in mean impact factor ($p = 0.001$, Mann-Whitney U), and the difference reflected income level rather than gender. The proportion of publications in Q1 journals was also comparable between female and male authors (34.9% vs 36.1%).

In Table 5B, which assessed only the subset of original research articles (OA subset, n = 568), the proportion of female authors was 23.4%. The proportion of female authors from HICs was 23.6%, and from LMICs 22.9%. Similarly, at the institutional level, the proportions were 23.9% for HIC institutions and 22.5% for LMIC institutions.

The quartile distributions by gender and institutional income level are presented in Figure 3, and the impact factor comparison (log-scale, median ± SD) is presented in Figure 4.

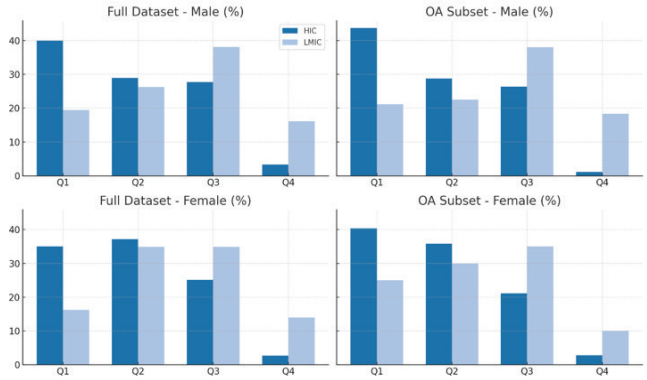

Figure 3. Percentage distribution of journal quartile ranks (Q1–Q4) stratified by gender and institutional income group for the full dataset and the OA subset. Each panel displays the within-group proportion (total = 100%). Across both datasets and genders, authors affiliated with institutions in high-income countries (HIC) are more frequently published in Q1–Q2 journals, whereas authors from low- and middle-income countries (LMIC) are over-represented in Q3–Q4 journals, indicating that visibility disparities are primarily income-based rather than gender-based.

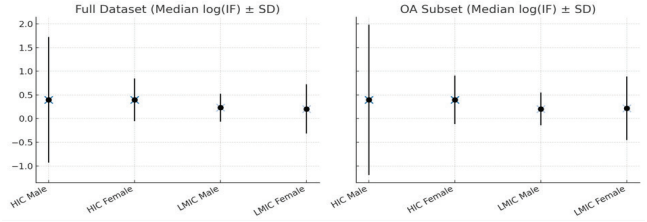

Figure 4. Impact factor (log-scale) by gender and institutional income level. Median journal impact factor is shown for each group, with SD represented as vertical error ranges. Values are plotted on a log10 scale. Across both the full dataset and the OA subset, HIC-affiliated authors have consistently higher median impact factors than LMIC-affiliated authors. The pattern is similar for male and female first authors, indicating that differences in journal impact occur primarily by institutional income level rather than gender.

Additional methodological variables were also evaluated in this analysis. There was no significant gender difference in study type (retrospective vs prospective; $p = 0.186$) or in the number of participating centers ($p = 0.145$). The mean study interval also did not differ significantly between genders ($p \approx 0.051$).

Across all analyses, income-based disparities were statistically significant ($p < 0.001$). Despite comparable methodological parameters between studies from high- and low- or middle-income countries, publications originating from HIC authors, institutions, and journals consistently demonstrated higher impact factors and greater representation in top-quartile journals. These findings quantitatively underscore the persistence of structural disparities in publication visibility, which will be further addressed in the Discussion section.

Discussion

This study demonstrates a marked visibility disparity among publications on PSP within the field of thoracic surgery, even when methodological characteristics are comparable. In both the full dataset and the subset of original research articles, authors and institutions from high-income countries were more frequently published in higher-impact journals and in upper quartiles compared with those from low- and middle-income countries. Importantly, this difference could not be explained by study design, sample size, number of participating centers, or prospective versus retrospective structure. These findings suggest that the observed disparity reflects structural factors embedded within editorial and publication processes rather than differences in scientific quality. In this study, publication visibility refers specifically to journal impact factor and quartile rank, rather than citation-based metrics.

In the existing literature, researchers from low- and middle-income countries have repeatedly been shown to be disadvantaged in terms of publication visibility within medicine and surgery. Bibliometric analyses across various disciplines have reported that journals and editorial decision-making processes are predominantly concentrated in high-income countries, which can influence publication acceptance and placement [1,2,4]. Moreover, even in international collaborative studies, leadership authorship roles are often shifted away from local researchers, thereby reinforcing a structural hierarchy [10-14]. However, because previous studies largely combined heterogeneous disease groups and broader surgical fields, it has remained unclear whether the observed disparities arise from clinical factors or from structural mechanisms within academic publishing. These patterns are consistent with findings from broader surgical and global health literature, where authors from high-income countries are more likely to publish in higher-impact journals and occupy leading authorship positions, independent of study context. This suggests that the observed disparities are not specific to thoracic surgery but reflect a wider structural phenomenon in academic publishing.

The choice of PSP in this study was intentional, as it represents a clinically homogeneous patient group with relatively standardized treatment approaches. PSP management is largely based on similar surgical decision-making algorithms across different countries and institutions, and published studies typically follow comparable methodological frameworks. This reduces the influence of disease severity, surgical indication variability, or clinical heterogeneity as factors that could affect publication visibility. Thus, the selection of a homogeneous clinical condition enabled a clearer assessment of whether the observed disparities stem from structural factors within publishing processes rather than from differences in scientific quality or clinical complexity. In summary, analyzing a uniform clinical topic allowed the identification of a visibility gap rooted in systematic and structural barriers rather than methodological differences.

The analyses conducted within the subset of original research articles further support this structural disparity. Key methodological variables such as study design, sample size, number of participating centers, national versus international scope, and study duration did not differ significantly between studies originating from high-income and low- and middle-income countries. Likewise, the rates of prospective study design, presence of randomization, and likelihood of being conducted as a multicenter study were comparable across all groups. This indicates that the likelihood of publication in higher-impact journals cannot be explained by methodological quality or scope. Rather, studies of similar scientific caliber are exposed to different levels of visibility during the publication process. Therefore, the observed disparity arises not from research design but from structural factors embedded within the scientific publishing ecosystem.

To address the possibility that differences in publication visibility may be driven by methodological quality rather than structural factors, we performed a detailed comparison of study-level characteristics within the original article subset. No significant differences were observed between HIC and LMIC studies in terms of sample size, study design, number of centers, geographic scope, or randomization. These findings suggest that the observed disparity is unlikely to be explained by differences in methodological rigor, but rather reflects structural factors within the publication process.

The potential mechanisms underlying this visibility disparity have been clearly described in the literature. Journals and editorial boards located in high-income countries often operate with implicit biases when evaluating language quality, narrative fluency, and perceived "scientific authority" [2]. Studies originating from low- and middle-income countries, even when they exhibit comparable methodological rigor, are more frequently subjected to revision and resubmission cycles on the grounds of "language improvement" or "academic writing standards" [11]. Furthermore, the centralized structure of the publishing system continuously reproduces the visibility and network advantages held by high-income institutions; even within collaborative research projects, this often results in first or senior authorship positions favoring HIC researchers [10,12,14]. In other words, the publication process evaluates not only scientific quality, but also the institutional and geographic position of the researcher. Thus, the disparity observed is not the result of individual capability, but of entrenched structural power asymmetries [1].

The dominant structural position of high-income countries in scientific publishing is linked not only to the geographic location of journals, but also to how global knowledge production networks are organized. Fifty-year analyses of global health literature demonstrate that research collaborations are centered around high-income countries, while low- and middle-income countries occupy peripheral positions within these networks [15]. A substantial proportion of articles published in high-impact medical journals lack local authorship even when the data originated from LMIC settings [16,17]. In the global surgery literature, this structural pattern results in systematic shifts of leadership and senior authorship roles toward HIC researchers, a dynamic that becomes even more pronounced among women researchers [18]. The consolidation of senior authorship authority within high-income institutions limits academic recognition and career advancement opportunities for LMIC researchers [19]. Additionally, authorship contributions in high-impact journals have become increasingly unequal, reflecting a redistribution of visibility as a form of academic capital [20]. The ethical implications of these structural imbalances highlight that scientific publishing processes reproduce power relations as much as they disseminate knowledge [3].

In this study, approximately one quarter of first authors were women, which is consistent with prior reports of gender representation in cardiothoracic surgery [5]. However, our findings indicate that the primary determinant of publication visibility for women was not gender itself, but the income level of the country in which their institution is located. The literature shows that women researchers, particularly those in low- and middle-income countries, are structurally underrepresented in leadership and senior authorship roles [21]. In high-impact journals, women remain markedly less represented as senior authors, and research visibility is directly linked to academic advancement [22]. Furthermore, some fields have shown lower citation rates for women compared to men, even when scientific content is similar [23]. In our dataset, however, the association between gender and journal impact factor lost significance once institutional income level was accounted for. This suggests that gender inequality does not operate in isolation, but rather intersects with income-based structural power asymmetries within the global publishing system [24,25]. Therefore, efforts to improve the visibility of women researchers must address not only gender equity but also the systemic publication barriers faced by LMIC institutions.

The principal strength of this study is its systematic examination of visibility and authorship representation within a clinically homogeneous domain of thoracic surgery over a 25-year publication period. The selection of PSP minimized variation in disease characteristics and treatment algorithms, allowing the observed disparities to be evaluated independently of clinical complexity. In addition, the use of two distinct income-related variables, author name origin and institutional country classification, demonstrated that the disparity operates not only at the individual level but also at the structural and institutional level. Finally, the methodological controls applied within the original research subset showed that the visibility gap cannot be explained by differences in study design or scientific rigor, supporting the interpretation that the disparity is rooted in the publishing process itself.

Several mechanisms may underlie the observed association between income level, gender, and publication visibility. Authors from high-income countries may benefit from greater access to research funding, established academic networks, and institutional support for manuscript preparation and submission. In addition, language proficiency, particularly in English, and familiarity with editorial expectations may further facilitate publication in higher-impact journals. Gender disparities may be influenced by differences in academic seniority, mentorship opportunities, and representation in leadership positions, which are known to affect authorship roles and publication outcomes. These factors likely operate together, contributing to structural advantages that extend beyond measurable study-level characteristics.

A formal multivariate regression model was not applied in this study. The primary outcomes were journal impact factor and quartile rank, which were analyzed directly in relation to author income classification using appropriate statistical methods. In addition, key methodological variables that could act as confounders, including study design, sample size, number of centers, and study duration, were systematically compared between groups, with no statistically significant differences observed. Together, these findings suggest that the observed disparities are unlikely to be explained by measurable study-level factors, but rather reflect structural determinants within the publication system.

Limitations of the Study

This study has several limitations. First, the analysis is based solely on published articles; because manuscripts that were submitted but rejected could not be examined, it was not possible to determine at which stage of the publication process the disparity arises. This suggests that visibility differences may occur not only during editorial decision-making, but also earlier, through strategic publication choices made by authors. Second, the study focuses specifically on the literature on PSP; although this choice increases clinical homogeneity, it may limit the direct generalizability of the findings to other areas of thoracic surgery. Third, as a bibliometric study, the analysis does not establish causality; the mechanisms under-

lying the disparity are inferred in relation to previously documented structural features of the publishing system. However, the methodological controls applied within the subset of original research articles strongly support that the visibility gap is not attributable to study quality.

Author name origin and gender were inferred using the NamSor API, which is based on probabilistic modeling. Although previously validated, this approach is subject to potential misclassification, particularly in cases of culturally overlapping or globally common names. Such misclassification may introduce a degree of classification bias; however, given the large sample size and the consistency of the observed patterns across both name-origin and institution-based analyses, the overall impact on the study findings is expected to be limited.

In conclusion, this study demonstrates that publication visibility in the thoracic surgery literature is shaped not only by scientific quality, but also by identity markers linked to institutional location and name origin. Even within a clinically homogeneous field such as PSP, institutions located in high-income countries benefit from an "institutional passport" that facilitates recognition and publication, while the geographic origin signaled by an author's name can similarly function as a "name passport" influencing perceived authority and acceptance. In other words, the likelihood of publication and the level of journal visibility are affected not only by methodological rigor, but also by the position of the author and institution within the global publishing system. These findings highlight persistent structural power asymmetries in the circulation of scientific knowledge and underscore the need for more transparent, structured, and geographically balanced evaluation mechanisms.

Implementing genuine double-blind editorial models that systematically mask both author identity and institutional affiliation, supported by technical systems that automatically remove metadata and institutional identifiers, may help reduce these disparities. In addition, regular reporting of the geographic and income-level composition of editorial boards and reviewer pools could increase transparency and encourage greater global diversity in decision-making. Such transparency would make structural imbalances visible and, over time, support more inclusive publishing policies.

Furthermore, for researchers in low- and middle-income countries, language barriers may contribute to reduced publication visibility. Independent, application-based language support programs, operating outside of editorial decision-making and managed according to objective, equitable criteria, could improve manuscript clarity without influencing acceptance decisions. Establishing a designated Authorship Equity Editor role within journals may also help ensure that reviewer assignments and revision communications are conducted with attention to geographic representation and structural fairness.

Finally, current article processing charge (APC) models create a strongly asymmetric cost burden: researchers at high-income institutions with subscription agreements often pay little or nothing, the lowest-income countries receive full waivers but publish infrequently, while the financial cost falls disproportionately on productive researchers in intermediate-income countries who lack institutional coverage and must pay APCs out of pocket. Revising APC support mechanisms to reflect institutional resource levels and individual funding availability, rather than broad country-income classifications, may promote more equitable financial access to publication.

Declaration of conflicting interests

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Ethics statement

This study was a descriptive bibliometric analysis based exclusively on publicly available, aggregated publication metadata retrieved from the Web of Science Core Collection. No human participants were recruited, no patient-level or private data were accessed, and no intervention, interaction, or identifiable personal information was involved. Therefore, institutional ethics committee approval and informed consent were not required for this type of study.

Authors' contribution

OY: conceived and designed the study, performed data acquisition and statistical analysis, interpreted the results, drafted the manuscript, and approved the final version. MI: contributed to study design, data interpretation, critical revision of the manuscript, and approval of the final version. EE: contributed to data collection, data analysis, manuscript drafting, and approval of the final version. RE: contributed to data extraction, literature review, manuscript drafting, and approval of the final version. MK: contributed to data validation, methodological review, critical revision of the manuscript, and approval of the final version. TD: contributed to literature review and approved the final version. AY: contributed to study supervision, critical revision of the manuscript for important intellectual content, and approval of the final version.

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Original Article

Prognostic factors for recurrence after surgical resection in early-stage non-small cell lung cancer

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ABSTRACT

Background: Non-small cell lung cancer (NSCLC) constitutes the majority of lung cancer cases, with surgical resection being the main treatment for stages 1 and 2. Despite advances, postoperative recurrence remains a major cause of mortality. Identifying recurrence risk factors could allow individualized follow-up strategies.

Materials and Methods: We retrospectively analyzed 246 patients with stage 1-2 NSCLC who underwent surgery between 2005-2022. Stage 3 disease and neoadjuvant-treated cases were excluded. Clinical, laboratory, radiological, and surgical data were collected. Recurrences (locoregional or distant) within at least two years of follow-up were recorded. Comparisons were made using Student's t-test or Chi-square test; survival was analyzed with Kaplan-Meier and Cox regression.

Results: VATS (Video-assisted thoracoscopic surgery) was more frequent in non-recurrence cases (p=0.017), while pneumonectomy was more common in recurrence cases (p=0.017). Advanced T and TNM stages, lymphatic and vascular invasion were significantly associated with recurrence. Cox regression identified N1 disease, pleural invasion, and lymphatic invasion as independent predictors of poor survival. Pneumonectomy and lymphatic invasion were significantly associated with reduced recurrence-free survival.

Conclusions: Recurrence after early-stage NSCLC surgery is linked to worse survival. Pneumonectomy and lymphatic invasion may predispose to recurrence, warranting closer follow-up and consideration of adjuvant therapy.

Keywords: non-small cell lung cancer, early stage, recurrence, prognosis

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Introduction

Non-small cell lung cancers (NSCLC) constitute the majority of newly diagnosed lung cancers [1]. Correct staging is very important to determine the appropriate treatment strategy and the 8th TNM staging system is used [2]. Treatment for non-small cell lung cancer (NSCLC) varies depending on the stage. For stage 1 and stage 2 NSCLC, surgical resection is the primary treatment modality, provided there are no contraindications. If surgery is contraindicated, patients are typically considered for conventional radiotherapy or stereotactic body radiotherapy (SBRT) [3].

In stage 3 patients and some stage 2 patients' cisplatin based combination regimens are indicated as adjuvant therapy. Furthermore, in recent years, immunotherapy has also been introduced in these patient groups [3].

Today, a uniform approach is recommended for all patients for postoperative follow-up [4]. It is recommended to conduct surveillance every six months for the first 2-3 years, which should include a review of the patient's medical history, a physical examination, and ideally a contrast-enhanced spiral chest Computed Tomography (CT) scan at the 12- and 24-month marks. After this period, annual follow-ups are advised, comprising a medical history review, physical examination, and chest CT to monitor for second primary tumors. Routine follow-up with PET-CT (positron emission tomography-computed tomography) is not advised [5].

Despite all advances, high recurrence rates are a serious problem in the treatment of lung cancer. Recurrence rates after complete resection in early stage lung cancer ranging from %20 to %41 [6,7]. The differences reported in the literature can be attributed to the examination of different stages of disease, the separate evaluation or exclusion of either local and distant metastases, and the variability in follow-up durations [8].

The majority of mortality in the post-resection period in non-small cell lung cancer is related to the development of recurrence [9]. Furthermore, the healthcare resource utilization is much higher in the recurrence group [10].

Overall recurrence is more likely in patients with a PET-CT maximum standard uptake value (SUVmax) over 5, advanced stage disease, or those who received preoperative radiation therapy. Local recurrence is more common in patients with specific risk factors including larger tumor size and lymphovascular invasion, which facilitate cancer spread and metastasis [8].

The factors related recurrence risk for early stage lung cancers are poorly defined, and the available data cannot clearly distinguish these factors based on time periods and relapse sites [11]. Our main aim in our study is to identify predisposing factors for recurrence and then to highlight which cases need more aggressive treatment methods and to create patient-specific follow-up options in the light of these factors.

Materials and Methods

Patients who were operated on for non-small cell lung carcinoma in our clinic between 2005 and 2022 were included in the study.

A total of 272 patients with stage 1-2 disease were included in our study. Twenty-six patients were excluded due to a history of neoadjuvant treatment. 246 patients with stages 1 and 2 were identified.

The patient's clinical, laboratory and respiratory data, radiological features of the tumor and surgical features were recorded retrospectively. Patients were further stratified by histological subgroups, resection types, stages, comorbidities and operation method (VATS/Thoracotomy). Patients were followed for a minimum of 2 years, with a median follow-up duration of 59.5 months for recurrence evaluation. Recurrence was defined as the appearance of locoregional or distant relapses, with sites and timing categorized according to the disease stage. Locoregional recurrence was defined as the development of tumors within the surgical field or adjacent lymph node stations, including bronchial stump recurrence, hilar or mediastinal lymph node involvement, and recurrence within the ipsilateral lung parenchyma. Distant recurrence was classified as the presence of lesions in the contralateral lung parenchyma or involvement of extrathoracic organs.

Recurrence was verified through radiological imaging and/or histopathological examination. In our clinical practice, asymptomatic patients were followed postoperatively with thoracic computed tomography every three months for the first two years, and every six months for the subsequent three years. In the presence

of additional clinical symptoms, Magnetic Resonance Imaging (MRI) and PET-CT were utilized for further investigation. All recurrences were histopathologically verified, except in cases where the anatomical location was not amenable to biopsy.

The study was approved by the Institutional Ethics Review Board of Istanbul University-Cerrahpasa (Number and Date: E-83045809-604.01.01-712053; 15/06/2023). Informed consent received. All patient data were anonymized and confidentiality was maintained.

Statistical Analysis

Patients were divided into two groups: those with recurrence (Group 1) and those without (Group 2). Groups were analyzed for parametric data with the Student-t test, and non-parametric data with the Chi-square test. Kaplan-Meier test was used for survival analysis, and multivariate analysis was performed for survival with Cox regression analysis. SPSS 27.00 was used. $p<0.05$ was considered statistically significant.

Results

This study includes 246 patients, comprising 73 women and 173 men. Among all patients, 87 (35.3%) experienced recurrence. The recurrence rate in male and female patients were 66 (75.8%) and 21 (24.1%), respectively. The mean age of patients without recurrence was 60.9 ± 10.4 years, while those with recurrence had a mean age of 62.1 ± 9.3 years (p=0.348) (Table 1).

Table 1. Table containing demographic data of the groups.

	No Recurrence n=159	Recurrence n=87	p
Gender -Male -Female	 107 (67.2%) 52 (32.7%)	 66(75.8%) 21(24.1%)	0.160
Age	60.9 ± 10.4	62.1 ± 9.3	0.348

In terms of smoking, patients without recurrence had a mean smoking duration of 41.4 ± 37.6 years, whereas those with recurrence had a mean duration of 43.6 ± 29.3 years (p=0.093). Furthermore, regarding postoperative hospital stay, patients without recurrence had an average stay of 6.0 ± 3.0 days, in contrast to those with recurrence, who had a significantly longer stay of 7.0 ± 5.0 days (p<0.001) (Table 2).

Table 2. Table containing parametric data of the groups.

	No Recurrence n=159	Recurrence n=87	p
Smoking (Pack Year)	41.1 ± 37.6	43.6 ± 29.3	0.093
Postoperative Hospital Stay (Days)	6.0 ± 3.0	7.0 ± 5.0	<0.001

In stage 1, local relapses were the most frequent, occurring in 25.4% of total cases, followed by distant relapses at 23.7%, and combined local and distant relapses at 6.8%. For stage 2, local relapses were observed in 18% of total cases, distant relapses in 22.7%, and combined relapses in only 3.4% (Table 3).

Regarding the Cardiac Risk Index, the majority of patients with recurrence (79, or 90.8%) had a score of 1, compared to 136 (85.5%) of patients without recurrence. 15 (9.4%) patients with Cardiac Risk Index Score 2 were without recurrence whereas, 8 (9.1%) patients were with recurrence. For scores of 3 and 5, recurrence was less common, with no patients in the recurrence group having a score of 3, and only one patient with a score of 5 in the no recurrence group. The difference of Cardiac Index scores between two groups was not statistically significant (p=0.079) (Table 3).

As for the Pulmonary Risk Index, 56 (35.2%) patients with recurrence had a score of 0, in contrast to 15 (7.2%) of patients without recurrence. 70 (44%) patients with score 1 experienced recurrence, same as without a recurrence. A score of 2 was seen in 25 patients (15.7%) with recurrence and 21 patients (24.1%) without recurrence. Moreover, 8 (5%) patients had a score of 3, compared to 2 (2.2%) patients without recurrence. The distinction between recurrence and without recurrence in terms of Pulmonary Risk Index was not statistically substantial (Table 3).

Five different surgical resection methods were utilized; lobectomy, bilobectomy, pneumonectomy, wedge resection and segmentectomy. These procedures were performed using video-assisted thoracoscopic surgery (VATS) or thoracotomy.

Most of the patients had stage 1 cancer (n:171 69.5%), whereas only %30.5 (n:75) had stage 2 cancer. The recurrence rate was 35.3%, with 87 out of 246 patients experiencing relapse. Among stage 1 patients, the recurrence rate was 30% (n=52), whereas it was significantly higher in stage 2 patients at 46.6% (n=35, p=0.014) (Table 3).

Table 3. Table containing non-parametric data of the groups.			
	No Recurrence n=159	Recurrence n=87	p
Diabetes	33 (20.7%)	10 (11.4%)	0.067
Cardiac Risk Index 1 2 3 5	 136 (85.5%) 15 (9.4%) 7 (4.4%) 1 (0.6%)	 79 (90.8%) 8 (9.1%) 0 0	0.079
Pulmonary Risk Index 0 1 2 3	 56 (35.2%) 70 (44%) 25 (15.7%) 8 (5%)	 15(17.2%) 49(56.3%) 21(24.1%) 2(2.2%)	0.066
Charlson Comorbidity Index 2 3 5	 117 (73.5%) 42 (26.4%) 0	 72(82.7%) 14(16.09%) 1(1.1%)	0.128
Vats Thoracotomy	91 (57.2%) 68 (42.7%)	36 (41.4%) 51(58.6%)	0.017
Resection Method -Lobectomy -Bilobectomy -Pneumonectomy -Wedge -Segmentectomy	 132 (83.0%) 4 (2.5%) 2 (1.3%) 12 (7.5%) 9 (5.7%)	 71 (81.6%) 1 (1.2%) 8 (9.2%) 6 (6.9%) 1 (1.1%)	0.017
Pathologic Diagnosis -Adenocarcinoma -Squamosus Cell Carcinoma -Other	 88 (55.4%) 50 (31.5%) 21 (13.1%)	 54 (62.1%) 21 (24.1%) 12 (13.8%)	0.464
N0	143 (89.9%)	72 (82.7%)	0.107
N1	16 (10.1%)	15 (17.2%)	0.184
T Staging -1A -1B -1C -2A -2B -3	 19 (11.9%) 47 (28.5%) 24 (15.2%) 46 (28.9%) 16 (10.1%) 7 (4.4%)	 9 (10.3%) 12 (13.8%) 13 (14.9%) 31 (35.6%) 10 (11.5%) 12 (13.8%)	0.021
TNM Staging -1A1 -1A2 -1A3 -1B -2A -2B	 18 (11.3%) 44 (27.6%) 17 (10.6%) 40 (25.1%) 13 (8.1%) 27 (16.9%)	 8 (9.2%) 11 (12.6%) 13 (14.9%) 20 (22.1%) 8 (9.2%) 27 (31%)	0.035 for Stage 1 and 2, p=0.014
Pleural Invasion	58 (36.4%)	40 (45.9%)	0.135
Perineural Invasion	44 (27.6%)	33 (37.9%)	0.199
Lymphatic Invasion	102 (64.2%)	74 (85.1%)	0.001
Vascular Invasion	70 (44.0%)	54 (62.1%)	0.008

Table 4. Survival of the patients.			
	5-Year Survival Rate (%)	Median Survival (Months)	95 % Confidence Interval
No recurrence	83.6	164.7 ± 6.9	151.2-178.2
Recurrence	59.8	131.3 ± 9.9	111.9-150.7
Overall	75.2	154.2 ± 6.3	141.9-166.5

The VATS surgery rate was statistically significantly higher in the group without recurrence (p=0.017). There were statistically significantly more pneumonectomies performed in the relapse group (p=0.017). Regarding histopathological distribution, the non-recurrence group comprised 55.4% adenocarcinoma and 31.5% squamous cell carcinoma, whereas the recurrence group showed 62.1% and 24.1%, respectively. There was no statistically significant difference in histopathological types between the two groups (p=0.464).

The relapse group had statistically significantly more advanced T stage and TNM stage (p=0.021, p=0.035, respectively). Statistically significant lymphatic invasion and vascular invasion were observed more frequently in the relapse group (p=0.001, p=0.008, respectively). Smoking history and number of postoperative hospital stay days were higher in the recurrence group (p=0.093, p<0.001, respectively) (Table 3).

For the non-recurrence group with operated stage 1 and stage 2 cancers, it was 164.7 months (±6.9; 95% CI: 151.2 - 178.2). In contrast, the recurrence group had a mean survival time of 131.3 months (±9.9; 95% CI: 111.9 - 150.7) (Table 4). The group in which relapse was monitored was statistically significantly worse in terms of survival data (p=0.002) (Figure 1).

In Cox regression analysis, the group with recurrence had a statistically significantly worse survival (p<0.001). In Cox regression analysis, the presence of N1, pleural invasion and lymphatic invasion were associated with poor survival as independent risk factors (p=0.019, p=0.005, p=0.004, respectively). The presence of N1 and pleural invasion were not statistically significant on relapse-free survival (p=0.125, p=0.111, respectively) (Figure 2,3). Pneumonectomy and the presence of lymphatic invasion were statistically significant on recurrence-free survival (p=0.023, p=0.001, respectively) (Table 5) (Figure 4,5).

Table 5. Multivariate Cox regression analysis of survival.

	Hazard Ratio	p Value	95 % Confidence Interval
N1	16.4	0.019	1.6-167.9
Pleural Invasion	6.25	0.005	0.04-0.56
Lymphatic Invasion	6.25	0.004	0.05-0.57

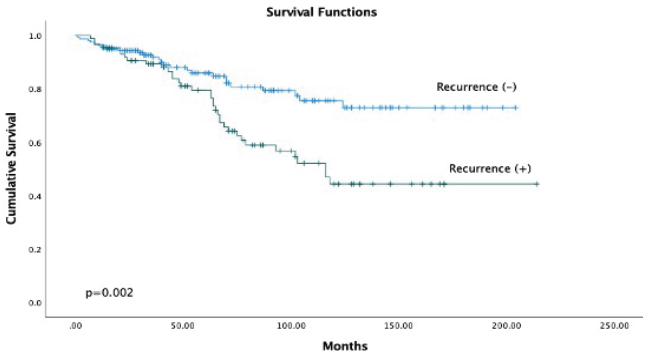

Figure 1. Survival graph of recurrence and non-recurrence groups in early stage non-small cell lung cancer patients.

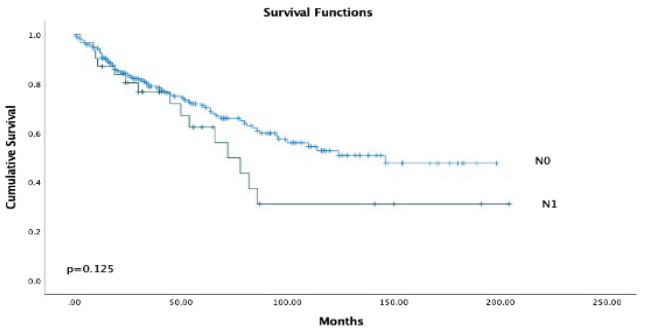

Figure 2. Survival graph showing the effect of the N factor on recurrence-free survival.

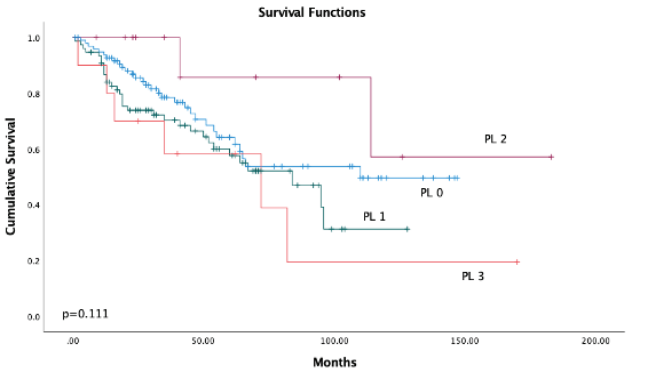

Figure 3. Survival graph showing the effect of the pleural invasion on recurrence-free survival.

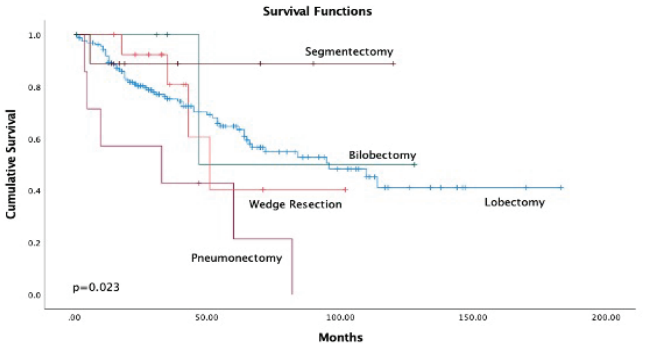

Figure 4. Survival graph showing the effect of the resection types on recurrence-free survival.

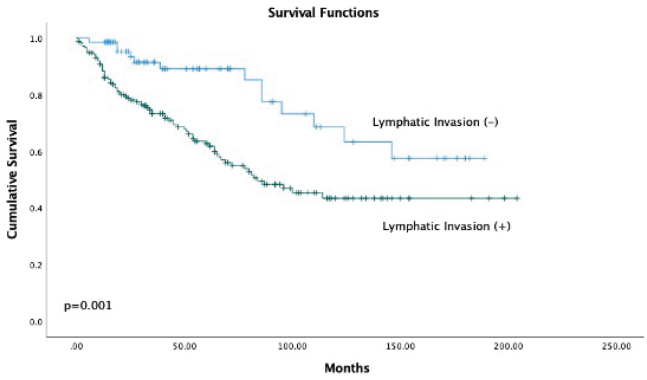

Figure 5. Survival graph showing the effect of the lymphatic invasion on recurrence-free survival.

Discussion

In this study, we retrospectively analyzed factors affecting recurrence in primary early stage lung cancer patients who were treated in our hospital between 2005 and 2022. Higher T and TNM stages, positive lymphatic and vascular invasion were significantly more common in the recurrence group. In contrast, the non-recurrence group showed a significantly higher rate of VATS surgery.

The Cox regression analysis confirmed recurrence as an independent predictor of poor survival ($p<0.001$). Additionally, the presence of N1, pleural invasion and lymphatic invasion were identified as significant risk factors for reduced survival ($p=0.019$, $p=0.005$, $p=0.004$, respectively). These findings highlight the importance of closely monitoring patients with these high-risk features and providing targeted interventions to help improve their outcomes [12].

Studies showed a strong association between locoregional recurrence and both visceral pleural invasion and N1 lymph node involvement [13,14]. Various studies have frequently discussed visceral pleural invasion concerning the prediction of postoperative recurrence. However, its prognostic significance is mostly confirmed through univariate analysis or found to be affected by tumor size [15,16]. However, a randomized controlled trial by Altorki et al. reported an increased recurrence rate and decreased disease-free survival in the presence of visceral pleural invasion [13]. In our study, the presence of pleural invasion was found to be an independent risk factor for survival, which is consistent with the literature, and it should be considered that additional treatment or close follow-up may be required in this patient group.

The presence of lymph node metastases (N1, N2) has been shown in multiple previous studies to significantly increase the risk of recurrence [17,18]. Furthermore, advanced N Stage (N1 compared to N0) and T stage (T3-T4 compared to T1-T2) have been found associated with loco-regional failure [19]. Similar to the literature, the presence of N1 was found to be an independent poor prognostic factor for survival. This highlights the importance of perioperative lymph node sampling.

In our study, the VATS surgery group had significantly lower recurrence rates compared to the Thoracotomy group. While other studies have also reported lower recurrence rates with VATS, even in larger tumors, the reasons for this remain unclear, particularly when considering the criteria used to determine the choice between VATS and thoracotomy [20,21]. Li et al., in their study presenting long-term outcomes after surgery for stage 1-3 NSCLC, demonstrated the advantage of VATS over thoracotomy in terms of overall and disease-free survival. However, when performing propensity score matching according to TNM stage, they found that VATS superiority in disease-free survival was observed only in stage 2 [22]. In our study, T stage was higher in the group that experienced recurrence. The lower recurrence observed in VATS patients may be due to the higher likelihood of performing thoracotomy in patients with larger tumors and more advanced T stage. However, this bias in incision selection should not be interpreted as recurrence caused by the type of incision [22].

Pneumonectomies were performed more frequently in the relapse group, and the number of postoperative hospital stay days was higher among the recurrence group. This may reflect the inclusion of patients with more advanced disease or worse overall health conditions in the relapse group, which could contribute to poorer survival outcomes and an increased likelihood of recurrence. In addition to advanced-stage disease, the necessity of a central pneumonectomy may also influence recurrence rates. Furthermore, pneumonectomy carries inherent risks of increased morbidity and mortality, which often result in prolonged hospitalizations and diminished overall health. Consequently, extended hospital stays likely reflect a more complex postoperative recovery driven by the patient's compromised health status or the presence of advanced-stage disease.

Limitations of the Study

Being a retrospective study conducted at a single institute, there are several limitations. First of all the study was conducted at a single center, which may limit the findings to broader population and variability in outcomes. Moreover, time-related bias was unavoidable due to our 17-year time interval. In order to mitigate this bias, we excluded the majority of patients (n = 506, 69%) with inconsistent, missing, or unexplainable data. Additionally, patients with advanced-stage disease were also excluded from the analysis. Although the study focused on stage I and II patients, these early-stage cases still exhibit significant heterogeneity and the variability within these groups may affect the interpretation of prognostic factors and outcomes. Despite these limitations, the strict exclusion of incomplete data and the long follow-up period enhance the reliability of our findings.

The TNM staging as well as the presence of lymphatic and vascular invasion were significantly linked to higher recurrence rates. Moreover, recurrence was more frequent in individuals with a smoking background and an extended hospital stay post-surgery. According to Cox regression analysis, lymphatic invasion was recognized as an independent factor associated with both lower survival rates and higher recurrence risk. Additionally, patients with pleural invasion, N1 involvement, advanced tumor stage, and those who underwent pneumonectomy also demonstrated a higher risk of recurrence and lower survival rate. Therefore, we recommend closer monitoring of these patient groups and a thorough assessment of adjuvant therapy strategies to enhance their prognosis.

In conclusion, recurrence in patients operated on for early-stage non-small cell lung carcinoma is important as it is associated with worse survival. In our study, the presence of N1, pleural invasion and lymphatic invasion were independently associated with poor survival in patients with early stage non-small cell lung carcinoma, indicating their effects as poor prognostic factors. The fact that pneumonectomy and the presence of lymphatic invasion have an impact on relapse-free survival shows that they are predisposing factors for relapse. In patients who underwent pneumonectomy and observed lymphatic invasion, more careful and close patient follow-up can be applied in terms of recurrence. Adjuvant treatment options may be considered. Moreover, recurrences occurring after five years may be more common than previously recognized, highlighting the need for stricter and longer surveillance programs for lung cancer patients. Consequently, high-risk patients require closer clinical surveillance. Incorporating adjuvant immunotherapy and chemotherapy into the treatment plan allows for personalized management strategies, optimizing patient outcomes.

Declaration of conflicting interests

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Ethics approval

The study was approved by the institutional ethics review board of Istanbul University-Cerrahpasa (Number and Date: E-83045809-604.01.01-712053; 15/06/2023).

Authors' contribution

GOI: contributed to the study's concept, design, data collection or processing, analysis or interpretation, literature search, and writing. AT: played a key role in the concept, design, analysis or interpretation, and writing of the manuscript. BSA: was involved in the design, data collection or processing, analysis or interpretation, and writing. BP, BK, EE, and HVK: focused on data collection or processing and conducted the literature search. MKK: contributed to the study's concept, analysis or interpretation, and final writing. All authors have read and approved the final version of the manuscript.

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Original Article

Changing phenotypes of pediatric empyema in the COVID-19 era

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ABSTRACT

Background: This study aimed to investigate whether the disease phenotype of pleural effusion and empyema in children changed across the COVID-19 periods, by analyzing clinical, biochemical, and radiological parameters among culture negative pediatric patients.

Materials and Methods: A retrospective analysis of 147 pediatric patients treated for thoracic empyema between 2012 and 2025 was conducted. Patients with current or previous SARS-CoV-2 infection were excluded. Patients were stratified into four groups: pre-COVID (≤2019), pandemic (2020-2021), early post-COVID (2022), and late post-COVID (≥2023). Worsening of the disease phenotype was assessed by the presence of lung abscess and necrotizing pneumonia. Demographic data, pleural fluid biochemistry (pH, glucose, lactate dehydrogenase (LDH)), and radiological findings were reviewed and compared.

Results: The prevalence of empyema-associated lung abscesses showed a trend toward increase across periods, being higher during the pandemic (33.3%) and late post-COVID (15%) compared with the pre-COVID era (7.4%, $p = 0.054$). Necrotizing pneumonia also increased numerically, reaching 35% in the late post-COVID period. LDH levels were significantly higher in the escalation group (4614.54 ± 4504.62 U/L) compared with the non-escalation group (2493.74 ± 4415.49 U/L, $p = 0.015$). Oxygen requirement ($p = 0.020$), ICU admission ($p < 0.001$) and secondary intervention requirements differed significantly across periods ($p = 0.046$), with the highest rates observed in the early post-COVID group.

Conclusions: In SARS-CoV-2 negative pediatric patients, empyema presenting in the post-pandemic period was associated with increased respiratory support requirements. These findings may reflect pandemic-related alterations in disease behavior and support earlier consideration of treatment escalation.

Keywords: empyema, COVID-19 era, pediatrics

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Introduction

Empyema is defined as collection of purulent fluid within the pleural space [1]. Pleural effusions (PEf) and empyema (PEm) are common pleural complications of pediatric community acquired pneumonia (CAP) causing significant morbidity [2]. While pleural involvement occurs in approximately 1% of CAP cases, it may be observed in up to 40% of hospitalized patients [3].

Pleural effusions are classified into three distinct stages by the American Thoracic Society, based on disease progression and biochemical analysis of the pleural fluid. Stage 1, the exudative phase, occurs within the first 1 to 3 days and is characterized by a clear fluid collection with normal glucose levels, normal pH, and an absence of bacteria or significant cellular activity. Stage 2, the fibrinopurulent phase, can last up to 10 days and is marked by purulent effusion with high cellularity, bacterial presence, low glucose concentration, a pH below 7.2, and the formation of septae and loculations. Finally, Stage 3, the organizing phase, develops over 2 to 4 weeks; during this period, fibroblast proliferation leads to the formation of a fibrous peel and pleural thickening, which may significantly limit lung expansion [4,5].

Although most effusions resolve with appropriate treatment of pneumonia, progression to empyema remains a clinical challenge and may require interventions ranging from chest drainage to video-assisted thoracoscopic surgery (VATS) [3].

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a global pandemic by the World Health Organization in March 2020, leading to profound changes in healthcare systems worldwide [6] . Public health measures such as social distancing and mask use led to reductions in respiratory infections including influenza and invasive bacterial diseases [7,8]. In parallel, changes in healthcare-seeking behavior, including a decline in emergency department visits during its early phases were reported [9].

These pandemic-related shifts have raised questions about potential changes in the clinical presentation and severity of pediatric empyema.

The aim of this study was to evaluate temporal changes in the clinical, biochemical, and radiological characteristics of pediatric pleural effusion and empyema across different COVID-19 periods, and to identify factors associated with disease severity and the treatment escalation in culture negative children.

Materials and Methods

This retrospective, single-center study was conducted in the Department of Pediatric Surgery at a tertiary referral hospital. 147 pediatric patients aged 1-18 years who were treated for pleural effusion and empyema between January 2012 and January 2025 were included.

Patients diagnosed with isolated parapneumonic pleural effusion or empyema were eligible for inclusion. Only patients with community-acquired pneumonia-related pleural disease were included. Patients with evidence of current or previous SARS-CoV-2 infection were excluded from the study. Cases with pleural effusion secondary to neonatal pneumonia, trauma, malignancy, postoperative causes, or non-pneumonic etiologies were also excluded.

Pleural effusion and empyema were diagnosed based on clinical presentation, radiological findings, and pleural fluid analysis. Pleural effusions were classified as exudative according to Light's criteria, defined by the presence of one or more of the following: a pleural fluid-to-serum protein ratio > 0.5, a pleural fluid-to-serum lactate dehydrogenase (LDH) ratio > 0.6, or pleural fluid LDH levels greater than two-thirds of the upper limit of normal serum LDH [10]. Empyema was defined as the presence of purulent pleural fluid and/or pleural fluid with biochemical characteristics consistent with infection.

Patients were categorized into four groups according to the period of admission in relation to the COVID-19 pandemic: pre-COVID period (≤2019), pandemic period (2020-2021), early post-COVID period (2022), and late post-COVID period (≥2023).

Disease severity was defined by the requirement for intensive care admission, supplemental oxygen support, treatment escalation, and the presence of lung abscess or necrotizing pneumonia. Treatment escalation was defined as the requirement for secondary invasive interventions following initial management, including additional chest tube insertion, video-assisted thoracoscopic surgery (VATS), or thoracotomy with decortication, excluding planned intrapleural fibrinolytic therapy as part of first-line management.

Demographic data, clinical characteristics, laboratory findings, radiological features, treatment modalities, and outcomes were retrospectively collected from hospital medical records and the institutional electronic database. Collected demographic variables included age and sex. Clinical data comprised symptom duration, laterality of pleural disease, respiratory support requirements (supplemental oxygen and ICU admission), and length of hospital stay.

Laboratory data included pleural fluid biochemical parameters obtained at the time of thoracentesis, including pH, glucose, lactate dehydrogenase (LDH), and leukocyte count. Radiological evaluation was performed using chest radiography and thoracic ultrasonography in all patients, with computed tomography reserved for selected cases to assess disease severity, loculations, lung abscess formation, or necrotizing pneumonia.

Treatment-related data included initial management strategy (chest tube drainage with or without intrapleural fibrinolytic therapy), the need for secondary interventions, and the type of surgical procedures performed. Outcome measures included treatment escalation requirements and duration of hospitalization. Culture-negative status was defined as the absence of bacterial growth in pleural fluid and blood cultures obtained prior to antibiotic modification. Most patients had received empirical antibiotic therapy before referral, which may have reduced culture yield.

This study was approved by the Ethics Committee of Health and Science University Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital (12.03.2026/ GOA-303) and it was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards, and informed consent was obtained from all patients.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software. Continuous variables were presented as mean ± standard deviation or median (minimum–maximum), depending on data distribution. Categorical variables were expressed as frequencies and percentages. Normality of continuous variables was assessed using the Shapiro-Wilk test. Comparisons between two groups were performed using the Student's t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Comparisons among multiple groups were conducted using the Kruskal-Wallis test for continuous variables and the Pearson chi-square test or Fisher's exact test for categorical variables, as appropriate. A p value < 0.05 was considered statistically significant.

Results

A total of 147 pediatric patients were included in the analysis. The mean age was 6.96 ± 4.72 years. Of the patients, 87 (59.2%) were male. Pleural involvement was located in the right hemithorax in 69 patients (46.9%), in the left hemithorax in 68 patients (46.3%), and was bilateral in 10 patients (6.8%). Patients were grouped according to the period of admission as pre-COVID (≤2019), pandemic (2020-2021), early post-COVID (2022), and late post-COVID (≥2023) (Table 1).

All patients included in the study were confirmed to be negative for SARS-CoV-2 infection at the time of diagnosis. Microbiological evaluation of pleural fluid and thoracic cultures revealed no growth of Mycobacterium tuberculosis or other specific pathogenic microorganisms. No significant comorbid condition was identified in the majority of patients. Symptom duration prior to hospital admission did not differ significantly across the COVID-19 periods ($p = 0.188$). The mean duration of symptoms was 10.1 ± 13.2 days in the pre-COVID period, 8.8 ± 5.6 days during the pandemic, 6.0 ± 3.7 days in the early post-COVID period, and 7.8 ± 7.4 days in the late post-COVID period.

Comparisons according to treatment escalation status are summarized in Table 2. Pleural fluid LDH levels were significantly higher in the escalation group (4614.54 ± 4504.62 U/L) compared with the non-escalation group (2493.74 ± 4415.49 U/L, $p = 0.015$). No statistically significant differences were observed between the two groups with respect to pleural fluid pH or glucose levels ($p > 0.05$). Similarly, the presence of empyema-associated lung abscess, necrotizing pneumonia, and pleural effusion volume did not differ significantly between patients with and without treatment escalation ($p > 0.05$).

Comparisons according to intrapleural fibrinolytic treatment success are summarized in Table 3. Pleural fluid biochemical parameters, including pH, lactate dehydrogenase (LDH), and glucose levels, were comparable between patients with successful and unsuccessful fibrinolytic therapy ($p > 0.05$). Similarly, the presence of empyema-associated lung abscess, necrotizing pneumonia, and the volume of pleural effusion did not differ significantly between patients with successful and unsuccessful fibrinolytic treatment ($p > 0.05$). No pleural fluid or radiological parameter was found to be significantly associated with fibrinolytic treatment success (Table 3).

Comparisons of secondary treatment requirements, fibrinolytic therapy outcomes, disease severity, and length of hospital stay across the COVID-19 periods are summarized in Table 4. The requirement for secondary treatment escalation differed significantly between the COVID-19 periods ($p = 0.046$). Secondary intervention was most frequently required in the early post-COVID period, while no patients required secondary treatment during the pandemic period. The requirement for supplemental oxygen differed significantly across the COVID-19 periods ($p = 0.020$), with higher proportions observed during the pandemic and post-COVID periods compared with the pre-COVID period. Similarly, ICU admission rates varied significantly between periods ($p < 0.001$), being most frequent in the early and late post-COVID groups. The rates of specific secondary interventions, including thoracoscopic debridement and thoracotomy with decortication, did not differ significantly across periods ($p > 0.05$). Similarly, the distribution of other secondary interventions was comparable between groups. The success rates of intrapleural fibrinolytic therapy did not differ significantly among the COVID-19 periods ($p > 0.05$), although a higher proportion of successful outcomes was observed in the early post-COVID period. Lung abscess formation was more frequently observed during the pandemic period compared with the pre-COVID period ($p = 0.054$). Although necrotizing pneumonia was more commonly observed during the pandemic and late post-COVID periods, this difference did not reach statistical significance ($p > 0.05$). The overall length of hospital stay did not differ significantly across the COVID-19 periods ($p > 0.05$).

Table 1. Baseline demographic characteristics of pediatric patients with parapneumonic pleural effusion and empyema, including distribution according to COVID-19 periods (n=147).

	value
Number of patients	147
Age (years), mean ± SD	6.96 ± 4.72
Sex, n (%)	
Male	87 (59.2)
Female	60 (40.8)
Side of pleural involvement, n (%)	
Right	69 (46.9)
Left	68 (46.3)
Bilateral	10 (6.8)
COVID-19 period of admission, n (%)	
Pre-COVID (≤2019)	81 (55.1)
Pandemic (2020–2021)	12 (8.2)
Early post-COVID (2022)	14 (9.5)
Late post-COVID (≥2023)	40 (27.2)

Values are presented as mean ± standard deviation or number (percentage), as appropriate

Table 2. Comparison of pleural fluid characteristics, lung abscess, necrotizing pneumonia, and pleural effusion volume according to treatment escalation status (n=147).

Variable	No escalation (n=127)	Escalation (n=20)	Z / χ^2	p
pH	7.24 ± 0.58	7.23 ± 0.78	-0.708	0.474
LDH (U/L)	2493.74 ± 4415.49	4614.54 ± 4504.62	-2.425	0.015
Glucose (mg/dL)	42.96 ± 84.37	40.14 ± 38.44	-1.056	0.291
Lung abscess, n (%)	14 (11.0)	3 (15.0)	—	0.705*
Necrotizing pneumonia, n (%)	34 (26.8)	8 (40.0)	0.904	0.342
Pleural effusion greater than half of hemithorax, n (%)	67 (52.8)	12 (60.0)	0.131	0.717

*Mann-Whitney U test for continuous variables; Pearson chi-square or Fisher's exact test for categorical variables, as appropriate. *Fisher's exact test.*

Table 3. Comparison of pleural fluid characteristics, lung abscess, necrotizing pneumonia, and pleural effusion volume according to intrapleural fibrinolytic treatment success (n=61).

	Unsuccessful (n=3)	Successful (n=58)	Z / χ^2	p
pH	7.60 ± 0.82	7.27 ± 0.70	0.212	0.845
LDH (U/L)	1171.33 ± 892.34	2917.09 ± 3864.52	-0.579	0.574
Glucose (mg/dL)	18.0 ± 19.7	36.98 ± 32.92	-0.545	0.603
Lung abscess, n (%)	2 (66.7)	10 (17.2)	—	1.000*
Necrotizing pneumonia, n (%)	2 (66.7)	19 (32.8)	—	1.000*
Pleural effusion > half hemithorax, n (%)	2 (66.7)	40 (69.0)	—	1.000*

**Fisher's exact test. Mann–Whitney U test and Fisher's exact test, as appropriate.*

Table 4. Comparison of secondary treatment requirements, fibrinolytic therapy success, disease severity, respiratory support, and length of hospital stay across COVID-19 periods (n=147).

	Pre-COVID (n=81)	Pandemic (n=12)	Early post-COVID (n=14)	Late post-COVID (n=40)	χ^2 / H	p
Secondary treatment required, n (%)	14 (17.3)	0 (0)	4 (28.6)	2 (5.0)	8.010	0.046
Thoracoscopic debridement, n (%)	1 (1.2)	0 (0)	1 (7.1)	0 (0)	4.215	0.239
Thoracotomy with decortication, n (%)	8 (9.9)	0 (0)	2 (14.3)	1 (2.5)	4.011	0.260
Other secondary interventions, n (%)	5 (6.2)	0 (0)	1 (7.1)	1 (2.5)	1.582	0.664
Fibrinolytic therapy successful, n (%)	27 (33.3)	5 (41.7)	9 (64.3)	19 (47.5)	5.813	0.121
Lung abscess, n (%)	6 (7.4)	4 (33.3)	1 (7.1)	6 (15.0)	7.658	0.054
Necrotizing pneumonia, n (%)	20 (24.7)	5 (41.7)	3 (21.4)	14 (35.0)	2.766	0.429
Oxygen requirement, n (%)	33 (40.7)	8 (66.7)	9 (64.3)	27 (67.5)	9.843	0.020
ICU admission, n (%)	30 (37.0)	7 (58.3)	11 (78.6)	30 (75.0)	19.873	<0.001
Length of hospital stay (days), mean ± SD	27.59 ± 20.49†	20.75 ± 15.74	26.36 ± 10.26	24.05 ± 20.75	5.650	0.130

Values are presented as number (percentage) or mean ± standard deviation. Pearson chi-square test was used for categorical variables and Kruskal-Wallis test for length of stay.

Discussion

In this retrospective cohort study, we evaluated changes in the clinical phenotype of pediatric parapneumonic pleural effusion and empyema across different COVID-19 periods.

The most notable finding of our study was the increased need for respiratory support, including supplemental oxygen and ICU admission, in the post-COVID era. Interestingly, this increase was not accompanied by a statistically significant rise in structural complications such as lung abscess or necrotizing pneumonia. Therefore, the post-pandemic shift in our cohort appears to reflect greater respiratory burden rather than increased destructive pulmonary involvement.

Recent reports have suggested that the COVID-19 pandemic altered the epidemiology of pleural infections. Chan et al. reported changes in microbiological etiology during the pandemic period, including an increase in polymicrobial infections, although overall clinical outcomes such as ICU admission and mortality were not significantly different between pre- and post-pandemic periods [7]. In contrast to their findings, our cohort demonstrated a clear increase in respiratory support requirements without parallel changes in structural complication rates.

Moreover, delayed presentation may lead to more advanced-stage empyema (fibrinopurulent or organizing phases), in which simple drainage is insufficient and early surgical intervention becomes necessary [5]. Although delayed presentation has been proposed as a potential explanation in other cohorts, symptom duration did not differ significantly across periods in our study and it does not explain the increased respiratory support requirements observed in the post-pandemic group.

We observed significant differences in the rate of secondary treatment escalation across COVID-19 periods, while specific surgical modalities did not individually differ. Current literature continues to debate the optimal first-line approach in pediatric empyema. A recent meta-analysis comparing VATS and tube thoracostomy with fibrinolytics showed shorter length of stay and faster recovery with VATS, although overall outcomes were comparable [5,11].

In our cohort, although escalation rates differed across periods, overall length of hospital stay remained comparable. This aligns with evidence suggesting that hospital stay in empyema is influenced by multiple clinical variables and is difficult to predict reliably [12]. Thus, increased respiratory support requirements did not necessarily translate into prolonged hospitalization.

Pleural fluid LDH levels were significantly higher in patients requiring secondary intervention. This finding supports the concept that biochemical markers may reflect disease intensity and inflammatory burden. The American Thoracic Society staging system recognizes elevated LDH as characteristic of the fibrinopurulent phase [5]. However, recent data suggest that pleural fluid biochemical parameters alone may not consistently predict fibrinolytic failure [13]. In our study, while LDH was associated with treatment escalation, pleural fluid pH and glucose were not. This may indicate that LDH reflects overall inflammatory activity rather than specific microbiological characteristics. Larger studies are required to validate LDH as a practical risk stratification tool.

Although lung abscess showed a numerical increase in certain periods among our patients, the difference did not reach statistical significance. Necrotizing pneumonia rates were also comparable across periods. These findings suggest that the post-pandemic shift in our cohort was characterized more by increased respiratory compromise than by a measurable rise in destructive parenchymal complications [3].

The increased frequency of oxygen requirement and ICU admission in the post-pandemic period highlights the need for careful respiratory monitoring in pediatric empyema patients. From a clinical perspective, elevated pleural fluid LDH may serve as an early warning marker to identify patients at higher risk of treatment escalation, prompting closer monitoring and earlier consideration of invasive interventions.

Limitations of the Study

Several limitations should be considered about this study. First of all, its retrospective design and single center setting may limit the generalizability of the findings. Secondly, the relatively small sample size within certain subgroups may have reduced the statistical power of some comparisons. In particular, the limited number of patients in the unsuccessful fibrinolytic therapy group restricts the interpretability of subgroup analyses. Additionally, the predominantly culture- negative results precluded pathogen-specific analyses, thereby limiting insights into microbiological trends across the studied periods.

In conclusion, pediatric empyema in the post-COVID-19 period appears to present with increased respiratory support requirements, without a clearly demonstrated rise in structural pulmonary complications. Elevated pleural fluid LDH levels were associated with the need for secondary treatment escalation, suggesting a potential role as a clinical indicator of disease severity. Further large-scale, multicenter studies are warranted to validate these findings and to better elucidate the long-term impact of pandemic-related factors on the clinical phenotype of pediatric empyema.

Declaration of conflicting interests

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Ethics approval

This study was approved by the Ethics Committee of Health and Science University Dr. Behcet Uz Pediatric Diseases and Surgery Training and Research Hospital (12.03.2026/ GOA-303).

Authors' contribution

AEB: contributed to the study's concept, design, data collection or processing, analysis or interpretation, literature search, and writing. ADP: played a key role in the data collection or processing, analysis or interpretation, and writing of the manuscript. AS: involved in the study's concept, design, and final writing of the manuscript. All authors have read and approved the final version of the manuscript.

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Original Article

Inflammatory and nutritional biomarker changes at postoperative days 25-34 after uniportal minimally invasive anatomical lung resection for non-small cell lung cancer

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ABSTRACT

Background: Blood-based inflammatory and nutritional biomarkers are increasingly used in non-small cell lung cancer (NSCLC), but their early postoperative behavior after uniportal minimally invasive anatomical lung resection remains unclear. This study evaluated perioperative changes in selected indices between the preoperative period and the standardized early postoperative outpatient assessment.

Materials and Methods: This retrospective observational study included 48 consecutive patients with histopathologically confirmed NSCLC who underwent uniportal minimally invasive anatomical lung resection between January 2024 and December 2025. Patients who underwent completion resection, had non-NSCLC histology, or lacked paired laboratory data were excluded. Preoperative laboratory values were compared with those obtained at the postoperative outpatient assessment between postoperative days 25 and 34. The primary endpoint was the change in hemoglobin, albumin, lymphocyte, and platelet score (HALP). Secondary endpoints were changes in neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, prognostic nutritional index, C-reactive protein-to-albumin ratio, and systemic immune-inflammation index.

Results: The cohort included 37 uniportal video-assisted thoracic surgery and 11 uniportal robotic-assisted thoracic surgery patients. HALP decreased significantly, whereas platelet-to-lymphocyte ratio and C-reactive protein-to-albumin ratio increased significantly. Hemoglobin and hematocrit decreased, while platelet count and C-reactive protein increased. No significant changes were observed in neutrophil-to-lymphocyte ratio, prognostic nutritional index, systemic immune-inflammation index, white blood cell count, neutrophil count, lymphocyte count, creatinine, or albumin.

Conclusions: The standardized postoperative outpatient assessment after uniportal minimally invasive anatomical lung resection for NSCLC suggested a selective biomarker pattern that may reflect a non-uniform early postoperative recovery process after uniportal anatomical lung resection.

Keywords: carcinoma, non-small cell lung, biomarkers, thoracic surgery, video-assisted, robotic surgical procedures, hemoglobin, albumin, lymphocyte, platelet score

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Introduction

Non-small cell lung cancer (NSCLC) remains the predominant histological subtype of lung cancer, and surgical resection continues to be the main curative treatment for patients with resectable disease. In recent years, increasing attention has been directed toward blood-based inflammatory and nutritional biomarkers because they can be obtained from routine laboratory tests at no additional cost and may reflect the interaction between tumor biology, host immunity, systemic inflammation, and nutritional status. In resected NSCLC, markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), prognostic nutritional index (PNI), and other composite scores have been widely investigated, mostly in relation to postoperative complications or long-term oncologic outcomes [1,2].

Among these markers, several indices are of particular interest because they capture complementary biological domains. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score integrates anemia, nutritional status, immune balance, and platelet-related inflammatory burden into a single composite measure [3]. The C-reactive protein-to-albumin ratio (CAR) reflects a CRP-dominant inflammatory and nutritional profile, whereas the systemic immune-inflammation index (SII) and PLR provide additional information on platelet-linked inflammatory activity [2,4,5]. These markers have been associated with prognosis in NSCLC and are increasingly viewed as practical host-related biomarkers in thoracic oncology [1].

However, most available studies have focused on preoperative values or long-term prognostic stratification rather than short-term postoperative biomarker behavior. This distinction is important because perioperative systemic changes after lung resection are influenced not only by cancer-related biology but also by surgical trauma and the subsequent recovery process. Previous work has shown that minimally invasive major lung resection is associated with a more attenuated inflammatory and immune disturbance than open surgery [6]. Recent reviews have also emphasized that perioperative systemic inflammation may itself be clinically relevant in lung cancer surgery [7]. Nevertheless, the early postoperative pattern of routinely available inflammatory and nutritional indices after uniportal minimally invasive anatomical lung resection remains insufficiently characterized, particularly at a standardized outpatient follow-up time point.

The present study was therefore designed to evaluate perioperative changes in inflammatory and nutritional indices between the preoperative period and the standardized early postoperative outpatient assessment in patients undergoing uniportal minimally invasive anatomical lung resection for NSCLC. HALP was assessed as the primary endpoint. Changes in NLR, PLR, PNI, CAR, and SII were examined as secondary indices to characterize the early postoperative biological recovery pattern after uniportal anatomical resection. We hypothesized that the standardized early postoperative follow-up after uniportal anatomical lung resection would demonstrate a selective exploratory biomarker recovery pattern, with more pronounced changes in composite and CRP/platelet-linked indices than in broader leukocyte- or albumin-based markers.

Materials and Methods

Study design and patient selection

This retrospective observational study included consecutive patients who underwent uniportal minimally invasive anatomical lung resection for NSCLC at our clinic between January 2024 and December 2025. The institutional database was reviewed to identify eligible patients.

Patients were included if they met all of the following criteria: (1) histopathologically confirmed NSCLC, including adenocarcinoma, squamous cell carcinoma, or adenosquamous carcinoma; (2) uniportal minimally invasive anatomical lung resection performed by either uniportal video-assisted thoracic surgery (UVATS) or uniportal robotic-assisted thoracic surgery (URATS); (3) anatomical resection in the form of lobectomy, segmentectomy, and pneumonectomy; and (4) availability of both preoperative and early postoperative laboratory measurements required for calculation of inflammatory and nutritional indices.

Patients were excluded if they underwent completion resection, had a non-NSCLC histology, or had missing paired laboratory data. After applying the eligibility criteria, 48 patients constituted the final study cohort. To reduce potential selection and information bias, we in-

cluded consecutive eligible patients from a single institutional database and restricted the analysis to patients with paired laboratory measurements obtained within a prespecified postoperative follow-up window.

Data collection

Demographic, clinical, operative, pathological, and laboratory data were obtained retrospectively from electronic medical records and the institutional surgical database. The following baseline variables were recorded: age, sex, body mass index, smoking history, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, and forced expiratory volume in 1 second (FEV_1).

Operative and pathological variables included surgical approach (UVATS or URATS), type of resection (lobectomy, segmentectomy, and pneumonectomy), tumor size, pathological T category, pathological stage, mediastinal lymph node dissection status, and total number of harvested lymph nodes. Postoperative descriptive variables included chest tube duration, length of hospital stay, in-hospital complications, and 30-day adverse events.

Laboratory assessment and follow-up window

Preoperative laboratory values were obtained from routine blood tests performed before surgery. Early postoperative laboratory values were collected from the postoperative outpatient assessment. To ensure a relatively homogeneous follow-up interval, only patients with postoperative laboratory assessment performed between postoperative days 25 and 34 were included in the final analysis. This interval was selected to reflect the standardized outpatient postoperative review in our practice and to approximate the 1-month postoperative time point used in prior NSCLC studies evaluating postoperative immunonutritional status [8,9]. It also captures an early recovery phase in which final pathology and postoperative oncologic planning are usually available while adjuvant systemic treatment has often not yet started.

The following laboratory parameters were recorded for both the preoperative and postoperative time points: white blood cell count, hemoglobin, hematocrit, platelet count, neutrophil count, lymphocyte count, C-reactive protein, serum creatinine, and albumin.

Inflammatory and nutritional indices

The following inflammatory and nutritional indices were calculated at both time points:

- Neutrophil-to-lymphocyte ratio (NLR): neutrophil count / lymphocyte count
- Platelet-to-lymphocyte ratio (PLR): platelet count / lymphocyte count
- Prognostic nutritional index (PNI): albumin (g/L) + 5 × lymphocyte count (10^9/L)
- C-reactive protein-to-albumin ratio (CAR): C-reactive protein / albumin
- Systemic immune-inflammation index (SII): platelet count × neutrophil count / lymphocyte count
- Hemoglobin, albumin, lymphocyte, and platelet (HALP) score: 10 × hemoglobin (g/dL) × albumin (g/L) × lymphocyte count (10^9/L) / platelet count (10^9/L)

For each index, change from the preoperative assessment to the standardized early postoperative follow-up was defined as the postoperative value minus the preoperative value in order to quantify the direction and magnitude of within-patient change over time.

Study endpoints

The primary aim of the study was to evaluate perioperative changes in inflammatory and nutritional indices between the preoperative period and the early postoperative follow-up after uniportal minimally invasive anatomical lung resection for NSCLC.

The primary endpoint was the change in HALP score between the preoperative and postoperative assessments. Secondary endpoints included changes in NLR, PLR, PNI, CAR, and SII. The study was designed as a descriptive and exploratory analysis intended to characterize early postoperative biomarker behavior and to generate hypotheses for future prospective studies, rather than to establish clinically actionable thresholds.

The study protocol was approved by the Institutional Review Board (Approval Date: 24.12.2025, Approval No: KAEK/24.12.2025.396). Written informed consent was obtained from all patients prior to surgery. The study

was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA). Data completeness was reviewed before analysis. Because all variables required for the predefined analyses were available in the final study cohort, a complete-case analysis was performed.

The distribution of continuous variables was assessed using visual inspection of histograms and the Shapiro–Wilk test. As most continuous variables, including the derived inflammatory and nutritional indices, did not follow a normal distribution, continuous data were expressed as median and interquartile range (IQR), whereas categorical variables were summarized as number and percentage.

The primary analysis of the study was based on within-patient paired comparisons between preoperative and early postoperative measurements. Changes in laboratory parameters and derived inflammatory/nutritional indices between the two time points were evaluated using the Wilcoxon signed-rank test. For paired comparisons, effect size for the Wilcoxon signed-rank test was expressed as r ($Z/\sqrt{N}$), and the magnitude of change was additionally summarized using the Hodges–Lehmann estimate of the paired difference with 95% confidence intervals. For each index, perioperative change was defined as the postoperative value minus the preoperative value.

The prespecified primary endpoint was the change in HALP score. Secondary endpoints were changes in NLR, PLR, PNI, CAR, and SII. Because the primary aim of the study was to characterize the shared early postoperative biomarker pattern after uniportal minimally invasive anatomical lung resection, operative approach was not used as a primary grouping variable for inferential analysis. Formal subgroup comparison between UVATS and URATS was not planned because of the small size of the URATS subgroup and the exploratory design of the study. Accordingly, operative approach was treated as a descriptive cohort characteristic. It was not used as a primary grouping variable for inferential analysis in order to avoid overlap with the separate perioperative outcomes study comparing URATS and UVATS.

Continuous baseline and postoperative descriptive variables were reported for the overall cohort using median (IQR), and categorical descriptive variables were reported as number (%). No predictive modeling, cutoff analysis, receiver operating characteristic analysis, or multivariable regression was performed, given the exploratory nature of the study and the limited sample size.

All tests were two-sided, and a p value of <0.05 was considered statistically significant. Because HALP change was defined a priori as the primary endpoint, analyses of the remaining indices were considered secondary and exploratory and were interpreted accordingly. No formal adjustment for multiple comparisons was applied, because HALP was prespecified as the single primary endpoint and the remaining biomarker analyses were exploratory in nature. Therefore, p values for secondary endpoints should be interpreted cautiously, with particular awareness of the increased risk of type I error.

Results

Study cohort and baseline characteristics

Among 57 preliminarily screened patients in the NSCLC biomarker cohort, 2 who underwent completion resection and 7 with missing laboratory data were excluded. The final analysis included 48 patients (Figure 1). Median age was 68.0 (IQR, 62.0–74.0) years, and 39 patients (81.2%) were male. The surgical approach was UVATS in 37 patients (77.1%) and URATS in 11 patients (22.9%). Lobectomy was performed in 35 patients (72.9%), segmentectomy in 11 patients (22.9%), and pneumonectomy in 2 patients (4.2%). Histopathology showed adenocarcinoma in 36 patients (75.0%), squamous cell carcinoma in 6 patients (12.5%), and adenosquamous carcinoma in 6 patients (12.5%). The early postoperative laboratory assessment was obtained at a median postoperative day of 29.5 (IQR, 27.0–31.0). Baseline and operative characteristics are summarized in Table 1.

Changes in routine laboratory parameters

Routine laboratory comparisons are presented in Table 2. Hemoglobin decreased from 13.85 (IQR, 11.85-

14.47) to 12.35 (IQR, 11.10-14.22) ($p < 0.001$), and hematocrit decreased from 41.25 (IQR, 36.25-43.90) to 38.05 (IQR, 33.98-41.95) ($p < 0.001$). Platelet count increased from 244.00 (IQR, 197.50-287.25) to 260.00 (IQR, 216.75-302.00) ($p = 0.038$), and C-reactive protein increased from 2.95 (IQR, 1.70-7.12) to 5.30 (IQR, 3.48–21.57) ($p = 0.005$). No significant differences were observed in white blood cell count, neutrophil count, lymphocyte count, creatinine, or albumin (all $p > 0.05$).

Changes in inflammatory and nutritional indices

Changes in inflammatory and nutritional indices are shown in Table 3, which also provides effect size estimates and Hodges-Lehmann confidence intervals for paired differences. The prespecified primary endpoint, HALP score, showed a significant decline from 44.14 (IQR, 34.48-65.76) preoperatively to 38.95 (IQR, 24.52-48.29) at early follow-up (median delta, -7.36 [IQR, -21.02 to 3.34]; $p = 0.010$; Figure 2). Figure 2 illustrates the paired within-patient decline in HALP score between the preoperative assessment and the standardized early postoperative follow-up. PLR increased significantly from 125.23 (IQR, 94.50-155.95) to 135.86 (IQR, 98.25-190.04) (median delta, 14.27 [IQR, -16.76 to 51.32]; $p = 0.047$; Figure 3), and Figure 3 demonstrates the overall upward shift in PLR values during the same interval. CAR increased from 0.067 (IQR, 0.040-0.157) to 0.121 (IQR, 0.086–0.521) (median delta, 0.039 [IQR, -0.004 to 0.262]; $p = 0.005$; Figure 4), while Figure 4 shows the postoperative increase in CAR across paired observations. In contrast, changes in NLR, PNI, and SII were not statistically significant ($p = 0.357$, $p = 0.134$, and $p = 0.065$, respectively).

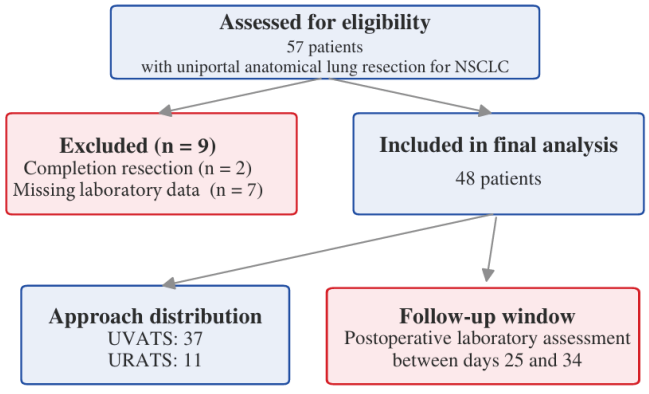

Figure 1. Study flow diagram.

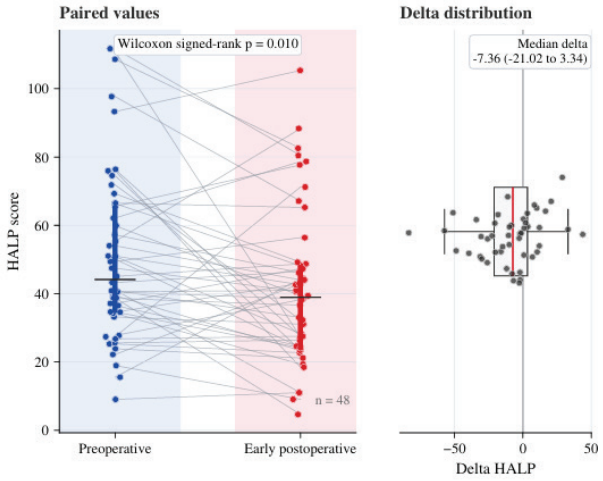

Figure 2. Paired change in HALP score between the preoperative period and the standardized postoperative outpatient assessment. Lower postoperative HALP values may reflect a less favorable early immunonutritional recovery profile.

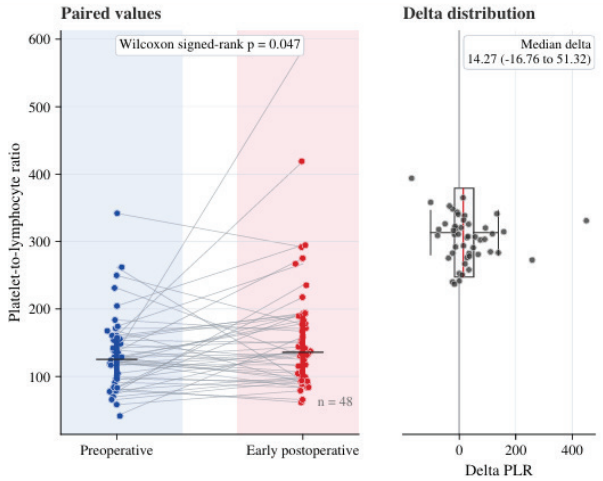

Figure 3. Paired change in platelet-to-lymphocyte ratio between the preoperative period and the standardized postoperative outpatient assessment. Higher postoperative PLR values may reflect greater platelet-predominant inflammatory activity during early recovery.

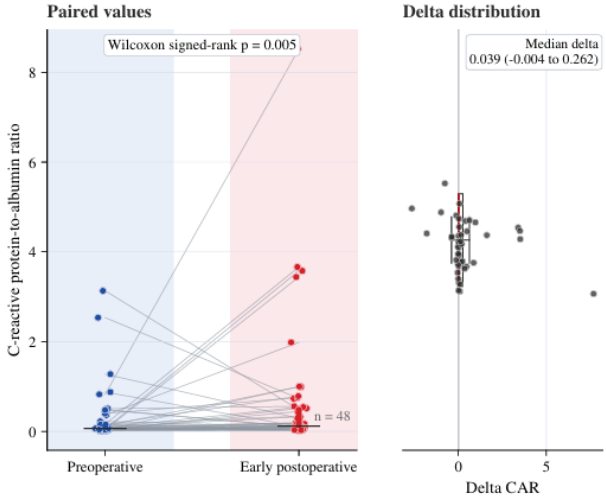

Figure 4. Paired change in C-reactive protein-to-albumin ratio between the preoperative period and the standardized postoperative outpatient assessment. Higher postoperative CAR values may reflect greater CRP-dominant inflammatory burden during early recovery.

Table 1. Baseline, operative, and pathological characteristics of the overall cohort.	
Variable	Overall cohort (n=48)
Demographic and clinical characteristics	
Age, years	68.0 (62.0-74.0)
Male sex	39 (81.2)
Body mass index, kg/m^2	26.6 (24.7-28.7)
Smoking status	
Never smoker	6 (12.5)
Current smoker	23 (47.9)
Former smoker	19 (39.6)
Pack-years	45.0 (32.2-62.5)
Chronic obstructive pulmonary disease	20 (41.7)
Diabetes mellitus	15 (31.2)
Hypertension	33 (68.8)
Forced expiratory volume in 1 second, % predicted	91.0 (78.0-104.0)
Operative and pathological characteristics	
Surgical approach	
Uniportal video-assisted thoracic surgery	37 (77.1)
Uniportal robotic-assisted thoracic surgery	11 (22.9)
Type of resection	
Lobectomy	35 (72.9)
Segmentectomy	11 (22.9)
Pneumonectomy	2 (4.2)
Tumor size on computed tomography, mm	25.5 (15.0-38.5)
Histopathology	
Adenocarcinoma	36 (75.0)
Squamous cell carcinoma	6 (12.5)
Adenosquamous carcinoma	6 (12.5)
Pathological T category	
Tis	1 (2.1)
T1	16 (33.3)
T2	22 (45.8)
T3	8 (16.7)
T4	1 (2.1)
Pathological stage	
Stage I	29 (60.4)
Stage II	16 (33.3)
Stage III	3 (6.2)
Harvested lymph nodes, total number	15.5 (10.0-22.0)
Postoperative descriptive characteristics	
Chest tube duration, days	2.0 (2.0-4.0)
Length of hospital stay, days	3.0 (2.0-5.0)
In-hospital complications	10 (20.8)
30-day adverse events	1 (2.1)
Postoperative laboratory assessment day	29.5 (27.0-31.0)

Table 2. Preoperative and early postoperative routine laboratory parameters.			
Parameter	Preoperative, median (IQR)	Early postoperative, median (IQR)	p value
White blood cell count, $\times 10^9$/L	7.790 (6.697-8.875)	7.960 (7.080-9.227)	0.369
Hemoglobin, g/dL	13.85 (11.85-14.47)	12.35 (11.10-14.22)	<0.001
Hematocrit, %	41.25 (36.25-43.90)	38.05 (33.98-41.95)	<0.001
Platelet count, $\times 10^9$/L	244.00 (197.50-287.25)	260.00 (216.75-302.00)	0.038
Neutrophil count, $\times 10^9$/L	4.770 (4.082-6.080)	4.985 (4.098-5.935)	0.988
Lymphocyte count, $\times 10^9$/L	1.965 (1.555-2.355)	1.910 (1.478-2.552)	0.562
C-reactive protein, mg/L	2.95 (1.70-7.12)	5.30 (3.48-21.57)	0.005
Creatinine, mg/dL	0.930 (0.835-1.120)	0.855 (0.808-1.005)	0.073
Albumin, g/L	43.00 (38.75-45.00)	42.00 (38.75-44.00)	0.181

Table 3. Preoperative and early postoperative inflammatory and nutritional indices.						
Index	Preoperative, median (IQR)	Early postoperative, median (IQR)	Delta (post - pre), median (IQR)	p	Effect size (r)	Hodges–Lehmann estimate (95% CI)
HALP score	44.14 (34.48–65.76)	38.95 (24.52–48.29)	-7.36 (-21.02 to 3.34)	0.010	0.367	-7.99 (-14.61 to -1.98)
Neutrophil-to-lymphocyte ratio	2.60 (1.96–3.67)	2.52 (1.63–4.08)	0.07 (-0.60 to 1.16)	0.357	0.135	0.21 (-0.19 to 0.69)
Platelet-to-lymphocyte ratio	125.23 (94.50–155.95)	135.86 (98.25–190.04)	14.27 (-16.76 to 51.32)	0.047	0.287	16.69 (0.20 to 38.46)
Prognostic nutritional index	51.98 (48.61–56.04)	51.62 (47.24–55.58)	-1.73 (-4.95 to 2.49)	0.134	0.216	-1.37 (-2.93 to 0.37)
C-reactive protein-to-albumin ratio	0.067 (0.040–0.157)	0.121 (0.086–0.521)	0.039 (-0.004 to 0.262)	0.005	0.401	0.07 (0.02 to 0.24)
Systemic immune inflammation index	584.35 (469.45–749.67)	725.13 (425.89–1117.80)	95.58 (-131.40 to 440.73)	0.065	0.266	126.94 (-11.46 to 279.68)
Data are presented as median (interquartile range). P values were obtained using the Wilcoxon signed-rank test. Effect size was expressed as r (Z/√N). The magnitude of paired change was additionally summarized using the Hodges–Lehmann estimate with 95% confidence intervals.						

Discussion

In this retrospective paired-cohort study, we found that the standardized postoperative outpatient assessment after uniportal minimally invasive anatomical lung resection for NSCLC was characterized by a biomarker pattern that appeared selective rather than global. The most relevant findings were a significant reduction in HALP score and significant increases in PLR and CAR, accompanied by lower hemoglobin and hematocrit values and higher platelet and CRP levels. In contrast, NLR, PNI, SII, total white blood cell count, neutrophil count, lymphocyte count, creatinine, and albumin did not change significantly. Overall, this pattern suggests that by postoperative days 25-34, the residual biological signal may be less consistent with a generalized leukocyte-driven inflammatory response. Instead, it appears more compatible with a selective profile marked by persistent CRP- and platelet-related activity together with incomplete hematologic recovery. This interpretation is consistent with the broader NSCLC literature showing that blood-based inflammatory and nutritional biomarkers are clinically relevant in resected disease, while perioperative systemic changes after lung surgery reflect both surgical trauma and subsequent biological recovery [1,7].

An important strength of the present study is that the evaluated biomarker panel was not assembled in an arbitrary fashion. Instead, the selected indices were predefined because they represent complementary biological domains derived from routine perioperative blood tests. HALP was chosen as the primary endpoint because it integrates anemia, nutritional status, immune balance, and platelet-related inflammatory burden into a single composite marker [3]. CAR was included as a CRP-dominant inflammation/nutrition index, whereas PLR and SII were used to reflect platelet-linked inflammatory activity [2,4,5]. NLR and PNI were retained as supportive secondary indices of immune balance and immunonutritional reserve. This selection strategy is aligned with current reviews of resected NSCLC, in which blood-based biomarkers are considered attractive

because they are simple, inexpensive, and widely available, even though most previous studies have primarily focused on baseline or prognostic value rather than short-term postoperative kinetics [1].

Among the evaluated markers, the decrease in HALP appears to be the most informative finding. HALP is driven upward by hemoglobin, albumin, and lymphocyte count and downward by platelet count. In our cohort, HALP decreased in parallel with significant reductions in hemoglobin and hematocrit and a concomitant rise in platelet count, whereas albumin and lymphocyte count remained relatively stable. This suggests that the early postoperative decline in HALP was mainly related to incomplete hematologic recovery and platelet-mediated inflammatory activity rather than to overt nutritional deterioration. This distinction is important, because HALP has mainly been studied as a prognostic marker in NSCLC, whereas our data indicate that it may also serve as a sensitive composite marker of short-term perioperative recovery after uniportal anatomical lung resection [3].

At the same time, the added value of these composite indices should be interpreted critically. The postoperative decrease in hemoglobin and the increases in CRP and platelet count observed in our cohort are expected findings after lung resection and do not, by themselves, establish the superiority of HALP, PLR, or CAR over their individual components. Rather, their potential value lies in summarizing multiple inflammatory and nutritional domains into a more integrated postoperative recovery signal. This interpretation is supported by the broader NSCLC biomarker literature and by thoracic surgical data on postoperative thrombocytosis after minimally invasive lung resection [1,10].

The increases in PLR and CAR support the same biological interpretation. In the case of CAR, the signal seems largely CRP-driven, as CRP increased significantly while albumin remained relatively stable. In the case of PLR, the increase is most plausibly explained by postoperative platelet elevation in the setting of relatively unchanged lymphocyte values. This pattern is clinically coherent, as CRP- and platelet-based indices may remain abnormal even when broader leukocyte-based measures are less disturbed. The relevance of CAR in lung cancer is supported by meta-analytic evidence showing that elevated CAR is associated with poorer survival outcomes, although our study was not designed to evaluate prognosis [4]. Therefore, our findings should not be interpreted as evidence that higher postoperative CAR or PLR predicts recurrence or survival; rather, they suggest that these indices may reflect incomplete early biological recovery and may warrant prospective evaluation in standardized postoperative follow-up windows.

Although these findings are not yet directly practice-changing, they may still have practical relevance for standardized postoperative follow-up. In routine thoracic surgical care, the outpatient postoperative review is often the time point when recovery status, final pathology, and adjuvant treatment planning are reassessed. Within this context, persistent reduction in HALP together with increases in CAR or PLR may be interpreted as candidate indicators of incomplete biological recovery rather than as immediate prognostic markers. If confirmed prospectively, such patterns may help identify patients who could benefit from closer laboratory reassessment or a more individualized early follow-up strategy. However, because the present study did not correlate biomarker changes with postoperative complications, recovery metrics, or oncologic outcomes, these findings should not yet be used to guide clinical decision-making.

Equally important are the biomarkers that did not change significantly. The lack of statistically significant shifts in NLR, SII, PNI, white blood cell count, neutrophil count, lymphocyte count, albumin, and creatinine should not be viewed as a negative result. Instead, it likely reflects the specific timing of assessment in the present study. We did not evaluate biomarkers during the immediate postoperative inflammatory surge; rather, we assessed them at a standardized follow-up visit between postoperative days 25 and 34. By that stage, leukocyte-based disturbances may already have partially resolved, particularly after minimally invasive surgery, whereas CRP, platelet, and anemia-related changes may persist for longer. This interpretation is supported by work showing that minimally invasive major lung resection is associated with a more attenuated postoperative inflammatory and immune disturbance than open surgery [6]. Recent

data also suggest that perioperative biomarker trajectories, including SII dynamics, may provide information beyond a single static postoperative measurement [8,11].

The present study should therefore be interpreted as hypothesis-generating rather than definitive. Its main contribution is to characterize the shared early postoperative biomarker profile after uniportal minimally invasive anatomical resection, rather than to establish postoperative cutoffs, predict recurrence, or compare the superiority of UVATS and URATS. Within that scope, our results support the hypothesis that early postoperative recovery after uniportal anatomical lung resection for NSCLC may follow a selective biomarker recovery pattern, with HALP reduction and increases in CAR and PLR remaining detectable at the standardized follow-up, whereas broader leukocyte-based or albumin-based changes are less prominent. If validated prospectively, this pattern may help identify which readily available biomarkers are most suitable for monitoring early recovery after minimally invasive lung cancer surgery [1]. In addition, because several secondary biomarkers were evaluated simultaneously without formal multiplicity adjustment, the observed secondary associations should be regarded as exploratory signals rather than confirmatory findings and interpreted with appropriate caution.

Limitations of the Study

Several limitations should be acknowledged. First, this was a retrospective single-center study, which limits external generalizability. In addition, the retrospective design introduces potential selection bias and information bias, particularly with respect to eligibility based on availability of paired laboratory data and the accuracy and completeness of retrospectively retrieved clinical variables. Second, the sample size was modest, and the analysis was therefore intentionally restricted to paired within-patient comparisons and descriptive cohort characterization. No formal a priori power analysis was performed because of the retrospective exploratory design of the study. Therefore, the cohort may have been underpowered to detect modest differences in secondary biomarker endpoints. Third, only one standardized early postoperative time point was evaluated; thus, we were unable to assess serial biomarker trajectories, delayed normalization patterns, or associations with long-term oncologic outcomes. In addition, we did not correlate biomarker changes with postoperative complications, recovery metrics, or other short-term clinical outcomes. Therefore, the observed biomarker shifts should not yet be interpreted as markers of clinical recovery, complication risk, or prognosis. In addition, the cohort included different extents of anatomical resection (lobectomy, segmentectomy, and pneumonectomy), which may differ in surgical stress and postoperative inflammatory response. Fourth, although both UVATS and URATS were represented in the cohort, the study was intentionally designed as a pooled uniportal analysis rather than a between-approach comparative study in order to preserve conceptual separation from our dedicated perioperative outcomes analysis. Potential differences in surgical trauma and postoperative inflammatory response between UVATS and URATS therefore cannot be excluded and should be evaluated in larger comparative cohorts. Furthermore, because multiple secondary biomarkers were analyzed without formal adjustment for multiple comparisons, the possibility of type I error should be acknowledged. Accordingly, the secondary results should be interpreted as exploratory findings that require confirmation in larger prospective cohorts. Finally, because the selected indices were derived from overlapping hematologic and inflammatory variables, the present work should be interpreted as a focused characterization of postoperative biological recovery rather than as a search for independent predictive markers. These limitations should temper interpretation, but they do not diminish the main methodological strength of the study: a homogeneous NSCLC cohort, anatomically comparable resections, and a tightly standardized postoperative laboratory window.

In conclusion, the standardized postoperative outpatient assessment after uniportal minimally invasive anatomical lung resection for NSCLC was characterized by a selective biomarker pattern, with reduced HALP and increased PLR and CAR despite stable NLR, SII, PNI, albumin, and leukocyte counts. These findings suggest that early postoperative recovery after uniportal minimally invasive anatomical lung resection may not

be biologically uniform. Among the evaluated indices, HALP, CAR, and PLR appeared to be the most responsive markers of residual postoperative biological stress and may deserve prospective evaluation in larger cohorts with serial postoperative follow-up.

Declaration of conflicting interests

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Ethics approval

This study was approved by the Institutional Review Board of Başakşehir Çam and Sakura City Hospital (Approval No: KAEK/24.12.2025.396)

Authors' contribution

MI: contributed to the study's concept, design, supervision, data collection or processing, literature search, statistical analysis, writing, and critical review. OY: was involved in the design, data collection or processing, literature search, and critical review of the manuscript. AY: contributed to the study's supervision and critical review. All authors have read and approved the final version of the manuscript.

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Original Article

Extended lung resections for NSCLC with adjacent structure involvement: a single-center experience

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ABSTRACT

Background: Extended lung resections for non-small cell lung cancer (NSCLC) requiring en bloc resection of adjacent structures remain technically demanding procedures and are associated with considerable perioperative risk. This study analyzes the outcomes of 29 consecutive patients undergoing extended lung resections, focusing on survival outcomes and potential prognostic factors.

Materials and Methods: We retrospectively analyzed 29 patients who underwent extended lung resections for non-small cell lung cancer (NSCLC) with suspected or confirmed invasion of adjacent structures between 2015 and 2023 at our institution. Extended resections included en bloc removal of structures such as the chest wall, pericardium, diaphragm, or vascular structures when necessary to achieve tumor clearance. Patient demographics, operative characteristics, pathological findings, postoperative complications, and long-term survival outcomes were evaluated using Kaplan–Meier survival analysis.

Results: The cohort included 26 males (89.7%) and 3 females (10.3%) with a mean age of 64.4 ± 10.7 years. Squamous cell carcinoma was the predominant histology (65.5%). TNM staging revealed Stage IB (34.5%) and Stage IIA (20.7%) as most frequent. All patients underwent thoracotomy with extended resections: chest wall (58.6%), pericardium (20.7%), and combined procedures (20.7%). R0 resection was achieved in 51.7% of patients. Mean operative time was 159 ± 62 minutes. Postoperative complications occurred in 27.6% of patients, with zero 30-day mortality. Mean follow-up was 29.4 ± 24.1 months with overall mortality of 72.4% and median survival of 24.0 months. Chest wall resection patients had higher mortality (82.4%) compared to other extended procedures (58.3%).

Conclusions: Extended lung resections may be performed with acceptable operative mortality in carefully selected patients. However, long-term survival remains limited, particularly in patients requiring chest wall resection. Rigorous patient selection and multidisciplinary evaluation are crucial for optimal outcomes.

Keywords: extended lung resection, non-small cell lung cancer, chest wall resection, survival analysis, locally advanced lung cancer

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Introduction

Non-small cell lung cancer (NSCLC) with invasion or suspected invasion of adjacent structures may require extended pulmonary resection to achieve complete tumor removal. Extended lung resections, defined as pulmonary resection combined with en bloc resection of invaded neighboring structures, offer the only potentially curative treatment option for selected patients with T3-T4 disease [1].

The evolution of extended resection techniques has been driven by advances in surgical methodology, improved perioperative care, and refined patient selection criteria [2]. These complex procedures typically involve resection of structures such as the chest wall, pericardium, great vessels, diaphragm, or adjacent organs, requiring specialized expertise and multidisciplinary coordination [3,4].

Current literature demonstrates variable outcomes for extended lung resections, with reported 5-year survival rates ranging from 23% to 71.7%, heavily dependent on patient selection criteria, completeness of resection, and institutional experience [5,6]. Critical prognostic factors consistently identified across studies include nodal status, achievement of R0 resection, histological subtype, and the specific anatomical structures involved in the extended procedure [7,8].

Patient selection remains the cornerstone of successful outcomes in extended lung resections. The presence of mediastinal nodal involvement (N2 disease) has been consistently identified as a relative contraindication to extended resection, while patients with N0-N1 disease demonstrate significantly improved survival outcomes [9,10]. Additionally, the ability to achieve complete microscopic resection (R0) is crucial for realizing long-term survival benefit [11,12].

Despite advances in surgical technique and perioperative management, extended lung resections continue to be associated with substantial morbidity and mortality, necessitating careful evaluation of the risk-benefit ratio for each individual patient [13,14]. The complexity of these procedures requires thorough preoperative assessment, including comprehensive staging, functional evaluation, and multidisciplinary team consultation [15].

This study presents our institutional experience with 29 consecutive patients undergoing extended lung resections for locally advanced NSCLC over an 8-year period. We provide detailed analysis of patient demographics, operative characteristics, postoperative complications, and long-term survival outcomes, with the aim of contributing to the evidence base supporting extended resections in appropriately selected patients and identifying prognostic factors that may guide future patient selection strategies.

Materials and Methods

This retrospective cohort study analyzed 29 consecutive patients who underwent extended lung resections for locally advanced NSCLC at our institution between January 2015 and December 2023. The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethics committee (Ethics Committee Approval Number: 21/18, Date: 11.12.2025). Patient informed consent was waived due to the retrospective nature of the study.

All patients had histologically confirmed NSCLC with clinical or radiographic evidence of invasion into adjacent structures, necessitating extended resection for complete tumor removal. Cases were reviewed and approved by a multidisciplinary thoracic oncology team including thoracic surgeons, medical oncologists, radiation oncologists, and pulmonologists. Although extended resections are commonly associated with T3-T4 disease, some patients in this cohort were pathologically staged as T1-T2 because invasion of adjacent structures was suspected preoperatively or identified intraoperatively. Extended resections were performed based on clinical, radiological, or intraoperative suspicion of adjacent structure invasion. However, in a subset of patients, histopathological examination did not confirm true tumor invasion of the resected adjacent structures. In such cases, pathological T staging was assigned according to the final histopathological findings, irrespective of the extent of surgical resection.

Patients were retrospectively identified from the institutional database. Eligible patients had a histologically confirmed diagnosis of primary non–small cell lung cancer (NSCLC) with clinical or radiographic evidence of T3-T4 disease requiring extended pulmonary resection. Adequate cardiopulmonary function was required, defined as a predicted $FEV_1 \geq 40\%$ and $DLCO \geq 40\%$. Only patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 and a multidisciplinary tumor

board consensus for surgery were included. Patients were excluded if they presented with distant metastatic disease (M1) confirmed by imaging, unresectable N2 disease (>3 involved mediastinal nodal stations or bulky nodes), insufficient cardiopulmonary reserve to tolerate extended resection, prior ipsilateral thoracic surgery, or a concurrent malignancy within the preceding five years.

All patients underwent a standardized preoperative evaluation. This included a comprehensive medical history, physical examination, ECOG performance status determination, and comorbidity assessment. Pulmonary function tests with spirometry and diffusion capacity for carbon monoxide (DLCO), arterial blood gas analysis, and cardiopulmonary exercise testing were performed when indicated. Patients at high cardiovascular risk underwent echocardiography or cardiac catheterization. Staging studies consisted of contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis, positron emission tomography-CT (PET-CT), and brain magnetic resonance imaging (MRI). Invasive mediastinal staging with endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) or mediastinoscopy was performed when required. Each case was discussed at a multidisciplinary thoracic oncology meeting, and all patients underwent preoperative anesthesiology consultation. Neoadjuvant therapy was considered according to disease stage and team consensus.

Surgical procedures were performed by experienced thoracic surgeons via posterolateral thoracotomy with patients in the lateral decubitus position under general anesthesia with single-lung ventilation. Extended resections were classified according to the invaded structures. Chest wall resections consisted of en bloc removal of the lung with involved ribs, intercostal muscles, and parietal pleura, with reconstruction indicated for defects exceeding 5 cm or involving three or more ribs, using prosthetic mesh, autologous grafts, or combined methods. Pericardial resections included partial or complete removal of the pericardium, with or without atrial involvement, and reconstruction with autologous pericardium, bovine pericardium, or synthetic substitutes when necessary. Diaphragmatic resections were repaired either primarily or with prosthetic material. Vascular resections involved reconstruction of pulmonary vessels, the superior vena cava, or other major vascular structures as indicated. Combined resections involving multiple structures were performed using multimodal reconstructive techniques.

In all cases, systematic mediastinal lymph node dissection was carried out in accordance with International Association for the Study of Lung Cancer (IASLC) recommendations. Completeness of resection was classified as R0 (microscopically complete), R1 (microscopically incomplete), or R2 (macroscopically incomplete).

Data were systematically retrieved from electronic medical records. Collected variables included demographics such as age, sex, body mass index, smoking history expressed in pack-years, and comorbidities including chronic obstructive pulmonary disease, coronary artery disease, hypertension, and diabetes mellitus, together with pulmonary function test results and clinical staging. Comorbidity burden was additionally quantified using the Charlson Comorbidity Index (CCI), which was retrospectively calculated based on age and documented comorbid conditions. The primary malignancy was not included in the CCI calculation to avoid artificial inflation of comorbidity scores. Tumor-related variables comprised histopathological diagnosis according to the World Health Organization classification, tumor size and anatomical location, TNM stage based on the 8th edition of the AJCC/UICC staging system, and histologic differentiation grade. Operative details included the type of pulmonary resection, the specific adjacent structures resected, operative time, estimated blood loss, and intraoperative complications. Postoperative outcomes assessed were intensive care unit stay, total hospital stay, postoperative complications categorized by the Clavien-Dindo classification, 30- and 90-day mortality, and resection margin status. Long-term data included overall survival, disease-free survival, recurrence patterns categorized as local, regional, or distant, and receipt of adjuvant therapy.

Patients were followed according to institutional protocol, with clinical examination and chest imaging every three months during the first two years, every six months between the third and fifth years, and annually thereafter. Additional imaging studies, including computed tomography or positron emission tomography-computed tomography, were performed when clinically indicated, and all recurrences were reviewed in a multidisciplinary setting.

Statistical Analysis

Statistical analyses were performed using SPSS software (version 28.0, IBM Corp., Armonk, NY, USA). Categorical variables were compared using the chi-square or Fisher's exact test, and continuous variables were analyzed with the Student's t test or Mann–Whitney U test, as appropriate. Survival outcomes, including overall survival and disease-free survival, were estimated by the Kaplan-Meier method and compared using the log-rank test. Due to the limited sample size, multivariable modeling was not performed. Survival comparisons were considered exploratory.

Descriptive statistics were applied to summarize patient characteristics and outcomes. Continuous variables were expressed as mean ± standard deviation for normally distributed data or as median with interquartile range for non-normally distributed data, while categorical variables were presented as absolute numbers and percentages. Overall survival was defined as the interval from the date of surgery to death from any cause or last follow-up, and disease-free survival was defined as the interval from surgery to the first documented recurrence, death, or last follow-up. Survival analyses were conducted using the Kaplan–Meier method, and survival curves were generated for overall survival as well as for relevant subgroups. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Results

During the study period, 29 patients underwent extended lung resections for locally advanced NSCLC. The cohort comprised 26 males (89.7%) and 3 females (10.3%) with a mean age of 64.4 ± 10.7 years (range: 41-83 years). The majority of patients (21, 72.4%) had a significant smoking history with a mean smoking exposure of 35.2 ± 18.6 pack-years among smokers.

Comorbidities were common, with chronic obstructive pulmonary disease present in 15 patients (51.7%), hypertension in 12 patients (41.4%), coronary artery disease in 8 patients (27.6%), and diabetes mellitus in 6 patients (20.7%). All patients had ECOG performance status 0-1 at the time of surgery. The mean Charlson Comorbidity Index (CCI) score was 2.83 ± 1.56, indicating a moderate comorbidity burden. Most patients were classified as having moderate comorbidity (CCI 2–3, 51.7%), while 31.0% had high comorbidity burden (CCI ≥4). Patient demographics and baseline clinical characteristics are summarized in Table 1.

Table 1. Patient demographics and clinical characteristics.

Characteristic	Value (n=29)
Age (years)	
Mean ± SD	64.4 ± 10.7
Median (range)	65.0 (41-83)
Gender, n (%)	
Male	26 (89.7)
Female	3 (10.3)
BMI (kg/m²), mean ± SD	26.8 ± 4.2
Smoking History, n (%)	
Current/Former smokers	21 (72.4)
Never smokers	8 (27.6)
Pack-years (smokers only), mean ± SD	35.2 ± 18.6
Comorbidities, n (%)	
COPD	15 (51.7)
Hypertension	12 (41.4)
Coronary artery disease	8 (27.6)
Diabetes mellitus	6 (20.7)
ECOG Performance Status, n (%)	
0	18 (62.1)
1	11 (37.9)
Preoperative PFTs	
FEV1 (% predicted), mean ± SD	78.5 ± 16.2
DLCO (% predicted), mean ± SD	72.3 ± 14.8

Squamous cell carcinoma was the predominant histological type, diagnosed in 19 patients (65.5%), followed by adenocarcinoma in 5 patients (17.2%). Other histological subtypes included large cell carcinoma (2 patients, 6.9%), adenosquamous carcinoma (1 patient, 3.4%), and neuroendocrine tumors (2 patients, 6.9%).

TNM staging according to the 8th edition AJCC classification revealed Stage IB disease in 10 patients (34.5%), Stage IIA in 6 patients (20.7%), Stage IA in 6 patients (20.7%), and Stage IIB in 7 patients (24.1%). The mean tumor size was 5.3 ± 2.3 cm (range: 2.0-10.0 cm). Although all patients underwent extended resection due to suspected adjacent structure invasion, histopathological confirmation of invasion was not present in all cases. In these patients, no tumor infiltration was identified in the resected adjacent tissues, leading to classification as lower T stage (T1-T2) and consequently early-stage disease according to the 8th edition TNM system.

Lymph node involvement was limited, with a mean of 6.5 ± 2.5 lymph nodes examined per patient and 0.3 ± 0.7 positive nodes. Lymphovascular invasion was present in 12 patients (41.4%), visceral pleural invasion in 15 patients (51.7%), and perineural invasion in 8 patients (27.6%). Detailed tumor characteristics and pathological findings are summarized in Table 2.

Table 2. Tumor characteristics and pathological findings.	
Characteristic	Value (n=29)
Histological Type, n (%)	
Squamous cell carcinoma	19 (65.5)
Adenocarcinoma	5 (17.2)
Large cell carcinoma	2 (6.9)
Adenosquamous carcinoma	1 (3.4)
Neuroendocrine tumors	2 (6.9)
TNM Stage (8th edition), n (%)	
Stage IA	6 (20.7)
Stage IB	10 (34.5)
Stage IIA	6 (20.7)
Stage IIB	7 (24.1)
T Stage, n (%)	
T1	6 (20.7)
T2	13 (44.8)
T3	8 (27.6)
T4	2 (6.9)
N Stage, n (%)	
N0	23 (79.3)
N1	5 (17.2)
N2	1 (3.4)
Tumor Size (cm)	
Mean ± SD	5.3 ± 2.3
Median (range)	5.0 (2.0-10.0)
Differentiation, n (%)	
Well differentiated	8 (27.6)
Moderately differentiated	15 (51.7)
Poorly differentiated	6 (20.7)
Lymph Node Data	
Total nodes examined, mean ± SD	6.5 ± 2.5
Positive nodes, mean ± SD	0.3 ± 0.7
Invasion Patterns, n (%)	
Lymphovascular invasion	12 (41.4)
Visceral pleural invasion	15 (51.7)
Perineural invasion	8 (27.6)

All 29 patients (100%) underwent extended resections through posterolateral thoracotomy. No video-assisted thoracoscopic surgery (VATS) procedures were performed due to the complexity and extent of resections required. The most commonly performed lung resections were left upper lobectomy (9 patients, 31.0%) and left lower lobectomy (8 patients, 27.6%).

Extended resections were categorized as follows:

- Chest wall resection only: 17 patients (58.6%)
- Pericardial resection only: 6 patients (20.7%)
- Combined chest wall and pericardial resection: 3 patients (10.3%)
- Diaphragmatic resection: 1 patient (3.4%)
- Other combined procedures: 2 patients (6.9%)

Among chest wall resections, the number of ribs resected ranged from 1-4 (mean: 2.3 ± 1.1). Chest wall reconstruction was performed in 12 of 17 patients (70.6%) using prosthetic mesh (8 patients), muscle flaps (3 patients), or combined techniques (1 patient).

All procedures were performed via posterolateral thoracotomy, and no video-assisted thoracoscopic surgery (VATS) approach was used. The most common type of lung resection was left upper lobectomy (31.0%), followed by left lower lobectomy (27.6%), right upper lobectomy (17.2%), and right lower lobectomy (10.3%). Bilobectomy and other types of resections were each performed in 6.9% of patients. Regarding the extent of resection, chest wall resection alone was the most frequent procedure (58.6%), while pericardial resection alone and combined resections were each performed in 20.7% of cases. Among patients undergoing chest wall resection, the mean number of ribs resected was 2.3 ± 1.1, and reconstruction was required in 60.0% of these cases. The mean operative time was 159 ± 62 minutes (median: 150 minutes, range: 90-280), and the mean estimated blood loss was 285 ± 195 mL (median: 250 mL, range: 100-800). Complete (R0) resection was achieved in 51.7% of patients, while 41.4% had microscopic residual disease (R1). No patients had macroscopic residual disease (R2), and resection margin status was not reported in 6.9% of cases.

There was no 30-day mortality, while 90-day mortality occurred in 1 patient (3.4%). The mean intensive care unit (ICU) stay was 0.5 ± 1.0 days, and the mean length of hospital stay was 6.1 ± 2.7 days. Overall postoperative complications were observed in 27.6% of patients. According to the Clavien–Dindo classification, minor complications (Grade I-II) occurred in 20.7% of patients, whereas major complications (Grade III-IV) were observed in 6.9%. No Grade V complications were recorded. The most common complications included atelectasis (13.8%) and prolonged air leak lasting more than 7 days (6.9%). Other complications included pneumonia (3.4%), cardiac arrhythmia (3.4%), and wound infection (3.4%). Readmission within 30 days occurred in 6.9% of patients.

Complete follow-up data was available for all 29 patients with a mean follow-up duration of 29.4 ± 24.1 months (range: 2-96 months). During the follow-up period, 21 patients (72.4%) died, while 8 patients (27.6%) remained alive at last follow-up.

Overall survival analysis revealed a median survival of 24.0 months (95% CI: 18.2-29.8). The 1-year, 2-year, and 3-year overall survival rates were 82.8%, 51.7%,

and 27.6%, respectively. Disease-free survival analysis showed a median disease-free survival of 18.0 months (95% CI: 12.4-23.6). Overall survival outcomes are illustrated using Kaplan-Meier analysis in Figure 1.

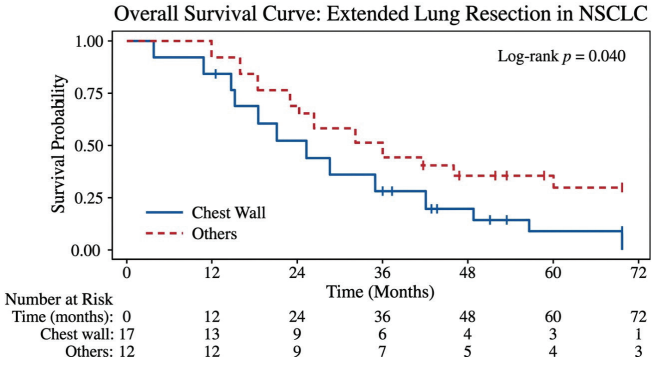

Figure 1. Kaplan-Meier Overall Survival Curve. Patients undergoing chest wall resection demonstrated significantly poorer survival compared with those undergoing other extended procedures (log-rank p = 0.040). The number of patients at risk at each time point is provided below the x-axis.

Recurrence occurred in 16 patients (55.2%) during follow-up, with patterns including local recurrence in 10 patients (34.5%), distant metastases in 6 patients (20.7%), and no evidence of recurrence in 13 patients (44.8%). The most common sites of distant recurrence were brain (3 patients), liver (2 patients), and bone (1 patient).

Subgroup analyses demonstrated variability in survival outcomes according to clinicopathological factors. Patients with adenocarcinoma exhibited longer mean survival compared with those with squamous cell carcinoma (47.6 vs. 26.5 months), although this difference did not reach statistical significance (p = 0.180), likely reflecting the limited sample size. Survival by TNM stage showed a trend toward improved outcomes in patients with stage I disease compared with stage II disease, with mean survival times of 30.3 and 26.8 months, respectively (p = 0.310). Type of extended resection was associated with significant differences in prognosis: patients undergoing chest wall resection experienced markedly poorer survival compared with those undergoing other types of extended procedures, with a mortality rate of 82.4% and mean survival of 26.7 months versus a mortality rate of 58.3% and mean survival of 33.2 months (p = 0.040). Resection margin status did not significantly influence survival, as no difference was observed between patients with R0 and R1 resections (p = 0.670), a finding that may be attributed to the aggressive biology of tumors necessitating extended resections or the limited cohort size. Subgroup survival analyses are detailed in Table 3.

Adjuvant therapy was administered to the majority of patients based on pathological findings and multidisciplinary team recommendations. Eighteen patients (62.1%) received adjuvant chemotherapy, typically consisting of platinum-based doublet regimens. Eight patients (27.6%) received adjuvant radiotherapy, and 5 patients (17.2%) received combined chemoradiotherapy.

The decision for adjuvant therapy was individualized based on factors including pathological stage, resection margin status, nodal involvement, and patient performance status. Patients with R1 resections were more likely to receive adjuvant radiotherapy (58.3% vs. 13.3% for R0 resections, p=0.020).

Table 3. Survival analysis by subgroups.

Subgroup	N	Deaths (%)	Mean Survival (months)	Median Survival (months)	p
Overall	29	21 (72.4)	29.4	24.0	-
Histology					0.180
SCC	19	15 (78.9)	26.5	24.0	
Adenocarcinoma	5	5 (100.0)	47.6	36.0	
Other	5	1 (20.0)	22.2	24.0	
TNM Stage					0.310
Stage I (IA+IB)	16	12 (75.0)	30.3	24.0	
Stage II (IIA+IIB)	13	9 (69.2)	26.8	24.0	
Extended Resection					0.040*
Chest wall	17	14 (82.4)	26.7	24.0	
Other procedures	12	7 (58.3)	33.2	33.0	
Resection Margins					0.670
R0	15	11 (73.3)	30.1	24.0	
R1	12	9 (75.0)	28.3	24.0	

**Statistically significant (p<0.05)*

Discussion

This study presents our institutional experience with extended lung resections for locally advanced NSCLC, demonstrating low perioperative mortality but limited long-term survival outcomes. Our findings add to the growing body of literature supporting the technical feasibility of extended resections in carefully selected patients, while underscoring the critical importance of rigorous patient selection and realistic discussions regarding expected outcomes.

The absence of 30-day mortality in our cohort compares favorably with previously reported operative mortality rates for extended lung resections, which range from 0% to 12.3% [16,17]. This favorable outcome likely reflects careful patient selection, advances in perioperative management, and accumulated institutional expertise in complex thoracic procedures. The overall complication rate of 27.6% is in line with contemporary series reporting major complication rates between 11.4% and 35% [18]. Respiratory complications such as atelectasis, pneumonia, and prolonged air leak predominated, as expected in procedures requiring single-lung ventilation and extensive resections. The low incidence of major complications (6.9%) suggests that extended resections can be performed safely in high-volume centers. Operative time and blood loss were within acceptable ranges for complex thoracic procedures, though these values likely underestimate the true technical demands of extended resections. The exclusive use of open thoracotomy in this series reflects the need for wide exposure and reliable reconstruction when multiple adjacent structures are involved.

Achieving complete resection with negative margins (R0) remains a cornerstone of oncologic surgery and is generally associated with improved long-term survival. In this study, the R0 resection rate was 51.7%, while 41.4% of patients had microscopic positive margins (R1). These findings highlight the inherent challenge of achieving adequate margins in tumors involving adjacent critical structures. The relatively low R0 rate observed in this cohort may reflect the complexity of tumors requiring extended procedures, borderline resectability in some patients, and the limitations of a small retrospective series. Reported R0 rates in the literature vary, suggesting that outcomes may be influenced by surgical technique, patient selection, and the use of neoadjuvant strategies.

Interestingly, survival did not differ significantly between patients with R0 and R1 resections. While this observation contrasts with most reports showing superior survival following complete resection, it may reflect small sample size, the aggressive biology of tumors necessitating extended procedures, or the mitigating effect of adjuvant therapy in cases with positive margins. The relatively low R0 resection rate observed in this study may be attributed to several factors. Many tumors were located in close proximity to critical anatomical structures such as major vascular structures, pericardium, and vertebral bodies, making complete resection technically challenging. In addition, some cases represented borderline resectable disease, in which extended resection was undertaken despite uncertain margins to achieve maximal tumor clearance. Another important consideration is the absence of neoadjuvant therapy in this cohort. Contemporary evidence supports the use of neoadjuvant chemotherapy and, more recently, chemoimmunotherapy in patients with locally advanced (T3-T4) NSCLC. These approaches have been shown to improve tumor downstaging, increase the likelihood of complete (R0) resection, and enhance long-term survival outcomes. Landmark trials have demonstrated significantly higher pathological response rates and improved resectability with neoadjuvant immunotherapy-based regimens. The lack of neoadjuvant treatment in our series may therefore have contributed to both the relatively low R0 resection rate and suboptimal long-term survival outcomes. This reflects historical treatment patterns and institutional practice variability during the study period. Future strategies incorporating neoadjuvant approaches may improve surgical and oncological outcomes in similar patient populations.

The median survival of 24 months and 3-year survival rate of 27.6% observed in this cohort are concerning but consistent with the poor prognosis of locally advanced NSCLC requiring extended resections. Published outcomes vary widely, with 5-year survival ranging from 23% to 71.7% placing our results at the lower end of this spectrum [19,20]. Several factors likely contributed to these outcomes. A high proportion of patients underwent chest wall resection, a subgroup that demonstrated significantly worse survival, with a mortality rate of 82.4% compared to 58.3% in patients undergoing other extended procedures ($p = 0.040$). This may reflect both the aggressive tumor biology associated with chest wall invasion and the technical challenges of achieving complete resection in this setting. The predominance of squamous cell carcinoma (65.5%) may also have contributed, as squamous histology is often associated with poorer prognosis compared to adenocarcinoma [21]. Furthermore, although most patients were staged as early disease (I-II), the requirement for extended resection indicates locally advanced behavior, diminishing the prognostic value of clinical stage. The apparent discrepancy between extended resections and early pathological stage observed in this study is explained by the lack of histopathological confirmation of invasion in some patients. Although these cases were managed surgically as locally advanced disease based on clinical, radiological, or intraoperative suspicion, fi-

nal pathology demonstrated no tumor infiltration of adjacent structures. This phenomenon represents a known limitation in preoperative and intraoperative assessment, where inflammatory adhesions or desmoplastic reactions may mimic true tumor invasion. Therefore, pathological staging in this study reflects definitive histological findings rather than the surgical indication for extended resection. Although extended resections are traditionally associated with locally advanced (T-T4) tumors, several patients in this cohort were pathologically staged as T1-T2. This discrepancy may reflect differences between clinical suspicion of adjacent structure invasion and final pathological staging, as well as intraoperative findings that necessitated extended resection to achieve adequate margins.

Among the types of extended resections, patients undergoing chest wall resections had the poorest outcomes, while those undergoing pericardial or vascular resections fared comparatively better, consistent with prior reports suggesting that cardiac resections, particularly limited atrial resections without cardiopulmonary bypass, can be performed with acceptable morbidity and survival [22,23]. The high recurrence rate of 55.2%, dominated by local recurrence (34.5%), further illustrates the challenge of achieving durable local control in this population. This finding may reflect the influence of tumor biology, patient selection, and treatment-related factors on survival outcomes [24]. Distant recurrences most frequently involved the brain, in keeping with the natural history of NSCLC and reinforcing the role of systemic therapy in disease management. The cohort included heterogeneous extended resections involving different anatomical structures such as the chest wall, pericardium, diaphragm, and combined resections. These procedures represent biologically and surgically distinct entities with potentially different prognostic profiles. However, due to the limited sample size, stratified analyses for each procedure type were not feasible, and the cohort was analyzed as a single group to present a descriptive institutional experience.

Adjuvant therapy was administered in the majority of cases, with 62.1% receiving chemotherapy. Patients with R1 resections were more likely to receive adjuvant radiotherapy, reflecting guideline-concordant efforts to improve local control in cases with positive margins. However, the lack of survival difference between R0 and R1 groups suggests either effective mitigation of margin positivity by adjuvant therapy or that systemic factors ultimately dominate survival irrespective of local control [25].

When compared with published literature, our findings are broadly consistent with previous reports demonstrating acceptable perioperative outcomes but limited long-term survival in patients undergoing extended resections for locally advanced NSCLC. Variability in survival outcomes across studies may be attributed to differences in patient selection, tumor biology, and extent of resection. These findings carry important clinical implications. Refinement of patient selection criteria is essential, particularly for patients requiring chest wall resections, in whom outcomes were significantly worse. Consideration of neoadjuvant or intensified adjuvant strategies, or enrollment in clinical trials, may be appropriate in this subgroup. The complexity of extended resections reinforces the importance of multidisciplinary evaluation and coordinated treatment planning involving thoracic surgeons, oncologists, radiation oncologists, and supportive care teams. The relatively poor long-term outcomes highlight the need for transparent discussions with patients regarding prognosis and quality-of-life expectations. Future research should focus on the development of molecular or imaging biomarkers to refine patient selection, optimization of neoadjuvant approaches, assessment of minimally invasive strategies where feasible, incorporation of quality-of-life outcomes, and cost-effectiveness analyses of extended resections in locally advanced NSCLC.

Limitations of the Study

This study has several limitations that should be acknowledged. The relatively small cohort of 29 patients limits the statistical power of subgroup analyses and multivariable modeling, raising the possibility of type II error in detecting clinically meaningful differences. Although comorbidity burden was assessed using the Charlson Comorbidity Index (CCI), its impact on survival could not be robustly evaluated due to the limited sample size. Its retrospective design introduces inherent biases, including selection bias, information bias, and potential confounding that may not be fully controlled. Being a single-institution experience, the results may not be generalizable to centers with different patient populations, surgical expertise, or perioperative protocols. Variability in follow-up duration and the potential for loss to follow-up could also influence the accuracy of survival analyses. Missing data, particularly with respect to detailed adjuvant therapy regimens and quality-of-life assessments, represent another constraint. Furthermore, the heterogeneity of extended resection types analyzed together may obscure procedure-specific outcomes and prognostic factors. Finally, the eight-year study period encompasses temporal changes in staging systems, adjuvant therapy recommendations, and surgical techniques, all of which may have influenced observed outcomes. In addition, the mean number of lymph nodes examined in this cohort was relatively low compared with values reported in studies adhering to strict mediastinal lymphadenectomy protocols. This may reflect variability in surgical sampling, pathological examination, or limitations inherent to retrospective data collection. As a result, the possibility of pathological understaging cannot be excluded and represents a limitation of this study.

Future research should focus on refining patient selection and treatment strategies. The development and validation of predictive models integrating clinical, pathological, and molecular variables may help identify patients most likely to benefit from extended resections. Prospective studies are needed to evaluate the role of neoadjuvant approaches, including chemotherapy, immunotherapy, or chemoradiotherapy, in improving resectability and long-term outcomes. The feasibility and safety of minimally invasive strategies, such as robotic or video-assisted approaches for selected cases, warrant investigation to potentially reduce morbidity without compromising oncological efficacy. Comprehensive assessment of quality of life, functional outcomes, and patient-reported measures in long-term survivors is also critical. Multi-institutional collaborations will be essential to increase sample size and enhance the generalizability of findings. Finally, the incorporation of molecular profiling into clinical decision-making may provide more individualized treatment pathways and help determine which patients are most likely to benefit from extended resections versus alternative modalities.

In conclusion, extended lung resections for locally advanced NSCLC can be performed with acceptable operative mortality and morbidity in carefully selected patients at experienced centers, yet long-term survival outcomes remain limited, particularly in those requiring chest wall resection. Our findings highlight that extended resections can be achieved with zero 30-day mortality and complication rates within the expected range, underscoring the importance of meticulous patient selection and standardized perioperative protocols. Nevertheless, overall survival remains poor, with a median survival of 24 months and a 3-year survival rate of only 27.6%. The type of extended resection emerged as a key prognostic factor, with chest wall resection associated with significantly worse survival compared with other procedures. Although R0 resection remains the oncologic ideal, the absence of survival difference between R0 and R1 resections in this cohort may reflect the aggressive biology of tumors necessitating extended procedures or the mitigating effects of adjuvant therapy.

These observations emphasize the critical role of rigorous selection criteria, incorporating functional reserve, nodal status, and multidisciplinary evaluation, in optimizing outcomes. The decision to proceed with extended resection should carefully balance potential survival benefit against the inherent risks and should be reserved for centers with substantial expertise and comprehensive multidisciplinary support. Realistic expectations regarding prognosis must be communicated to patients and families, and for high-risk subgroups, alternative strategies or enrollment in clinical trials may be appropriate.

Looking forward, research should prioritize refinement of patient selection, optimization of multimodal treatment strategies, and exploration of less invasive techniques while preserving oncologic integrity. The integration of molecular profiling and predictive modeling holds promise for identifying patients most likely to benefit from these complex operations. Extended lung resection remains an important therapeutic option for selected patients with locally advanced NSCLC, but continued innovation and collaborative research are essential to improve long-term outcomes.

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Ethics approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Antalya Training and Research Hospital Scientific Research Ethics Committee (Approval Number. 21/18, Date: 11 December 2025). Due to the retrospective nature of the study, the requirement for informed consent was waived by the Ethics Committee.

Authors' contribution

All authors made a significant contribution to the work reported, including the conception and design of the study, execution, acquisition of data, analysis, and interpretation. All authors participated in drafting the article or revising it critically for important intellectual content, gave final approval of the version to be published, agreed on the journal to which the manuscript was submitted, and accept accountability for all aspects of the work.

AI Use Disclosure

In the preparation of this manuscript, an artificial intelligence tool (Chatgpt 5.2) was used solely to assist with literature review support and improvement of English language, including grammar and stylistic refinement. All content generated or suggested by the AI tool was carefully reviewed, verified, and edited by the authors. The AI tool was not used for data generation, data analysis, or interpretation of results. The authors take full responsibility for the originality, accuracy, validity, and integrity of the content of this manuscript.

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Original Article

Video-assisted thoracoscopic lung-sparing tracheobronchial and carinal resections: a single-center experience

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ABSTRACT

Background: In selected patients, lung-sparing airway resections may achieve complete oncological resection while preserving pulmonary parenchyma. With increasing experience in video-assisted thoracoscopic surgery (VATS), these complex procedures can now be performed using minimally invasive techniques. We aimed to present our single-center experience with VATS lung-sparing tracheobronchial and carinal resections, focusing on perioperative outcomes.

Materials and Methods: Data from 7 patients who underwent VATS lung-sparing airway resections in our clinic between February 2022 and December 2024 were retrospectively evaluated in terms of surgical indications, as well as preoperative, intraoperative, and postoperative conditions.

Results: The surgical procedures included isolated carinal resection and reconstruction in two patients, main bronchial bronchotomy with bronchoplastic resection and reconstruction in two patients, segmental sleeve resection of the right main bronchus in one patient, and segmental sleeve resection of the bronchus intermedius in two patients, including one posterior biportal and one anterior uniportal approach. The mean age was 46.4 ± 17.1 years (range: 26-67). Pathological diagnoses included four typical carcinoid tumors, one glomus tumor, one sarcoma, and one squamous cell carcinoma. All resections achieved negative surgical margins. Postoperatively, the mean time to chest drain removal was 1.86 ± 0.38 days, and the mean length of hospital stay was 4.43 ± 1.40 days. No intraoperative mortality occurred, and no major postoperative complications or anastomotic failures were observed.

Conclusions: VATS lung-sparing tracheobronchial and carinal resections are feasible and safe in carefully selected patients. These procedures allow complete oncological resection while preserving lung parenchyma, with favorable perioperative outcomes and short hospital stays. Minimally invasive lung-sparing airway surgery may offers a valuable alternative to more extensive resections in selected tracheobronchial tumors.

Keywords: VATS, tracheobronchial resection, carinal resection, lung-sparing surgery, minimally invasive surgery, bronchoplasty

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Introduction

Sleeve lobectomy resections help avoid pneumonectomy, which is associated with high rates of morbidity and mortality [1-3]. However, in cases of tumors located solely in the carina or low-grade neoplasms such as carcinoid tumors arising in the tracheobronchial tree, curative surgical resection may be achieved without any parenchymal removal. Various terms have been used to describe this surgical strategy in which no lung parenchyma is resected. These include bronchoplastic and sleeve resections of the tracheobronchial tree without parenchymal removal, as well as isolated carina resections. Airway control and effective ventilation are particularly critical in carinal surgery. For this purpose, different techniques such as cross-field ventilation and high-frequency jet ventilation [HFJV] may be employed [4].

Historically, the standard approach to access the carina, right main bronchus, and bronchus intermedius has been via a right posterolateral thoracotomy through the fourth or fifth intercostal space [5]. Recently, with growing experience in VATS, these complex procedures have become feasible in experienced centers [2]. VATS has demonstrated clear advantages over open surgery, including reduced postoperative pain, shorter hospital stays, decreased morbidity, and improved cosmetic outcomes [6].

This study presents technical details of seven cases: two isolated carinal resections with reconstruction due to malignancies localized to the carina; one isolated right main bronchus resection and sleeve anastomosis for a glomus tumor in the right main bronchus; two bronchoplastic resections and reconstructions of the main bronchus for typical carcinoid tumors, one in the right main bronchus and the other in the left main bronchus; and two segmental sleeve resections of the bronchus intermedius for typical carcinoid tumors confined to that region.

Materials and Methods

A retrospective analysis was performed on seven patients who underwent VATS lung-sparing airway resections and reconstruction at our clinic between February 2022 and December 2024, evaluating surgical indications and preoperative, intraoperative, and postoperative outcomes. The study was approved by the Ethics Committee of Dr. Ismail Fehmi Cumalıoglu City Hospital (2024/107).

Preoperative evaluation

A comprehensive preoperative evaluation was performed to assess surgical eligibility and to plan the operative strategy. Contrast-enhanced thoracic computed tomography (CT) was used to define tumor location, size, anatomical relationships, and possible invasion of adjacent structures. Positron emission tomography-computed tomography (PET-CT) was performed to evaluate metabolic activity and to identify regional lymph node involvement and distant metastases. Rigid or fiberoptic bronchoscopy (FOB) was utilized for direct visualization of the lesion, histopathological confirmation via biopsy, and airway patency restoration when required. Pulmonary function was assessed using forced expiratory volume in one second (FEV_1), with diffusing capacity for carbon monoxide (DLCO) measured in selected patients. Only patients deemed suitable from both respiratory and cardiological perspectives were considered candidates for surgical intervention.

Perioperative evaluation andsurgical technique

All patients were positioned in lateral decubitus. Selective intubation was utilized in cases requiring main bronchus or bronchus intermedius resection, while in patients undergoing isolated carinal resection, single-lumen intubation in combination with either an endobronchial blocker or high-frequency jet ventilation (HFJV) was employed. In one segmental sleeve resection of the bronchus intermedius, a uniportal technique was used, whereas a biportal approach was adopted in all other cases. A 30º thoracoscope was used for visualization, and a soft tissue retractor such as Alexis® (Applied Medical Resources Corporation, Rancho Santa Margarita, CA, USA) was placed in the utility incision to facilitate retraction. Following intubation, all patients underwent fiberoptic bronchoscopy (FOB) to reassess the tumor localization and the planned surgical intervention. In long-segment resections of the tracheobronchial tree, release maneuvers are recommended to reduce anastomotic tension [7]. In a total of 5 cases involving isolated carinal sleeve resections, segmental sleeve resections of the intermediate bronchus, and main bronchus sleeve resections, the inferior pulmonary ligament was released as a releasing maneuver. In the first case of isolated carinal resection and reconstruction, additional distal tracheal mobilization was performed. To further reduce tension at the anastomotic site and prevent in-

voluntary neck extension, the chin was sutured to the manubrium of the sternum in both cases of isolated carinal resection/reconstruction. This technique reduced anastomotic tension and mitigated the risk of sudden neck hyperextension. These sutures were removed after approximately one week. To achieve optimal exposure and facilitate anastomosis in procedures involving the carina and right main bronchus, the azygos vein was divided, and both ends were anchored to the chest wall and mediastinal pleura.

In bronchoplastic resections, the tumor-containing airway segment was removed via bronchotomy, and the bronchial defect was repaired with primary sutures. In sleeve resections, anastomosis was started at the membranocartilaginous junction of the proximal airway using an inside-to-outside suturing technique along the cartilaginous wall. To avoid suture entanglement during thoracoscopic anastomosis, the first proximal stitch was passed through the parietal pleura, brought out through the utility incision, and temporarily secured under tension. After completion of two-thirds of the cartilaginous portion, the suture was retrieved, and the membranous portion was completed in the opposite direction. The anastomosis was finalized using an endoscopic knot pusher. For isolated carinal resections, the trachea was first partially anastomosed end-to-end with the left main bronchus. The right main bronchus was subsequently anastomosed end-to-side to the remaining tracheobronchial opening.

Intraoperative frozen section analysis was performed in all patients to confirm negative bronchial margins. As no positive margins were identified on frozen section examination in any case, additional bronchial resection prior to anastomosis or bronchoplasty was not required. Additionally, to adhere to oncological principles and ease the anastomotic procedure, the right lower paratracheal and subcarinal lymph nodes were excised at this stage. To enhance anastomotic healing and prevent minor leaks, viable tissue flaps such as omentum, parietal pleura, or pericardial fat may be used. The application of fibrin sealants (e.g., Tisseel) over the anastomotic site is another option to prevent minor air leaks and reduce the risk of dehiscence. In our series, a parietal pleural flap was used in one case, and fibrin sealant (Tisseel) was applied in four cases.

Postoperative evaluation

Patients were extubated and monitored in the intensive care unit ICU for one day before transfer to the thoracic surgery ward. Chest drains were removed when daily drainage was <100 mL, no air leak was present, and complete lung expansion was confirmed on posteroanterior chest radiographs. Carinal resection patients were monitored until chin sutures were removed. Outpatient follow-up was scheduled 10 days post-discharge. No FOB was required postoperatively in any case.

Results

Between February 2022 and December 2024, a total of 858 VATS anatomical lung resections were performed at our institution. Among these procedures, 40 cases (4.6%) consisted of bronchoplastic or sleeve resections. Video-assisted thoracoscopic lung-sparing tracheobronchial and carinal resections were performed in 7 patients, representing 0.8% of all VATS anatomical lung resections and 17.5% of the bronchoplastic/sleeve resections.

The cohort consisted of seven patients with a mean age of 46.4 ± 17.1 years (range: 26-67). Pathological diagnoses included four typical carcinoid tumors, one glomus tumor, one sarcoma, and one squamous cell carcinoma. All resections achieved negative surgical margins.

Postoperatively, the mean time to chest drain removal was 2.00 ± 0.58 days, and the mean length of hospital stay was 4.43 ± 1.81 days. No intraoperative mortality occurred. No major or minor complications or anastomosis failures occurred in the postoperative period. The mean follow-up duration was 22 months, during which no local or distant recurrence was observed, and all patients were alive at the last follow-up.

Case 1. Right VATS bronchotomy and bronchoplastic resection and reconstruction of the right main bronchus

A patient evaluated due to a typical carcinoid tumor localized in the proximal right main bronchus underwent FOB, which revealed a 1×1 cm lesion on the posterior wall of the distal right main bronchus extending toward the carina. The lesion was located in the right main bronchus on thorax CT (Figure 1). Selective intubation was performed, and with the patient in the left lateral decubitus position, thoracic access was achieved through a 3 cm utility incision at the 4th intercostal space in the anterior-mid axillary line. The camera port was inserted through the 7th intercostal space along the posterior axillary line. The surgical assistant retracted the lung inferiorly using a lung retractor inserted through the camera port to expose the paratracheal area. For ex-

posure, the azygos vein was divided, and its posterior stump was sutured to the chest wall. The hilar (10R) lymph node was excised. The right main bronchus was circumferentially dissected and suspended with a vessel loop. Macroscopically, a bulging lesion over the membranous portion at the carinal level was observed. The distal trachea was mobilized close to the carinal plane, with careful preservation of the vagus nerve. Using a scalpel and endoscopic scissors, a bronchotomy was performed from the distal right main bronchus toward the carina, ensuring negative surgical margins, and the lesion was excised over a 1 cm^2 area. The resulting defect was closed with a continuous suture using 3-0 polypropylene with a round needle. The anastomotic line was reinforced with a parietal pleural flap, and fibrin sealant (Tisseel) was applied to support the repair site (Figure 2). The operation lasted 125 minutes with an estimated blood loss of 100 mL. The chest drain was removed on postoperative day 2, and the patient was discharged on postoperative day 3.

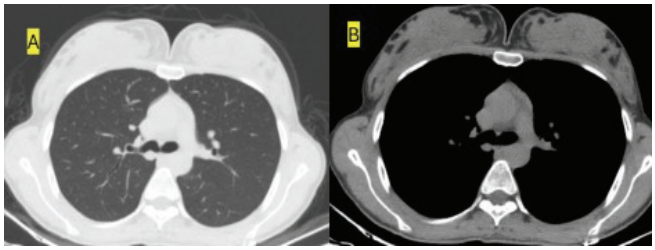

Figure 1. CT image of the lesion localized in the right main bronchus. **A:** Thoracic computed tomography parenchymal section image of the lesion in the right main bronchus localization, **B:** Mediastinal section image.

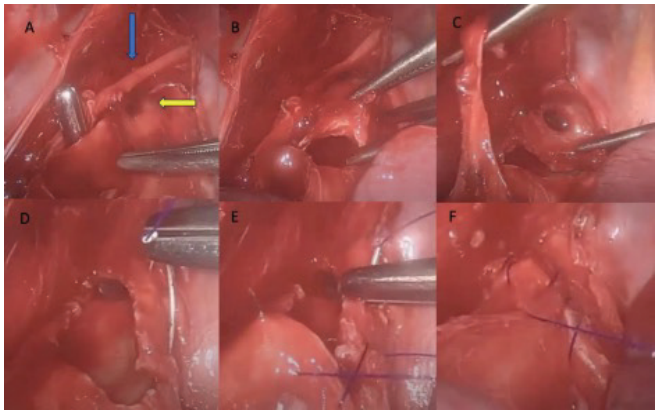

Figure 2. Right VATS Bronchotomy and Bronchoplastic Resection and Reconstruction of the Right Main Bronchus. **A:** Right main bronchus. Blue arrow: Vagus nerve, yellow arrow: Lesion**, B:** Bronchotomy proximal to the lesion, **C:** Bronchotomy distal to the lesion. **D, E, F:** Continuous suture of the right tracheobronchial defect.

Case 2. Left VATS left main bronchus bronchotomy and bronchoplastic resection and reconstruction

Due to a 1 cm typical carcinoid tumor located in the distal left main bronchus, surgery was performed in the right lateral decubitus position under selective intubation. Thoracic access was achieved through a 3 cm utility incision at the 4th intercostal space in the midaxillary line. The camera port was inserted at the 7th intercostal space along the posterior axillary line. The lung was retracted anteriorly to expose and dissect the left main bronchus, which was circumferentially mobilized and suspended using a vessel loop. To localize the lesion intraoperatively, an angiocatheter was inserted intraluminally through the distal left main bronchus. The catheter was visualized via FOB, confirming the lesion's position. A bronchotomy was performed on the membranous portion of the left main bronchus using a scalpel, and the lesion was resected with negative surgical margins. The defect was closed with a continuous suture using 3-0 polypropylene with a double round needle. Lymph nodes from the aortopulmonary window and subcarinal region were excised. No air leak was observed during the leak test. A single 28 Fr chest drain was placed through the camera port, and the procedure was concluded. The operation lasted 90 minutes with an estimated blood loss of 150 mL. The chest drain was removed on postoperative day 3, and the patient was discharged on day 4 (Figure 3).

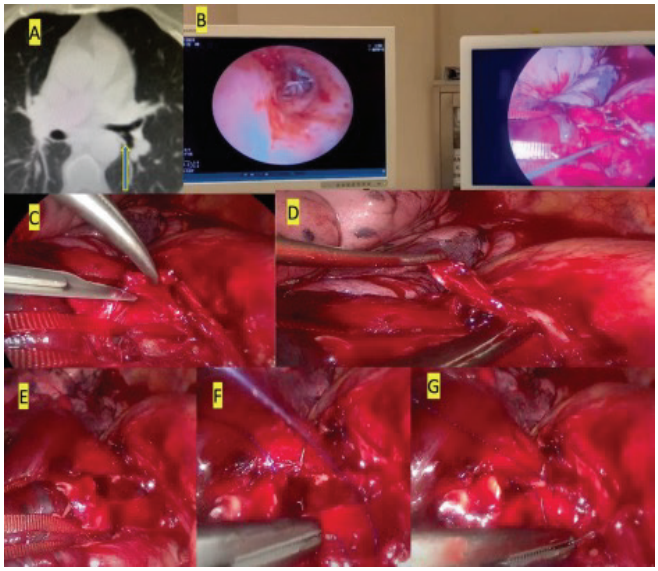

Figure 3. Left Vats Left Main Bronchus Bronchotomy and Bronchoplastic Resection and Reconstruction **A:** CT image of the lesion in the distal main bronchus, **B:** Screenshot of angiocut application to the bronchus during the operation (FOB and VATS visual), **C, D:** Excision of the lesion with scissors, **E:** Defect area in the main bronchus, **F, G:** Continuous suturing of the defect area

Case 3. Right VATS segmental sleeve resection of the right main bronchus

Due to a glomus tumor localized on the lateral wall of the distal right main bronchus, surgery was performed under selective intubation with the patient in the left lateral decubitus position. Thoracic access was achieved via a 3 cm utility incision at the 4th intercostal space. A camera port was inserted at the 7th intercostal space along the posterior axillary line. The azygos vein was divided using an endoscopic stapler, and its ends were anchored to the chest wall and mediastinal pleura to provide adequate exposure. With careful preservation of the vagus nerve, the trachea and right main bronchus were dissected circumferentially and suspended using a vessel loop. A bronchotomy was performed with a scalpel on the right main bronchus, allowing direct visualization of the tumor. The affected segment of the right main bronchus, including the lesion, was partially resected, ensuring negative microscopic margins at both proximal and distal ends. An end-to-end anastomosis was then performed using a continuous suture technique with 3-0 polypropylene and a double round needle. After confirming the absence of an air leak, the divided ends of the azygos vein were reapproximated and sutured over the anastomotic line to provide additional support. A single 28 Fr chest drain was placed in the thoracic cavity. The operation lasted 130 minutes with an estimated blood loss of 250 mL. The chest drain was removed on postoperative day 2, and the patient was discharged on day 3 (Figure 4).

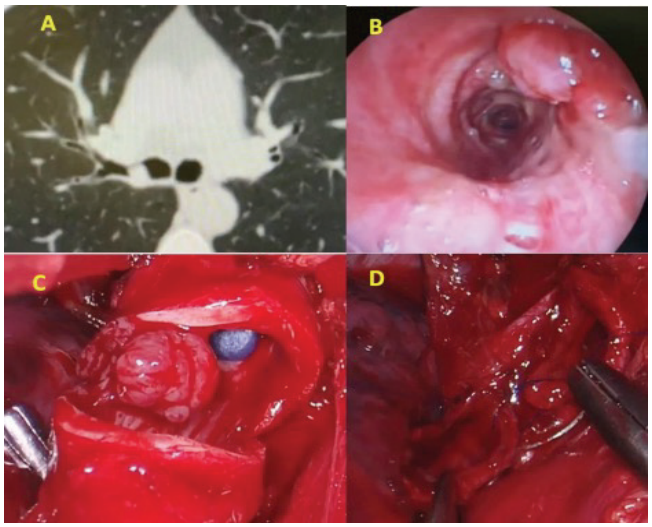

Figure 4. Right VATS Segmental Sleeve Resection of the Right Main Bronchus. **A:** Thoracic CT of endobronchial tumor localized in the right main bronchus, **B:** Fiberoptic bronchoscopy images of endobronchial tumor localized in the right main bronchus, **C:** Glomus tumor in the right main bronchus, **D:** Sleeve anastomosis of the right main bronchus.

Case 4. Right VATS isolated carina resection and reconstruction

Rigid bronchoscopy was performed by the interventional pulmonology team due to a follicular dendritic cell sarcoma localized at the carina. The lesion was causing near-total obstruction of the right main bronchus and approximately 70% obliteration of the left main bronchus (Figure 5). Airway patency was partially restored via argon plasma coagulation (APC), and definitive surgical resection was planned and performed 10 days later. Under general anesthesia, the patient was placed in the left lateral decubitus position. Endotracheal intubation was performed with an 8.0-mm tube, and an endobronchial blocker was positioned in the right main bronchus. A 3 cm utility incision was made through the 4th intercostal space, and the camera port was placed at the 7th intercostal space along the posterior axillary line. The azygos vein was divided using an endovascular stapler to facilitate exposure. The trachea was circumferentially mobilized and suspended with a vessel loop. The main pulmonary artery and the superior pulmonary vein were dissected, looped, and retracted inferiorly to expose the right main bronchus and carina. The right main bronchus was then dissected and suspended with a vessel loop. Macroscopically, the tumor was protruding approximately 2 cm outward from the membranous portion at the posterior aspect of the carinal level. The right main bronchus was first transected at its most proximal margin using a scalpel. The left main bronchus was then visualized and dissected distally, circumferentially mobilized, and suspended with a vessel loop. For traction, a 2-0 polyglactin was placed on the cartilaginous wall of the left main bronchus. The distal trachea was transected at the level corresponding to the proximal carina using a scalpel. Before this step, the patient's oxygen saturation was optimized, and the endobronchial blocker was withdrawn. Finally, using the traction suture placed on the left main bronchus, the left main bronchus was transected with a scalpel, and the specimen was removed en bloc. At this stage, the patient's ventilation was maintained via a high-frequency jet ventilation (HFJV) cannula inserted from the trachea into the left main bronchus. The inferior pulmonary ligament was released, and the head was placed in flexion. End-to-end anastomosis between the left main bronchus and the trachea was initiated using 3- 0 polypropylene with a double round needle in a continuous suture technique. The suture was advanced over approximately 1 cm, af-

ter which both ends were temporarily secured by tying them to newly placed anchoring sutures, intentionally leaving a gap at the medial aspect of the anastomosis. Subsequently, a parabolic (crescent-shaped) cartilage segment was excised from the tracheal edge at the remaining gap to create an adequate opening for the end-to-side anastomosis of the right main bronchus. The right main bronchus was then anastomosed to this site using continuous sutures with 3-0 polypropylene and a double round needle. No air leak was observed. For reinforcement, fibrin sealant (Tisseel) was applied to the anastomotic site. A single 28 Fr chest drain was placed in the thoracic cavity. To reduce tension on the anastomosis postoperatively, the patient's chin was sutured to the sternum using a No. 1 silk suture. The total operative time was 4 hours, with an estimated blood loss of 350 mL. The chest drain was removed on postoperative day 2. On day 7, the chin suture was removed, and the patient was discharged.

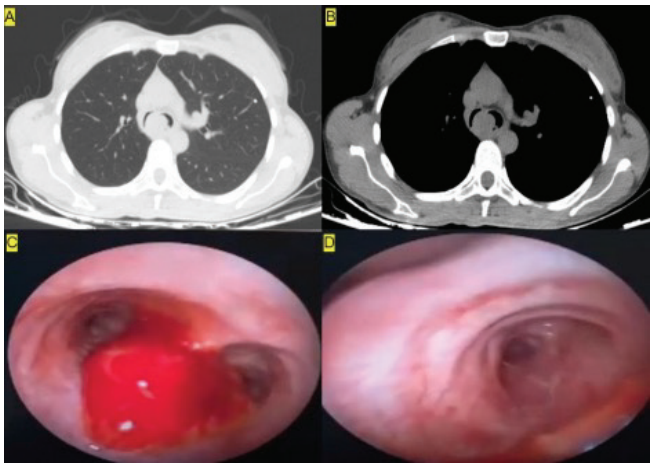

Figure 5. CT bronchoscopy and images of the lesion localized in the carina. **A:** Parenchymal section CT image of the lesion in the carina localization, **B:** Mediastinal section, **C:** FOB image of the lesion, **D:** Open image of the left main bronchus after the carina.

Case 5. Right VATS isolated carina resection and reconstruction

A patient diagnosed with squamous cell carcinoma localized at the carina underwent surgery in the left lateral decubitus position. The lesion was seen at the carina level in the thorax CT and FOB examination (Figure 6). The patient was intubated with an 8.5 mm endotracheal tube. Using FOB through the tube, an endobronchial blocker was placed into the right main bronchus. A working incision was made at the 4th intercostal space along the mid-axillary line. The camera port was inserted through the 8th intercostal space at the posterior axillary line. Through the camera port, the surgical assistant used a lung retractor to displace the lung inferiorly, exposing the paratracheal region. The azygos vein was dissected, suspended, and divided using an endovascular stapler. The distal trachea was circumferentially mobilized and suspended with a vessel loop. Subsequently, the right main bronchus was also dissected and suspended. With the aid of FOB, the proximal resection margin on the right main bronchus was identified. At this point, the endobronchial blocker was withdrawn, and bilateral ventilation was achieved using low tidal volumes. The right main bronchus was transected with negative surgical margins. The left main bronchus was dissected distally, and a 2-0 polyglactin traction suture was placed to facilitate exposure and manipulation. The left main bronchus was transected near the carina with negative surgical margins. Ventilation was maintained via cross-field ventilation, using a sterile 5.5 mm spiral endotracheal tube introduced directly into the left main bronchus through the operative field. The carina was then resected from the distal trachea using a scalpel, ensuring negative surgical margins. The excised specimen was sent for frozen section analysis, which confirmed margin negativity. To reduce tension at the anastomotic site, the inferior pulmonary ligament was released, and the patient's head was placed in neck flexion. Reconstruction began with an end-to-end anastomosis of the left main bronchus to the trachea. The first stitch was placed using 3-0 polypropylene with a double round needle, starting from the junction between the cartilaginous and membranous portions of the trachea (inside-out), and continuing at the corresponding site on the left main bronchus (outside-in), near the junction of the cartilage and membranous wall. The end-to-end anastomosis was completed, leaving a 1 cm gap on the medial aspect. The free suture ends were tied to newly placed sutures and then cut. To create a suitable opening for the right main bronchus, a crescent-shaped piece of cartilage was excised from the tracheal side. The right main bronchus was then anastomosed end-to-side to this newly formed opening. Near completion of the anastomosis, a caliber mismatch was noted, prompting the excision of an additional small cartilage segment from the tracheal edge to ensure proper alignment. After confirming the absence of air leaks, fibrin sealant (Tisseel) was applied to the anastomotic site for reinforcement, and the ends of the divided azygos vein were reapproximated and sutured together. To prevent inadvertent neck hyperextension,

the chin was sutured to the manubrium of the sternum using No. 1 silk suture. A single 28 Fr chest drain was placed. The total operative time was 180 minutes, and the estimated blood loss was 350 mL. The chest drain was removed on postoperative day 2, and the chin sutures were taken down on day 7, at which point the patient was discharged (Figure 7).

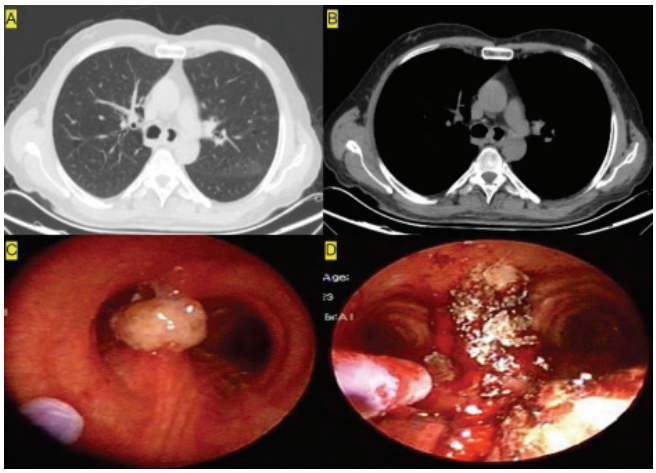

Figure 6. CT bronchoscopy and images of a tumor localized in the carina. **A:** Parenchymal section CT image of the tumor in the carina localization, **B:** Mediastinal section, **C:** FOB image of the tumor **D:** FOB image after endobronchial treatment.

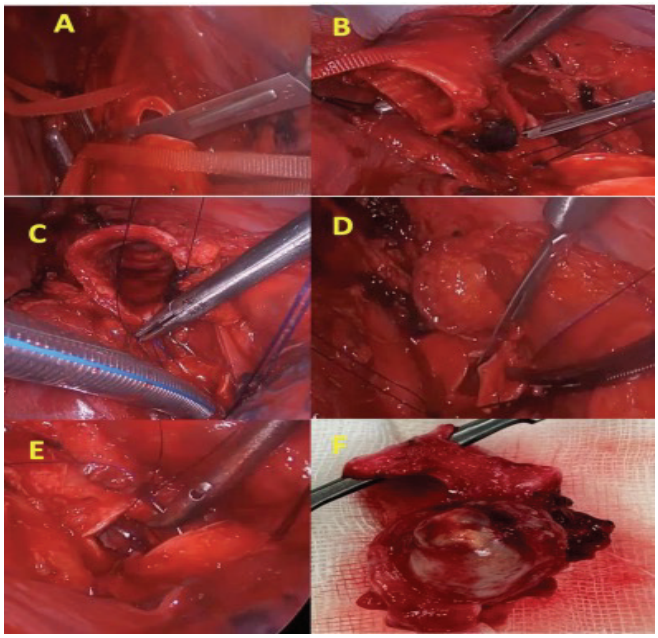

Figure 7. The surgical technique of VATS isolated carina resections and reconstructions **A:** Division of the right main bronchus, **B:** Division of the left main bronchus, **C:** Continuous end to end anastomosis of trachea to left main bronchus, **D:** After the trachea is anastomosed to the left main bronchus, leaving 3/4 of the area open, partial cartilage resection is performed to provide sufficient clearance for the anastomosis of the right main bronchus over the trachea, **E:** End-to-side continuous anastomosis of the right main bronchus to the trachea and left main bronchus anastomosis line, **F:** Carinal tumor. The right main bronchus is marked.

Case 6. Right VATS segmental sleeve resection of the bronchus intermedius: posterior approach

A patient diagnosed with a carcinoid tumor localized in the right bronchus intermedius underwent surgery in the left lateral decubitus position under selective intubation. The lesion was seen in the intermediate bronchus in the thorax CT and FOB examination (Figure 8). A 3 cm utility incision was made through the 4th intercostal space along the posterior axillary line. The camera port was placed at the 7th intercostal space, also along the posterior axillary line. The mediastinal pleura was incised posteriorly, and dissection was performed down to the distal right main bronchus and the right lower lobe bronchus to fully expose the bronchial anatomy. Care was taken to avoid injury to the pulmonary artery during dissection. The right upper lobe bronchus and the middle lobe bronchus were mobilized proximally, and the bronchus intermedius was circumferentially dissected and suspended using a vessel loop. Intraoperative FOB evaluation revealed that the lesion extended from the posterior wall of the bronchus intermedius at the level of the upper lobe bronchus distally. Therefore, to preserve the upper lobe and ensure negative margins, a curved (tangential) incision rather than a linear one was made proximally on the bronchus intermedius. The upper limit of the incision extended up to the posterior wall of the upper lobe bronchus. A similar curved incision was then made at the proximal portion of the middle lobe bronchus, and the bronchus intermedius was resected en bloc. Frozen section analysis confirmed tumor-free surgical margins. To reduce tension on the anastomosis, the inferior pulmonary ligament was released. The bronchial reconstruction was performed with a continuous end-to-end anastomosis using 3-0 polypropylene with a double round needle (Figure 9). The procedure lasted 130 minutes, and the estimated blood loss was 200 mL. The chest drain was removed on postoperative day 1, and the patient was discharged on day 3.

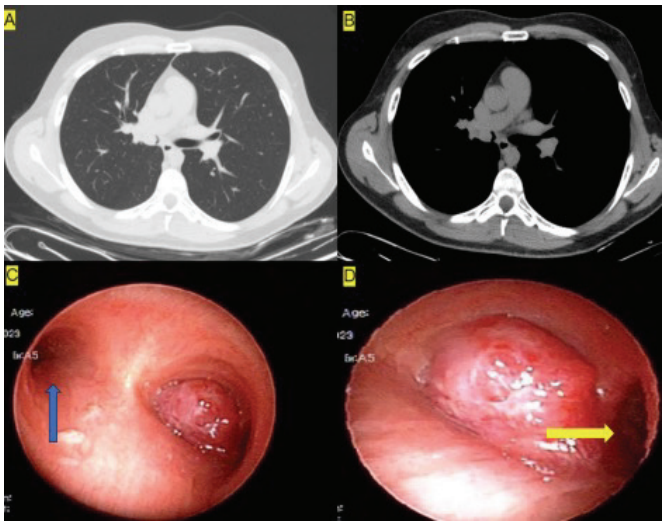

Figure 8. CT bronchoscopy and images of a tumor localized in the intermediate bronchus **A:** CT parenchymal section image of the lesion in the intermediate bronchus localization. **B:** Mediastinum section, **C:** FOB image, blue arrow, upper lobe entrance, lesion at the intermediate bronchus entrance, **D:** FOB image, yellow arrow, middle lobe.

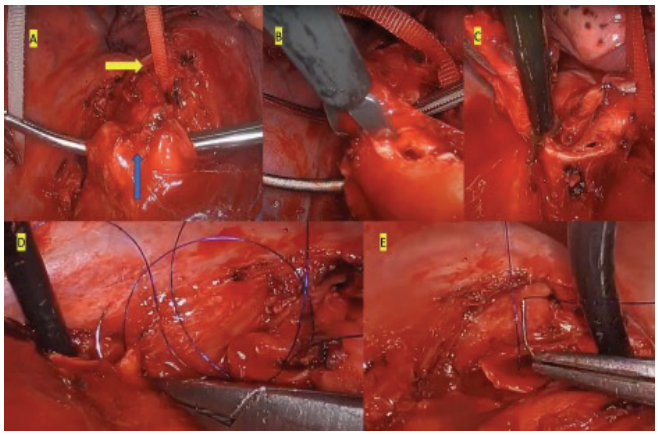

Figure 9. Right VATS Segmental Sleeve Resection of the Bronchus Intermedius – Posterior Approach **A:** Bronchial structures are suspended with tape. Blue arrow: intermediate bronchus, yellow arrow: upper lobe bronchus, **B:** Tangential section of the intermediate bronchus, **C:** Tangential section of the upper lobe bronchus, **D:** Sleeve anastomosis of the bronchial ends with continuous suture.

Case 7. Right VATS segmental sleeve resection of the bronchus intermedius: anterior uniportal approach

A patient diagnosed with a typical carcinoid tumor localized in the bronchus intermedius underwent surgery in the left lateral decubitus position under selective intubation. The tumor was seen in the intermediate bronchus in the thorax CT and FOB examination (Figure 10). Thoracic access was achieved through a 3 cm uniportal utility incision made at the 5th intercostal space along the mid-axillary line. The procedure began with the opening of an incomplete fissure to access the basal pulmonary artery. The lung was then retracted anteriorly, and the posterior mediastinal pleura was incised to expose and excise a paraesophageal lymph node. Using a tunneling technique posterior to the bronchus intermedius, the dissection proceeded through the posterior mediastinal pleura to reach the oblique fissure, which was divided using an endoscopic stapler. Through the fissure, the basal segmental pulmonary artery was looped with a vessel tape and retracted anteriorly, allowing exposure of the bronchus intermedius. The bronchus intermedius was carefully dissected and encircled using a dissector. It was transected just distal to the upper lobe take-off. To ensure complete resection of the tumor, an additional proximal ring of the bronchus intermedius was excised. Macroscopically, the tumor showed protrusion through the membranous wall toward the extrabronchial space; this extension was dissected bluntly and sharply. After proximal resection of the bronchus intermedius, subcarinal and paraesophageal lymph nodes were removed. The distal bronchus intermedius, including the proximal portion of the middle lobe bronchus, was also resected. Frozen section analysis confirmed negative margins at both proximal and distal ends. Bronchial reconstruction was performed with a continuous anastomosis using 3-0 polypropylene with a double round needle. During the leak test, a small air leak was observed at the junction of the cartilaginous and membranous portions on the posterior side of the anastomosis. This defect was repaired with an additional 3-0 polypropylene suture, and no further air leak was detected upon retesting (Figure 11). The operation lasted 180 minutes, with an estimated blood loss of 270 mL. The chest drain was removed on postoperative day 2, and the patient was discharged on day 4.

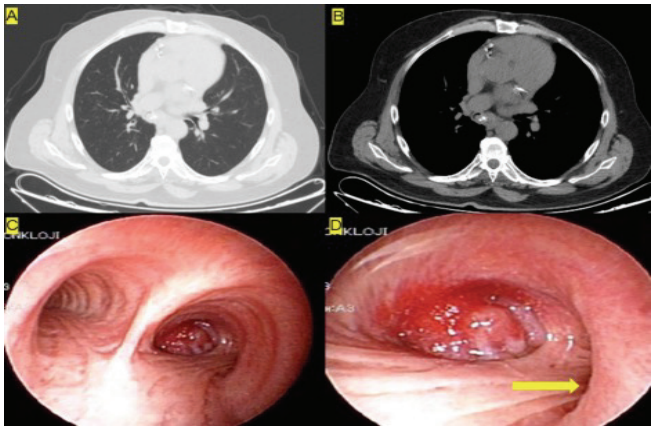

Figure 10. CT bronchoscopy and images of a lesion localized in the intermediate bronchus **A:** CT parenchymal section image of the lesion in the intermediate bronchus localization. **B:** Mediastinum section, **C:** FOB view of main bronchi, **D:** FOB image, yellow arrow, upper lobe entrance.

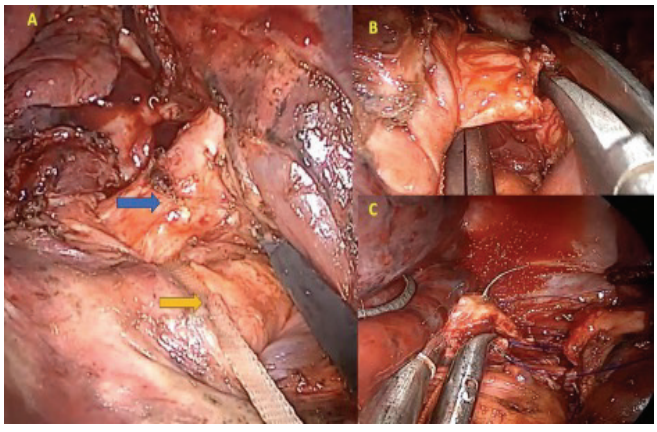

Figure 11. Right VATS Segmental Sleeve Resection of the Bronchus Intermedius – Anterior Uniport Approach **A:** Blue arrow intermediate bronchus, yellow arrow basal artery retracted anteriorly with tape, **B:** Division of the intermediate bronchus **C:** Anastomosis of proximal and distal edges after segmental resection of intermediate bronchus.

Discussion

Sleeve resections have long been performed using both open and minimally invasive approaches, yet curative resection of only the bronchial tree without parenchymal removal remains rare [7]. These procedures require high technical expertise but have become feasible via minimally invasive techniques in skilled centers [2]. Indications include tumors isolated to the carina, low-grade tumors such as carcinoids in the main or intermediate bronchus, and selected benign pathologies [8]. In cases where there is no systemic spread and R0 resection is performed, surgically isolated airway resection and reconstruction significantly increase survival [9]. For airway-limited tumors without parenchymal invasion, lung-sparing resections are preferred. Historical reports of bronchoplastic resections date to the 1980s and 1990s [8,10]. Complex tracheobronchial resections with full parenchymal preservation have recently been achieved with minimally invasive techniques [2]. Diego et al. [2], in their 2020 review, described the technique using a uniportal approach. Although the preferred technique in our clinic for such complex minimally invasive procedures is often the biportal approach, uniportal access is also utilized in selected cases. Airway continuity during these procedures requires coordination between surgery and anesthesia teams, employing cross-field ventilation or HFJV [4]. Tubeless spontaneous ventilation techniques have also been reported [11]. In our series, cross-field ventilation was primarily used, with HFJV in one case. Current literature suggests that, due to the lack of a safe and functional interposition graft for tracheal segments, there are anatomical limits to the length of the trachea that can be surgically resected [14]. Mortality for carinal resections ranges 7.2–29% [12], but adequate patient selection, surgical technique, and postoperative management have lowered rates. Lung-sparing approaches reduce mortality, mainly due to fewer anastomotic complications compared to carinal pneumonectomies [13]. Reinforcement flaps are optional, with mixed evidence [14,15]. Fibrin sealants (Tisseel) were used in some cases to prevent minor leaks [16]. Continuous and interrupted suture techniques yield similar outcomes; success relies on suture quality and tension-free anastomosis [17,18]. In parenchyma-sparing sleeve resections, complete oncologic resection is achieved without lung tissue loss. This case series highlights surgical nuances and technical considerations in minimally invasive VATS lung-sparing airway procedures.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

The study was approved by the Ethics Committee of Dr. Ismail Fehmi Cumalıoglu City Hospital (2024/107).

Authors' contribution

MEF: contributed to the definition of intellectual content, VE: was involved in the manuscript preparation and design, MÜ: contributed to the statistical analysis, design, and editing, ACK: was involved in the clinical studies, EK: contributed to the data acquisition, MSOM: contributed to the editing, NY: contributed to the definition of intellectual content, AÇ: was involved in the literature search, MM: contributed to the review of the manuscript, all authors have read and approved the final version of the manuscript

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Review Article

Technological evolution of uniportal video-assisted thoracoscopic surgery in lung cancer: a comprehensive review

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ABSTRACT

In this review, we will examine how uniportal video-assisted thoracoscopic surgery (U-VATS) compares in the management of non-small cell lung cancer (NSCLC) in terms of effectiveness, safety, and advancements in technology, as supported by recent literature. The change from multiportal techniques to uniportal techniques has expanded the limits of minimal invasiveness in thoracic surgery. In all aspects evaluated in the literature included in this review, U-VATS is comparable to multiportal techniques in postoperative pain, drainage time, and oncologic outcomes. The learning curve criteria set by the ESTS consensus for the safe adoption of U-VATS provides a sound basis for promoting this technique. In essence, Uniportal VATS is an evolving technique that is equally minimally invasive and has great oncologic potential, given advancements in technology.

Keywords: uniportal VATS, lung cancer, minimally invasive surgery, sleeve resection

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Introduction

In the past three decades, the surgical approach to the treatment of NSCLC has witnessed a revolutionary change from the traditional and morbid approach of thoracotomy to the minimally invasive surgical approach. The minimally invasive approach, as described in the early 1990s by Roviaro et al., marked the beginning of a new era in the surgical treatment of thoracic malignancies [1]. Although the approach at the outset used the conventional three- and four-port "multiportal" technique, VATS rapidly gained acceptance as the gold standard in the treatment of early-stage NSCLC due to its proven benefits over the traditional approach of thoracotomy, including reduced postoperative pain, hospital stay, and immunological stress [2-4].

In parallel to the evolution of multi-portal techniques, the trend towards reduced port access was first seen in the early 2000s. While the initial attempt to perform minor video-assisted thoracoscopic surgery (VATS) procedures via a uniportal approach was made by Gaetano Rocco et al. in 2001, thereby indicating a significant learning curve for the specialty, the second landmark was seen in 2011 [5]. Following on from this, Gonzalez-Rivas et al. were successful in proving the viability of performing major pulmonary procedures via a single incision, thereby establishing the term Uniportal VATS (U-VATS) [6]. Although the approach follows the same principles as the traditional approach, U-VATS has proven to be a more refined approach in the treatment of NSCLC, in which the aim is to minimize the trauma and the injury to the intercostal nerves.

Although U-VATS has achieved worldwide popularity, controversy still exists with regard to technical difficulties and oncological outcomes compared with conventional M-VATS. M-VATS allows for a triangulated view with instruments moving parallel to each other within the thoracic cavity, whereas with U-VATS, the surgeon gets a direct cranio-caudal view, similar to that of conventional open surgery. In addition, with all instruments being inserted through one incision, a new set of ergonomics must be mastered by the surgeon, thus creating a steep learning curve. Current meta-analysis and randomized controlled trials involving thousands of patients have shown that U-VATS achieves better results with regard to chest drainage, hospital stay, and postoperative pain, with comparable results with regard to oncological outcomes compared with M-VATS.

The main objective of this review article is to assess the effectiveness of U-VATS in lung cancer surgeries with regard to its clinical outcomes, safety, and oncological adequacy based on recent comparative studies, systematic reviews, and meta-analyses. By combining the short-term benefits of U-VATS without compromising long-term oncological outcomes, this study aims to provide an updated perspective with regard to recent literature.

Uniportal surgical technique and ergonomics

The uniportal video-assisted thoracic surgery (U-VATS) technique marks an advanced level of achievement in the history of thoracic surgery, realized through the consolidation of the multiportal videothoracoscopic technique, which started in the 1990s, into a single incisional approach by 2011. Though initially considered to be more demanding than the multiportal technique in terms of the learning curve, the U-VATS technique provides a surgical view similar to the traditional open thoracotomy approach while offering direct access to the hilar structures. The technique allows for the excellent visualization of the whole hilar area, thus being considered a very effective technique. The major technical problem to be overcome by the surgeon is the problem of instrument collisions, i.e., the passage of the camera system and the instruments through a single incision, called the utility incision. Among the major solutions proposed to overcome this problem is the utilization of special instruments, which are longer and thinner than those used in the traditional VATS approach. These instruments have tips that allow for the manipulation of the instruments in different directions. This feature allows the hands of the operator to be located at a greater distance from the incision, thus reducing the incidence of hand collisions in the extracorporeal area while allowing for the manipulation of several instruments in a small space (Figure 1).

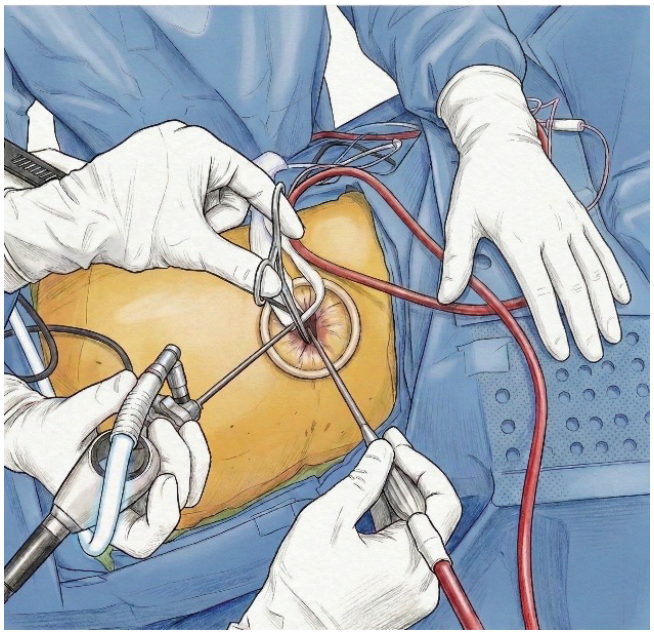

Figure 1. Uniportal video-assisted thoracic surgery.

A further factor in the determination of optimized ergonomics is the hierarchical placement of the instruments within the incision site. To avoid obstruction of the visual field and instrument overlap, the camera is best placed at the most superior (posterior) aspect of the incision site, while the surgical instruments are placed inferior to the camera (anterior). This placement allows for a natural working angle, analogous to the hand-eye coordination phenomenon observed during open procedures. This placement also reduces the fulcrum effect between the instrument's angle of insertion and the hand position. During the dissection of deep hilar structures such as vascular elements and the bronchus, maneuvers that either draw the lung tissue towards or away from the incision site using a cautery device or dissector are particularly useful in improving depth perception and comfort during the procedure. In cases of peripheral nodules, manipulation of the lung tissue towards the incision site allows for digital palpation in some cases, thereby improving diagnostic accuracy.

The use of a stapler in uniportal video-assisted thoracoscopic surgery (U-VATS) requires more sophisticated movements compared to multiportal VATS. To overcome this limitation of using a stapler, the concept of "mobile tissue against a fixed stapler line" is used. Dynamic traction of the lung tissue in the anterior, posterior, or superior direction is used to achieve the desired angle of the vessel or bronchus. This technique helps to align the hilar structures parallel to the stapler line.

In the subxiphoid uniportal approach, a semi-lateral position with a 70° posterior tilt is used with the help of the operating table. The access for the uniportal VATS is obtained through a longitudinal incision in the infrasternal area. After the incision, the rectus abdominis muscle fibers are longitudinally sectioned to access the xiphoid process. Complete excision of the xiphoid process facilitates the approach by providing an optimal view of the surgical area without the need to retract the sternum. After the tunnel is created behind the sternum, the pleural layer is entered under thoracoscopic vision, followed by the placement of a wound protector retractor. To maintain ergonomic positions, a 30° angled 10-mm diameter videothoracoscope is inserted from the caudal (inferior) part of the incision, while the VATS instruments are inserted from the cranial (superior) part of the incision to avoid instrument conflicts (Figure 2).

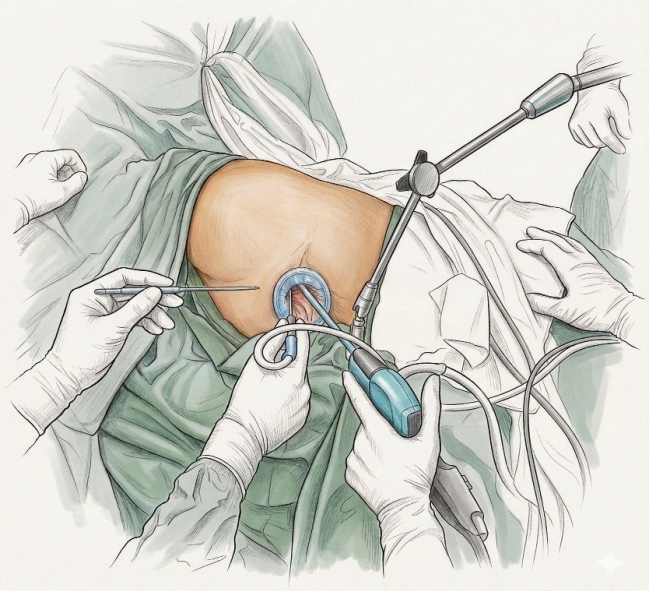

Figure 2. Subxiphoid uniportal approach.

Learning curve

Uniportal video-assisted thoracoscopic surgery (U-VATS) is believed to be technically challenging, as all the surgical manipulations are performed through a single incision. Even for thoracoscopic surgeons familiar with conventional multiportal video-assisted thoracoscopic surgery (M-VATS), the learning curve for the new technique involves improvements in depth perception and management of instrument interference.

The Cumulative Sum (CUSUM) analyses reported in the literature have evaluated the number of cases that need to be performed to acquire technical competence in the new technique of U-VATS lobectomy. The Consensus report from the ESTS Uniportal VATS Interest Group (UVIG) concluded that at least 50 cases need to be performed by the surgeon under mentorship/supervision to acquire competency in the technique of uniportal lobectomy [7]. Nachira et al. reported that the experienced team reached the technical proficiency threshold after 25 cases, with a reduction in the mean operative time from 191 to 164 min ($p = 0.04$) after the threshold cases [8]. Liu et al. divided the learning curve into three stages, with the initial 30 cases being the ascending phase, cases 30 to 60 being the plateau phase, and cases greater than 60 being the proficiency phase, with significant stabilization of the operative time and improvement in surgical safety from cases 30 to 60 [9].

Conversion Rates and Causes of ConversionConversion to open surgery is one of the key parameters used to evaluate the safety of U-VATS and the challenges associ-

ated with its learning curve. Meta-analyses conducted by Yan et al. and Magouliotis et al. demonstrated that there is no statistically significant difference in conversion rates between U-VATS and M-VATS ($p > 0.05$) [3,10]. The main causes of conversion are generally classified as pleural adhesions, calcified lymph nodes, and uncontrollable vascular injuries. Drevet reported that the majority of conversions occur during the first half of the learning curve, emphasizing the importance of surgical experience [11]. Table 1 summarizes the studies related to the learning process of Uniportal VATS.

At the early learning curve stage, particularly within the first 30 cases, the major problem encountered by the surgeon is the stapler's maneuverability. Liu et al. found that during the early learning curve phase, the attempts to insert the stapler had to be repeated in 73% of cases; however, the rate reduced to 5% once proficiency was achieved [9]. Recent research suggests that the learning curve for U-VATS does not have a negative effect on the length of stay and morbidity; the procedure can be safely performed with an appropriate training background.

A series of meta-analyses by Harris et al. has established that U-VATS is as safe as traditional M-VATS while also showing significant advantages in terms of postoperative recovery time [12].

Operative time was initially considered a limitation of U-VATS due to the steep learning curve required for surgeons. Indeed, data reported by Al-Ameri et al. [13] and more recently by Zheng et al. [2] demonstrated that operative times in the uniportal group were longer during the early phases compared with M-VATS. However, large-scale meta-analyses by Yan et al. [10] and Magouliotis et al. [3] have confirmed that as the surgical team's experience increases, this difference diminishes, and no statistically significant difference remains between the two techniques in terms of operative time or intraoperative blood loss.

The Uniportal VATS (U-VATS) method for major pulmonary resections has enjoyed significant popularity in the literature since the publication of the initial large case series by Gonzalez-Rivas et al. This initial study established the premise that the U-VATS method is a highly precise technique in terms of hilar dissection and does not violate any oncological principles [14].

The most consistently reported advantage of U-VATS in the literature is its ability to minimize thoracic tissue trauma, thereby reducing postoperative drainage volume and shortening the length of hospital stay. Nachira et al. demonstrated that these clinical advantages are much more pronounced when compared with open surgery (thoracotomy) [8]. Furthermore, when postoperative complication rates are evaluated, Magouliotis et al. [3] reported that the overall morbidity risk (arrhythmia, air leak, etc.) was significantly lower in the uniportal group compared with the M-VATS group (OR: 0.76), providing strong evidence supporting the safety of the technique (Table 2).

Table 1. Comparison of U-VATS learning curve and conversion data.

Study (Author)	Year	Threshold number of cases for learning	Conversion rate (%)	Key findings
Bertolaccin [7]	2019	50 cases	–	Training standard under mentorship.
Nachira et al. [8]	2018	25 cases	4.3%	Operative time decreases after 25 cases.
Liu et al. [9]	2018	30–60 cases	17% → 2%*	Stapler success increases after the first 30 cases.
Drevet et al. [11]	2016	~90 cases	15%	Rates stabilize after the first 10 months.

**In the study by Liu et al., the change between the first 30 cases and the subsequent 60 cases is presented.*

Table 2. Chronological comparison of perioperative outcomes between U-VATS and M-VATS.

No	Study (Author)	Year	Study Type	Patients (U/M)*	Operative Time	Drainage (Days)	Hospital Stay (Days)
1	Gonzalez-Rivas [14]	2013	Cohort	102 (U-VATS)	154 min (mean)	1.5 vs 2.3	2.5 vs 3.7
2	Harris et al. [12]	2016	Meta-analysis	1815 (total)	Similar	U-VATS <	U-VATS <
3	Al-Ameri et al. [13]	2019	Cohort	122 / 211	147 vs 133 min	2 vs 3	3 vs 4
4	Sihoe et al. [15]	2019	Review	–	Safe	Advantage	Advantage
5	Yan et al. [10]	2020	Meta-analysis	1869 / 2273	Comparable	3.8 vs 4.7	5.6 vs 6.5
6	Magouliotis et al. [3]	2021	Meta-analysis	1469 / 3231	Comparable	U-VATS <	U-VATS <
7	Nachira et al. [8]	2022	Comparative	115 / 115 (Open)	Comparable	4 vs 6	5 vs 8
8	Zheng et al. [2]	2024	Retrospective	60 / 68	U-VATS longer	3.5 vs 4.3	4.8 vs 6.0

** U: Uniportal VATS, M: Multiportal VATS.*

Oncological outcomes

The success of minimal invasive techniques in lung surgery for cancer is not only measured by the quick recovery of patients but also by the strict adherence to oncological principles, including lymph node dissection. One of the concerns regarding the extensive adoption of Uniportal Video-Assisted Thoracoscopic Surgery (U-VATS) for lung cancer has been the adequacy of exposure for all mediastinal stations through a single incision.

In fact, recent meta-analyses have demonstrated that U-VATS is equally effective as multiportal techniques (M-VATS) in lymph node dissection. In fact, in the meta-analysis by Yan et al., which included 20 studies, no significant difference was found between U-VATS and M-VATS in terms of the number of lymph nodes removed, with $p = 0.41$ for the comparison between the two techniques in terms of the total number of lymph nodes removed [10]. Magouliotis et al. have also demonstrated that with the uniportal technique, it is possible to adequately sample lymph nodes in both the hilar and mediastinal regions (N1 and N2) for staging purposes [3]. In their study comparing U-VATS for lobectomy with open thoracotomy, Nachira et al. [8] found that there was no difference in terms of the number of lymph nodes removed between the two techniques, thus demonstrating the oncological radicality of U-VATS for lung cancer surgery.

The ability to clear all the lymph nodes completely is of paramount importance to ensure the accuracy of the disease staging and the administration of adequate adjuvant treatment. The literature has shown that the incidence of upstaging of the lymph nodes with U-VATS is similar to that with M-VATS and even open surgery. The data from the ESTS Uniportal VATS Interest Group have shown that the use of the uniportal technique does not interfere with the en bloc dissection of the mediastinal fatty tissue and the lymph nodes [7].

Moreover, the data regarding the long-term results of U-VATS are emerging. Zheng et al. have shown that there were no significant differences in the rates of recurrence and metastasis between U-VATS and M-VATS during the postoperative period [2]. In the case of early-stage lung cancer, the rates of survival at 3 and 5 years are similar with the use of the conventional technique and the U-VATS, suggesting the oncological safety of the procedure.

Advanced techniques and extended resections

The evolution of Uniportal VATS (U-VATS) has gone beyond the initial indications, which were generally limited to simple resections, and has entered the extended phase, which allows for the execution of complex oncologic procedures safely. In this regard, the execution of bronchial and vascular sleeve resections for centrally located tumors has proven that such procedures can be fully executed in accordance with oncologic principles. Notably, the reliability of Uniportal VATS sleeve resections for locally advanced central-type non-small cell lung cancer (Stage IIB-IIIB) after the administration of neoadjuvant chemo-immunotherapy has been proven. Yang et al. have shown that, despite the fibrosis in the hilar region induced by the immunotherapy, the execution of sleeve resections with the aid of U-VATS has been technically possible and has been associated with satisfactory results with regard to the duration of the surgical procedures and the rates of complications [16]. These advanced techniques, with the simultaneous instrumentation ergonomics of the Uniportal technique, make it possible to avoid pneumonectomy in the case of pulmonary artery involvement.

The subxiphoid approach of the Uniportal SVATS, which has further enhanced the minimally invasive nature of the technique, has revolutionized the management of postoperative pain by avoiding the injury to the intercostal nerves. Studies by Pfeuty et al. and Sezen et al. have shown that the subxiphoid approach offers better perioperative results not only for routine lobectomies but also for complex operations like segmentectomy, which requires anatomical knowledge [17,18]. Sezen et al. have shown that the subxiphoid approach significantly reduces the hospital stay compared to the conventional intercostal approach (3.8 days vs. 4.8 days; $P = 0.004$) and significantly reduces the intensity of early postoperative pain, as measured by the VAS score [19]. One of the major strategic advantages of the subxiphoid approach is the ability to perform operations bilaterally, allowing for the treatment of lesions in both lungs through a single incision. Elkhayat et al. emphasized the advantage of the SVATS technique in improving the efficiency of the surgical procedure, especially for operations like the bilateral pulmonary metastasectomy, which allows for simultaneous access to

both hemithoraces through a single incision, avoiding the need for two separate operations. Thus, the minimally invasive nature of the technique has been taken to the next level by avoiding the need for two separate thoracotomies and the attendant increase in the duration of the surgical procedure [20].

In addition, the minimally invasive nature of the Uniportal VATS technique has been extended to the anesthetic management, as emphasized by Elkhayat and Gonzalez-Rivas, who have shown that the non-intubated (awake) approach to the Uniportal VATS technique could reduce the complications associated with endotracheal intubation and the use of muscle relaxants, allowing for tubeless surgery, which optimizes the recovery process [21]. Thus, the spectrum of operations, from the complex sleeve operations to the bilateral subxiphoid metastasectomy, and the non-intubated approach, clearly demonstrates that the Uniportal VATS technique is a dynamic and ever-expanding field.

Conclusion

In the field of minimal access surgery for lung cancer, Uniportal VATS surgery represents the pinnacle of minimal access surgery that has been achieved over the last decade. The advantage that is most consistently highlighted for U-VATS surgery is that it results in a significant reduction in postoperative pain, as measured by VAS scores, by limiting trauma to one intercostal space. This has significant benefits for postoperative mobilization, adherence to respiratory physiotherapy regimens, shorter durations of postoperative chest drainage, and shorter durations of postoperative stay in the hospital. With regards to lymph node dissection capabilities and nodal staging, which are critical for any oncologic surgery, U-VATS surgery is completely equivalent to multiportal techniques and open surgery. The future of uniportal surgery is likely to be even more closely aligned with advancements in technology and expertise, as represented by robotic uniportal VATS surgery (RUVATS) and advancements in artificial intelligence-based imaging.

In summary, Uniportal VATS surgery is a rapidly evolving field that is capable of providing minimal access surgery without compromising oncologic principles, improving quality of life for patients, and increasing its applications in parallel with advancements in technology.

Declaration of conflicting interests

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Authors' contribution

Both authors contributed equally to the concept, design, supervision, data collection, literature search, writing, and critical review of the manuscript. all authors have read and approved the final version of the manuscript.

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Case Report

Traumatic pneumopericardium: a rare clinical condition developing on the fifth day after trauma

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ABSTRACT

Pneumopericardium is a rare pathology that may occur following blunt or penetrating thoracic trauma, iatrogenically after certain medical interventions, or due to specific infections. It is most commonly observed after trauma and presents with a wide spectrum of clinical manifestations. The presented case is noteworthy as it involves pneumopericardium that developed on the fifth day of follow-up for a rib fracture sustained after a fall from height. This case highlights the diagnosis, monitoring, and treatment approach to traumatic pneumopericardium.

Keywords: trauma, pneumopericardium, rib fracture

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Introduction

Pneumopericardium is defined as the presence of air in the pericardial cavity. Its cause is mostly trauma; it may be seen in conjunction with severe blunt chest trauma, pneumothorax, pneumoperitoneum, or other causes of pneumomediastinum. Although spontaneous resolution is often observed, tension pneumopericardium is life-threatening and requires urgent, life-saving intervention. It can lead to severe cardiovascular complications and may require emergency drainage. Diagnosis is made using thoracic computed tomography (CT), which also helps identify accompanying injuries [1].

Close monitoring of vital signs is required in its treatment. In patients who do not develop tension pneumopericardium, spontaneous regression may be observed. The early detection of tamponade development in pneumopericardium treatment is of vital importance [2].

Case Report

A 55-year-old male patient was admitted to the emergency department with a history of falling from a height of approximately 4 meters. On physical examination, the patient's general condition was good, he was conscious, oriented, and cooperative. Oxygen saturation was measured as 95% with a finger probe, blood pressure was 130/75 mmHg, and pulse rate was 86 beats per minute (bpm). On palpation, tenderness was present on the lateral wall of the left hemithorax. On auscultation, breath sounds were diminished in the lower zone of the left hemithorax. Thoracic CT was performed. Thoracic CT revealed displaced fractures in the lateral aspects of the 5th, 6th, and 7th ribs on the left hemithorax, with subcutaneous emphysema adjacent to the fractures. Additionally, pleural effusion measuring 2 cm at its thickest point and minimal pneumothorax were present in the left hemithorax. (Figure 1). The patient's blood test results were as follows on the first day: WBC: 14.79 K/μL, Hb: 16.7 g/dL, and CRP: 3.28 mg/L. The patient was admitted to the thoracic surgery clinic for trauma follow-up. The patient was started on systemic analgesia with intravenous paracetamol and a nonsteroidal anti-inflammatory drug (tenoxicam). The patient continued respiratory exercises and mobilization. On the fifth day after the trauma, the patient developed a burning-type left-sided chest pain accompanied by cold sweating. At this time, his vital signs were assessed: oxygen saturation at the fingertip was measured as 85%, the pulse was tachycardic (110 bpm), normotensive (120/70 mmHg), and body temperature was recorded as 37°C. The patient was monitored closely. An echocardiography (ECHO) was performed on the patient, who was actively mobile and exhibited no respiratory symptoms, due to the description of angina-like chest pain. Echocardiography revealed minimal pericardial effusion without compression or presence of air. No acute pathology was detected in the bedside chest X-ray or blood tests. Pulmonary CT angiography was performed with a preliminary diagnosis of pulmonary embolism, which was not detected. However, diffuse infiltrative areas suspicious of pneumonia in both lungs and pneumopericardium were observed (Figure 2). Infection markers were evaluated, and the results were as follows: CRP: 147 mg/L, WBC: 7.63 K/μL, and procalcitonin: 0.19 μg/L. Respiratory tract swab and sputum culture samples were collected. The patient was started on antibiotic therapy with moxifloxacin 400 mg once daily and piperacillin-tazobactam 3.5 g four times daily. No growth was detected in the collected sputum culture or respiratory tract swab samples. Nasal oxygen support was provided to the patient, and analgesic therapy was continued. It was observed that the patient's existing symptoms had regressed. Follow-up imaging demonstrated a reduction in the areas of infiltration. The patient was clinically followed for the resolution of pneumopericardium, and improvement was observed without the need for invasive intervention. The patient was discharged on the 13th day after the trauma. Informed consent was obtained from the patient for publication of this case report and accompanying images.

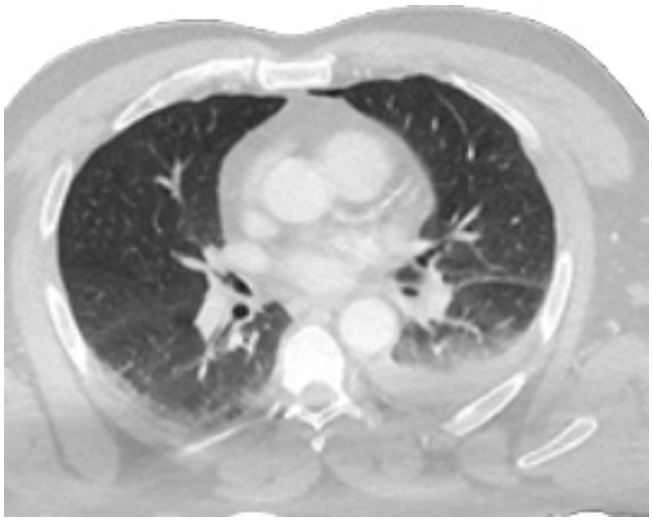

Figure 1. Thoracic CT scan of the patient taken after trauma.

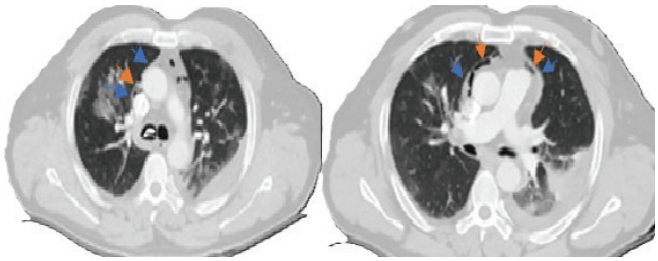

Figure 2. Thoracic CT scan obtained on the 5th day after trauma (Blue arrows: pericardial border, red arrows: pneumopericardium).

Discussion

In the literature, the mechanism of air entry into the pericardial space in blunt trauma was first proposed by Macklin. Macklin suggested that air escaping from ruptured alveoli advances along the sheaths of pulmonary vessels to the hilum, where it spreads into the mediastinum. Mediastinal emphysema can enter the pericardial space through the ostia of the pulmonary veins, leading to pneumopericardium [3].

Pneumopericardium may be self-limited; however, in one-third of cases, tension pneumopericardium develops, leading to a clinical presentation similar to tamponade, which has been shown to be associated with a 60% mortality rate [4].

Pneumopericardium can be asymptomatic, but it may also cause symptoms such as chest pain, dyspnea, syncope, and upper quadrant pain. On physical examination, Hamman's sign is typical on auscultation [2].

Although the diagnosis of pneumopericardium can be made with chest radiographs, their utility in pericardial and cardiac injuries is limited. Differentiating pneumomediastinum and medial pneumothorax from pneumopericardium on direct radiographs is challenging. CT imaging is a highly sensitive modality for evaluating pneumopericardium and associated pathologies [5].

In the presented case, pneumopericardium was detected on thoracic CT on the fifth day post-trauma following the emergence of burning-type chest pain and sweating in a patient with blunt thoracic trauma. This finding demonstrates that pneumopericardium may not develop immediately after trauma but can occur days later. Therefore, long-term and meticulous monitoring of trauma patients is of great importance.

In this case, the patient's elevated WBC level prior to the onset of chest pain was considered secondary to trauma. Following the onset of chest pain, imaging revealed infiltrative areas, which gradually regressed over time as observed through daily follow-up with posteroanterior (PA) chest radiographs.

In the literature, pneumopericardium findings are generally observed during the acute phase of trauma. In contrast to the existing literature, in the presented case, pneumopericardium was not detected on the initial CT scan performed on the first day of trauma but was identified on the fifth day. The occurrence of late-onset chest pain after adequate pain control in a trauma patient, accompanied by the subsequent detection of pneumopericardium in diagnostic studies, is a remarkable and rare finding that contributes to the literature.

The delayed onset of pneumopericardium following trauma is a critical point to consider in clinical follow-up. In patients presenting with mechanisms such as falls from height or blunt thoracic trauma, dynamic assessment of symptoms during follow-up and the use of advanced imaging modalities when necessary are essential.

In conclusion, traumatic pneumopericardium, while rare and potentially fatal, can be successfully managed with early diagnosis and prompt intervention. This case highlights the importance of meticulous clinical monitoring and post-trauma care in trauma patients. Furthermore, a better understanding of the pathophysiological mechanisms of pneumopericardium may facilitate the development of new approaches for preventing and managing this rare complication.

Declaration of conflicting interests

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Authors' contribution

All authors contributed to the conception, data collection, writing, and final approval of the manuscript.

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Case Report

Glomus tumour of the trachea: a rare case

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ABSTRACT

This case report presents a rare case of a benign tracheal glomus tumor in a 48-year-old male who presented with progressive cough and dyspnea. Imaging revealed a proximal tracheal mass causing partial airway obstruction, and bronchoscopy demonstrated a highly vascularized lesion. Due to the risk of bleeding, biopsy was not performed, and PET/CT findings supported a benign etiology. The tumor was excised via a cervical approach, and histopathological examination confirmed a benign glomus tumor with typical immunohistochemical features. Postoperative recovery was uneventful; no recurrence was observed during one year of follow-up. This case highlights the diagnostic challenges of tracheal glomus tumors, the importance of imaging and surgical flexibility in management, and the favorable prognosis achievable with complete surgical resection and vigilant long-term follow-up.

Keywords: glomus tumor, tracheal neoplasms, airway obstruction, bronchoscopy

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Introduction

Glomus tumors are rare neoplasms that most commonly occur in the upper extremities [1]. These tumors originate from glomus bodies, mesenchymal structures responsible for thermoregulation. While they are typically found in the subungual region, glomus tumors have also been reported in unusual extraneous sites such as the stomach, abdominal wall, mandible, and bronchi [2-4].

Glomus tumors arising within the airway are exceedingly rare, with only a limited number of cases described in the literature. A recent literature review has shown that there were 77 published articles on tracheal glomus tumors in the English-language medical literature up to 2020 [5]. They usually occur in the upper and middle portions of the trachea, where they lead to airway obstruction. The rarity of these tumors in the trachea creates diagnostic challenges, as their symptoms such as cough and dyspnea are nonspecific and often mimic more common respiratory disorders. In these patients, imaging modalities such as computed tomography, bronchoscopy, and PET-CT are commonly utilized to evaluate the lesion and its extent within the airway. The low FDG uptake of glomus tumors on PET/CT may help differentiate them from other malignant neoplasms; however, the definitive diagnosis of glomus tumors is based on histopathological examination and immunohistochemical staining.

In this report, we present a case of a 48-year-old male initially misdiagnosed with a tracheal papilloma, in whom surgical excision confirmed a glomus tumor. This case emphasizes the need to consider glomus tumors among the differential diagnoses of tracheal lesions and highlights the curative potential of complete surgical resection.

Case Report

A 48-year-old male, with a history of Behcet's disease and no comorbidities or smoking history, presented to pulmonology clinic with a persistent cough and increasing exertional dyspnea. The patient reported these symptoms had increased over the past six months and were impacting his quality of life. Physical examination was unremarkable.

Behcet's disease is a systemic disease that can affect the vascular system. The literature presents data showing that the disease causes vascular involvement and inflammatory processes in the airways and lungs. The patient's complaints could be related to this. Given the severity of his symptoms, further diagnostic workup was warranted.

The initial thoracic computed tomography (CT) scan revealed a 15x10 mm soft tissue mass in the proximal trachea (Figure 1). The lesion was located approximately 2 cm below the vocal cords and partially obstructed the tracheal lumen. The patient was subsequently referred to our thoracic surgery clinic for further evaluation. Flexible bronchoscopy demonstrated a highly vascularized polypoid lesion arising from the posterior membranous wall of the trachea, causing nearly 50% luminal narrowing. Bronchoscopic biopsy was considered high risk and therefore not performed for previous case reports showing that massive bleeding has been encountered during biopsy of highly vascular tracheal tumors [5]. To further characterize the lesion, a positron emission tomography/computed tomography (PET/CT) scan was obtained, revealing minimal fluorodeoxyglucose (FDG) uptake with a maximum standardized uptake value (SUVmax) of 2.34, consistent with a benign process. Despite the imaging findings, the patient's persistent respiratory symptoms warranted surgical intervention.

The patient underwent an open surgical excision via a cervical collar incision. Intraoperatively, the tumor was found to be arising from the posterior tracheal wall at second tracheal cartilage ring. The tumor was only dissected from the posterior tracheal wall with sharp dissection for the tumor was located in the superior trachea, no deep infiltration, and no submucosal extension was detected. The lesion was excised en bloc without complications. Intraoperative frozen section analysis revealed no evidence of malignancy and there was no need for further tracheal resection.

The resected specimen was subjected to histopathological examination, revealing a neoplasm composed of uniform cells with round nuclei and eosinophilic cytoplasm surrounding numerous blood vessels. There was minimal cellular atypia and a low mitotic index (Figure 2). Immunohistochemical staining showed strong positivity for smooth muscle actin (SMA) and H-Caldesmon, with weaker staining for Desmin. The Ki67 proliferation index was below 5%, consistent with a benign glomus tumor.

Benign glomus tumors are histologically monotonous, with low mitotic activity and uniform cells; malignant glomus tumors show mitosis with atypical mitotic figures or marked nuclear atypia. Although the immunohistochemical profile (SMA and h-caldesmon positivity) is generally common in all glomus tumors, a low Ki-67 index and the absence of atypical cytological features characterize benign tumors [6].

Postoperative recovery was uneventful. Follow-up bronchoscopy performed one week and four months after surgery showed no evidence of tumor recurrence (Figure 3). The patient remained symptom-free with no signs of recurrence at the one-year follow-up. Informed consent was obtained from the patient for publication of this case report and accompanying images.

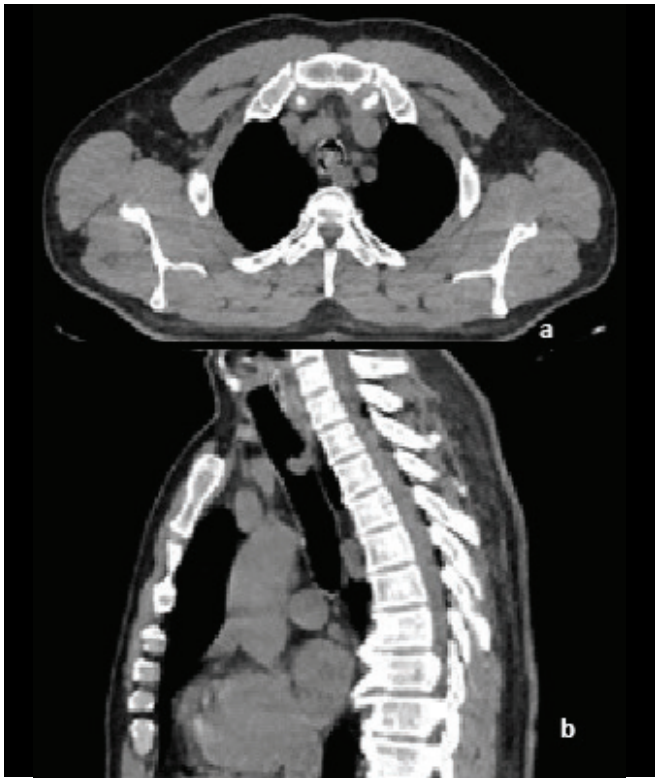

Figure 1. Preoperative axial CT imaging shows a tumor narrowing the trachea by %50 **(a)**, preoperative sagittal CT imaging shows that the tumor originates from the posterior wall of the trachea **(b)**.

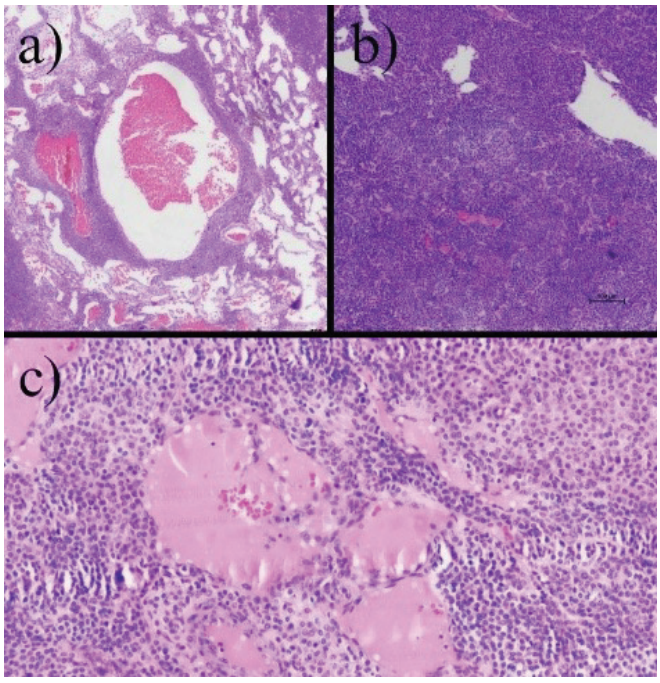

Figure 2. At low magnification, layers of glomus cells surrounding the vascular spaces can be observed, HEx40 **(a)**, glomus cells with round nuclei, eosinophilic cytoplasm, and minimal atypia are observed to solid growth pattern, HEx100 **(b)**, round nuclei with indistinct borders, eosinophilic cytoplasm, minimal atypia, and low mitotic activity glomus cells are observed HEx200 **(c)**.

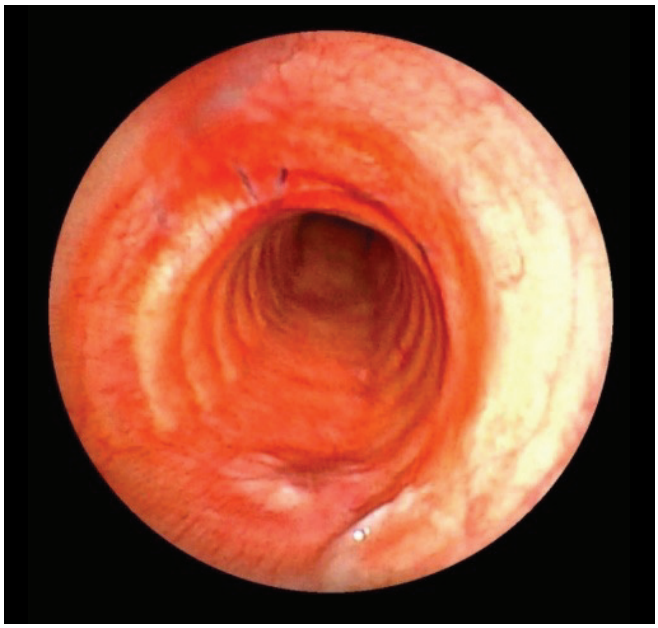

Figure 3. Bronchoscopy performed in the 4th month postoperatively shows no signs of recurrence.

Discussion

Tracheal glomus tumors present significant clinical and pathological challenges in diagnosis due to their rarity. In the present case, several important aspects were observed. Firstly, because the symptoms overlapped with other respiratory conditions, imaging studies played a crucial role in detecting the lesion and assessing its extent. Secondly, the lesion appeared highly vascularized during bronchoscopy, which modified the diagnostic and therapeutic approach. Instead of performing a high-risk biopsy, a PET-CT scan was obtained. Low SUVmax value (2.34) is consistent with benign glomus tumors based on previously reported cases. Surgical excision through tracheotomy was performed. The intraoperative frozen section confirmed removal of the tumor with clear surgical margins, emphasizing the importance of flexibility in diagnostic and treatment planning. Finally, histopathological evaluation revealed an exceptionally rare diagnosis, leading to a review of the literature and implementation of a long-term follow-up strategy.

Complete surgical excision with clear margins is essential to prevent local recurrence and achieve long-term disease control. The selection of the surgical approach should be individualized according to the tumor's size, vascularity, and precise tracheal location. In reported cases, techniques such as rigid bronchoscopic resection, tracheotomy, segmental resection, or sleeve resection have been successfully employed, each with

specific indications and limitations [2]. Rigid bronchoscopic resection is less invasive but carries a high risk of bleeding and local recurrence. Segmental or sleeve tracheal resection is generally curative for preventing local recurrence, especially in cases with deep invasion. However, it is a major surgical procedure. It carries a risk of serious postoperative complications such as anastomosis leak and tracheal stenosis.

Intraoperative frozen section examination may be valuable, confirming complete tumor removal and guiding the extent of resection when malignancy cannot be excluded. For this case, open surgical excision via a cervical approach provided optimal exposure and ensured complete resection without the need for segmental tracheal reconstruction.

The prognosis for benign glomus tumors is generally favorable, with low recurrence rates following complete surgical excision. Nevertheless, long-term follow-up remains essential to detect potential recurrence or malignant transformation. Although glomus tumors are predominantly benign, rare cases with malignant behavior have been reported; therefore, regular postoperative surveillance using bronchoscopy and imaging is recommended.

Given the rarity of these tumors, further case reports are needed to improve understanding of their biological behavior, optimal treatment strategies, and long-term outcomes. This case reinforces the importance of including glomus tumors in the differential diagnosis of tracheal masses, highlights the value of a multidisciplinary approach in diagnosis and treatment, and emphasizes the necessity of follow-up to ensure favorable patient outcomes.

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Authors' contribution

All authors contributed to the conception, data collection, writing, and final approval of the manuscript.

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Case Report

Chest wall epithelioid hemangioendothelioma unmasked by a hematoma: case report

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ABSTRACT

Epithelioid hemangioendothelioma (EHE) is a rare neoplasm originating from vascular endothelial cells, which can arise in varied tissue sites. We describe a case of EHE presented with submammary mass of the left chest wall in a 25-year-old male, and his chest CT scan revealed a hematoma. The patient underwent a resection of the mass and the pathologic examination confirmed the diagnosis of epithelioid hemangioendothelioma. Five months later, He developed a firm nodule at his surgical scar. He had a second surgery consisting of excision of the local recurrence and partial resection of the sixth rib, including the intercostal space of the chest wall. To cover the remaining defect, we used polypropylene mesh, with muscle advancement and primary skin closure. The patient subsequently received radiotherapy and remains under active surveillance. This case highlights the challenges of preoperative diagnosis and that EHE should be considered in the differential diagnosis of chest wall masses.

Keywords: epithelioid hemangioendothelioma, chest wall tumor, vascular tumor, soft tissues, surgical treatment

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Introduction

Epithelioid hemangioendothelioma (EHE) is an exceptionally rare vascular malignancy, representing less than 1% of all vascular tumors [1]. According to the 2020 World Health Organization (WHO) Classification of Soft Tissue Tumors. EHE is categorized among vascular sarcomas and exhibits highly heterogeneous clinical presentations, arising from sites such as bone, liver, soft tissues, or lung [2]. Chest wall involvement is extremely uncommon. We describe a case of chest wall EHE that developed local recurrence after R0 resection involving the ribs, managed with surgical excision followed by radiotherapy.

Case Report

A 25-year-old man presented with a left submammary mass that had been evolving for approximately one year. He underwent ultrasound-guided biopsies, but the histopathological findings were inconclusive. The patient denied any history of trauma and had no significant medical history, including no tobacco or alcohol use. On physical examination, a 5 cm mass was palpated in the left submammary region of the anterior chest wall. Preoperative thoracic computed tomography (CT) revealed a hematoma-like collection measuring 50×64×36 mm, with peripheral enhancement after contrast injection (Figure 1). Following multidisciplinary discussion, surgical management was decided, and the patient underwent en bloc resection including the mass and the pectoralis major muscle (without costal invasion). Histological examination of the surgical specimen showed a proliferation of endothelial cells arranged in small vascular channels. The tumor cells appeared large and epithelioid, with abundant cytoplasm, prominent nucleoli, and marked nuclear atypia. Mitotic activity was estimated at 6 per 10 high-power fields, with no necrosis identified. Immunohistochemistry demonstrated positive staining for CD31, EMA, and ERG, Ki-67 (approximately 20%), while CD34 was negative (Figure 2). These findings supported the diagnosis of epithelioid hemangioendothelioma with negative microscopic (R0) margins. As part of the metastatic workup, computed tomography (CT) scans of the head, neck, chest, abdomen, and pelvis were performed and showed no abnormalities.

Five months later, the patient developed a small, firm, fixed subcutaneous nodule on his surgical scar. A second surgery was performed consisting of excision of the tumor and partial resection of the sixth rib, including the intercostal chest wall, for definitive diagnosis and treatment. The tumor was a smooth, soft mass located primarily within the intercostal soft tissues and adherent to the sixth rib, but without lung involvement. The chest wall defect was reconstructed using polypropylene mesh, and the wound was closed by dissecting and advancing by three muscles, the latissimus dorsi, pectoralis minor, and rectus abdominis. Given the good skin elasticity, primary closure of the incision was achieved (Figure 3). The postoperative course was uneventful, and the patient was discharged on postoperative day 3. Pathological examination revealed local recurrence with aggressive features, including focal tumor necrosis and a mitotic count of 14 per 10 high-power fields. As the recurrence developed five months after the initial surgery, the patient underwent radiotherapy and remains under active surveillance. The patients gave written informed consent to collect, analyze, and publish his medical data in this study.

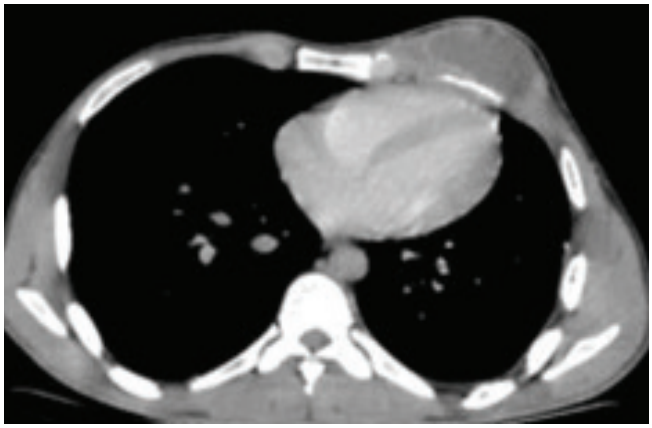

Figure 1. A computed tomographic (CT) scan of the chest showing a hematoma-like collection with peripheral contrast enhancement.

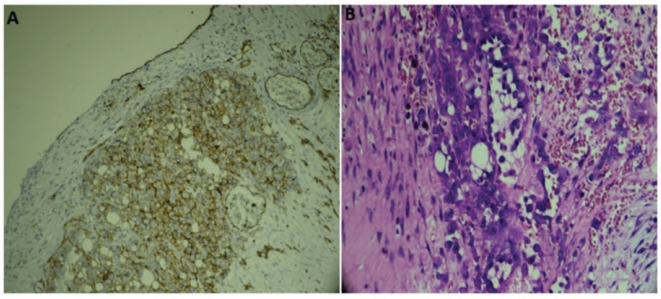

Figure 2. Histopathological features of epithelioid hemangioendothelioma: Proliferation of vascular structures and large epithelioid cell sheets with marked anisokaryosis and vesicular nuclei (A), nuclear staining of tumor cells with anti-CD31 antibody (magnification ×20) (B).

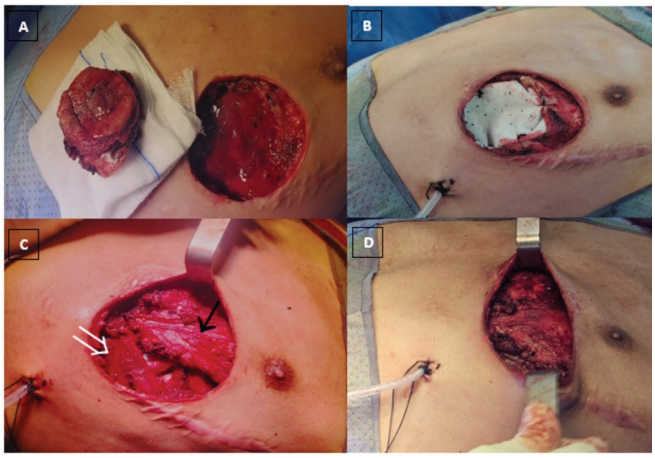

Figure 3. Clinical images of the representative case. Defect after excision of the local recurrence with the mass resected **(A)**, intraoperative view after placement of a polypropylene mesh to close the defect **(B)**, closure achieved by dissecting and advancing three muscles: the latissimus dorsi (black arrow), pectoralis minor, and rectus abdominis (white arrow) **(C)**, final appearance after reconstruction and closure of the defect **(D)**.

Discussion

Epithelioid hemangioendothelioma (EHE) is an ultrarare vascular sarcoma with two distinct morphological and molecular variants (CAMTA1-related and TFE3-related). Its rarity, with an incidence of 0.038 per 100,000 per year, accounts for the limited literature, which is primarily composed of case reports and small case series showing variations in demographic characteristics [3]. The median age at diagnosis is typically in the fourth to fifth decades of life [1-4]. However, in our case, the patient was young.

EHE can occur in any part of the body and may present as a unifocal lesion, with locoregional metastases, or with systemic metastases [5]. Furthermore, intrathoracic EHE usually presents as bilateral pulmonary nodules, and to our knowledge, this case represents the second reported case of chest wall EHE. The clinical presentation at diagnosis is highly variable; patients may exhibit respiratory symptoms such as pleuritic chest pain, pleural effusion, or hemoptysis, although some cases may remain asymptomatic [6]. A review of the literature reveals that chest wall involvement is very uncommon [7]. In the present case, we initially suspected a spontaneous hematoma because of the negative result of the needle biopsy.

Epithelioid hemangioendothelioma of the soft tissues may arise in either supra- or sub-aponeurotic compartments. These tumors frequently develop in proximity to blood vessels, reported in 50–70% of cases, and can sometimes cause vascular lumen obstruction. Magnetic resonance imaging (MRI) is recommended for the primary soft tissue disease, it presents as heterogeneous mass close, particularly following the administration of contrast agents, and may include calcifications, spontaneous hemorrhages, peripheral edema, or bone erosions [8].

EHE is diagnosed based on histological, immunohistochemical, and molecular features [5]. Histologically, the tumor is composed of nests and cords of epithelioid endothelial cells, occasionally admixed with spindle cells. Cytological features of EHE include cells with moderate to abundant cytoplasm and pleomorphic nuclei with frequent intranuclear pseudoinclusions [5]. Approximately 10% of cases demonstrate marked nuclear atypia with prominent nucleoli, areas of necrosis, and elevated mitotic activity (>2 mitoses per 10 high-power fields); these features are associated with more aggressive clinical behavior, which was the case in our patient and may explain the recurrence despite an R0 resection at the first operation [1]. Immunohistochemically, EHE typically expresses vascular markers such as Fli-1, CD31, ERG, and CD34 [5].

The treatment of choice for confirmed unifocal epithelioid hemangioendothelioma (EHE) is complete surgical excision. Resection should be performed in specialized referral centers with expertise in sarcoma surgery [7]. The tumor must be resected en bloc, including the biopsy tract, with microscopic negative (R0) margins, achieving a cure rate of approximately 70-80%. The risk of local recurrence remains in the range of 10-15%. The tumor is considered relatively radiosensitive, although the role of radiotherapy (RT) is not well established. Adjuvant RT is recommended in selected cases, particularly when margins are close or positive and the risk of local recurrence is significant [1], which was indicated in our case. Systemic treatment is not routinely indicated for localized disease. In contrast, in metastatic settings with unequivocal progression, symptom aggravation, or organ impairment, systemic therapy may be considered, although no established standard of care currently exists [1].

In conclusion, chest wall epithelioid hemangioendothelioma represents a rare entity with unpredictable behavior. Complete surgical resection remains the cornerstone of treatment when feasible, even in the setting

of local recurrence, which highlights the crucial role of long-term surveillance.

Declaration of conflicting interests

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Authors' contribution

I.A.: Conceptalization, data curation, investigation, software, project administration, visualization, writing - original draft, writing - review & editing, H.H.: Conceptualization, formal analysis, methodology, project administration, visualization, writing - original draft, writing - review & editing, M.L.: Funding acquisition, resources, supervision, validation, writing - review & editing, Y.O.: Funding acquisition, resources, supervision, validation, writing - review & editing, M.S.: Funding acquisition, supervision, validation, writing - review & editing.

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Case Report

Cough-induced spontaneous intercostal lung herniation: a case report

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ABSTRACT

Spontaneous lung herniation is a rare clinical entity caused by protrusion of lung tissue through a weakened chest wall in the absence of trauma. Due to its nonspecific presentation, diagnosis may be delayed or overlooked, particularly on initial imaging. We report the case of a 71-year-old obese male who presented with acute-onset right-sided chest pain following a severe coughing episode. Initial thoracic computed tomography revealed no significant pathology, and the patient was discharged with conservative treatment. Due to progression of symptoms, repeat imaging demonstrated a prominent lung herniation through the right 8th intercostal space, accompanied by minimal pleural effusion. Magnetic resonance imaging revealed a 9x1 cm intercostal defect. Surgical repair was performed via thoracotomy with reduction of the herniated lung tissue, approximation of the ribs, and reconstruction of the defect using a nonabsorbable polypropylene mesh. The postoperative course was uneventful, and the patient was discharged on postoperative day seven. This case highlights the diagnostic challenge of false-negative initial computed tomography and emphasizes the importance of repeat advanced imaging in patients with progressive symptoms. Spontaneous lung herniation should be considered in obese male patients presenting with localized chest pain and chest wall swelling following severe coughing. Initial imaging may fail to detect the condition, and repeat evaluation with computed tomography or magnetic resonance imaging is crucial in cases of clinical progression. Surgical repair is a safe and effective treatment option for symptomatic patients or those with large defects, leading to favorable outcomes and low recurrence rates.

Keywords: spontaneous lung herniation, intercostal, cough-induced chest wall defect

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Introduction

Lung herniation is a clinical condition characterized by the protrusion of lung tissue beyond the thoracic cavity due to an anatomopathological weakness of the chest wall and may develop secondary to a wide range of etiologies [1,2]. Spontaneous lung herniation represents a rarer subgroup that occurs in the absence of any traumatic cause. In this report, we aim to present and discuss a case of spontaneous intercostal lung herniation-an entity rarely described in the literature and with an imprecisely defined incidence-with particular emphasis on its etiology, diagnostic approach, and management strategies in the context of current literature. This case is particularly noteworthy due to the initial false-negative computed tomography findings, the delayed radiological diagnosis following symptom progression, and the presence of morbid obesity and severe cough as the primary predisposing factors in the absence of trauma, chronic lung disease, or corticosteroid use.

Case Report

A 71-year-old male patient with a long-standing history of cough presented to the emergency department 10 days earlier with right inferolateral hemithoracic pain that was exacerbated by coughing and movement. Thoracic computed tomography (CT) performed at the initial presentation revealed no remarkable pathology; therefore, the patient was discharged with nonsteroidal anti-inflammatory drug therapy (Figure 1). Due to progression of his respiratory-related symptoms, the patient re-presented 10 days later and was subsequently admitted for further diagnostic evaluation. The decision to pursue repeat imaging was prompted by worsening localized chest pain, newly apparent chest wall tenderness and ecchymosis on physical examination, and the emergence of subtle radiographic changes suggestive of pleural involvement.

The patient had no history of trauma, known comorbidities, prior surgical interventions, or use of tobacco or corticosteroids. His body mass index was calculated as 41.8 kg/m^2. He reported that the chest pain began after a severe coughing episode and was described as a "stabbing" sensation localized to the right hemithorax. The pain was exacerbated by maneuvers that increased intrathoracic pressure, such as coughing, sneezing, and deep inspiration.

On admission, the patient's vital signs were as follows: oxygen saturation (SpO_2) 97%, heart rate 81 beats/min, and blood pressure 135/75 mmHg. Physical examination revealed ecchymosis and marked tenderness on palpation over an approximately 4-cm area at the level of the 8th intercostal space on the lateral aspect of the right hemithorax. Widening of the intercostal space was also noted in the same region. Examination of the other systems was unremarkable.

Laboratory investigations revealed no abnormalities. Following the detection of blunting of the right costophrenic angle on posteroanterior chest radiography, thoracic CT was performed, demonstrating minimal pleural effusion in the right hemithorax and a prominent lung herniation at the level of the right 8th intercostal space (Figure 2). To better delineate the extent of the herniation, thoracic magnetic resonance imaging (MRI) was obtained, revealing a 9x1 cm intercostal defect (Figure 3). The initial CT images were retrospectively re-evaluated after the diagnosis; however, no definite signs of lung herniation were identified. After multidisciplinary discussion at a joint Pulmonology and Thoracic Surgery board meeting, surgical intervention was recommended.

Following completion of the preoperative evaluations, the patient was taken to the operating room. Exploration was initiated through a 4th intercostal space port for videothoracoscopic assessment, while the definitive thoracotomy incision was made at the level of the 8th intercostal space directly overlying the defect to achieve optimal exposure and secure mesh placement. The localization of the defect directly influenced the choice of thoracotomy site. Intraoperative videothoracoscopic assessment revealed that the defect measured approximately 25×1 cm, the discrepancy between measurements was attributed to the oblique course of the defect and its extension into the subcutaneous tissues (Figure 4). The discrepancy between radiological and intraoperative measurements was attributed to the fact that MRI measurements were obtained in the axial plane, whereas intraoperative assessment revealed the total oblique length of the defect, including its extension into the subcutaneous tissues. A skin incision of approximately 20 cm was made at the level of the 8th intercostal space. After reduction of the herniated lung tissue back into the thoracic cavity, the ribs were approximated, and the defect was reconstructed using a nonabsorbable polypropylene mesh (Figure 5). An open thoracotomy was preferred over a minimally invasive approach due to the considerable length of the defect, its oblique extension into the chest wall, the need for stable rib approximation, and secure placement of a prosthetic mesh.

The postoperative course was uneventful, and the patient was discharged on postoperative day 7. Informed consent was obtained from the patient for publication of this case report and accompanying images.

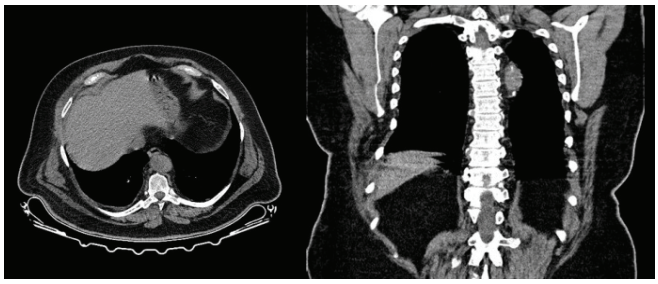

Figure 1. Initial presentation CT scan.

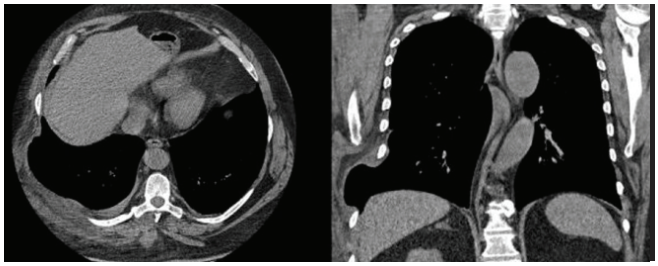

Figure 2. CT scan at the second presentation demonstrating minimal pleural effusion in the right hemithorax and a prominent lung herniation at the level of the right 8th intercostal space.

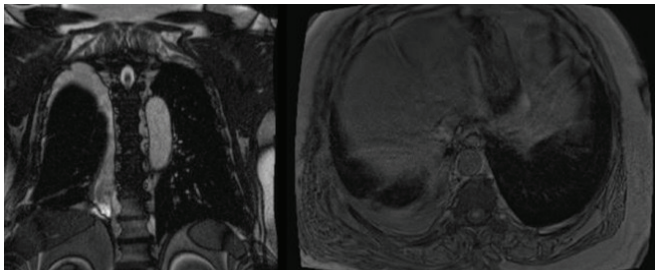

Figure 3. Thoracic magnetic resonance imaging revealing a 9x1 cm intercostal defect.

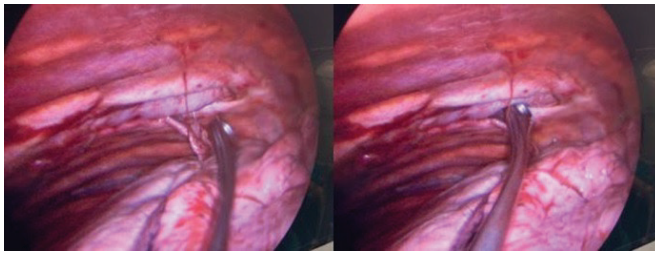

Figure 4. Thoracoscopic view of the hernia.

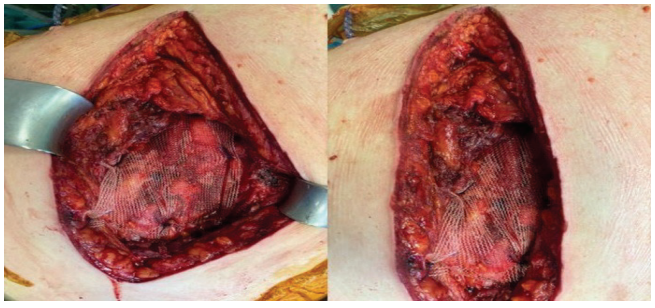

Figure 5. View after polypropylene mesh placement.

Discussion

Spontaneous lung herniation is a rare clinical entity that may be underestimated or overlooked during the diagnostic process. According to etiological classification, approximately 29% of lung herniations are spontaneous, as observed in our case, whereas the majority (52%) are post-traumatic in origin [2].

Although the exact etiology of spontaneous lung herniation has not been fully elucidated, it is widely believed to result from a combination of underlying medical conditions that weaken the chest wall and episodes of increased intrathoracic pressure [1,2]. In patients with chronic obstructive pulmonary disease or emphysema, weakening of the chest wall musculature together with chronically elevated intrathoracic pressure due to persistent coughing may predispose to herniation. The proposed pathogenic mechanism involves acute or chronic increases in intrathoracic pressure during activities such as severe coughing, sneezing, heavy lifting, or straining [1]. Obesity, male sex, and tobacco use are also recognized as relevant risk factors for spontaneous lung herniation. Additionally, corticosteroid use is considered a significant risk factor, as it may contribute to weakening of the thoracic wall [3]. In the present case, the patient's elevated body mass index and history of a severe coughing episode were considered potential predisposing factors.

From a mechanical perspective, lung herniations most commonly occur in the anterior thoracic wall, particularly between the 8th and 9th ribs, where muscular support is relatively weak [4]. However, intercostal herniation has also been reported in the parasternal region due to insufficient muscular coverage in this area [5]. Congenitally weak areas of the chest wall are typically described as the anterior region near the sternum, the medial region adjacent to the costochondral junction, and the posterior region near the vertebral bodies, where the intercostal musculature is composed of a single muscle layer [1,2]. In cases involving spontaneous, non-traumatic rib fractures induced by forceful coughing, the typical fracture locations are most commonly reported in the lateral or anterior portions of the ribs [2].

The clinical manifestations of spontaneous lung herniation are generally nonspecific and may include chest pain, dyspnea, and cough. On physical examination, the main findings may consist of localized swelling (bulging) and ecchymosis over the affected area. The bulge

often becomes more prominent during physical exertion or coughing, particularly with the Valsalva maneuver. Chest pain is most likely attributable to irritation of the parietal pleura. In some cases, unexplained elevations in non-cardiogenic creatine kinase (CK) levels accompanying chest pain have been reported, which may reflect injury to the thoracic musculature [1,2,6].

The diagnosis is established through a combination of physical examination and medical imaging. It may be challenging because the symptoms are nonspecific and can mimic other conditions such as pulmonary embolism, pneumonia, malignancies, lipomas, and subcutaneous emphysema [1,2,7]. On physical examination, a chest wall bulge that becomes more apparent with coughing and localized tenderness on palpation are important diagnostic clues. However, findings may not always be evident, and lung protrusion may only be palpable during the Valsalva maneuver [8].

Posteroanterior chest radiography has limited sensitivity, although findings such as a "lung beyond the rib" or a "lucent lung" sign may occasionally be observed [4]. High-resolution thoracic computed tomography and, when necessary, magnetic resonance imaging are considered the gold standard for evaluating the size of the defect, its relationship with adjacent structures, and potential complications [7]. In our case, no herniation was detected on the initial CT scan; however, repeat CT and MRI performed after symptom progression revealed a 9-cm defect. This underscores the importance of meticulous image interpretation, as also emphasized by Bresler et al. [8].

The therapeutic approach is determined by the patient's symptoms, the size of the herniation, and the presence of associated complications. Although conservative management with observation and cough-suppressive therapy may be appropriate for small, asymptomatic cases, surgical repair is considered the standard of care for symptomatic or complicated herniations [2,4]. In the management algorithm proposed by Ugolini et al., the presence of pleural effusion is identified as an indication for surgical intervention [9].

In our patient, surgical repair via thoracotomy using a nonabsorbable polypropylene mesh was performed due to severe pain, the large size of the defect, and the potential risk of compression of intrathoracic organs; no postoperative complications were observed. Leivaditis et al. emphasized the importance of postoperative rehabilitation following successful surgical repair in a case of spontaneous lung herniation secondary to ventral rib dislocation [2]. Similarly, early mobilization and respiratory physiotherapy were implemented in our patient during the postoperative period.

In conclusion, spontaneous lung herniation should be considered in obese male patients presenting with nonspecific symptoms such as acute-onset localized chest pain and chest wall swelling following severe coughing. Clinicians should be aware that herniation may be overlooked on initial imaging studies, and detailed reevaluation with computed tomography or magnetic resonance imaging is warranted in cases of clinical progression. Surgical repair represents a safe and effective treatment option for symptomatic patients, those with large defects, or cases accompanied by pleural effusion. With early diagnosis and appropriate surgical management, long-term outcomes are favorable and recurrence rates are low. This report highlights the potential for spontaneous intercostal lung herniation to be overlooked on initial imaging and underscores the importance of maintaining a high index of suspicion and performing repeat advanced imaging in patients with progressive symptoms, even in the absence of traditional risk factors. The primary learning point of this case is that spontaneous lung herniation may be missed on initial CT imaging, and repeat advanced imaging should be strongly considered in clinically progressive patients.

Declaration of conflicting interests

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Authors' contribution

All authors contributed to the conception, data collection, writing, and final approval of the manuscript.

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Case Report

Asymptomatic discovery of a rare congenital vascular anomaly in a 33-year-old male: a case of Pulmonary Sling Syndrome

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ABSTRACT

Pulmonary sling (PS) syndrome is a rare congenital vascular anomaly characterized by the anomalous origin of the left pulmonary artery (LPA) from the right pulmonary artery (RPA). While it typically presents in infancy with severe respiratory distress, its diagnosis in adulthood is exceedingly rare and often incidental. A 33-year-old male presented with acute, severe right-sided pleuritic chest pain. Initial suspicion was pulmonary embolism (PE); however, laboratory markers (D-dimer, troponin) were normal. Pulmonary CT angiography ruled out PE but revealed an incidental pulmonary sling, where the LPA originated from the RPA and coursed between the trachea and esophagus. A 10 mm pleural effusion was noted. The patient was diagnosed with idiopathic pleurisy, treated with anti-inflammatory agents, and symptoms resolved. This case underscores the possibility of PS remaining asymptomatic until the fourth decade of life. Clinicians should be aware of such vascular variants, as they may have significant implications for airway management and thoracic surgery.

Keywords: pulmonary artery, vascular ring, incidental findings

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Introduction

Pulmonary sling syndrome, first described by Glaevecke and Doehle in 1897, is a unique form of vascular ring [1]. Unlike other vascular rings that encircle both the trachea and esophagus, the pulmonary sling specifically involves the anomalous origin of the left pulmonary artery (LPA) from the posterior aspect of the right pulmonary artery (RPA). As the LPA courses toward the left hilum, it passes between the distal trachea and the anterior esophagus, creating a "sling" or "lasso" effect that can lead to mechanical compression of these structures [2].

The incidence of this anomaly is estimated to be approximately 1 in 17,000 live births. Due to the high frequency of associated tracheobronchial tree malformations, such as complete tracheal rings (O-shaped rings) and tracheal stenosis, most patients present with life-threatening respiratory distress, stridor, or recurrent pneumonia shortly after birth [3]. However, in a very small subset of patients where the airway is structurally robust or the compression is mild, the condition may remain clinically silent. The literature regarding adult-onset or incidentally discovered pulmonary sling is sparse, making each documented adult case vital for understanding the natural history of this congenital malformation [4].

Case Report

A 33-year-old male with no prior significant medical history presented to the emergency department with acute, stabbing right-sided chest pain. The pain was exacerbated by deep inspiration and physical movement, typical of pleuritic irritation. On physical examination, the patient was hemodynamically stable (BP: 120/80 mmHg, HR: 86 bpm, SpO2: 97%). Lung auscultation revealed equal breath sounds without rales or rhonchi.

Laboratory workup showed a normal D-dimer level and negative cardiac troponins. C-reactive protein (CRP) was initially 4.1 mg/L. Despite the low probability based on the Wells criteria and normal D-dimer, the severity and persistence of the pain necessitated a pulmonary CT angiography (CTA) to definitively rule out pulmonary embolism (PE).

The CTA excluded PE but revealed an incidental pulmonary sling. The LPA was observed arising from the RPA and coursing posteriorly between the trachea and esophagus, just above the carina, toward the left lung (Figures 1-3). A concurrent 10 mm right-sided pleural effusion was identified. The patient was monitored; on the second day, his CRP rose to 10.5 mg/L, supporting the diagnosis of idiopathic pleurisy. Treatment with non-steroidal anti-inflammatory drugs (NSAIDs) was initiated. At the one-week follow-up, the CRP had decreased to 4.9 mg/L, and the patient's symptoms had completely resolved. The pulmonary sling was documented as an incidental, asymptomatic finding.

Following the initial identification of the anomaly on CT, a cardiovascular surgery consultation was performed to assess the potential for surgical intervention. A comprehensive evaluation, including axial MIP and 3D reconstructions, revealed no evidence of critical hemodynamic compromise or hemodynamically significant tracheobronchial stenosis. Consequently, in the absence of symptoms, a conservative strategy involving regular clinical and radiological monitoring was adopted by the multidisciplinary team. Written informed consent for publication was obtained from the patient.

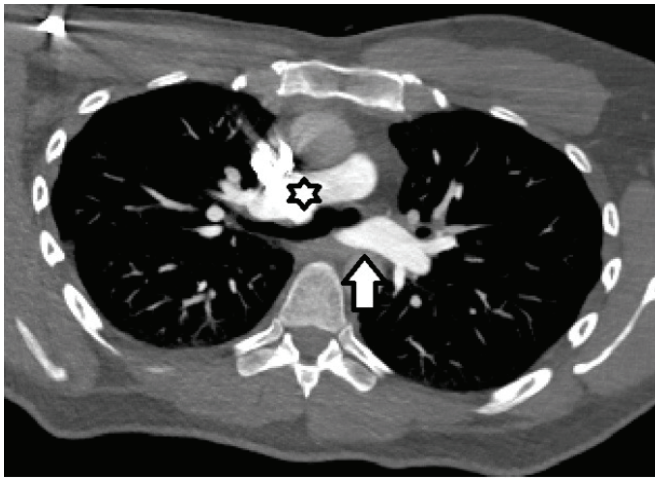

Figure 1. Axial CT angiography image demonstrating the left pulmonary artery (LPA) originating from the right pulmonary artery (RPA) and its course posterior to the trachea (asterisk: RPD, arrow: LPA).

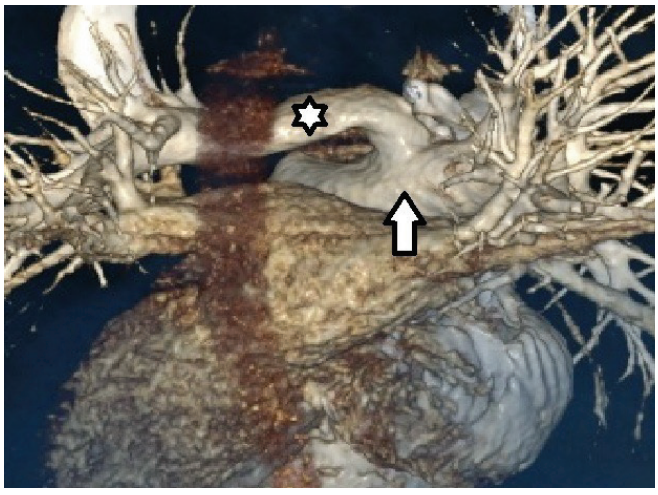

Figure 2. Posterior view of the three-dimensional volume-rendered CT reconstruction. The image demonstrates the heart, left atrium (black arrowhead), and pulmonary veins (white arrowheads). The right main pulmonary artery is visualized (black arrow), along with the anomalous left pulmonary artery (asterisk), which originates from the right pulmonary artery and follows a retro-cardiac course. The esophagus is observed as a columnar structure positioned anterior to the anomalous left pulmonary artery (white arrows).

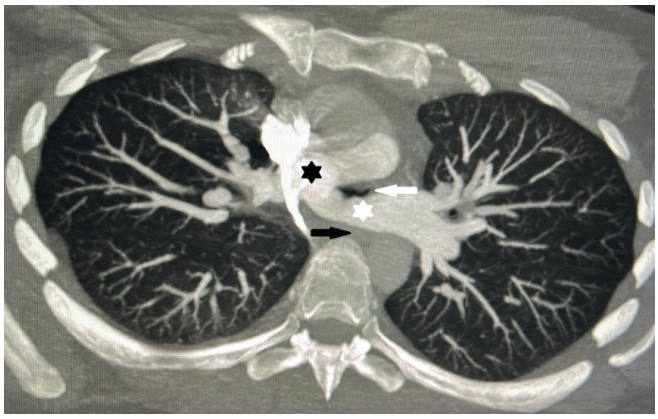

Figure 3. Axial Maximum Intensity Projection (MIP) image showing the anomalous left pulmonary artery (white asterisk) arising from the right pulmonary artery (black asterisk) and passing between the trachea (white arrow) and the esophagus (black arrow), confirming the diagnosis of pulmonary artery sling syndrome.

Discussion

The embryological development of the pulmonary arteries is a complex process occurring between the 4th and 7th weeks of gestation. Normally, the pulmonary arteries develop from the proximal part of the sixth branchial arches. A pulmonary sling occurs when the left sixth arch fails to develop correctly, and a persistent postbranchial vessel (capillary plexus) from the right side connects to the left lung bud [5]. This abnormal connection forces the developing left pulmonary artery to originate from the right pulmonary artery, crossing the midline to reach the left lung.

Pulmonary slings are classified into two main types based on the Landing and Wells system [6]:

Type 1 (Classic): The LPA arises from the RPA, and the bifurcation of the trachea (carina) is at the normal level (T4-T5). The sling compresses the right main bronchus and the lower trachea.

Type 2 (Complex): This is more common and involves an abnormally low carina (T6 level) and "T-shaped" bronchi. This type is frequently associated with "bridging bronchus" and long-segment tracheal stenosis due to complete O-shaped rings.

Our case likely represents a Type 1 variant, given the absence of chronic respiratory symptoms and the normal carinal position observed on imaging.

While the classic presentation involves 'the ring-sling complex' in neonates, adult cases are often discovered incidentally during routine lung screenings or during the evaluation of unrelated clinical symptoms [7,8]. The lack of symptoms in adults is generally attributed to the absence of intrinsic tracheal abnormalities. In our patient, the discovery was purely incidental during an evaluation for chest pain. This highlights that while the "sling" is anatomically present, it may not always be physiologically obstructive.

In symptomatic infants, the gold standard of treatment is surgical reimplantaton. This involves detaching the LPA from the RPA and anastomosing it to the main pulmonary trunk, anterior to the trachea [9]. If tracheal stenosis is present, simultaneous slide tracheoplasty is performed. In contrast, for asymptomatic adults, the management is controversial. Most experts recommend a conservative "wait and watch" approach, as the risks of major thoracic surgery usually outweigh the benefits in the absence of airway compromise [10]. However, its presence should be noted, as it can complicate endotracheal intubation, transbronchial biopsy, or future mediastinal surgeries [11].

Although PAS is classically associated with severe respiratory distress in infancy, this case demonstrates that the anomaly can remain clinically silent until the fourth decade of life. We hypothesize that the lack of intrinsic tracheal abnormalities and a relatively preserved airway diameter provided a compensatory mechanism that prevented early clinical manifestation.

In conclusion, pulmonary sling syndrome in adults is a rare but important diagnostic entity. This case demonstrates that the anomaly can remain silent for over three decades. CT angiography remains the definitive tool for diagnosis; however, its incidental finding should prompt a comprehensive evaluation of the airway using both advanced radiological imaging and, when clinically indicated, bronchoscopy to exclude underlying tracheobronchial malformations

Declaration of conflicting interests

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Authors' contribution

All authors contributed to the conception, data collection, writing, and final approval of the manuscript.

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Case Report

Coexistence of achalasia cardia and Hirschsprung's disease in a child: a rare case report

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ABSTRACT

Achalasia cardia and Hirschsprung's disease are distinct pediatric gastrointestinal motility disorders that rarely manifest in a single patient. While both involve a failure of muscular relaxation within the enteric nervous system, they typically present with disparate clinical features. We report an exceedingly rare case of a 3-year-old girl who initially presented with classic signs of achalasia cardia, including progressive dysphagia and regurgitation. Following a successful Heller's cardiomyotomy, the patient's esophageal symptoms improved; however, her recovery was hampered by emerging constipation and significant abdominal distension. Initially attributed to protein-energy malnutrition, these lower gastrointestinal symptoms prompted further investigation, which ultimately revealed a concurrent diagnosis of Hirschsprung's disease. The patient subsequently underwent a posterior anal myectomy, which led to the complete resolution of her symptoms and a full recovery. This case underscores the diagnostic complexity of dual motility pathologies. It emphasizes that persistent or evolving symptoms following a primary surgical intervention should prompt a high index of suspicion for additional underlying conditions, requiring a comprehensive and multidisciplinary diagnostic approach to ensure favorable pediatric outcomes.

Keywords: achalasia cardia, Hirschsprung's disease, pediatric GI disorders, Heller's cardiomyotomy, anal myectomy

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Introduction

Achalasia cardia is an uncommon esophageal motility disorder characterized by degeneration of neurons within the myenteric plexus, leading to impaired relaxation of the lower esophageal sphincter and uncoordinated esophageal peristalsis [1]. Though more common in adults, it can occur in children and is often misdiagnosed due to overlapping symptoms with other gastrointestinal disorders [2]. Hirschsprung's disease is a congenital enteric neuropathy in which ganglion cells are absent in segments of the distal intestine, resulting in impaired bowel motility and functional intestinal obstruction [3].

Although both conditions involve neuronal dysfunction of the digestive tract, they differ in pathophysiology and clinical presentation. The simultaneous occurrence of achalasia and Hirschsprung's disease is exceedingly rare and poses a diagnostic challenge [4,5]. We report such a case to highlight the importance of thorough evaluation in pediatric patients' persistent or evolving gastrointestinal symptoms. This case adds to the limited global literature and emphasizes the importance of considering coexisting enteric neuropathies in persistent pediatric GI dysfunction

Case Report

A 3-year-old female presented with a six-month history of progressive dysphagia to both solids and liquids, associated with regurgitation of undigested food and failure to thrive. On presentation, she appeared chronically ill with evidence of poor nutritional status, and anthropometric assessment was consistent with failure to thrive for age. Laboratory investigations were within acceptable limits for surgery.

A contrast esophagogram demonstrated a markedly dilated esophagus with smooth tapering ("birdbeak" appearance) at the gastroesophageal junction and delayed esophageal emptying, findings highly suggestive of achalasia cardia. Based on the characteristic clinical presentation and radiologic features, a working diagnosis of achalasia was made. Esophageal manometry, which remains the diagnostic gold standard for confirming achalasia, was not available in our center at the time of evaluation and therefore could not be performed.

This limitation is acknowledged; however, in resource-limited settings, the combination of typical symptoms and classical radiologic findings on contrast esophagography is often relied upon to establish the diagnosis. The patient was optimized nutritionally and medically before undergoing a modified open Heller's cardiomyotomy, with initial postoperative relief of symptoms. (Figure 1).

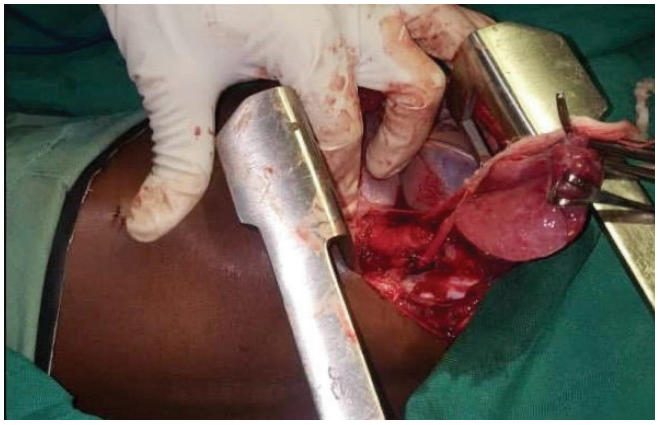

Figure 1. Open Modified Heller's cardiomyotomy via thoracotomy.

However, within a few weeks, she developed progressive constipation and abdominal distension. These symptoms were initially misdiagnosed as protein–energy malnutrition and managed conservatively.

As the symptoms persisted, further evaluation with a contrast enema demonstrated a narrowed distal rectal segment with proximal colonic dilatation, suggestive of a transition zone. A provisional diagnosis of Hirschsprung's disease was made.

Six months after the cardiomyotomy, the patient underwent a diverting colostomy with procurement of a full-thickness rectal biopsy taken approximately 2 cm above the dentate line. Histopathological examination using hematoxylin and eosin staining demonstrated absence of ganglion cells within the submucosal and myenteric plexuses, with associated hypertrophy of submucosal nerve fibers, confirming aganglionosis consistent with Hirschsprung's disease.

A posterior anal myectomy was performed several months later. One year after the initial presentation, the patient subsequently underwent colostomy takedown following satisfactory postoperative recovery and improvement in bowel function.

Following the staged surgical procedures, the patient achieved complete resolution of her gastrointesti-

nal symptoms. Six months after definitive surgery, she demonstrated regular bowel habits, satisfactory weight gain, and evidence of catch-up growth. Continued follow-up confirmed sustained clinical improvement and a satisfactory quality of life. Informed consent was obtained from the patient's parents for publication of this case report and accompanying images.

Discussion

Achalasia and Hirschsprung's disease are rare but significant pediatric digestive tract disorders with overlapping clinical features yet distinct pathophysiological mechanisms. Achalasia cardia is characterized by failure of the lower esophageal sphincter (LES) to relax and, absence of esophageal peristalsis, primarily due to loss of inhibitory ganglion cells in the myenteric (Auerbach's) plexus [6]. Hirschsprung's disease similarly results from a lack of ganglion cells, but in the distal colon and rectum, leading to chronic functional intestinal obstruction [3].

While achalasia is commonly recognized in adults, pediatric achalasia is far less common and often underdiagnosed or misdiagnosed [7]. Pediatric achalasia accounts for less than 5% of all achalasia cases [8]. The annual incidence in children is estimated at 0.11 per 100,000 children, with a peak presentation age between 8 and 12 years, though cases in younger children and infants have been reported [9].

Achalasia may occur as part of the rare AAA syndrome, also referred to as Allgrove syndrome, which is characterized by the triad of alacrima, achalasia, and adrenal insufficiency (Addison disease). This condition results from mutations in the AAAS gene located on chromosome 12q13, which encodes the ALADIN protein involved in nuclear pore complex function. These manifestations are incorporated into the Eckardt scoring system, a clinical tool widely used to assess symptom severity and treatment outcomes in patients with achalasia [10].

In young children, the clinical presentation of achalasia is often nonspecific and may mimic other conditions such as gastroesophageal reflux disease (GERD), esophageal stricture, or feeding aversion disorders. Affected patients commonly present with progressive dysphagia, regurgitation of undigested food, recurrent vomiting, chronic cough, weight loss, and failure to thrive. Retrosternal chest discomfort may also occur in older children and adults. Because these symptoms develop gradually and overlap with more common pediatric gastrointestinal conditions, the diagnosis is frequently delayed.

The diagnosis is typically established using a combination of barium swallow (which reveals the classic "bird-beak" sign), esophageal manometry (demonstrating incomplete LES relaxation and aperistalsis), and upper gastrointestinal endoscopy to rule out structural causes. In many low-resource settings, as in our case, diagnosis is made using barium swallow studies due to limited access to manometry and endoscopic equipment [11].

Treatment options for achalasia in children include Heller's cardiomyotomy (open or laparoscopic), pneumatic balloon dilation, and, more recently, peroral endoscopic myotomy (POEM), with Heller's myotomy remaining the standard surgical approach in resource-limited settings. The long-term outcomes in pediatric patients undergoing

Heller's myotomy is generally favorable, with improvement in dysphagia and weight gain reported in up to 90% of cases [12].

Hirschsprung's disease, in contrast, is a congenital condition typically diagnosed in the neonatal period or early infancy [13]. However, in ultra-short segment or atypical cases, diagnosis may be delayed until later in childhood [14]. Common symptoms include delayed passage of meconium, chronic constipation, abdominal distension, and failure to thrive. Diagnosis is confirmed by rectal biopsy demonstrating absence of ganglion cells. A contrast enema revealing a transition zone between aganglionic and ganglionic bowel segments supports the diagnosis [7].

The simultaneous presence of achalasia and Hirschsprung's disease has been reported only rarely in the medical literature [4]. Only a handful of cases have been reported in the literature [5]. The shared involvement of the enteric nervous system in both conditions has prompted speculation about a common embryological or genetic origin. Some researchers have postulated that both disorders may fall within the spectrum of neurocristopathies diseases arising from aberrant development of neural crest cells. Mutations in genes such as RET, EDNRB, and SOX10, which are implicated in the develop-

ment of the enteric nervous system, have been associated with Hirschsprung's disease and may also play a role in esophageal motility disorders [14,15]. However, definitive genetic or mechanistic links remain unclear due to the rarity of co-presentation and limited data.

Our case exemplifies the diagnostic difficulty in identifying dual pathologies, particularly when the second condition presents shortly after surgical correction of the first. In this case, postoperative constipation and abdominal distension were initially attributed to malnutrition and reduced motility following Heller's myotomy. The delay in diagnosing Hirschsprung's disease could have been avoided with earlier consideration of dual pathology, especially in the presence of hallmark signs such as persistent constipation and a distended abdomen. This diagnostic oversight has been reported in other pediatric cases, underscoring the need for vigilance [16,17].

Surgical management of Hirschsprung's disease typically involves a pull-through procedure (e.g., Soave or Duhamel), although limited distal disease may be treated with posterior anal myectomy, as was done in this patient. This approach also provides tissue for histological confirmation of aganglionosis.

The favorable outcome following staged surgical management underscores the importance of maintaining a high index of suspicion for dual pathology in children with persistent or unexplained symptoms despite initial treatment. Timely diagnostic reassessment can significantly improve outcomes. Awareness of such rare coexisting conditions is essential to avoid diagnostic delays and ensure appropriate surgical intervention.

In conclusion, this report emphasizes the importance of considering coexisting digestive tract pathologies in pediatric patients with persistent or atypical symptoms. Early diagnosis and multidisciplinary management are key to optimizing outcomes. The rare combination of achalasia and Hirschsprung's disease should be considered in complex pediatric gastrointestinal presentations.

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Authors' contribution

All authors contributed to the conception, data collection, writing, and final approval of the manuscript.

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Images in Thoracic Surgery

Calcified fibrothorax as a sequela of long-standing untreated empyema

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Chronic empyema thoracis represents the end stage of pleural infection when early drainage and antimicrobial therapy are inadequate or absent. Progression of untreated empyea resulted in lung entrapment and fibrothorax. In rare, long-standing untreated cases, this pleural peel may undergo extensive dystrophic calcification, forming a rigid shell around the lung and causing severe restriction, chronic chest pain, and functional disability [1,2]. Computed tomography is the imaging modality of choice for chronic empyema and fibrothorax. Typical findings include circumferential pleural thickening, dense pleural calcification, reduction in hemithoracic volume, and compression of the underlying lung [3]. Clinically, patients develop restrictive ventilatory impairment, dyspnea, and reduced quality of life due to mechanical limitation of lung expansion. Chronic chest pain further contributes to morbidity.

Once calcified fibrothorax is established, surgery becomes the definitive treatment. Open thoracotomy with pleural decortication remains the standard approach in heavily calcified disease, allowing complete removal of the fibrous rind and restoration of lung expansion [4,5]. This case highlights the natural history and classic imaging appearance of chronic calcified empyema with fibrothorax. It emphasizes the critical importance of early diagnosis and timely management of pleural infections to prevent progression to this rare but disabling late sequela. Informed written consent has been taken from the participant before enrollment. Anonymizing data maintained patient confidentiality.

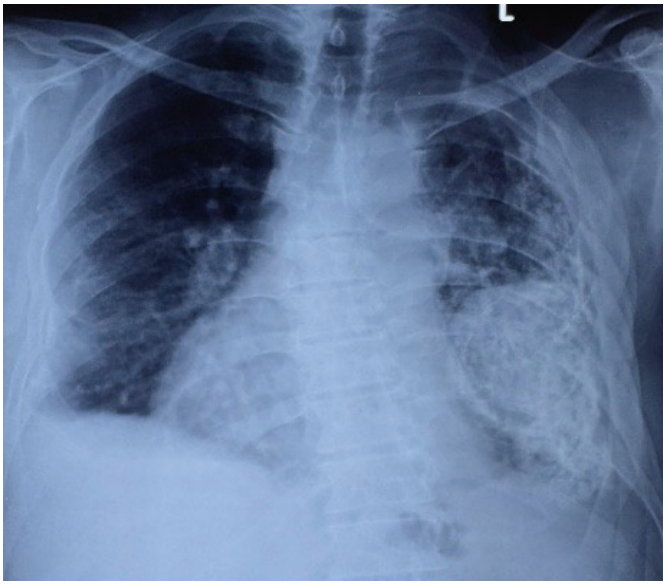

Figure 1. PA chest X-ray showing a large, dense, left-sided calcified mass occupying the hemithorax with associated volume loss, consistent with pleural pathology.

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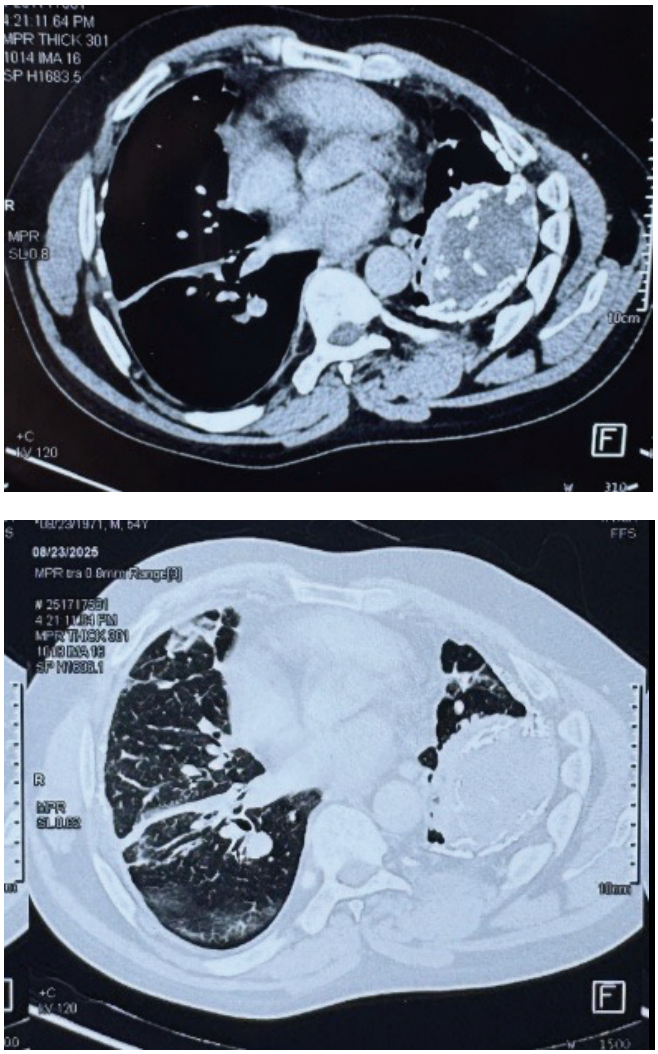

Figure 2. Axial contrast-enhanced CT scan demonstrating long-standing untreated empyema thoracis with a markedly thickened and calcified pleural peel adherent to the left lung, causing fibrothorax.

Keywords: empyema thoracis, fibrothorax, thoracotomy, computed tomography

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ZS,MSN; design, review, editing and co-writing the paper equally.

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Authors of secondary analyses using shared data must attest that their use was in accordance with the terms (if any) agreed to upon their receipt. They must also reference the source of the data using its unique, persistent identifier to provide appropriate credit to those who generated it and allow searching for the studies it has supported. Authors of secondary analyses must explain completely how theirs differ from previous analyses. In addition, those who generate and then share clinical trial data sets deserve substantial credit for their efforts. Those using data collected by others should seek collaboration with those who collected the data. As collaboration will not always be possible, practical, or desired, the efforts of those who generated the data must be recognized.

Statistical Knowledge

The statistical method used should be reported in a way that a reader whoever could reach the original data could understand the results. The terms used, abbreviations, symbols, the pc programme used and the statistical method should all be defined.

When reporting the results, especially when giving means and percentages, two digits should be given after the comma (112.20 or 112.21 instead of 112.2). P, t, Z values are exceptional and three digits should be given after the comma ($p = 0{,}001$, instead of $p < 0{,}05$).

Briefly, except whole numbers, two digits after the comma should be given, but for statistical values like p,t,z,F,Chi-square, three digits after the comma should be given. When presenting p values, the exact p value together with the test statistics should be given, except for the case when this value is smaller than one percent or one per thousand (this time $p < 0.01$ or $p < 0.001$, respectively should be given).

Preparation of Manuscript

Cover Letter

The Current Thoracic Surgery requires authors to disclose in the "cover letter" any commercial association (eg, employment, direct payments, stock holdings, retainers, consultantship, patent licensing arrangements, or honoraria) that might pose a conflict of interest issue concerning the manuscript. All funding sources supporting the work should be acknowledged in a footnote. Also authors should mention that none of the material in the manuscript has been published previously, and that none of this material is currently under consideration for publication elsewhere. This includes symposia, transactions, books, articles published by invitation, and preliminary publications of any kind except an abstract of 400 words or fewer.

Style and Format

Manuscripts should be double-spaced with 3-cm margins on all sides of the page, in Times New Roman font. Every page of the manuscript, including the title page, references, tables, etc., should be numbered. All copies of the manuscript should also have line numbers starting with 1 on each consecutive page.

Symbols, Units and Abbreviations

In general, the journal follows the conventions of Scientific Style and Format, The CSE Manual for Authors, Editors, and Publishers, Council of Science Editors, Reston, VA, USA (7th ed.). If symbols such as ×, μ, η, or ν are used, they should be added using the Symbols menu of Word. Degree symbols (°) must be used from the Symbol menu, not superscripted letter o or number 0. Multiplication symbols must be used (×), not the letter x. Spaces must be inserted between numbers and units (e.g., 3 kg) and between numbers and mathematical symbols (+, –, ×, =, <, >), but not between numbers and percent symbols (e.g., 45%). Please use SI units. All abbreviations and acronyms should be defined at first mention. Latin terms such as et al., in vitro, or in situ should not be italicized.

Manuscript Content

Research articles should be divided into the following sections. Principal sections should be Introduction, Materials and Methods, Results, Discussion, Acknowledgements and References sections. Please see below for information about other types of manuscripts.

Title and Contact Information

The first page should contain the full title in sentence case, the full names (last names fully capitalized) and affiliations (in English) of all authors (University, Faculty, Department, City, Country), and the contact address and e-mail for the clearly identified corresponding author.

Abstract

An informative abstract of not more than 250 words must accompany each manuscript. The abstract must be structured to include the study's background, materials and methods, results, and conclusions and key words under 5 separate headings. Abstracts of review articles should be a brief overview of the main points from the review.

Keywords

Please provide at least 3 key words or phrases to enable retrieval and indexing. Acronyms should be avoided.

Always try to use terms from the Medical Subjects Headings (MeSH) list from PubMed https://www.ncbi.nlm.nih.gov/pubmed.

Introduction

This should argue the case for your study, outlining only essential background, and should not include the findings or the conclusions. It should not be a review of the subject area, but should finish with a clear statement of the question being addressed.

Materials and Methods

Explain clearly but concisely your clinical, technical, or experimental procedures. Previously published papers related to the methods should be cited with appropriate references. Brand names and company locations should be supplied for all mentioned equipment, instruments, chemicals, etc.

Results

Findings must be described without comment. The same data or information given in a Table must not be repeated in a Figure and vice versa. It is not acceptable to repeat extensively the numbers from Tables in the text or to give lengthy explanations of Tables or Figures.

Discussion

Statements from the Introduction and Results sections should not be repeated here. The final paragraph should highlight the main conclusions of the study. Names of funding organizations should be written in full.

References

In the text, references should be identified using numbers in square brackets in which they appear consecutively. The titles of journals should be abbreviated according to the style used in Index Medicus. Ageneral guide limit the number of references to 25 for original articles, to 6 for case reports and to 85 for reviews. For articles with 1 to 6 authors, list all authors. For articles more than 6 authors, list the first 6 authors followed by "et al.". Do not use individual sets of parentheses for citation numbers that appear together, e.g., [2,3,5-9], not [2],[3],[5]–[9]. For other styles of publication or Internet articles, see http:// www. nlm.nih.gov/ bsd/ uniform_requirements.html References should be formatted as follows (please note the punctuation and capitalization)

Journal titles should be abbreviated according to ISI Web of Science abbreviations. Authors are solely responsible for the accuracy and completeness of references.

Articles in Journals

Özpolat B, Gürpınar ÖA, Ayva EŞ, Gazyağcı S, Niyaz M. The effect of Basic Fibroblast Growth Factor and adipose tissue derived mesenchymal stem cells on wound healing, epithelization and angiogenesis in a tracheal resection and end to end anastomosis rat model. Turk Gogus Kalp Dama 2013; 21: 1010-9.

For other styles of publication or Internet articles, see http:// www.nlm.nih.gov/bsd/uniform_requirements.html

Tables and Figures

All illustrations (photographs, drawings, graphs, etc.), not including tables, must be labeled "Figure." Figures must be submitted both in the manuscript and as separate files.

All tables and figures must have a caption and/or legend and be numbered (e.g., Table 1, Figure 2), unless there is only one table or figure, in which case it should be labeled "Table" or "Figure" with no numbering. Captions must be written in sentence case (e.g., Macroscopic appearance of the samples.). The font used in the figures should be Times New Roman. If symbols such as ×, μ, η, or ν are used, they should be added using the Symbols menu of Word.

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Graphs and diagrams with a line weight of less than 0.5 point or more than 1 point are not accepted. Scanned or photocopied graphs and diagrams are not accepted.

Charts must be prepared in 2 dimensions unless required by the data used. Charts unnecessarily prepared in 3 dimensions are not accepted.

Figures that are charts, diagrams, or drawings must be submitted in a modifiable format, i.e. our graphics personnel should be able to modify them. Therefore, if the program with which the figure is drawn has a "save as" option, it must be saved as *.ai or *.pdf. If the "save as" option does not include these extensions, the figure must be copied and pasted into a blank Microsoft Word document as an editable object. It must not be pasted as an image file (tiff, jpeg, or eps) unless it is a photograph.

Tables and figures, including caption, title, column heads, and footnotes, must not exceed 16×20 cm and should be no smaller than 8 cm in width. For all tables, please use Word's "Create Table" feature, with no tabbed text or tables created with spaces and drawn lines. Please do not duplicate information that is already presented in the figures.

Tables must be clearly typed, each on a separate sheet, and double-spaced. Tables may be continued on another sheet if necessary, but the dimensions stated above still apply.

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The Current Thoracic Surgery is a current periodical, peer-reviewed and open access official e- journal of the Turkish Society of Thoracic Surgery which its funded and published three times annually. In April, August and December.

The language of the journal is English.

The Current Thoracic Surgery is dedicated to publishing clinical research, clinical analysis, laboratory and experimental studies, editorials, invited current reviews, case reports, interesting images and "How to Do It" papers.

The journal is based on independent and unbiased double-blinded peer-reviewed principles. Only unpublished papers that are not under review for publication elsewhere can be submitted. Current Thoracic Surgery does not accept multiple submission and duplicate submission even though the previous one was published in a different language. The authors are responsible for the scientific content of the material to be published. The Current Thoracic Surgery reserves the right to request any research materials on which the paper is based.

The Current Thoracic Surgery encourages and enables academicians, researchers, specialists to publish their valuable research in branches of general thoracic surgery, thoracic disease and thoracic surgery anesthesia. The primary aim of the journal is to publish original articles with high scientific and ethical quality and serve as a good example of medical publications in the World.

The Editorial Board of the Current Thoracic Surgery and the Publisher adheres to the principles of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the US National Library of Medicine (NLM), the World Medical Association (WMA), the US Office of Research Integrity (ORI), the European Association of Science Editors (EASE), and the International Society of Managing and Technical Editors (ISMTE).

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All articles submitted for publication are strictly reviewed for their

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importance,

quality,

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The Current Thoracic Surgery uses a well-constructed scheme for the evaluation process.

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Manuscripts that comply with the main rules of the journal are sent to at least two external reviewers, and the reviewers are asked for their opinion about the suitability of the paper for publication. The reviewed manuscripts are then re-reviewed by the Editor in Chief and the Editorial Board and a decision of rejection or acceptance is shaped.

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mals (8th edition, 2011)" and/or "International Guiding Principles for Biomedical Research Involving Animals (2012)" is required for all research studies. If the submitted manuscript does not include ethics committee approval, it will be reviewed according to COPE's guideline (Guidance for Editors: Research, Audit and Service Evaluations). If the study should have ethical approval, authors will be asked to provide ethical approval. If they cannot provide ethical approval, their manuscript will be rejected and also their institutions and when needed, the related bodies in their country will be informed that such studies must have ethics committee approval. If the study does not need ethics committee approval after the editorial board's review, the authors will be asked to provide an ethics committee approval or a document given by a related independent committee that indicates the study does not need ethics committee approval according to the research integrity rules in their country. If the authors provide either an approval or a document showing that ethics approval is not needed, the review process will continue. If the authors cannot provide either documents, the manuscript will be rejected. For articles concerning experimental research on humans, a statement should be included that shows informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo.

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