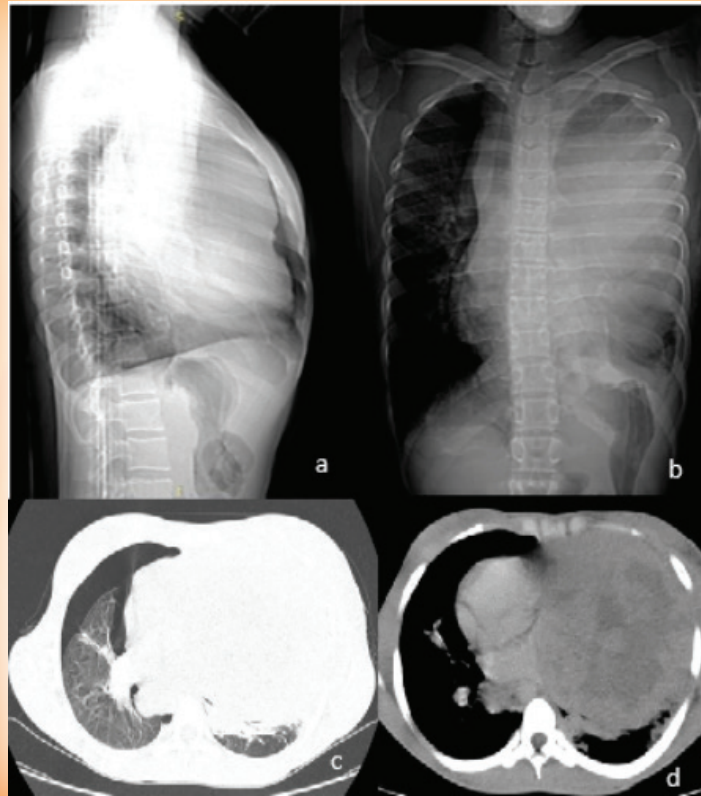


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Original Article

Thoracic injury profile in the geriatric population: an analysis of age-specific patterns and independent risk factors

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ABSTRACT

Background: The aim of this study was to evaluate the association between geriatric age and the presence of specific thoracic injuries in patients who presented to the emergency department with trauma and were diagnosed with thoracic injury.

Materials and Methods: This retrospective observational study included 486 adult patients with thoracic trauma, categorized into young adults (18-64 years, $n = 366$) and geriatric patients (≥ 65 years, $n = 120$). Data on demographics, trauma etiology, thoracic pathologies, and concomitant injuries were analyzed using univariate and multivariate binary logistic regression models to identify independent predictors of specific thoracic injuries.

Results: Significant differences were observed in trauma mechanisms; ground-level falls were the predominant mechanism in the geriatric group ($p < 0.001$), while high-energy mechanisms such as penetrating trauma, assault, and falls from height were significantly more frequent in young adults ($p < 0.001$). Regarding specific injuries, rib fractures were significantly more common in the geriatric group ($p < 0.001$). Conversely, pneumothorax and pneumomediastinum were significantly more prevalent in the young adult group ($p < 0.001$ and $p = 0.01$, respectively). Multivariate logistic regression analyses revealed that geriatric age was an independent risk factor for the development of rib fractures (OR: 3.99; $p = 0.01$) and was independently associated with a decreased risk of pneumothorax (OR: 0.36; $p = 0.01$).

Conclusions: This study revealed that thoracic injury patterns vary with age. Geriatric age is independently associated with rib fractures, whereas pneumothorax and pneumomediastinum are more frequent in young adults. These findings highlight the importance of considering age-specific injury patterns in the evaluation of thoracic trauma.

Keywords: emergency service, hospital, geriatric, pneumothorax, rib fractures, risk factors, thoracic injuries

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Introduction

Trauma remains a leading cause of global morbidity and mortality and constitutes a significant portion of emergency department admissions. With respect to trauma cases, thoracic injuries hold a critical position because of their frequent association with multisystem injuries and their potential for severe clinical outcomes. With increasing life expectancy and an aging population, the proportion of the geriatric population (≥ 65 years) among thoracic trauma patients is steadily increasing. In these geriatric patients, detailed investigations of trauma mechanisms and early prediction of associated thoracic pathologies are vital for the timely implementation of appropriate diagnostic and therapeutic strategies in the emergency department [1,2].

Trauma mechanisms in the geriatric population differ significantly from those in young adults because of decreased cardiopulmonary and musculoskeletal reserves, impaired balance and reaction times, concomitant neurological and psychiatric diseases, polypharmacy, and the presence of environmental risk factors. As a result of this risk profile, low-energy trauma, such as ground-level falls, is the predominant mechanism in geriatric patients, whereas high-energy trauma, such as penetrating injuries, assault, motor vehicle accidents, and falls from height, is more common in young adults [2]. Similarly, thoracic injury patterns following trauma also vary across age groups. Even when individuals are exposed to low-energy trauma, such as ground-level falls, rib fractures are observed more frequently in geriatric patients than in younger individuals because of decreased bone mineral density and reduced chest wall elasticity. Conversely, specific thoracic injuries such as hemothorax and pneumothorax are reported to occur at higher rates in young adults because of their exposure to penetrating and high-energy trauma [3,4].

Despite the increase in the number of emergency department admissions among the aging population, comprehensive studies on which specific thoracic pathologies are more predominant in geriatric patients and the clinical predictability of these conditions are needed [5].

The aim of this study was to evaluate the association between geriatric age and the presence of specific thoracic injuries in patients who presented to the emergency department with trauma and who were diagnosed with thoracic injury.

Materials and Methods

Study design and population

This retrospective observational study was conducted at a tertiary training and research hospital. The study protocol was approved by the Clinical Research Ethics Committee of University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital (No: KAEK/2022.04.95). Owing to the retrospective nature of the study, the requirement for informed consent was waived by the same committee. The study was also conducted in compliance with ethical standards and the principles of the Declaration of Helsinki.

Within the scope of the study, patients aged 18 and older who presented to the emergency department with trauma and who were diagnosed with thoracic injury between 01.01.2017 and 31.12.2021 were retrospectively reviewed via the hospital information management system and archive records. A total of 559 consecutive patients with complete clinical records and radiological data were included in the preliminary evaluation; of these, 73 patients with unclear trauma mechanisms were excluded. Following the evaluation, the 486 patients included in the study were divided into two groups for comparison on the basis of age: young adults (18-64 years) and geriatric (≥ 65 years) (Figure 1).

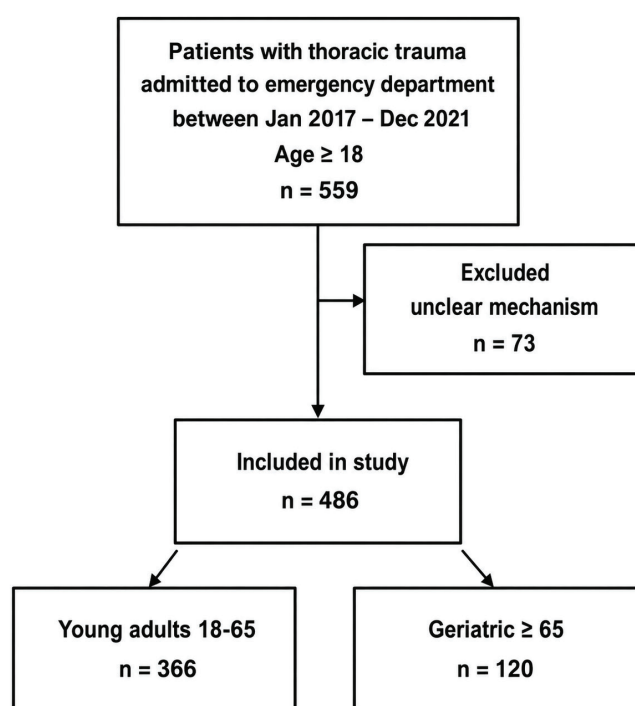


Figure 1. Flowchart of the study population selection and group distribution.

Data collection

Demographic data (age and sex), trauma mechanisms (penetrating thoracic trauma, ground-level falls, motor vehicle accidents, assault, and falls from height), thoracic pathologies (pneumothorax, hemothorax, rib fracture, sternum fracture, tension pneumothorax, pneumomediastinum, and pulmonary contusion), concomitant injuries (cranial, abdominal, extremity, and vertebral), emergency department outcomes (admission and discharge), and in-hospital mortality status were retrospectively reviewed and recorded on a preformatted data collection form. In our study, trauma mechanisms such as motor vehicle accidents (including both in-vehicle accidents with an estimated speed >60 km/h and pedestrian/cyclist-vehicle collisions with an estimated speed >30 km/h), falls from a height (≥ 3 meters), assault, and penetrating injuries were considered high-energy traumas. Conversely, ground-level falls (falls from a standing height or <1 meter) were defined as low-energy traumas. Gunshot wounds and stab wounds were defined as penetrating trauma. Thoracic pathologies were identified through a retrospective review of official computed tomography reports issued by attending radiologists. Diagnoses were based on standardized radiological criteria: pulmonary contusion was defined as non-segmental parenchymal opacification or consolidation; pneumothorax, hemothorax, and pneumomediastinum were defined by the presence of ectopic air or fluid in their respective anatomical compartments. Tension pneumothorax was diagnosed based on radiological signs of significant pressure effect, such as mediastinal shift or diaphragmatic inversion accompanying a pneumothorax. Fractures (ribs and sternum) were defined as a loss of cortical continuity on CT sections. All data were extracted directly from these validated clinical reports. Data were collected by a single researcher who was blinded to the study's objective; to ensure data quality and consistency, 10% of the randomly selected cases were independently audited by a second researcher.

Statistical Analysis

Statistical analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY, USA) and R-based Jamovi version 2.3.28. Nominal categorical variables are presented as numbers and percentages, whereas continuous variables are presented as medians and interquartile ranges because of their nonnormal distribution. No statistical imputation methods were used during the analysis of missing data; observations with missing data were excluded from the relevant analyses. The distribution characteristics of the continuous variables were evaluated using visual methods (histograms and box-plots) and analytical tests

(Kolmogorov-Smirnov, Shapiro-Wilk, skewness, and kurtosis). The Mann-Whitney U test was used to compare continuous variables between the young adult and geriatric groups, as they did not follow a normal distribution. For the comparison of categorical variables, Pearson's chi-square or Fisher's exact test was used as appropriate. Within the scope of the study's objective, univariate and multivariate binary logistic regression models were constructed to evaluate whether geriatric age is an independent predictor of specific thoracic pathologies. Variables found to be significant at $p < 0.20$ in the univariate analysis were included in the multivariate model. Multicollinearity was assessed using variance inflation factor (VIF) values, and variables with a $VIF > 5$ were excluded from the model. It was observed that certain clinical variables had zero occurrences in specific age subgroups, which may lead to unstable estimates or large standard errors in the logistic regression models. Consequently, variables with zero cell counts were interpreted with caution and, where appropriate, excluded from the final multivariable models to ensure statistical stability. The results of the logistic regression analysis are reported as odds ratios (OR) and 95% confidence intervals (CI). All hypothesis tests were two-tailed, and a p value of < 0.05 was considered to indicate statistical significance.

Results

A total of 486 patients were included in the study, of whom 120 (24.7%) were in the geriatric group. A significant difference was observed between the age groups in terms of sex distribution ($p < 0.001$). Trauma mechanisms significantly differed according to age group. While ground-level falls were significantly more frequent in the geriatric group ($p < 0.001$), penetrating trauma, assault, and falls from height were significantly greater in the young adult group ($p < 0.001$). No significant difference was found between the groups in terms of the frequency of motor vehicle accidents (Table 1).

When specific thoracic injuries were evaluated, rib fractures were significantly more frequent in the geriatric group ($p < 0.001$). Conversely, the presence of pneumothorax and pneumomediastinum was significantly greater in the young adult group ($p < 0.001$ and $p = 0.01$, respectively). No significant difference was observed between the age groups in terms of other thoracic injuries. Among the concomitant injuries, only extremity injuries were significantly more common in the young adult group ($p = 0.02$). The in-hospital mortality rate was 2.06%, and no significant difference was found between the age groups (Table 1).

Table 1. Baseline demographic and clinical characteristics of the study population.

Variables [Median (IQR) or n (%)]	Total (n=486)	Geriatric (n=120)	Young Adult (n=366)	p
Age (years)	49 (36-64)	74 (69-80)	43 (31-53)	<0.001
Sex				
Male	364 (74.90)	65 (54.17)	299 (81.69)	<0.001
Female	122 (25.10)	55 (45.83)	67 (18.31)	
Trauma Mechanism				
Penetrating Trauma	49 (10.08)	0 (0.00)	49 (13.39)	<0.001
Ground-level Fall	245 (50.41)	95 (79.17)	150 (40.98)	<0.001
Motor Vehicle Accident	104 (21.40)	21 (17.50)	83 (22.68)	0.23
Assault	45 (9.26)	2 (1.67)	43 (11.75)	<0.001
Falls From Height	43 (8.85)	2 (1.67)	41 (11.20)	<0.001
Thoracic Pathologies				
Pneumothorax	132 (27.16)	10 (8.33)	122 (33.33)	<0.001
Hemothorax	71 (14.61)	18 (15.00)	53 (14.48)	0.89
Rib Fracture	395 (81.28)	116 (96.67)	279 (76.23)	<0.001
Pulmonary Contusion	83 (17.08)	17 (14.17)	66 (18.03)	0.33
Sternum Fracture	10 (2.06)	0 (0.00)	10 (2.73)	0.13*
Tension Pneumothorax	3 (0.62)	0 (0.00)	3 (0.82)	1.00*
Pneumomediastinum	21 (4.32)	0 (0.00)	21 (5.74)	0.01
Concomitant Injuries				
Any Concomitant Trauma	172 (35.39)	31 (25.83)	141 (38.52)	0.01
Cranial Trauma	31 (6.38)	4 (3.33)	27 (7.38)	0.12
Abdominal Trauma	29 (5.97)	3 (2.50)	26 (7.10)	0.07
Extremity Trauma	107 (22.02)	17 (14.17)	90 (24.59)	0.02
Vertebral Trauma	49 (10.08)	8 (6.67)	41 (11.20)	0.15
Mortality				
Yes	10 (2.06)	3 (2.50)	7 (1.91)	0.71*
No	476 (97.94)	117 (97.50)	359 (98.09)	

*Fisher's exact test

According to univariate logistic regression analyses, geriatric age was significantly associated with a decreased risk of pneumothorax development ($p < 0.001$) and an increased risk of rib fracture development ($p < 0.001$). Multivariate logistic regression analyses revealed that geriatric age was an independent risk factor for the development of rib fractures (OR: 3.99; 95% CI:

1.36-11.67; $p = 0.01$), whereas it was independently associated with a decreased risk of pneumothorax development (OR: 0.36; 95% CI: 0.17-0.74; $p = 0.01$) (Table 2). Other thoracic injuries, including sternum fractures and tension pneumothorax, were excluded from Table 2 due to the low number of cases and lack of statistical significance in regression analyses.

Table 2. Univariate and multivariate logistic regression analyses identifying independent risk factors for specific thoracic injury patterns.						
	Univariate Logistic Regression Analysis			Multivariate Logistic Regression Analysis		
	OR	95% CI	p	OR	95% CI	p
Pneumothorax						
Age groups*	0.18	0.09-0.36	<0.001	0.36	0.17-0.74	0.01
Sex†	1.72	1.05-2.84	0.03	0.93	0.52-1.65	0.80
Penetrating Trauma	12.61	6.20-25.61	<0.001	8.57	3.34-22.05	<0.001
Ground-level Fall	0.24	0.15-0.37	<0.001	0.53	0.25-1.15	0.11
Motor Vehicle Accident	0.71	0.43-1.19	0.19	0.69	0.31-1.57	0.38
Assault	1.10	0.56-2.17	0.78			
Falls From Height	3.92	2.07-7.43	<0.001	2.01	0.77-5.24	0.15
Cranial Trauma	1.76	0.83-3.74	0.14	1.28	0.53-3.05	0.58
Abdominal Trauma	4.21	1.95-9.09	<0.001	2.57	1.07-6.19	0.04
Extremity Trauma	1.34	0.84-2.13	0.23			
Vertebral Trauma	2.20	1.20-4.04	0.01	1.95	0.95-3.98	0.07
Hemothorax						
Age groups*	1.04	0.58-1.86	0.89			
Sex†	2.58	1.24-5.36	0.01	1.90	0.89-4.07	0.10
Penetrating Trauma	7.17	3.80-13.54	<0.001	4.13	1.42-12.01	0.01
Ground-level Fall	0.56	0.33-0.93	0.03	0.73	0.27-1.93	0.52
Motor Vehicle Accident	0.64	0.32-1.26	0.19	0.68	0.24-1.93	0.47
Assault	0.39	0.12-1.30	0.13	0.39	0.09-1.68	0.21
Falls From Height	1.15	0.49-2.70	0.75			
Cranial Trauma	1.13	0.42-3.06	0.81			
Abdominal Trauma	1.95	0.80-4.76	0.14	1.83	0.67-4.97	0.24
Extremity Trauma	0.61	0.31-1.21	0.15	0.77	0.36-1.63	0.49
Vertebral Trauma	1.16	0.52-2.59	0.72			
Rib Fracture						
Age groups*	9.04	3.24-25.21	<0.001	3.99	1.36-11.67	0.01
Sex†	0.24	0.11-0.51	<0.001	0.55	0.24-1.25	0.15
Penetrating Trauma	0.02	0.01-0.04	<0.001	0.04	0.02-0.11	<0.001
Ground-level Fall	4.70	2.75-8.02	<0.001	2.09	1.05-4.16	0.04
Motor Vehicle Accident	1.04	0.59-1.82	0.89			
Assault	1.94	0.74-5.06	0.18	2.13	0.74-6.18	0.16
Falls From Height	2.38	0.83-6.85	0.11	2.60	0.82-8.21	0.10
Cranial Trauma	0.64	0.28-1.48	0.30			
Abdominal Trauma	2.07	0.61-6.98	0.24			
Extremity Trauma	1.40	0.78-2.53	0.26			
Vertebral Trauma	1.73	0.71-4.20	0.23			
Pulmonary Contusion						
Age groups*	0.75	0.42-1.34	0.33			
Sex†	1.64	0.90-2.99	0.11	1.73	0.92-3.27	0.09
Penetrating Trauma	-	0.00-Inf	0.98			
Ground-level Fall	0.53	0.32-0.86	0.01	2.46	0.97-6.22	0.06
Motor Vehicle Accident	2.89	1.73-4.81	<0.001	4.67	1.78-12.27	0.002
Assault	0.73	0.30-1.78	0.49			
Falls From Height	2.62	1.32-5.21	0.01	3.27	1.03-10.30	0.04
Cranial Trauma	3.42	1.59-7.35	0.002	2.61	1.09-6.29	0.03
Abdominal Trauma	2.77	1.24-6.20	0.01	1.94	0.77-4.91	0.16
Extremity Trauma	3.14	1.89-5.20	<0.001	2.18	1.23-3.85	0.01
Vertebral Trauma	2.99	1.57-5.69	<0.001	1.93	0.92-4.03	0.08
Pneumomediastinum						
Age groups*	-	0.00-Inf	0.99			
Sex†	N/A	0.00-Inf	0.99			
Penetrating Trauma	5.04	1.93-13.17	<0.001	5.68	1.72-18.72	0.004
Ground-level Fall	0.22	0.07-0.66	0.01	0.55	0.15-2.01	0.37
Motor Vehicle Accident	1.50	0.57-3.96	0.42			
Assault	1.03	0.23-4.59	0.97			
Falls From Height	1.09	0.25-4.84	0.91			
Cranial Trauma	3.82	1.20-12.13	0.02	3.42	0.95-12.35	0.06
Abdominal Trauma	4.14	1.30-13.23	0.02	2.64	0.76-9.15	0.13
Extremity Trauma	1.44	0.55-3.81	0.46			
Vertebral Trauma	2.99	1.05-8.55	0.04	3.69	1.11-12.25	0.03

*Reference group is young adults; †Reference group is female

Discussion

In this study, the association between the geriatric age group and specific thoracic injury patterns was evaluated in adult patients who presented to the emergency department with trauma and who were diagnosed with thoracic injury. Our findings reveal that rib fractures are significantly more frequent in geriatric patients than in young adults and that geriatric age is an independent risk factor for the development of rib fractures. Conversely, pneumothorax and pneumomediastinum occur at higher rates in young adults, and geriatric age was inversely associated with the risk of pneumothorax development. These results suggest that age-related physiological changes and differences in trauma mechanisms play significant roles in determining thoracic injury patterns.

It has been frequently reported in the literature that the proportion of females among all trauma cases is greater in older age groups. This trend is attributed to the higher female ratio in the elderly population, resulting from the longer life expectancy of women than that of men. This demographic structure is also reflected in trauma cohorts [6,7]. With age, a distinct shift in trauma mechanisms is observed. In young adults, thoracic trauma occurs more frequently because of penetrating and high-energy mechanisms, which are more common in males. Conversely, in older age groups, ground-level falls become the predominant trauma mechanism [8,9]. In our study, the higher proportion of females in the geriatric age group and the identification of ground-level falls as the predominant trauma mechanism are consistent with the literature. These findings suggest that sex distribution and trauma mechanisms shift simultaneously with age and that these two phenomena may be interrelated. Clinically, these findings indicate that the possibility of thoracic injury must be carefully evaluated in elderly and female patients, even in the absence of a high-energy trauma history.

The inverse association found between geriatric age and pneumothorax in our study is consistent with several epidemiological observations reported in the literature. These findings are thought to be related to age-dependent shifts in trauma mechanisms, as well as structural changes in chest wall biomechanics. Pneumothorax is strongly associated with high-energy trauma and penetrating injuries that specifically disrupt pleural integrity, and such mechanisms are more prevalent in younger individuals. In contrast, trauma in the geriatric population frequently

occurs via low-energy mechanisms, such as ground-level falls, combined with an age-related increase in chest wall rigidity, leading to the absorption of trauma energy by bony structures rather than its transmission to lung and pleural tissues. These biomechanical characteristics may contribute to the lower incidence of pneumothorax in geriatric patients [10,11]. The significant increase in the risk of pneumothorax development associated with penetrating trauma and thoracoabdominal injuries suggestive of high-energy trauma is also consistent with findings in the literature. Clinically, these findings highlight the importance of considering trauma mechanisms and concomitant injuries alongside age when evaluating the development of pneumothorax.

Numerous studies have reported that rib fractures are more frequent in the geriatric age group and that advanced age is an independent risk factor for the development of rib fractures. This increased risk is attributed to physiological changes such as decreased bone mineral density, loss of chest wall elasticity, and increased age-related frailty [3,12]. In our study, the finding that geriatric age is significantly and independently associated with the development of rib fractures is consistent with these findings. Furthermore, the independent association found between ground-level falls and the risk of rib fractures in our study may reflect the characteristics of the exposed population rather than a direct causal effect of the mechanism itself. Indeed, it has been reported in the literature that the risk of rib fractures is increased in the geriatric population, where ground-level falls are more prevalent [13]. In this context, the association of ground-level falls with rib fractures despite the inclusion of the age variable in the model can be explained by the partial representation of age-related frailty and exposure patterns through this mechanism. Specifically, underlying osteoporosis may further increase the risk of rib fractures, while neurodegenerative conditions such as Parkinson's disease often contribute to the high frequency of ground-level falls observed in our geriatric cohort [3,14]. Clinically, these findings highlight that low-energy falls, particularly in older patients, should not be considered minor trauma and underscore the importance of careful clinical and radiological evaluation for rib fractures in this patient group.

The inverse association found between the penetrating trauma mechanism and the development of rib fractures in our study is consistent with findings reported

in the literature. In blunt trauma, high-energy forces transmitted to the chest wall over a broad impact area exceed the bending capacity of the ribs, thereby facilitating fracture development. In contrast, in penetrating thoracic injuries, because the trauma energy remains localized along a limited entry path, rib fractures typically occur only when the entry path directly coincides with the bony structure [15,16]. Clinically, these findings indicate that the trauma mechanism must be considered when evaluating the risk of rib fractures.

Although differences were observed in the distribution of pneumomediastinum between age groups in this study, the geriatric population was not identified as a risk factor for the development of pneumomediastinum in the logistic regression analysis. Conversely, the penetrating trauma mechanism was found to be associated with the development of pneumomediastinum. These findings differ from those of studies in the literature that report posttraumatic pneumomediastinum is more commonly associated with blunt trauma [16,17]. This discrepancy may be related to the study's methodology, the limited patient population, and the distribution of trauma mechanisms within the current sample.

According to the multivariate logistic regression analysis, the inability to identify geriatric age as a significant risk factor for the development of pneumomediastinum, sternal fracture, and tension pneumothorax may be attributed to the absence of these pathologies in the geriatric age group within our sample. The fact that the number of cases was zero in this group hindered the ability of the model to statistically evaluate these associations in a reliable manner. Therefore, rather than indicating a lack of effect of geriatric age, these results reflect statistical limitations inherent to the current data structure.

In the univariate logistic regression analyses for the development of hemothorax and pulmonary contusion, the age variable was not found to be statistically significant and was therefore not included in the multivariate model. These findings suggest that these specific thoracic pathologies may be related to the mechanism and severity of trauma rather than an age-specific risk. Indeed, the development of hemothorax and pulmonary contusion is more closely associated with trauma mechanisms and energy transfer [17-21]. Multivariate logistic regression analysis revealed a significant association between hemothorax development and penetrating trauma, as well as between pulmonary contusion development and high-energy trauma mechanisms such as motor vehicle

accidents and falls from height, which is consistent with the literature. Clinically, these findings suggest that focusing on the trauma mechanism independently of age when evaluating the risk of hemothorax and pulmonary contusion may provide more guidance in determining diagnostic approaches and imaging strategies.

Limitations of the study

This study has several limitations. First, the retrospective and single-center design presents limitations regarding the establishment of causal relationships and the generalizability of the findings. Second, the absence of certain rare thoracic pathologies, such as pneumomediastinum, sternal fracture, and tension pneumothorax, in the geriatric age group hindered the interpretation of the multivariate analyses. Additionally, specific comorbidities, including osteoporosis and neurodegenerative diseases, were not individually analyzed due to data constraints. Furthermore, the lack of standardized trauma scoring systems (e.g., injury severity score or new injury severity score) restricts a more comprehensive assessment of overall anatomical injury severity. Consequently, these factors may limit a broader interpretation of trauma-related outcomes. Given these limitations, the results need to be validated by larger-scale studies with prospective designs.

In conclusion, this study demonstrated that geriatric age is associated with specific thoracic injury patterns among patients who are diagnosed with thoracic injury and who are presenting to the emergency department with trauma. While geriatric age was associated with the development of rib fractures, pneumothorax and pneumomediastinum were observed more frequently in young adults. These findings indicate that age and age-specific injury patterns must be considered together during the diagnostic evaluation of patients with thoracic trauma.

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 protocol was approved by the Clinical Research Ethics Committee of University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital (No: KAEK/2022.04.95).

Authors' contribution

YC: Conceptualization, methodology, data curation, writing - original draft, project administration. FC: Investigation, resources, validation, writing - review and editing. BY: Data curation, formal analysis, visualization. EU: Investigation, resources, writing - review and editing. BD: Supervision, validation, writing - review and editing. AC: Conceptualization, supervision, validation, writing - review & editing.

Use of Generative AI and AI-assisted technologies in the writing process

The authors used generative artificial intelligence (GenAI) and AI-assisted technologies during the preparation of this manuscript solely to improve language, grammar, and formatting. The authors declare that all scientific content, data analysis, and conclusions were independently conceived and validated by the authors, and the authors take full responsibility for the accuracy and integrity of the work.

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Original Article

Short-term effects of respiratory physiotherapy training on pulmonary function test parameters

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ABSTRACT

Background: In this study, we aimed to determine the effect of preoperative respiratory exercise training and practice on spirometric parameters, which are among the most critical factors evaluated prior to surgery.

Materials and Methods: Fifth-year medical students consisting of healthy individuals were included in the study. The participants were divided into a study group and a control group. The study group received respiratory physiotherapy training and was instructed to perform the exercises for four days. Pulmonary function tests were administered to both groups on the first and fifth days.

Results: A total of 118 healthy individuals with a mean age of 24.27 ± 1.18 years were included in the study. Of these, 66 participants constituted the study group and 52 the control group. In the study group, the second measurement of forced vital capacity (FVC) was significantly lower than the first measurement ($p < 0.001$). In the control group, no statistically significant difference was observed between pre- and post-measurements. The FVC% predicted was also significantly lower in the second measurement compared to the first in the study group ($p < 0.001$). Furthermore, the second FVC measurement in the study group was significantly lower than that of the control group ($p = 0.045$). The change in forced expiratory volume in one second (FEV_1) differed significantly between the study and control groups ($p = 0.018$). While a decrease in FEV_1 was observed in the study group, an increase was noted in the control group.

Conclusions: We suggest that individualized physiotherapy protocols and targeted interventions are required to accurately determine the true impact of respiratory physiotherapy in preoperative settings.

Keywords: enhanced recovery after surgery (ERAS), thoracic surgery, pulmonary rehabilitation, spirometry

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Introduction

Lung cancer is the third most commonly diagnosed malignancy and remains one of the leading causes of cancer-related mortality worldwide. In non-small cell lung cancer (NSCLC), which constitutes the majority of lung cancer cases, lobectomy is considered the gold standard treatment, particularly in early-stage disease. In selected cases and in patients with limited pulmonary reserve, segmentectomy or wedge resection may also be performed [1]. Preoperative risk assessment in resectable patients heavily relies on cardiopulmonary functional evaluation. A significant proportion of patients diagnosed with lung cancer, particularly males, also have concomitant chronic obstructive pulmonary disease (COPD). Approximately 37% of patients deemed resectable are ultimately considered inoperable due to insufficient pulmonary functional capacity [1-3].

Pulmonary resection surgery may lead to a reduction in lung volumes and respiratory muscle strength, potentially resulting in postoperative respiratory failure. In recent years, video-assisted thoracoscopic surgery (VATS) has become increasingly widespread, and due to its minimally invasive nature with smaller incisions, it reduces respiratory muscle impairment and significantly lowers postoperative morbidity and mortality rates. Nevertheless, reduced preoperative pulmonary function remains a major factor associated with increased postoperative morbidity and mortality [1,2].

In recent years, considerable emphasis has been placed on the development and systematic implementation of perioperative care protocols aimed at reducing postoperative morbidity and mortality. Within this context, Enhanced Recovery After Surgery (ERAS) protocols have been shown to decrease hospital length of stay and postoperative complications. One of the key objectives of ERAS protocols is to improve postoperative pulmonary capacity in the remaining lung and to prevent respiratory failure [4].

In the present study, we aimed to evaluate the impact of short-term preoperative respiratory physiotherapy training on baseline spirometric parameters in healthy individuals to assess its potential role in optimizing preoperative pulmonary capacity.

Materials and Methods

Fifth-year medical students attending the thoracic surgery clerkship were prospectively enrolled in the

study on a voluntary basis. All participants underwent pulmonary function testing on the first day. Subsequently, participants were randomly assigned to either the study group or the control group. The internship groups consisted of 25 participants each, and allocation was performed randomly using a lottery-based method. According to the results of the randomization process, the internship groups were assigned to either the control group or the study group. Participants in the control group received no training or intervention, and pulmonary function testing was repeated on day 5. In the study group, following the initial pulmonary function test on day 1, participants received respiratory exercise training from a respiratory physiotherapist and were instructed to perform these exercises daily. After four days of presumed adherence to the exercise program, pulmonary function testing was repeated on day 5. Height and weight of all participants were measured, and body mass index (BMI) was calculated. Participant characteristics and all obtained data were recorded and analyzed statistically. Participants were excluded if they had a known chronic disease, a history of thoracic surgery or thoracic trauma, a history of inflammatory airway disease such as asthma, an upper respiratory tract infection within one week prior to or during the five-day study period, or if they declined participation or failed to complete either of the pulmonary function tests.

This study was conducted with the approval of Non-Interventional Clinical Research Ethics Committee of Izmir Katip Çelebi University (Approval No. 2023/597).

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as number (n), percentage (%), mean $\pm$ standard deviation (mean $\pm$ SD), median (M), and minimum (min)–maximum (max) values. Comparisons of measurements between groups were performed using Mixed Design ANOVA. Bonferroni correction was applied for pairwise comparisons of main effects. Differences between pre- and post-measurements were calculated and compared between groups. Variables were analyzed using the independent samples t-test when parametric assumptions were met, and the Mann–Whitney U test when these assumptions were not satisfied. After categorization of FEV₁ and FVC values, pre- and post-intervention differences were evaluated using the McNemar test. A p-value of <0.05 was considered statistically significant.

Results

A total of 118 healthy individuals (53 females and 65 males) with a mean age of 24.27 ± 1.18 (range, 23-27) years were included in the study. Of these, 66 participants were assigned to the study group and 52 to the control group. The mean height, weight, and body mass index (BMI) of the participants were 173.78 ± 9.65 cm, 69 ± 14.83 kg, and 22.78 ± 3.37 kg/m², respectively. No significant differences were observed between the groups in terms of baseline demographic characteristics.

Pulmonary function test parameters, including FEV₁, FVC, FEV₁/FVC, peak expiratory flow (PEF), maximal expiratory flow at 25% (MEF25), 50% (MEF50), and 75% (MEF75), were compared before and after training and exercise within each group. The results are presented in Table 1. Accordingly, no statistically significant differences were observed in FEV₁, FEV₁/FVC, MEF50, and MMEF values between pre- and post-measurements in either group. MEF25 decreased significantly from pre- to post-measurement in the study group ($F = 5.764$; $p = 0.018$), whereas no statistically significant change was observed in the control group ($F = 0.015$; $p = 0.902$).

Table 1. Comparison of values within and between groups.

	Groups		Test Statistics		
	Study Group	Control Group	F	p	η^2
FEV1					
Pre	3.74±0.92	3.91±1.03	0.927	0.338	0.008
Post	3.67±0.87	3.98±1.02	3.192	0.077	0.027
Test Statistics	F=2.106; p=0.149; η^2=0.018	F=1.858; p=0.175; η^2 =0.016			
FEV1 (% predicted)					
Pre	89.77±12.56	93.01±15.71	1.556	0.215	0.013
Post	88.12±11.31	93.65±14.38	5.470	0.021	0.045
Test Statistics	F=1.840; p=0.178; η^2 =0.016	F=0.214; p=0.645; η^2 =0.002			
FVC					
Pre	4.62±1.05	4.77±1.03	0.587	0.445	0.005
Post	4.46±0.97	4.78±1.09	2.807	0.097	0.024
Test Statistics	F=21.117; p<0.001; η^2 =0.154	F=0.045; p=0.833; η^2 =0.001			
FVC (% predicted)					
Pre	94.31±10.13	96.30±11.66	0.981	0.324	0.008
Post	91.22±10.10	95.15±10.89	4.097	0.045	0.034
Test Statistics	F=18.414; p<0.001; η^2 =0.137	F=2.022; p=0.158; η^2 =0.017			
FEV1/FVC					
Pre	80.95±8.42	81.89±9.97	0.311	0.578	0.003
Post	82.24±7.48	83.20±8.05	0.444	0.506	0.004
Test Statistics	F=2.076; p=0.152; η^2 =0.018	F=1.663; p=0.200; η^2 =0.014			
PEF					
Pre	5.73±2.08	6.80±2.65	6.047	0.015	0.050
Post	6.18±2.06	7.21±2.59	5.796	0.018	0.048
Test Statistics	F=6.083; p=0.015; η^2=0.050	F=3.990; p=0.048; η^2=0.033			
MEF25					
Pre	2.25±0.74	2.40±0.88	0.942	0.334	0.008
Post	2.11±0.72	2.39±0.89	3.337	0.070	0.028
Test Statistics	F=5.764; p=0.018; η^2=0.047	F=0.015; p=0.902; η^2 =0.001			
MEF50					
Pre	4.31±1.43	4.72±1.69	1.968	0.163	0.017
Post	4.27±1.25	4.75±1.56	3.350	0.070	0.028
Test Statistics	F=0.110; p=0.740; η^2 =0.001	F=0.055; p=0.812; η^2 =0.001			
MEF75					
Pre	5.48±1.99	6.36±2.49	4.518	0.036	0.037
Post	5.82±1.96	6.57±2.30	3.656	0.058	0.031
Test Statistics	F=3.700; p=0.057; η^2 =0.031	F=1.163; p=0.283; η^2 =0.010			
MMEF					
Pre	3.87±1.23	4.32±1.56	3.012	0.085	0.025
Post	3.84±1.08	4.25±1.36	3.396	0.068	0.028
Test Statistics	F=0.149; p=0.700; η^2 =0.001	F=0.384; p=0.536; η^2 =0.003			

F: Mixed Design ANOVA. Effect Size (η^2). Descriptive statistics are given as mean $\pm$ standard deviation. Sections highlighted in bold are statistically significant ($p < 0.05$).

In the study group, the second measurement of FVC was significantly lower than the first measurement ($p < 0.001$), whereas no significant difference was observed in the control group. Similarly, the percentage of FVC in the study group was significantly lower in the second measurement compared to the first ($p < 0.001$). Furthermore, the second FVC measurement in the study group was significantly lower than that of the control group ($p = 0.045$). For MEF75, the initial measurement in the study group was significantly lower than that in the control group ($p = 0.036$). The PEF value in the study group was significantly higher in the second measurement compared to the first ($p = 0.015$). A similar increase was observed in the control group ($p = 0.048$). Both the first and second PEF measurements in the study group were significantly lower than those in the control group ($p = 0.015$ and $p = 0.018$, respectively).

Intergroup comparisons of the differences between pre- and post-training measurements are presented in Table 2. The change in FEV_1 differed significantly between the study and control groups ($p = 0.018$), with a decrease observed in the study group and an increase in the control group. The percentage change in FEV_1 was statistically similar between the groups. The change in FVC also differed significantly between the groups ($p = 0.002$), with a decrease in the study group and an increase in the control group. All remaining variables showed no statistically significant differences between the study and control groups.

In addition, when FEV_1 and FVC values were categorized based on whether they were below or above 80% of the predicted values, no statistically significant differences were observed between the groups in either measurement period.

Table 2. Comparison of variable difference values by groups.

	Groups		Test Statistics	
	Study Group	Control Group	Test value	p value
FEV1	0.06±0.35 0.11 (0.42)	-0.07±0.40 -0.08 (0.36)	z=2.374	0.018
FEV1 (% predicted)	1.65±8.99 3 (10.5)	-0.63±10.92 1 (10.75)	z=1.362	0.173
FVC	0.16±0.28 0.20 (0.48)	-0.01±0.28 0.01 (0.39)	t=3.209	0.002
FVC (% predicted)	3.09±6.25 4 (10)	1.15±5.28 2 (7.75)	z=1.773	0.076
FEV1/FVC	-1.29±5.91 -0.40 (5.60)	-1.30±8.77 -0.15 (5.10)	z=0.298	0.766
PEF	-0.44±1.40 -0.37 (1.79)	-0.40±1.57 -0.37 (1.53)	t=0.143	0.886
MEF25	0.13±0.38 0.14 (0.47)	0.01±0.54 -0.02 (0.49)	z=1.827	0.068
MEF50	0.03±0.89 -0.01 (1.17)	-0.03±1.02 0.01 (0.87)	z=0.035	0.972
MEF75	-0.34±1.34 -0.32 (1.69)	-0.21±1.57 -0.25 (1.77)	t=0.470	0.639
MMEF	0.03±0.65 0.08 (0.71)	0.06±0.91 0.01 (1.04)	z=0.393	0.694

Descriptive values are given as mean ± standard deviation and median (interquartile range). z: Mann Whitney U test, t: Independent two-sample t-test. Differences (Δ) were calculated as pre-intervention minus post-intervention values (Pre – Post); therefore, positive values indicate a decrease, and negative values indicate an increase from pre- to post-intervention.

Discussion

The primary aims of respiratory physiotherapy are to increase lung volumes, facilitate secretion clearance, and enhance respiratory muscle strength, thereby improving overall respiratory capacity. Previous studies have demonstrated that preoperative respiratory muscle training can lead to improvements in spirometric parameters, particularly FEV_1 and FVC. However, the magnitude of these effects varies depending on the duration of the intervention and the target population, with exercise programs longer than six weeks reported to yield more substantial benefits [5-7]. Additionally, supervised and device-assisted respiratory exercises have been shown to be more effective than unsupervised home-based programs [7]. In the present study, the lack of expected improvement in FEV_1 and FVC values may be attributed to several factors, including the inclusion

of healthy individuals, the short duration of the exercise program (four days), and the possibility of suboptimal adherence due to the study population consisting of students.

Studies conducted in patients with chronic obstructive pulmonary disease (COPD) have demonstrated that respiratory muscle training has significant effects on respiratory capacity and dyspnea, while its impact on FEV_1 and FVC remains limited. Similarly, in patients undergoing thoracic surgery, preoperative respiratory physiotherapy has been shown to improve functional lung capacity and reduce postoperative complications; however, its short-term effects on spirometric parameters appear to be minimal [8-10]. While patients with impaired pulmonary reserve may exhibit a more pronounced response to such interventions, studies involving healthy individuals generally do not demonstrate significant

improvements. This phenomenon may be explained by a ceiling effect, as healthy individuals are already operating near their maximal pulmonary capacity [8,10,11]. Consistent with these findings, the absence of expected spirometric improvements in our study may be attributed to the inclusion of a healthy study population.

In our study, a significant increase in PEF values was observed in both the study and control groups. This finding is likely attributable to a learning effect. The learning effect in spirometry refers to improved patient performance with repeated testing, particularly in effort-dependent parameters, as a result of increased familiarity and compliance with the procedure. Current guidelines published by the European Respiratory Society (ERS) and the American Thoracic Society (ATS) recommend repeated respiratory maneuvers to ensure reliable spirometry measurements [12].

In recent years, with the increasing implementation of Enhanced Recovery After Surgery (ERAS) protocols, the importance of respiratory physiotherapy has become more evident. Respiratory physiotherapy integrated within ERAS protocols has been shown to reduce postoperative pulmonary complications and shorten hospital length of stay [13].

In this study, we aimed to evaluate the effects of short-term respiratory physiotherapy training in healthy individuals. In line with the existing literature, we observed a decrease rather than an improvement in FEV₁ and FVC values, likely due to factors such as the inclusion of healthy participants, the short duration of the intervention, and the characteristics of the selected population. The observed increase in PEF values was consistent with the literature and can be attributed to repeated testing and the associated learning effect.

Limitations of the study

The greatest limitation of our study stemmed from the characteristics of the study population. Because the study was conducted on young and healthy individuals, the intended objectives of the research could not be fully achieved, thereby limiting the overall clinical applicability and guiding value of the findings. Another important limitation was the inability to monitor the extent to which participants adhered to and regularly performed the prescribed breathing exercises for which they had received training.

In conclusion, our findings suggest that short-term

respiratory physiotherapy interventions in healthy individuals do not significantly improve spirometric parameters, in accordance with the existing literature. To accurately evaluate the true impact of respiratory physiotherapy, future studies should focus on high-risk patient populations with limited pulmonary reserve and employ longer-duration, individualized, and targeted physiotherapy programs.

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 conducted with the approval of the İzmir Katip Çelebi University Non-Interventional Clinical Research Ethics Committee (Approval No. 2023/597).

Authors' contribution

MU: Conceptualization, methodology, data curation, project administration, writing-original draft, formal analysis, validation. BCS: data curation, resources, investigation, formal analysis. OB: data curation, resources. MK: Writing, review, editing, visualization, supervision. SST: data curation, resources. KIT: Conceptualization, data curation, resources. SS: data curation, resources.

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Original Article

Dual-axis learning curve of a newly established robotic mediastinal surgery program: an approach-adjusted CUSUM analysis

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ABSTRACT

Background: To objectively evaluate the dual-axis learning curve and safety profile of a newly established robotic mediastinal surgery program using an approach-adjusted methodology to account for anatomical and procedural heterogeneity.

Material and Methods: A retrospective analysis of 41 consecutive patients who underwent robotic-assisted thoracic surgery (RATS) for mediastinal lesions between December 2023 and December 2025 was conducted. Procedures included lateral decubitus and subxiphoid approaches. To mitigate variations in case complexity, an Observed-Expected (O-E) approach-adjusted Cumulative Sum (CUSUM) model was employed for both access/docking time (operating room team adaptation) and console time (procedural adaptation). Phase 1 (learning) and Phase 2 (proficiency) were compared.

Results: The mean age was 44.8 ± 13.4 years. The approach-adjusted console time CUSUM demonstrated an inflection point at case 16, whereas the access/docking time CUSUM reached inflection at case 24. Comparing Phase 1 ($n = 16$) and Phase 2 ($n = 25$), the median O-E console time deviation showed a trend toward improvement from +10.0 to -13.9 minutes ($p = 0.219$), despite an increased proportion of technically demanding subxiphoid cases in Phase 2. Estimated blood loss significantly decreased in Phase 2 (0.0 mL vs. 10.0 mL, $p = 0.025$). The safety profile remained high, with no conversions in the learning phase, low postoperative complications ($n = 2$ vs. $n = 2$), and zero mortality.

Conclusions: The implementation of a newly established robotic mediastinal surgery program demonstrates feasibility with acceptable short-term outcomes when preceded by structured training. A dual-axis approach-adjusted CUSUM analysis suggests that procedural proficiency and team adaptation occur at different phases, guiding safe expansion to complex approaches.

Keywords: Robotic-assisted thoracic surgery, thymectomy, mediastinal diseases, learning curve

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Introduction

Robotic-assisted thoracic surgery (RATS) has gained widespread acceptance for the management of mediastinal pathologies, ranging from thymic diseases to neurogenic tumors [1]. Compared to standard video-assisted thoracoscopic surgery (VATS), the robotic platform offers three-dimensional high-definition visualization, tremor filtration, and wristed instrumentation with seven degrees of freedom. These technological enhancements are particularly advantageous in the narrow and rigid anatomical confines of the mediastinum, allowing for safe and precise dissection [2].

Despite these clear technical advantages, the implementation of a newly established robotic surgery program requires navigating a steep and multifaceted learning curve. The adaptation process in robotic surgery is inherently dual-axis; it involves not only the primary console surgeon's procedural proficiency but also the spatial orientation and operational efficiency of the entire operating room (OR) team, which is predominantly reflected in the access and docking times [3,4]. Furthermore, modern mediastinal robotic programs increasingly utilize tailored approaches, incorporating both lateral decubitus and multi-portal subxiphoid techniques depending on the target compartment. This procedural and anatomical heterogeneity significantly complicates the objective assessment of surgical proficiency.

Traditional learning curve analyses that rely solely on raw operative times often fail to account for these inherent variations in case complexity (e.g., radical thymectomy versus simple cyst enucleation), potentially leading to inaccurate estimations of surgical proficiency. The Cumulative Sum (CUSUM) methodology has been firmly established as a robust statistical tool to sequentially monitor surgical performance and ensure patient safety during the learning phase [3,5]. However, to accurately evaluate a heterogeneous cohort without penalizing the surgeon for adopting complex techniques later in the series, an approach-adjusted methodology is imperative.

Therefore, the objective of this study was to evaluate the safety profile and the dual-axis learning curve, distinguishing between OR team adaptation and procedural proficiency, of a newly established robotic mediastinal surgery program. By employing an approach-adjusted CUSUM methodology, this study aimed to objectively define the proficiency thresholds across a mix of anatomical compartments and diverse surgical approaches.

Materials and Methods

Study design and patient selection

Following approval by the Institutional Review Board of Başakşehir Çam and Sakura City Hospital (Approval Date: 29.12.2025, No:KA EK/24.12.2025.397) regarding the retrospective analysis of clinical data, a review of the maintained database was performed. Between 15 December 2023 and 15 December 2025, 41 consecutive patients who underwent robotic-assisted thoracic surgery (RATS) for mediastinal lesions at a single institution were included in the study. All procedures were performed by a dedicated thoracic surgery team as part of a newly established institutional robotic surgery program. Prior to the initiation of the program, formal structured robotic thoracic surgery training was completed to ensure a standardized approach to console mechanics, team coordination, and patient safety.

Surgical technique and data collection

All procedures were performed using a multi-portal technique with the da Vinci robotic surgical system (Intuitive Surgical, Sunnyvale, CA, USA). The surgical approach - right lateral decubitus, left lateral decubitus, or a multi-portal subxiphoid approach (utilizing a subxiphoid camera port combined with bilateral subcostal or intercostal working arms) - was tailored according to the lesion's location (anterior vs. posterior mediastinum), pathology, and the patient's anatomical characteristics. Three robotic arms were utilized in all cases, while the necessity of an additional assistant port was determined dynamically based on the complexity of the case.

Definition of variables

The primary endpoints of the study were the surgical proficiency metrics, specifically separated into team adaptation and procedural adaptation:

Access and docking time: Defined as the time (in minutes) from the initial skin incision for port placement to the successful attachment of the robotic arms to the trocars. This metric was utilized to evaluate the OR team's learning curve regarding spatial orientation and setup.

Console time: Defined as the duration (in minutes) the primary surgeon spent operating at the console. This metric evaluated the procedural learning curve.

Total operative time: Defined as the time from skin incision to skin closure.

Secondary endpoints included safety profile metrics: estimated blood loss, conversion to VATS or thoracotomy, intraoperative complications, and 30-day postoperative morbidity graded according to the Clavien-Dindo classification.

Statistical Analysis

Statistical analysis was performed using Python version 3.10 (Python Software Foundation, Wilmington, DE, USA) utilizing the SciPy and Pandas libraries. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on the normality of distribution assessed by the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages.

To objectively define the learning phases, the Cumulative Sum (CUSUM) methodology was employed. Due to the inherent temporal differences between distinct surgical approaches, an Observed-Expected (O-E) approach-adjusted CUSUM model was utilized for both access/docking time and console time. The expected time (μ) was explicitly derived from the mean time of the corresponding surgical approach group (subxiphoid vs. lateral). Therefore, this methodology serves to mitigate approach-related temporal confounding and should be interpreted as an approach-adjusted O-E CUSUM, rather than a multivariable approach-adjusted model incorporating individual patient factors and specific pathologies. The CUSUM series was defined by the equation: $CUSUM_n = \sum (X_i - \mu)$ where X_i represents the observed time for the i -th case.

The inflection point on the CUSUM curve identified the transition from the "learning phase" (Phase 1) to the "proficiency phase" (Phase 2). Patient demographics, operative parameters, and safety metrics were compared between these two phases using the Student's t-test or Mann-Whitney U test for continuous variables, and the Chi-square or Fisher's exact test for categorical variables. A p-value of <0.05 was considered statistically significant.

Results

Patient demographics and operative characteristics

A total of 41 consecutive patients (24 females, 17 males) underwent robotic-assisted mediastinal surgery. The mean age was 44.8 ± 13.4 years. The surgical approaches utilized included the lateral decubitus approach (right/left) in 27 patients (65.9%) and the subxiphoid approach

in 14 patients (34.1%). Baseline patient demographics and operative characteristics of the study cohort are summarized in Table 1. The overall mean access and docking time was 12.9 ± 5.6 minutes, while the expected mean console times were 90.0 minutes for lateral approaches and 138.9 minutes for subxiphoid approaches.

Learning curve and CUSUM analysis

The procedural learning curve, based on the approach-adjusted console time CUSUM, demonstrated an inflection point at Case 16, dividing the cohort into Phase 1 (Learning Phase, cases 1-16) and Phase 2 (Proficiency Phase, cases 17-41) (Figure 1). Conversely, the OR team's adaptation curve, based on the approach-adjusted access and docking time CUSUM, reached its inflection point slightly later, at Case 24 (Figure 2).

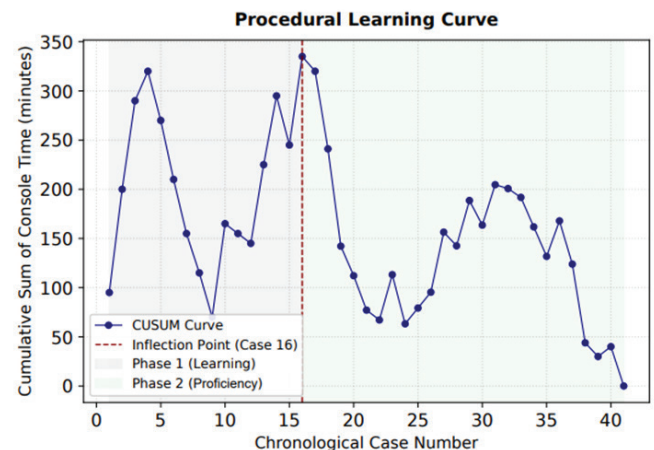


Figure 1. Approach-adjusted cumulative sum (CUSUM) analysis of the console time demonstrating the procedural learning curve. The dashed line indicates the inflection point at case 16.

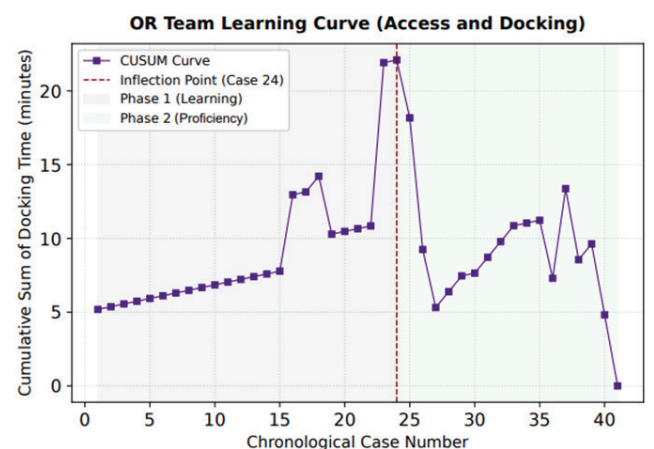


Figure 2. Approach-adjusted cumulative sum (CUSUM) analysis of the access and docking time demonstrating the operating room team's learning curve. The dashed line indicates the inflection point at case 24.

As shown in Figure 3, the raw console times initially trended downwards for the lateral approach. The subsequent introduction of the subxiphoid approach initially presented longer console times, which subsequently exhibited their own independent downward trend. The shift in surgical complexity over time is illustrated in Figure 4, confirming that as surgical proficiency increased, the proportion of cases performed via the technically more demanding subxiphoid approach progressively expanded.

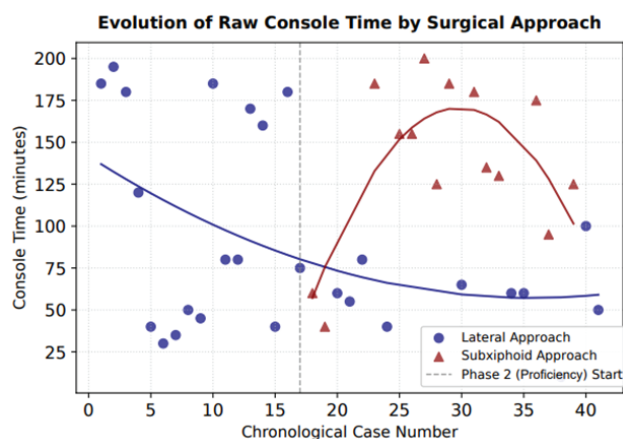


Figure 3. Scatter plot illustrating raw console times across chronological case numbers. Trendlines (second-degree polynomial) highlight the independent learning progress for lateral (navy) and subxiphoid (crimson) approaches. The vertical dashed line marks the start of Phase 2 (proficiency).

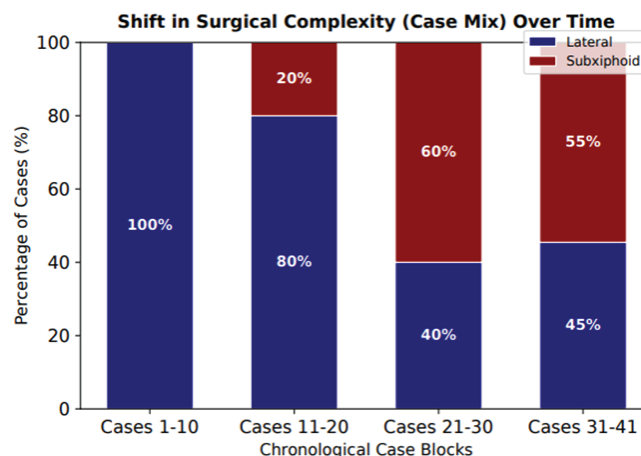


Figure 4. Stacked bar chart demonstrating the shift in case complexity over time. As surgical proficiency increased, the proportion of cases performed via the technically more demanding subxiphoid approach progressively expanded.

Comparison of Phase 1 and Phase 2

A detailed comparison between Phase 1 and Phase 2, based on the procedural inflection point, is presented in Table 2. The approach-adjusted console time deviation showed a trend toward improvement, shifting from a median of +10.0 minutes in Phase 1 to -13.9 minutes in Phase 2 ($p = 0.219$). Although the raw total operative time showed a decreasing trend in Phase 2, the difference was not statistically significant ($p = 0.915$), primarily due to the

Table 1. Baseline patient demographics and operative characteristics of the study cohort.

Variable	Total Cohort (n=41)
Age (years), mean $\pm$ SD	44.8 $\pm$ 13.4
Gender, n (%)	
Female	24 (58.5)
Male	17 (41.5)
BMI (kg/m ²), mean $\pm$ SD	28.5 $\pm$ 4.7
Surgical Approach, n (%)	
Lateral Decubitus	27 (65.9)
Subxiphoid	14 (34.1)
Pathology, n (%)	
Thymic Cyst / Hyperplasia	19 (46.3)
Thymoma	8 (19.5)
Bronchogenic / Mesothelial / Pericardial Cyst	8 (19.5)
Schwannoma / Neurogenic	6 (14.6)
Estimated Blood Loss (mL), median (IQR)	0.0 (0.0-10.0)
Total Operative Time (min), median (IQR)	120.0 (80.0-180.0)
Access and Docking Time (min), mean $\pm$ SD	12.9 $\pm$ 5.6
Console Time (min), median (IQR)	100.0 (60.0-155.0)

Table 2. Comparison of surgical proficiency metrics and safety outcomes between Phase 1 (learning phase) and Phase 2 (proficiency phase).

Variable	Phase 1 (n=16)	Phase 2 (n=25)	p-value
Access & Docking Time Deviation (min), median (IQR)	0.2 (0.2 to 0.2)	0.2 (-3.9 to 1.1)	0.694
Console Time Deviation (min), median (IQR)	10.0 (-46.2 to 90.0)	-13.9 (-35.0 to 16.1)	0.219
Estimated Blood Loss (mL), median (IQR)	10.0 (0.0 to 30.0)	0.0 (0.0 to 0.0)	0.025
Total Operative Time (min), median (IQR)	132.5 (68.8 to 200.0)	120.0 (80.0 to 180.0)	0.915
Conversion to Open/VATS, n (%)	0 (0.0)	1 (4.0)	0.390
Intraoperative Complication, n (%)	0 (0.0)	1 (4.0)	0.390
Postoperative Complication, n (%)	2 (12.5)	2 (8.0)	0.635
30-day Mortality, n (%)	0 (0.0)	0 (0.0)	>0.999

mentioned clustering of complex subxiphoid cases in the latter phase. It is crucial to note that Phase 1 consisted exclusively of lateral approaches (100%), whereas all subxiphoid cases were clustered in Phase 2. Therefore, raw temporal comparisons between the phases are inherently confounded by this shift in surgical approach, reinforcing the necessity of relying on the approach-adjusted (O-E) deviations as the primary indicator of procedural progression. Importantly, the intraoperative estimated blood loss was significantly reduced in Phase 2 compared to Phase 1 [0.0 mL (0.0-0.0) vs. 10.0 mL (0.0-30.0), $p = 0.025$]. The safety profile remained consistently high throughout the entire series. There were no conversions to VATS or open surgery in the learning phase (0% in Phase 1 vs. 4.0% [$n = 1$] in Phase 2, due to difficulty in anesthesia management). Postoperative complication rates were identically low across both phases ($n=2$ in Phase 1 vs. $n=2$ in Phase 2), with no 30-day or 90-day mortality observed.

Discussion

The widespread adoption of robotic platforms in mediastinal surgery necessitates a rigorous evaluation of the learning process, particularly in newly established programs where diverse anatomical compartments and surgical approaches are utilized sequentially [3,6]. This study aimed to objectively assess the dual-axis learning curve and safety profile of a newly established robotic mediastinal surgery program. By employing an approach-adjusted CUSUM methodology to account for procedural heterogeneity, we identified a procedural consolidation signal at 16 cases and an OR team adaptation inflection points at 24 cases, all while maintaining a consistently high safety profile.

A critical challenge in evaluating learning curves in thoracic surgery is the inherent variation in case com-

plexity [3,7]. In our cohort, the initial learning phase predominantly consisted of lateral decubitus approaches, whereas the technically more demanding subxiphoid approach was introduced and utilized more frequently in the latter half of the series. Standard temporal analyses often misinterpret this shift as a lack of progress, as raw operative times may not significantly decrease [8,9]. However, the approach-adjusted O-E CUSUM analysis successfully mitigated this confounding factor. Although the raw console time did not show a statistically significant reduction between Phase 1 and Phase 2 ($p = 0.957$), the O-E deviation demonstrated a trend toward improvement, transitioning from a median of +10.0 minutes to -13.9 minutes. This finding aligns with the learning curve thresholds of 15 to 25 cases previously reported for robotic thymic diseases, confirming that the primary surgeon achieved proficiency and subsequently applied it to more complex anatomical orientations [10-13].

Furthermore, true surgical consolidation is reflected not only in operative speed but also in tissue handling and intraoperative safety [14]. In the present study, the estimated blood loss significantly decreased from a median of 10.0 mL in Phase 1 to 0.0 mL in Phase 2 ($p = 0.025$). While the absolute clinical difference is small, this reduction may reflect improved tissue handling during wristed instrument manipulation and precise vascular dissection within the confined mediastinal space [15].

The dual-axis nature of our analysis revealed that OR team adaptation (access and docking time) required a slightly longer learning phase (24 cases) compared to the surgeon's console adaptation (16 cases). The subxiphoid approach, which involves a different spatial configuration and complex port placement compared to the stand-

ard lateral decubitus position, inherently prolongs setup times during the initial adoption phase [16]. The later inflection points for docking time highlights the importance of maintaining a dedicated robotic OR team to ensure standardized workflows and progressive efficiency when introducing new patient positioning techniques.

Patient safety must remain the primary priority during the adoption of any novel surgical technique. Our results demonstrated zero conversions to open surgery or VATS in the initial learning phase, with an identically low rate of postoperative complications across both phases and zero mortality. We attribute this safe transition to the completion of formal, structured robotic thoracic surgery training prior to the program's initiation. Such prerequisite training likely acts as a safeguard, ensuring that the initial learning phase represents a refinement of technique and workflow integration rather than a period of hazardous trial and error.

Limitations of the study

This study has several limitations. It is a retrospective analysis from a single center with a relatively modest sample size ($n = 41$). While the cohort size is sufficient for exploratory CUSUM assessment, the findings reflect the experience of a specific dedicated team and may not be universally generalizable. Additionally, while our approach-adjusted methodology effectively mitigated the temporal confounding caused by patient positioning (lateral vs. subxiphoid), we must emphasize that this is not a fully risk-adjusted model. It did not statistically account for other critical determinants of operative time, such as pathological diagnosis, lesion complexity, extent of resection, tumor size, and patient-related variables (e.g., BMI). This heterogeneity introduces inherent variability into the learning curve. Furthermore, the chronological clustering of all subxiphoid cases in Phase 2 introduces significant case-mix heterogeneity, which inherently confounds raw temporal comparisons between the phases. Due to the modest sample size of the cohort, further subgroup analyses to isolate these variables were not feasible. Future multicenter prospective studies with larger, pathology-specific subgroups are warranted to validate these proficiency thresholds. Furthermore, the identified proficiency thresholds (16 cases for the surgeon and 24 for the team) are model-

dependent outcomes derived specifically from our approach-adjusted CUSUM methodology. While these numbers align with broader thymectomy learning curve literature, they should be interpreted as institutional benchmarks rather than absolute universal cut-offs.

In conclusion, our early experience suggests that a newly established robotic mediastinal surgery program can be implemented feasibly after structured training, with acceptable short-term postoperative outcomes. An approach-adjusted dual-axis CUSUM analysis reveals that the transition toward procedural proficiency and OR team adaptation occur at different phases. Objective monitoring of these distinct learning curves provides valuable insights for optimizing team workflows and safely expanding surgical indications to more complex approaches.

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 the Institutional Review Board of Başakşehir Çam and Sakura City Hospital (Approval Date: 29.12.2025, No:KA EK/24.12.2025.397).

Authors' contribution

MI: Concept, design, supervision, data collection, literature search, statistical analysis, writing, and critical review. AY: Design, supervision, and critical review. OY: Data collection, literature search, and critical review. All authors read and approved the final version of the manuscript.

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Original Article

Outcomes and prognostic factors following surgical treatment of pulmonary large cell neuroendocrine carcinoma

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ABSTRACT

Background: Pulmonary large cell neuroendocrine carcinoma (LCNEC) is a rare subtype of lung cancer with a poor prognosis, making its management challenging. This study aimed to evaluate the surgical outcomes of patients who underwent resection for LCNEC at our clinic during the past 10 years and to identify prognostic factors.

Materials and Methods: Patients who underwent surgery for lung cancer were retrospectively reviewed. Those with a postoperative histopathological diagnosis of LCNEC were included. Demographic and clinicopathological characteristics were analyzed, and factors affecting survival were investigated.

Results: Between January 2016 and December 2025, pulmonary resection was performed in 1066 patients with primary lung cancer, of whom 36 (3.4%) had LCNEC. The mean overall survival (OS) was 56.4 ± 8.0 months, with a 5-year OS rate of 42.8%. The mean disease-free survival (DFS) was 37.7 ± 7.4 months, with a 5-year DFS rate of 26.1%. Patients who received adjuvant therapy had significantly better OS ($p < 0.001$) and a trend toward improved DFS ($p = 0.215$) compared to those who did not, particularly in stage II and higher disease ($p < 0.001$ and $p = 0.177$, respectively). The presence of spread through air spaces (STAS) and higher N stage were associated with worse survival outcomes, although these differences did not reach statistical significance.

Conclusions: Adjuvant therapy is associated with improved survival in patients undergoing surgery for LCNEC.

Keywords: pulmonary large cell neuroendocrine carcinoma, surgical resection, prognosis

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Introduction

Large-cell neuroendocrine carcinoma (LCNEC) of the lung is a rare and aggressive malignancy. Histopathologically, it exhibits features that overlap with both small-cell lung cancer (SCLC) and non-small cell lung carcinoma (NSCLC). LCNEC accounts for approximately 3% of all lung cancer cases [1]. Due to its low incidence, heterogeneous histopathological structure, and aggressive clinical course, LCNEC presents a significant diagnostic and therapeutic challenge.

Under the World Health Organization (WHO) classification of lung tumors, LCNEC is categorized within the neuroendocrine neoplasms group, alongside typical carcinoid, atypical carcinoid, and SCLC. Compared to carcinoid tumors, LCNEC exhibits a higher Ki-67 proliferation index and increased mitotic counts. This profile is directly associated with tumor aggressiveness and a poor prognosis [2]. The Ki-67 index, even when obtained from small biopsies, serves as a crucial diagnostic aid for neuroendocrine tumors. Due to its aggressive nature and high propensity for early metastasis, LCNEC is classified as a high-grade neuroendocrine tumor, similar to SCLC [3]. In light of these characteristics, adjuvant therapy is recommended to prevent recurrence and improve overall survival [4].

Due to the rarity of pulmonary large cell neuroendocrine carcinoma (LCNEC), the number of studies focusing on this tumor is limited. In this study, we aimed to analyze the 10-year surgical outcomes of patients who underwent surgery for LCNEC, and to evaluate their demographic characteristics as well as tumor-related clinicopathological factors.

Materials and Methods

Patients

Patients who underwent surgery for lung cancer at our clinic were retrospectively reviewed. Among these cases, those whose postoperative pathology reports identified LCNEC or an LCNEC component were included in the study. Patients who did not undergo therapeutic surgery or those with incomplete medical records were excluded. This study was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (Approval No: 2026/010.99/26/1, date: 01.04.2026) and was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from each participant.

Data collection

The demographic characteristics of the included patients, the type of surgical treatment performed, tumor

invasion parameters, PET/CT findings, the administration of adjuvant therapy, staging according to the 9th edition of the TNM system [5], overall survival, and disease-free survival were evaluated. Overall survival (OS) and disease-free survival (DFS) were defined as the time from the date of surgery to the date of death or recurrence, respectively.

Preoperative period

All patients who underwent surgical treatment for lung cancer at our institution were preoperatively evaluated using computed tomography (CT) and positron emission tomography (PET/CT). Patients presenting with lesions suggestive of primary lung malignancy on PET/CT without evidence of mediastinal lymph node involvement or distant metastasis underwent direct surgical intervention. In these cases, wedge resection followed by intraoperative frozen section examination was performed and upon confirmation of malignancy, subsequent anatomical resection was carried out. For central lesions and tumors larger than 3 cm, transthoracic needle aspiration biopsy (TTNA) was utilized as the initial diagnostic modality. Invasive mediastinal staging, via endobronchial ultrasonography (EBUS) or mediastinoscopy, was indicated for tumors exceeding 3 cm in diameter. Patients with confirmed single-station N2 disease on preoperative invasive staging proceeded to surgery following neoadjuvant therapy, whereas those with multi-station N2 involvement were excluded from surgical resection [6]. Patients who received neoadjuvant therapy due to pN2 disease and were downstaged to cN0 in the preoperative period were included in the study. Functional status was evaluated through pulmonary function tests and echocardiography, while preoperative risk stratification was documented using the Charlson Comorbidity Index.

Surgical approach

The extent of anatomical resection comprising lobectomy, bilobectomy, sleeve lobectomy, or pneumonectomy was determined based on tumor size and localization. Complete macroscopic tumor clearance was achieved in all patients. In cases with chest wall involvement, additional en bloc chest wall resection was performed. Furthermore, systematic mediastinal lymph node dissection was carried out in every patient to ensure accurate pathological staging.

Postoperative follow-up

Patients who underwent surgical resection for LCNEC were monitored with thoracic CT scans every 3 months for

the first 2 years and subsequently every 6 months for up to 5 years. While adjuvant therapy is conventionally recommended in routine NSCLC practice for patients with tumors larger than 4 cm or those with N1/N2 disease, in our study cohort, adjuvant treatment was recommended for LCNEC patients starting from Stage I. Adjuvant therapy was not administered in cases of patient refusal or due to an inability to tolerate chemotherapy-related toxicities. If follow-up assessments suggested recurrence, further evaluation via PET/CT was conducted and biopsy procedures were performed when clinically indicated.

Statistical Analysis

Categorical variables were presented as frequencies and percentages. Continuous variables were expressed as mean $\pm$ standard deviation and compared using the Student's t-test. Overall survival (OS) and disease-free survival (DFS) were estimated using the Kaplan–Meier method, with statistical differences assessed by the log-rank test. Survival analyses are carried out after excluding operative mortality. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were carried out using SPSS version 26.0 (IBM Corporation, Armonk, NY, USA).

Results

Between January 2016 and December 2025, a total of 1,066 patients underwent anatomical resection for lung cancer at the Thoracic Surgery Clinic of Kartal Dr. Lütfi Kırdar City Hospital. Among these patients, 36 patients (3.4%) were diagnosed with LCNEC.

Demographic characteristics, surgical approaches, invasion parameters, and TNM stages of the patients are presented in Table 1.

The mean age of the patients included in the study was 62.8 ± 8.7 years and the average tumor size was 4.56 ± 2.33 cm. On PET/CT examination, the mean maximum standardized uptake (SUVmax) value was calculated as 11.9 ± 7.3 . In the resected tumors, the mean Ki-67 proliferation index was found to be 72.6 ± 14.7 .

During the follow-up period, 19 patients (52.8%) remained alive, while 17 patients (47.2%) died; of these, 3 patients (8.3%) passed away within the first three post-operative months. The mean overall survival (OS) of the study cohort was 56.4 ± 8.0 months, with a 5-year OS rate of 42.8%. During the follow-up process, recurrence or metastasis was observed in 17 patients (47.2%). The mean disease-free survival (DFS) was 37.7 ± 7.4 months, and the 5-year DFS rate was found to be 26.1% (Figure 1). The sites of recurrence are presented in Table 2.

Analysis on spread through air spaces (STAS) reveals mean overall survival was 52.7 ± 9.6 months for STAS-positive patients, with a 5-year OS rate of 51.1%. For STAS-negative patients, mean OS was 61.5 ± 11.8 months, with a 5-year OS rate of 52.5% ($p = 0.517$). STAS-positive patients had a mean DFS of 40.4 ± 8.4 months and a 5-year DFS rate of 47.3%, whereas STAS-negative patients exhibited a mean DFS of 39.0 ± 12.0 months, with a 5-year DFS rate of 22.2% ($p = 0.910$).

All patients included in the study were preoperatively staged as cN0. Occult hilar/mediastinal lymph node metastasis was observed in 11 patients (30.5%). In patients with mediastinal lymph node positivity, the mean overall survival was 36.4 ± 7.7 months, with a 5-year survival rate of 44.2%. For patients without mediastinal lymph node involvement, the mean overall survival was 56.7 ± 9.3 months, with a 5-year OS rate of 42.1% ($p = 0.906$). Regarding disease-free survival, the mean DFS for patients with mediastinal lymph node metastasis was 17.7 ± 2.8 months, with a 5-year DFS rate of 26.5%. In the group without mediastinal lymph node metastasis, these values were calculated as 40.2 ± 8.5 months and 29.5%, respectively ($p = 0.769$).

The impact of adjuvant therapy on mean survival values is detailed in Table 3 and illustrated in Figure 2.

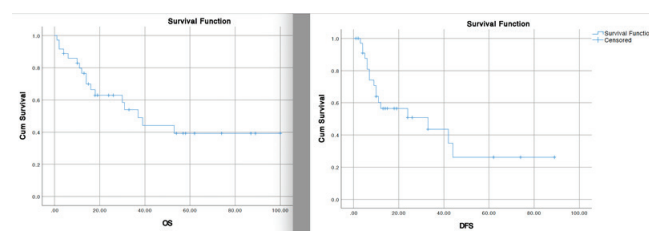


Figure 1. Overall survival and disease-free survival of patients included in the study.

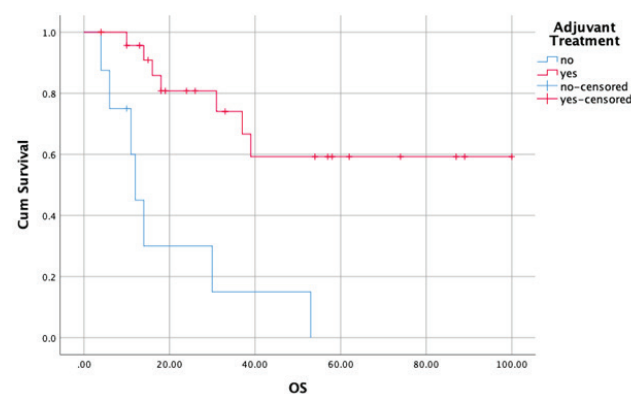


Figure 2. Overall survival depending on adjuvant treatment.

Table 1. Demographics of the patients, surgical approach, invasion parameters and staging.

Gender		STAS	
Male	33 (91.66%)	Negative	10 (27.77%)
Female	3 (8.33%)	Positive	20 (55.55%)
Preoperative Biopsy		Not investigated	6 (16.66%)
Malignant	24 (66.66%)	Pleural invasion	
LCNEC/NE	5 (13.88%)	PL0	26 (72.22%)
AdC	1 (2.77%)	PL1	5 (13.88%)
SqCC	2 (5.55%)	PL 2	0 (0.00%)
Non-diagnostic	1 (2.77%)	PL 3	1(2.77%)
Not performed	3 (8.33%)	Vascular invasion	
Definitive diagnosis		No	21 (58.33%)
Pure LCNEC	22 (61.11%)	Yes	15 (41.66%)
AdC component	8 (22.22%)	Perineural invasion	
SqCC component	4(11.11%)	No	32 (88.88%)
Pleomorphic C component	1 (2.77%)	Yes	4 (11.11%)
SCLC component	1 (2.77%)	T Status	
Symptoms		T1b	5 (13.88%)
Incidental	9 (25.00%)	T1c	7 (19.44%)
Chronic cough	13 (36.11%)	T2a	8 (22.22%)
Fatigue	6 (16.66%)	T2b	4 (11.11%)
Hemoptysis	1 (2.77%)	T3	6 (16.66%)
Dizziness	1 (2.77%)	T4	6 (16.66%)
Surgery		N Status	
RUL	11 (30.55%)	N0	25 (69.44%)
RML	1 (2.77%)	N1	7 (19.44%)
RLL	4 (11.11%)	N2a	3 (8.33%)
LUL	7 (19.44%)	N2b	1 (2.77%)
LLL	9 (25.00%)	M Status	
Lower bilobectomy	1 (2.77%)	M0	33 (91.66%)
Right Pneumonectomy	1 (2.77%)	M1b	3 (8.33%)
Left Pneumonectomy	2 (5.55%)	Stage	
Incision		IA2	3 (8.33%)
VATS	11 (30.55%)	IA3	5 (13.88%)
Thoracotomy	18 (50.00%)	IB	5 (13.88%)
Conversion	7 (19.44%)	2A	3 (8.33%)
Neoadjuvant Treatment		2B	9 (25.00%)
No	33 (91.66%)	3A	5 (13.88%)
Yes	3 (8.33%)	3B	3 (8.33%)
Mediastinal Staging		IVA	3 (8.33%)
Not performed	13 (36.11%)		
EBUS	18(50.00%)		
Mediastinoscopy	5 (13.88%)		

Abbrev.: AdC: Adenocarcinoma, EBUS: Endobronchial ultrasound, LCNEC/NE: Large cell neuroendocrine carcinoma/neuroendocrine carcinoma, LLL: Left lower lobectomy, LUL: Left upper lobectomy, RLL: Right lower lobectomy, RML: Right middle lobectomy, RUL: Right upper lobectomy, SCLC: Small Cell carcinoma, SqCC: Squamous cell carcinoma, STAS: Spread through air spaces, VATS: Video-assisted thoracoscopic surgery

Table 2. Recurrence sites of patients included in the study.

Recurrence Site	
Lung	2 (5.55%)
Mediastinum	7 (19.44%)
Brain	3 (8.33%)
Bone	4 (11.11%)
Liver	1 (2.77%)
Total	17 (47.22%)

Table 3. Survival based on adjuvant treatment. DFS: Disease-free survival, OS: Overall survival.

	Mean OS (months) based on presence of adjuvant treatment			Mean DFS (months) based on presence of adjuvant treatment		
	Adjuvant (-)	Adjuvant (+)	p value	Adjuvant (-)	Adjuvant (+)	p value
All stages	19.25±6.61	69.76±9.05	<0.0001	23.05±8.01	42.35±8.75	0.215
Stage 1	41.50±11.50	73.64±15.26	0.248	27.00±17.00	35.85±11.63	0.925
Stage 2-3-4	9.88±1.68	62.17±9.41	<0.0001	8.67±2.12	45.09±10.56	0.177

Discussion

Pulmonary LCNEC was previously classified as a sub-type of large-cell lung cancer in the 2004 World Health Organization (WHO) classification [7]. With subsequent updates to immunohistochemical criteria, it was recategorized in 2015 within the neuroendocrine tumor group of the lung, along with typical carcinoid, atypical carcinoid, and small-cell lung cancer [8]. In the 2021 WHO classification, neuroendocrine neoplasms were categorized as low-grade (typical carcinoid), intermediate-grade (atypical carcinoid), and high-grade neuroendocrine carcinomas, the latter consisting of LCNEC and SCLC [9].

Despite improvements in the diagnostic yield of small-needle biopsies in recent years, establishing a preoperative diagnosis of LCNEC remains challenging using limited biopsy specimens. Due to the presence of excessive necrosis typically associated with these tumors, larger tissue samples are required to identify neuroendocrine morphology and perform specific immunohistochemical staining for neuroendocrine markers [10]. Consequently, patients with a final pathology of LCNEC are frequently preoperatively misdiagnosed as having

other types of NSCLC or SCLC [11,12]. In a study by Chen et al., it was reported that a diagnosis of LCNEC was achieved in only 6 out of 20 patients who underwent preoperative bronchoscopic or transthoracic biopsy [13]. Consistent with these findings, the majority of patients in our study could not be diagnosed with LCNEC preoperatively through small biopsies obtained via TTNA or transbronchial biopsy.

In patients with good performance status and adequate cardiopulmonary function, surgical intervention remains the primary therapeutic approach for early-stage LCNEC [14]. Previous studies have demonstrated that sublobar resections, such as segmentectomy and wedge resection, do not provide survival benefits comparable to those of lobar resections [15-18]. Due to the high growth potential of these tumors, extensive tumor necrosis and hemorrhage may be encountered intraoperatively [19], necessitating heightened caution, particularly when managing large masses. It has also been documented that spontaneous tumor rupture can lead to hemorrhagic shock [20]. At our clinic, the minimum extent of resection performed for all LCNEC patients

was lobectomy. Our surgical experience indicates that these tumors contain significant necrosis and are prone to persistent, oozing-type bleeding due to excessive angiogenesis—though not necessarily massive hemorrhage. Consequently, this characteristic may contribute to an increased rate of conversion from video-assisted thoracoscopic surgery (VATS) to thoracotomy in this specific tumor type.

The optimal stage at which adjuvant therapy should be recommended for resectable LCNEC remains a subject of ongoing debate. Existing studies have reported benefits of postoperative adjuvant treatment in Stage I disease [21], Stage IB or higher disease, and Stage IIB or higher disease [15]. Although the number of studies on this topic is limited, the standard approach for early-stage LCNEC similar to that for SCLC is platinum-etoposide or irinotecan combinations. When all stages included in our study were analyzed, adjuvant therapy was found to provide a statistically significant benefit in OS. While a survival benefit was also observed in Stage I disease, it did not reach statistical significance. In contrast, for Stage II and higher disease, a statistically significant improvement in OS was observed. These findings suggest that while adjuvant therapy benefits the entire cohort, its efficacy is more pronounced in Stage II and higher disease. In DFS analyses, although adjuvant therapy appeared more beneficial, this advantage did not achieve statistical significance.

First described by Kadota et al. in 2015 [22], spread through air spaces (STAS) refers to clusters of tumor cells or single tumor cells within the air spaces beyond the edge of the main tumor. Although STAS was formally recognized as a prognostic feature only for non-mucinous adenocarcinoma in the 2021 WHO classification of lung tumors [23], it has been shown to adversely affect prognosis in other histopathological subtypes as well, despite its prevalence and prognostic significance being more extensively documented in adenocarcinomas [24-26]. In a study by Aly et al. focusing on STAS in neuroendocrine lung cancers, the prevalence of STAS in LCNEC was reported as 43%, and its presence was identified as a poor prognostic factor for both disease-

free survival and overall survival [27]. Consistently, our study suggested that STAS is a poor prognostic factor for LCNEC, although this association did not reach statistical significance.

Preoperative PET/CT is mandatory for patients with confirmed or suspected lung cancer. Invasive mediastinal staging is indicated when the tumor size exceeds 3 cm or if PET/CT reveals suspicious uptake in mediastinal or hilar lymph nodes [28]. Nodal upstaging is recognized as a poor prognostic factor in lung cancer. Previous studies have demonstrated nodal upstaging rates of 10% in clinical Stage I LCNEC and 8% in clinical Stage II LCNEC [15]. In our study, the rates of occult pN1 and pN2 disease were consistent with the literature. Furthermore, although the association did not reach statistical significance, nodal upstaging was found to be associated with a worse prognosis.

Ki-67 is an antigen expressed by the MKI67 gene and has been identified as a parameter associated with a poor prognosis [29]. In neuroendocrine lung tumors, the Ki-67 proliferation index is typically below 20% to 30% in typical and atypical carcinoids, whereas it often exceeds 50% and frequently surpasses 70% to 80% in LCNEC and SCLC [30]. Consequently, the Ki-67 index plays a pivotal role in refining the differential diagnosis of neuroendocrine neoplasms, particularly in small-needle biopsy specimens where tissue samples are limited.

Due to the rarity of LCNEC and the limited number of publications in the literature, reported survival rates vary within a wide range, despite the well-established aggressive nature and poor prognosis of this tumor. Studies have demonstrated that 5-year OS rates for all stages of LCNEC range from 18% [31] to 53.8% [32], and even in Stage I disease alone, these values fluctuate between 18% and 88%. These studies indicate that adjuvant therapy following surgery in resectable patients is associated with improved OS, with N and M stages being the most prominent factors influencing OS [13]. The number of publications reporting DFS rates for this tumor is considerably lower. One study reported a 5-year DFS of 32.2% and identified adjuvant chemotherapy and TNM stage as the primary factors affecting DFS [33].

In conclusion, our study reveals the administration of adjuvant therapy provides a statistically significant benefit in overall survival, it was also observed that STAS status and N status influence survival outcomes. These parameters were further found to be associated with disease-free survival.

Limitations of the study

Our study has several limitations. First is its retrospective design; however, clinical records at our institution were meticulously maintained and documented. The second limitation is the relatively small number of the sample size. This constraint is commonly encountered in the majority of existing literature on this specific subject. The primary reason why parameters such as STAS presence and N status did not reach statistical significance in their impact on overall and disease-free survival is likely the limited sample size. Nevertheless, this limitation is inherent to most studies focusing on this exceptionally rare tumor type.

Declaration of conflicting interests

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Ethics approval

This study was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (Approval No: 2026/010.99/26/1, date: 01.04.2026).

Use of Generative AI and AI-assisted technologies in the writing process

Artificial intelligence was utilized solely for writing assistance, grammar correction, and to enhance the clarity and understandability of the manuscript.

Authors' Contribution

BC: Conceptualization, Methodology, Writing - original draft, Project administration. MB: Data curation. FTO: Formal analysis, investigation. MTD: Data curation, software. AO: Validation, Supervision. RD: Conceptualization, Supervision

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Original Article

Clinical access restrictions in totally implantable venous access port (TIVAP) implantation: revision and malposition outcomes in a 1,224-patient cohort

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ABSTRACT

Background: Current guidelines recommend the right internal jugular vein as the primary access route for totally implantable venous access port (TIVAP) implantation. However, oncologic patients frequently present with anatomical or clinical constraints that necessitate alternative venous access routes. This study aimed to evaluate whether clinical conditions restricting guideline-preferred access planning are associated with increased revision or catheter malposition rates in TIVAP implantation.

Material and Methods: This retrospective single-center, single-operator study included 1,224 consecutive adult patients who underwent TIVAP implantation between June 2022 and January 2026. Patients with clinical conditions limiting cervical or pectoral access were classified as the restricted-access group ($n = 115$), while the remaining patients comprised the standard-access group ($n = 1,109$). Primary outcomes were revision and catheter malposition. Logistic regression analyses were performed to evaluate potential risk factors.

Results: Left-sided access (12.2% vs 1.4%, $p < 0.001$) and subclavian vein use (47.0% vs 20.2%, $p < 0.001$) were significantly more frequent in the restricted-access group. Revision rates (4.3% vs 3.7%, $p = 0.612$) and catheter malposition rates (1.7% vs 0.7%, $p = 0.240$) did not differ significantly between groups. Restricted-access status was not independently associated with revision (OR 1.08, 95% CI 0.38-3.01, $p = 0.887$) or malposition (OR 0.86, 95% CI 0.15-4.70, $p = 0.861$). Subclavian vein use was associated with catheter malposition (OR 34.84, 95% CI 4.31-281.2, $p = 0.001$).

Conclusions: No statistically significant increase in revision or catheter malposition risk was observed in patients with clinical conditions restricting guideline-preferred access planning. When applied within a standardized procedural framework, alternative venous access strategies may be feasible according to patient-specific anatomical conditions.

Keywords: vascular access device, revision surgery, subclavian vein, head and neck neoplasm

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Introduction

Oncologic treatment requires reliable vascular access for the safe and continuous administration of cytotoxic agents. Peripheral vein damage caused by irritant drugs and the physical and psychological burden of repeated interventions necessitate the use of central venous access devices. In this context, totally implantable venous access ports (TIVAPs) are one of the most effective methods, significantly enhancing patient comfort.

The surgical implantation of these devices requires careful selection of the access vein. Current international guidelines recommend the right internal jugular vein as the primary choice because it provides the most direct and linear anatomical path to the right atrium [1-3].

Many studies in the literature focus on comparing various venous access routes and techniques to identify the optimal TIVAP insertion site [4,5]. However, there is a lack of large cohort studies [4,6] investigating the safety and clinical outcomes of situations where surgeons are obliged to utilize non-guideline routes, such as left-sided access or the subclavian vein, due to anatomical constraints or clinical barriers inherent in oncological surgery. This gap in the literature leads to clinical uncertainty regarding procedural safety, particularly in terms of revision requirements and catheter malposition, when practitioners must operate outside the idealized conditions proposed by current guidelines.

We evaluated whether the use of alternative TIVAP access routes in patients with anatomical or clinical constraints was associated with increased revision or catheter malposition rates. Accordingly, the aim of our study was to evaluate revision and malposition outcomes in patients with clinical conditions restricting guideline-preferred access planning and requiring alternative access strategies when necessary.

Material and Methods

Patient selection and study groups

This retrospective, single-center, single-operator study included 1,224 consecutive patients aged 18 years or older who underwent TIVAP implantation at our institution between June 2022 and January 2026. Cases in which port implantation could not be completed (n =

28) were excluded. Failed implantation cases were excluded from the main revision and malposition analyses because these outcomes require a successfully implanted port system. However, these cases were reviewed separately as technical failures. The study was approved by the Clinical Research Ethics Committee of Basakşehir Çam and Sakura City Hospital (approval number: KAEK/11.02.2026.48). The requirement for study-specific informed consent was waived given the retrospective nature of the study.

Real-time ultrasound guidance was not routinely available at our institution; therefore, all procedures were performed using the anatomical landmark technique.

Patients were divided into two groups based on their diagnoses and clinical characteristics that could affect cervical and pectoral anatomy, regardless of the venous access route ultimately used for implantation. A total of 115 patients with clinical conditions influencing side selection and/or complicating access to the cervical region, including head and neck malignancies, prior neck surgery, a history of cervical radiotherapy, tracheostomy, conditions causing distortion of cervical anatomy (e.g., large goiter), as well as conditions potentially affecting pectoral access planning, including breast cancer and lymphoma, were defined as the restricted-access group. Although these conditions may not directly alter venous anatomy, they were considered clinical factors that could influence side selection or surgical planning for venous access. These conditions were considered clinical factors potentially restricting guideline-preferred access planning. Restricted-access status was defined according to preoperative clinical or anatomical conditions that could influence access planning, rather than according to the venous route ultimately used. Therefore, the term restricted-access group refers to patients with potential clinical constraints on guideline-preferred access, not to patients in whom deviation from the right internal jugular route was individually documented as mandatory in every case.

The remaining 1,109 patients without such clinical characteristics were classified as the standard-access group. After group allocation, the distribution of venous access routes (right/left and jugular/subclavian), along with demographic characteristics, comorbidities, and clinical

cal outcomes, were analyzed in both groups. Median follow-up duration was 7.3 months (IQR: 3.0-13.0 months).

Procedure

All procedures were performed in a day-surgery operating room under sedation and local anesthesia by the same surgeon using a standardized institutional protocol. Venous access was obtained using the anatomical landmark technique. Guideline recommendations were considered during procedural planning, and the right internal jugular vein was preferred whenever anatomically feasible. When right internal jugular vein access was not feasible, the procedure was performed via the right subclavian, left internal jugular, or left subclavian veins.

To minimize the risk of procedure-related pneumothorax, ipsilateral alternative access was preferred, and contralateral attempts were avoided within the same session whenever possible. If both right-sided veins were deemed unsuitable, the procedure was performed on the left side.

Post-procedural control was achieved with posteroanterior chest radiography, and patients were discharged on the same day.

Outcomes

The primary outcomes were defined as port revision and catheter malposition. Revision was defined as any surgical reintervention performed to restore the functionality or safety of the port system following the initial implantation. This included port removal, repositioning, or corrective procedures involving the catheter. In this cohort, revision procedures were performed for skin erosion at the port site. Because all revision procedures in this cohort were performed for skin erosion at the port site, revision was evaluated as a clinically relevant port-system reintervention outcome rather than as a direct route-specific technical complication.

Catheter malposition was defined as the catheter tip being located outside the intended anatomical position, typically the cavoatrial junction, and was evaluated using posteroanterior chest radiography obtained after the procedure in all patients. Only technical placement errors related to the initial implantation were considered within the scope of malposition.

Statistical Analysis

The normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with normal distribution were presented as mean $\pm$ standard deviation, whereas non-normally distributed variables were reported as median and interquartile range (IQR). Comparisons of continuous variables between groups were performed using the Student's t-test or the Mann-Whitney U test, as appropriate. Categorical variables were expressed as numbers and percentages and were compared using the chi-square test or Fisher's exact test.

To identify potential risk factors for revision and catheter malposition, univariable analyses were first conducted; variables with $p < 0.10$ in univariable analysis were entered into logistic regression models. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Associations between continuous variables and complications were evaluated using Spearman's correlation analysis.

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA), and a p -value < 0.05 was considered statistically significant.

Results

A total of 1,224 consecutive patients were included in the study. Among them, 115 patients with clinical characteristics potentially limiting vascular access were classified as the restricted-access group, while 1,109 patients without such features comprised the standard-access group. The patient selection process and group allocation are illustrated in Figure 1. The demographic and baseline clinical characteristics of both groups are presented in Table 1. The distribution of restricted-access indications is summarized in Supplementary Table 1.

Among all attempted implantations, 28 procedures could not be completed and were excluded from the main revision and malposition analyses because these outcomes required successful port implantation. These failed cases are summarized separately in Supplementary Table 2. Of these, 3 patients belonged to the restricted-access group and 25 to the standard-access group. Right-sided access was attempted in 25 patients and left-sided access in 3 patients. Both jugular and subcla-

vian access were attempted in these cases. All patients were subsequently referred to interventional radiology.

Patients in the restricted-access group were significantly younger than those in the standard-access group (median age: 58 [IQR 46-64] vs 62 [54-69]; $p < 0.001$) and had a higher median body mass index (28 [24-30] vs 25 [23-29]; $p = 0.004$). Female sex was more frequent in the restricted-access group (59.1% vs 37.5%; $p < 0.001$).

Procedural characteristics and clinical outcomes according to the restricted-access and standard-access groups are presented in Table 2. Left-sided access was significantly more frequent in the restricted-access group (12.2% vs 1.4%; $p < 0.001$). Similarly, subclavian vein use was more common in this group (47.0% vs 20.2%; $p < 0.001$). The distribution of venous access side between groups is shown in Figure 2.

In terms of clinical outcomes, no significant differences were observed between the groups with respect to revision rates (4.3% vs 3.7%; $p = 0.612$) or catheter malposition (1.7% vs 0.7%; $p = 0.240$). Pneumothorax occurred in 5 patients (0.4%) in the overall cohort.

Multivariable logistic regression analysis for revision risk according to the restricted-access and standard-access groups is presented in Table 3. Being in the restricted-access group was not independently associated with revision (OR: 1.08; 95% CI: 0.38-3.01; $p = 0.887$). Although left-sided access showed a tendency toward an increased risk of revision, it did not reach statistical significance (OR: 3.44; 95% CI: 0.88-13.28; $p = 0.073$). No significant associations were observed between revision and either age or body mass index.

Multivariable logistic regression analysis for catheter malposition is presented in Table 4 and illustrated in Figure 3. Being in the restricted-access group was not independently associated with malposition (OR: 0.86; 95% CI: 0.15-4.70; $p = 0.861$). Subclavian vein use was independently associated with catheter malposition (OR: 34.84; 95% CI: 4.31-281.2; $p = 0.001$). Increasing age was associated with a lower risk of malposition (OR: 0.95; 95% CI: 0.90-0.99; $p = 0.029$). The distribution of catheter malposition events according to venous access route is presented in Supplementary Table 3. Most catheter malposition events occurred following right subclavian vein access.

The distribution of comorbidities between the groups is presented in Table 5. No significant differences were observed between the groups with respect to diabetes mellitus, hypertension, smoking status, chronic steroid use, or organ failure. Thyroid disorders were more frequent in the restricted-access group (12.2% vs 6.2%; $p = 0.026$).

Correlations between continuous variables and clinical outcomes were evaluated using Spearman correlation analysis, and the results are provided in Supplementary Table 4. Associations between comorbidities and clinical outcomes are presented in Supplementary Table 5. Overall, patient-related comorbidities were not significantly associated with procedural complications in this cohort.

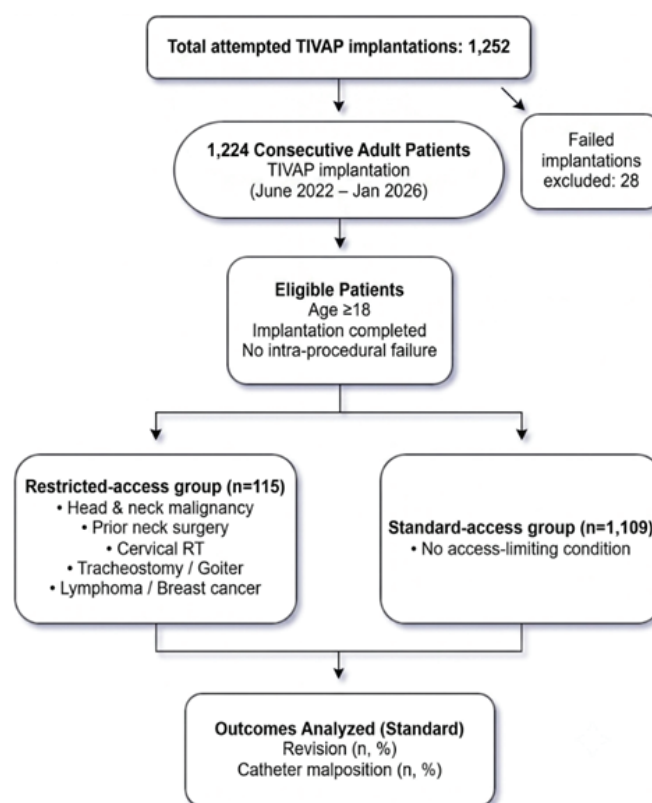


Figure 1. Study flow diagram. Flowchart showing patient selection, exclusion of failed implantations, and group allocation. A total of 1,252 TIVAP implantation attempts were identified. Of these, 28 failed implantations were excluded, leaving 1,224 consecutive adult patients with completed implantation and no intra-procedural failure. Eligible patients were then classified into the restricted-access group ($n = 115$) and the standard-access group ($n = 1,109$). Revision and catheter malposition outcomes were analyzed in both groups.

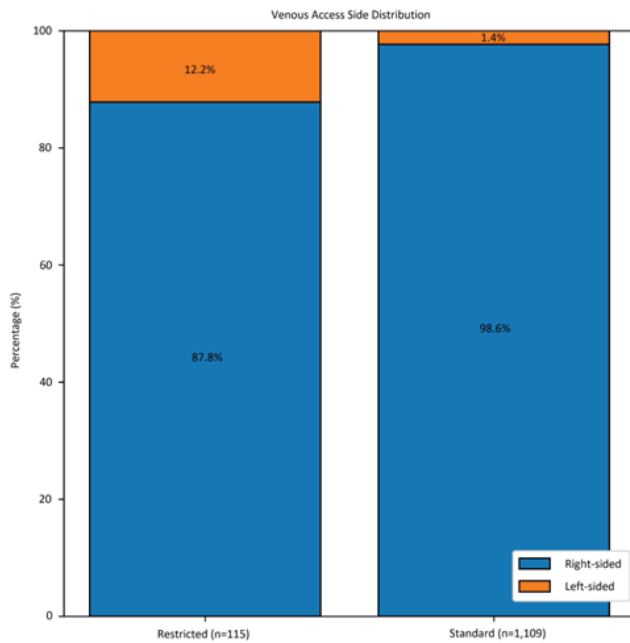


Figure 2. Venous access side distribution. Stacked bar chart showing the percentage distribution of right- and left-sided venous access in the restricted-access (n = 115) and standard-access (n = 1,109) groups. Left-sided access was more frequent in the restricted-access group.

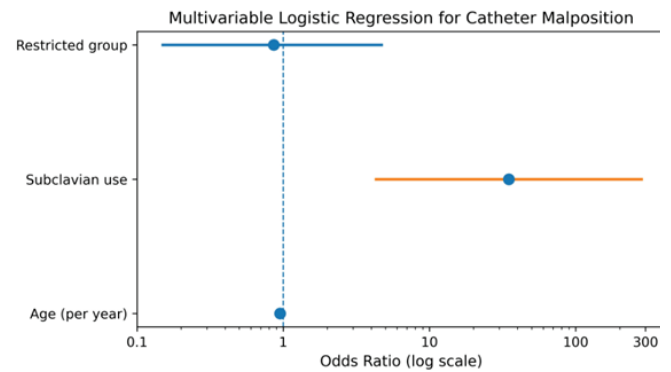


Figure 3. Multivariable logistic regression analysis for catheter malposition. Forest plot showing odds ratios (ORs) with 95% confidence intervals (CIs) for variables independently associated with catheter malposition. The dashed vertical line indicates OR = 1. Restricted-access status was not associated with malposition, whereas subclavian vein use was an independent predictor (OR 34.84, 95% CI 4.31–281.2; $p = 0.001$). Increasing age was associated with a lower risk (OR 0.95 per year, 95% CI 0.90–0.99; $p = 0.029$). Odds ratios are presented on a logarithmic scale.

Table 1. Baseline characteristics of the restricted-access and standard-access groups.

Variable	Restricted-access (n=115)	Standard-access (n=1,109)	p
Age, median (IQR) [†]	58 (46–64)	62 (54–69)	<0.001
Body mass index, median (IQR) [†]	28 (24–30)	25 (23–29)	0.004
Female sex, n (%) [‡]	68 (59.1)	416 (37.5)	<0.001

[†] Mann–Whitney U test; [‡] Chi-square test; IQR: interquartile range

Table 2. Procedural characteristics and clinical outcomes according to access group.

Variable	Restricted-access (n=115)	Standard-access (n=1,109)	p
Left-sided access, n (%) [§]	14 (12.2)	16 (1.4)	<0.001
Subclavian vein use, n (%) [‡]	54 (47.0)	224 (20.2)	<0.001
Revision, n (%) [§]	5 (4.3)	41 (3.7)	0.612
Catheter malposition, n (%) [§]	2 (1.7)	8 (0.7)	0.240

[‡] Chi-square test; [§] Fisher's exact test.

Table 3. Multivariable Logistic Regression Analysis for revision risk.

Variable	Odds Ratio (OR)	95% Confidence Interval	p
Restricted-access group	1.08	0.38–3.01	0.887
Left-sided access	3.44	0.88–13.28	0.073
Body mass index	1.02	0.95–1.08	0.591
Age	0.99	0.96–1.01	0.436

Table 4. Multivariable Logistic Regression Analysis for catheter malposition.

Variable	Odds Ratio (OR)	95% Confidence Interval	p
Restricted-access group	0.86	0.15–4.70	0.861
Subclavian vein use	34.84	4.31–281.2	0.001
Age	0.95	0.90–0.99	0.029

Table 5. Distribution of comorbidities between the groups.

Comorbidity	Restricted-access (n=115)	Standard-access (n=1,109)	p
Diabetes mellitus, n (%)‡	26 (22.6)	292 (26.3)	0.451
Hypertension, n (%)‡	37 (32.2)	404 (36.4)	0.422
Smoking, n (%)‡	33 (28.7)	298 (26.9)	0.757
Chronic steroid use, n (%)§	2 (1.7)	18 (1.6)	0.711
Thyroid disorder, n (%)‡	14 (12.2)	69 (6.2)	0.026
Organ failure, n (%)‡	5 (4.3)	54 (4.9)	0.984

‡ Chi-square test; § Fisher's exact test.

Supplementary Table 1. Distribution of clinical conditions defining the restricted-access group.

Restricted-access indication	n
Breast cancer	48
Head and neck malignancies	45
Lymphoma	8
Other conditions associated with cervical/pectoral access limitation	14

Supplementary Table 2. Characteristics of failed implantation cases.

Variable	Data
Failed implantation cases, n	28
Restricted-access group, n	3
Standard-access group, n	25
Right-sided attempt, n	25
Left-sided attempt, n	3
Attempted venous access	Internal jugular and subclavian access were attempted
Subsequent management	Referred to interventional radiology

Supplementary Table 3. Distribution of catheter malposition according to venous access route.

Venous access route	Total procedures, n	Catheter malposition, n (%)
Right internal jugular vein	940	1 (0.1%)
Left internal jugular vein	6	0 (0.0%)
Right subclavian vein	254	9 (3.5%)
Left subclavian vein	24	0 (0.0%)

Supplementary Table 4. Correlation analysis of age and Body Mass Index with clinical outcomes.

Variable	Outcome	Correlation coefficient (r)	p
Body mass index	Revision	0.03	0.905
Body mass index	Malposition	-0.032	0.249
Age	Revision	-0.017	0.538
Age	Malposition	-0.079	0.005

Supplementary Table 5. Association between comorbidities and clinical outcomes.		
Comorbidity	Revision (p)*	Malposition (p)*
Diabetes mellitus	0.088	1.000
Hypertension	0.531	0.346
Smoking	0.613	0.473
Chronic steroid use	0.171	1.000
Thyroid disorder	0.765	0.506
Organ failure	1.000	1.000
<i>*Fisher's exact test was used for all comparisons due to the low number of events.</i>		

Discussion

Guidelines recommend the right internal jugular vein as the primary access route for TIVAP implantation [1-3]. However, in clinical practice, particularly among oncologic patients, cervical and pectoral anatomy may be altered or side selection constrained. In this large consecutive patient cohort, no statistically significant increase in revision or catheter malposition rates was observed in patients with clinical conditions restricting guideline-preferred access planning. These findings suggest that, when performed within a standardized procedural framework, these alternative access strategies may not necessarily increase procedural risk.

Anatomical and treatment-related factors inherent to oncologic care may directly influence venous access planning. Prior surgery, radiotherapy, bulky tumors, and regional anatomical distortion can restrict the use of guideline-preferred pathways and necessitate alternative strategies [7]. Under these conditions, access site selection becomes a context-dependent decision in which procedural safety must be balanced against anatomical feasibility. Therefore, adapting the access strategy to patient-specific constraints should be interpreted not as a departure from guideline-based care, but as a pragmatic application of surgical judgment.

Notably, the absence of increased complications in the restricted-access group suggests that anatomical complexity alone does not inevitably translate into technical failure. Rather than functioning as an independent determinant of risk, restricted access may represent a contextual modifier whose impact depends on how procedural strategy is adapted. This perspective is consistent with previous investigations reporting comparable complication profiles between alternative venous access routes and traditional internal jugular approaches [8].

In the restricted-access group, the significantly higher rates of left-sided access and subclavian vein use indicate that clinical factors limiting access directly influenced surgical planning. In contrast, no statistically significant differences were observed between the groups in terms of revision or catheter malposition rates. However, the revision endpoint should be interpreted cautiously. In this cohort, all revisions were performed for skin erosion, which is a multifactorial outcome and may be influenced by port pocket location, nutritional status, cachexia, local radiotherapy, infection, skin quality, and device-related factors rather than the venous access route alone. Moreover, multivariable analysis confirmed that restricted-access status was not an independent predictor of either revision or malposition. Although subclavian access was more frequent in the restricted-access group, restricted-access status itself was not independently associated with malposition. This discrepancy may reflect the limited number of events and the heterogeneity of technical strategies within the restricted-access cohort. Although left-sided access is often considered technically more demanding because of its longer intrathoracic course and the need for the catheter to traverse the left brachiocephalic vein before reaching the superior vena cava, our findings did not demonstrate a measurable increase in complications. Previous studies have nevertheless reported a higher incidence of malposition after left internal jugular access compared with right internal jugular access [9]. Although a numerical trend toward higher revision risk was observed with left-sided access, this did not reach statistical significance. Taken together, these findings suggest that approaches traditionally considered technically more demanding, such as left-sided and subclavian access, may be performed within the overall safety profile of the cohort when applied with appropriate planning and experience. Although the restricted-access group differed

significantly from the standard-access group in terms of age, body mass index, and sex distribution, these variables were not independently associated with revision or malposition in multivariable analysis. The absence of an association between age, body mass index, and revision risk may reflect the consistency of a standardized single-operator procedural approach.

In our study, the use of the subclavian vein was independently associated with catheter malposition, representing a noteworthy finding. In the subclavian approach, there is a more pronounced angulation at the junction of the vein with the right innominate vein and subsequently the superior vena cava [10]. Compared with the more linear course of the right internal jugular vein, this configuration may render catheter advancement technically more challenging and predispose to directional deviation before reaching the intended cavoatrial junction. This anatomical characteristic may partly explain the increased risk of malposition observed in subclavian access [11]. Notably, increasing age was associated with a modest reduction in malposition risk, suggesting that patient-related anatomical or physiological factors may also influence catheter positioning outcomes. Nevertheless, this finding should be interpreted cautiously given the low number of malposition events in the cohort.

Thyroid disorders were more frequent in the restricted-access group, which may reflect the higher prevalence of cervical anatomical alterations in this cohort; however, comorbid conditions overall were not independently associated with procedural outcomes.

All procedures in this series were performed using a standardized anatomical landmark technique without routine ultrasound guidance. Although real-time ultrasound is widely recommended and has been shown to improve success rates and reduce complications in many settings [12], our findings suggest that a carefully standardized landmark-based approach may remain a viable alternative in contexts where imaging is unavailable or limited. Nevertheless, current evidence and contemporary guidelines generally favor ultrasound-guided venous access because of its lower complication profile. Our findings should therefore be interpreted within the context of a landmark-based institutional practice envi-

ronment. In such environments, procedural consistency, operator experience, and adherence to anatomical principles may be critical determinants of safety.

Limitations of the study

This study has several limitations. First, its retrospective design inherently carries the risk of documentation bias. Although failed implantations were excluded from the main revision and malposition analyses, their exclusion may still introduce selection bias. Therefore, these cases were reviewed and reported separately. Second, the data were derived from a single center, which may limit the direct generalizability of the findings to institutions with different practice patterns. The low number of catheter malposition events may have limited the stability of the regression coefficients and contributed to the wide confidence intervals observed for some estimates. Revision events in this cohort were limited to skin erosion, and detailed data on port pocket characteristics, cachexia, nutritional status, local radiotherapy fields, infection, and skin quality were not available. In addition, all procedures were performed using an anatomical landmark technique without ultrasound guidance, which may limit direct comparisons with centers routinely employing imaging support. Nevertheless, this uniform technical approach also allowed for a consistent evaluation of a standardized procedural strategy.

In conclusion, no statistically significant increase in catheter malposition or revision requiring surgical reintervention was observed in patients with clinical conditions restricting guideline-preferred access planning. However, revision findings should be interpreted as port-system reintervention outcomes related to skin erosion rather than direct route-specific technical complications. The increased risk of malposition was related not to restricted-access status itself but to specific technical choices, particularly the use of the subclavian vein. Our findings suggest that, when supported by appropriate planning and a standardized surgical approach, alternative venous access routes may be feasible in selected patients with anatomical or clinical access restrictions.

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 Clinical Research Ethics Committee of Basaksehir Çam and Sakura City Hospital (approval number: KAEK/11.02.2026.48).

Authors' contribution

OY: Concept, design, supervision, surgical procedures, data collection, statistical analysis, writing, and critical review. Mİ: Design, statistical analysis, writing, and critical review. MK: Data collection, literature search, and critical review. RE: Data collection, literature search, and critical review. AY: Supervision and critical review. All authors read and approved the final version of the manuscript.

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Original Article

Lower body mass index is associated with prolonged air leak after pulmonary resection

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ABSTRACT

Background: Prolonged air leaks are one of the most common complications following pulmonary resection and are associated with increased morbidity, prolonged hospital stays, and higher healthcare costs. This study evaluated factors associated with prolonged air leak, with emphasis on body mass index and surgical characteristics.

Material and Methods: This retrospective single-center study included 152 patients who underwent pulmonary resection between October 2022 and October 2025. Prospectively collected data were analyzed retrospectively. Patients were divided into two groups: Group 1 (air leak >5 days) and Group 2 (no air leak or ≤5 days). Demographic, clinical, and perioperative variables were compared.

Results: Prolonged air leaks occurred in 20 patients (13.2%). Patients in Group 1 had lower body mass index compared to Group 2 (23.6 ± 3.8 vs. 27.1 ± 4.7 kg/m², $p = 0.0009$). Anatomical resection was more frequent in Group 1 (85.0% vs. 50.0%, $p = 0.007$). Diffusing capacity of the lung for carbon monoxide (%) was lower in Group 1 (64.0 ± 19.1 vs. 74.0 ± 22.6 , $p = 0.042$). The length of hospital stay was longer in Group 1 (6.0 ± 2.7 vs. 4.0 ± 2.2 days, $p = 0.004$). No significant differences were observed in other variables.

Conclusions: Prolonged air leak remains a common complication following pulmonary resection and is associated with prolonged hospital stay. Lower body mass index and anatomical resection were significant factors associated with its development. These findings suggest that body mass index, evaluated as a continuous variable, may help identify patients at higher risk and guide perioperative management.

Keywords: prolonged air leak, pulmonary resection, body mass index, risk factors, length of stay

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Introduction

Pulmonary resection remains the cornerstone of treatment for a wide spectrum of thoracic diseases, including both malignant and benign conditions. Despite advances in surgical techniques, prolonged air leak (PAL) continues to be one of the most frequent postoperative complications, with a reported incidence ranging between 7% and 18% in patients undergoing lung resection [1-3]. PAL has been associated with delayed chest tube removal, prolonged hospital stays, increased postoperative morbidity, and higher healthcare costs. Given its clinical and economic impact, PAL represents a significant challenge in the perioperative management of patients undergoing pulmonary resection [4].

PAL is generally defined as an air leak persisting for more than 5 days after pulmonary resection and is widely accepted in the literature as a standard definition [5]. This definition reflects the expected postoperative recovery period and provides a practical threshold for identifying patients with delayed resolution of air leak.

Several risk factors for PAL have been identified in previous studies, including male sex, impaired pulmonary function, and the extent and type of resection. Large database analyses have demonstrated that lower body mass index (BMI), reduced pulmonary reserve, and anatomical resections are associated with an increased risk of PAL [2]. However, despite these findings, the impact of BMI on the development of PAL remains insufficiently explored and is not consistently emphasized in clinical practice. More recent studies have also highlighted the potential role of BMI as an independent predictor of PAL, suggesting that lower BMI may reflect reduced tissue resilience and impaired healing capacity, thereby predisposing patients to prolonged air leakage [6].

The aim of this study was to evaluate the risk factors associated with PAL in patients undergoing pulmonary resection, with particular emphasis on the role of BMI and surgical characteristics.

Material and Methods

This retrospective single-center study included patients who underwent pulmonary resections between October 2022 and October 2025. Prospectively maintained institutional data were reviewed retrospectively. Both anatomical and non-anatomical pulmonary resections were included in the study. Patients who underwent biopsy procedures only or those with incomplete key clinical data were excluded. A total of 152 patients were included in the final analysis.

Demographic, clinical, and perioperative data were collected from a prospectively maintained institutional database. Recorded variables included age, sex, height, weight, and body mass index (BMI). Clinical characteristics such as cardiac and other comorbidities, smoking status, and pulmonary function test parameters (FEV1, FVC, and DLCO) were documented. Diagnosis (benign or malignant) and type of pulmonary resection (anatomical or non-anatomical) were also recorded. Postoperative data included complications, presence of prolonged air leak (PAL), length of hospital stay, and in-hospital morbidity and mortality.

PAL was defined as an air leak persisting for more than 5 days after pulmonary resection. Air leak was assessed through chest tube drainage systems during the postoperative period. Patients were divided into two groups based on the presence of prolonged air leak: Group 1 consisted of patients with prolonged air leak (>5 days), while Group 2 included patients without air leak or with air leak lasting 5 days or less. Body mass index was calculated as weight in kilograms divided by the square of height in meters (kg/m^2).

Smoking status was categorized as never smoker, ex-smoker, and active smoker. Patients who had quit smoking for at least 2 months prior to surgery were classified as ex-smokers, while those who continued smoking up to the day of surgery were defined as active smokers.

Cardiac comorbidity was defined as the presence of coronary artery disease, valvular heart disease, or hypertension. Other comorbidities were defined as the presence of diabetes mellitus, history of malignancy, or previous major surgical procedures.

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Memorial Atasehir Hospital (No: 23.04.2026/27)

Statistical Analysis

Statistical analysis was performed using SPSS software (version 25, IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation and compared using the Student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were expressed as numbers and percentages and compared using the chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

Results

A total of 152 patients who underwent pulmonary resection were included in the study. The mean age was 59.1 ± 15.1 years, and 52 patients (34.2%) were female. The mean body mass index of the entire study population was 26.6 ± 4.7 kg/m². Cardiac comorbidities were present in 70 patients (46.1%), while other comorbidities were observed in 90 patients (59.2%).

Regarding smoking status, 50 patients (32.9%) were active smokers, 59 (38.8%) were ex-smokers, and 43 (28.3%) had never smoked. A total of 126 patients (82.9%) underwent surgery for malignant disease, while 26 (17.1%) had benign pathology. Anatomical resection was performed in 83 patients (54.6%), whereas 69 patients (45.4%) underwent non-anatomical resection.

The mean length of hospital stay was 3.9 ± 2.4 days (median: 4 days, range: 1-16 days), and no in-hospital mortality was observed.

Prolonged air leaks were observed in 20 patients (13.2%), who were classified as Group 1, while 132 patients (86.8%) without prolonged air leak constituted Group 2. The mean length of hospital stay was significantly longer in Group 1 compared to Group 2 (6.0 ± 2.7 vs. 4.0 ± 2.2 days, $p = 0.004$).

Comparisons between the two groups are summarized in Table 1. Patients in Group 1 had a significantly lower body mass index compared to those in Group 2 (23.6 ± 3.8 vs. 27.1 ± 4.7 kg/m², $p = 0.0009$). Similarly, DLCO (%) values were significantly lower in Group 1 (64.0 ± 19.1 vs. 74.0 ± 22.6 , $p = 0.042$).

Anatomical resection was more frequently performed in Group 1 than in Group 2 (85.0% vs. 50.0%, $p = 0.007$). When anatomical resections were further categorized according to procedure type, wedge resection was significantly less frequent in Group 1 than in Group 2 (15.0% vs. 50.0%, $p = 0.003$). In contrast, lobectomy (including sleeve lobectomy) (60.0% vs. 37.1%, $p = 0.084$), segmentectomy (15.0% vs. 9.1%, $p = 0.420$), and bilobectomy (10.0% vs. 3.8%, $p = 0.230$) were more common in Group 1, although these differences did not reach statistical significance. No significant differences were observed between the groups in terms of age, sex, comorbidities, pulmonary function parameters, smoking status, or pathological diagnosis (Table 1). The distribution of body mass index according to group is illustrated in Figure 1.

Table 1. Comparison of patients with and without prolonged air leak.

Variable	Group 1 (PAL) (n=20)	Group 2 (No PAL) (n=132)	p-value
Age (years)	55.7 ± 21.1	59.6 ± 14.0	0.43
Female sex, n (%)	3 (15.0%)	49 (37.1%)	0.09
BMI (kg/m ²)	23.6 ± 3.8	27.1 ± 4.7	0.0009
Cardiac comorbidity, n (%)	9 (45.0%)	61 (46.2%)	1.00
Other comorbidity, n (%)	12 (60.0%)	78 (59.1%)	0.93
FEV1 (L)	2.62 ± 0.58	2.75 ± 0.83	0.39
FEV1 (%)	91.0 ± 21.8	97.0 ± 22.4	0.26
FVC (L)	3.49 ± 0.73	3.48 ± 0.98	0.96
FVC (%)	95.0 ± 20.7	99.0 ± 20.1	0.43
DLCO	5.39 ± 2.13	6.34 ± 2.11	0.075
DLCO (%)	64.0 ± 19.1	74.0 ± 22.6	0.042
Smoking status, n (%)			0.45
Active smoker	9 (45.0%)	41 (31.1%)	
Ex-smoker	6 (30.0%)	53 (40.2%)	
Never smoker	5 (25.0%)	38 (28.8%)	
Malignant disease, n (%)	16 (80.0%)	110 (83.3%)	0.96
Anatomical resection, n (%)	17 (85.0%)	66 (50.0%)	0.007
Procedure type, n (%)			
Wedge resection	3 (15.0%)	66 (50.0%)	0.003
Segmentectomy	3 (15.0%)	12 (9.1%)	0.420
Lobectomy	12 (60.0%)	49 (37.1%)	0.084
Bilobectomy	2 (10.0%)	5 (3.8%)	0.230
Length of hospital stay (days)	6.0 ± 2.7	4.0 ± 2.2	0.004

Abbrev.: BMI: body mass index; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; DLCO: diffusing capacity for carbon monoxide.
Values are presented as mean $\pm$ standard deviation or number (percentage).

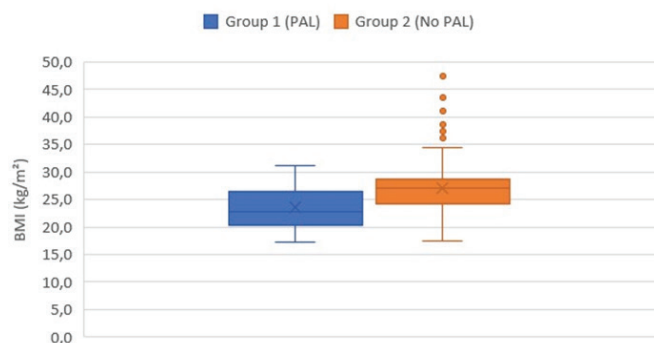


Figure 1. Distribution of body mass index according to Group 1 and Group 2.

Discussion

In this study, we evaluated the factors associated with PAL following pulmonary resection and found that the overall incidence of PAL was 13.2%. The most important findings of our analysis were that lower BMI and anatomical resection were significantly associated with the development of PAL. In addition, patients in Group 1 experienced a significantly longer hospital stay compared to those in Group 2. These findings highlight the clinical relevance of PAL and suggest that both patient-related and surgical factors play a role in its development.

Several studies have identified various risk factors associated with PAL following pulmonary resection, including patient-related and surgical variables [1,7]. Large database analyses have demonstrated that lower BMI is an important predictor of PAL, together with factors such as reduced pulmonary function and the extent of resection [2]. In this context, our findings are consistent with previous reports, as patients in Group 1 had significantly lower BMI values compared to those in Group 2.

Recent studies have further emphasized the role of BMI as a clinically relevant risk factor. Gioutsos et al. reported that lower BMI was associated with an increased risk of PAL following uniportal segmentectomy [6]. Similarly, risk stratification models derived from large datasets, such as the STS database, have also included lower BMI as a significant predictor of PAL [2]. These findings further support the association between lower BMI and susceptibility to postoperative complications such as PAL.

The underlying mechanisms linking relatively lower BMI to the development of PAL are not fully understood but are likely multifactorial. In the present study,

BMI was evaluated as a continuous variable rather than according to a predefined underweight cutoff. Therefore, the observed association should be interpreted as a difference in relative BMI between groups, not as an indication that patients in Group 1 were underweight according to standard BMI classifications. Patients with relatively lower BMI may have less parenchymal and soft tissue reserve, which may increase susceptibility to alveolar disruption during surgical manipulation [8]. In addition, BMI may be a surrogate marker of general nutritional and physiological reserve rather than a direct causal factor. Supporting this concept, Li et al. demonstrated that body composition parameters, particularly fat-free mass index, may be more closely associated with the risk of PAL than BMI alone [9].

In addition to BMI, the type of resection was also associated with PAL in our cohort. Procedure-specific analysis demonstrated that PAL occurred less frequently after wedge resection, whereas it was observed more often following anatomical resections, particularly lobectomy and bilobectomy. Although the differences among individual anatomical resection subtypes did not reach statistical significance, the overall distribution was consistent with the well-established association between increasing resection extent and the risk of PAL reported in previous studies [1,2]. From a technical perspective, anatomical resections require wider hilar dissection and a greater parenchymal staple line, which may increase the likelihood of persistent postoperative air leakage. In this regard, our findings support the view that surgical factors, in addition to patient-related characteristics, play an important role in the development of PAL.

The clinical impact of PAL was also evident in our study, as patients in Group 1 had a significantly longer hospital stay compared to those in Group 2. Prolonged hospitalization not only delays patient recovery but also increases the burden on healthcare systems. Previous studies have consistently demonstrated that PAL is associated with increased treatment costs, primarily driven by extended length of stay and a higher rate of postoperative complications. In a landmark study, Varela et al. showed that PAL was associated with a significant increase in hospital stay, postoperative morbidity, and overall healthcare costs following pulmonary resection [10]. More recently, Ponholzer et al. confirmed these findings and reported substantially higher healthcare expenditures in patients who developed PAL compared

to those without PAL [4]. Taken together, these findings highlight that PAL is not only a clinical complication but also a significant contributor to healthcare resource utilization and cost burden.

In contrast to these findings, no significant differences were observed between the groups in terms of age, sex, smoking status, comorbidities, or pulmonary function parameters. Although previous studies have identified some of these variables as potential risk factors for PAL, the results have been inconsistent across different cohorts. These discrepancies may be related to variations in patient populations, surgical techniques, and study design.

Lower DLCO values were also observed in patients who developed PAL. Although DLCO was not the primary focus of the present study, this finding is consistent with previous reports suggesting that impaired diffusing capacity may be associated with an increased risk of PAL. Divisi et al. identified reduced DLCO as a predictor of PAL following pulmonary resection, possibly reflecting impaired parenchymal integrity and reduced pulmonary reserve [11]. However, further studies are needed to clarify the independent contribution of DLCO to PAL development.

Limitations of the study

This study has several limitations. First, it is a retrospective analysis from a single center, which may limit the generalizability of the findings. Second, certain intraoperative and postoperative factors that may influence the development of PAL, such as surgical technique, use of surgical sealants, and chest tube management strategies, were not evaluated. Furthermore, multivariate analysis was not performed because the limited number of PAL events did not allow construction of a reliable multivariable model without a substantial risk of overfitting; therefore, the findings should be interpreted as associative rather than causative. In addition, air leak assessment was based on conventional chest tube drainage systems, which may introduce a degree of subjectivity, as previously described in the literature [12]. Despite these limitations, the present study provides clinically relevant data regarding the association between BMI and PAL.

In conclusion, PAL remains a common complication following pulmonary resection and is associated with prolonged hospital stay. In this study, relatively lower BMI and anatomical resection were identified as

significant factors associated with the development of PAL. These findings suggest that simple preoperative parameters such as BMI may help identify patients at higher risk of developing PAL and guide perioperative management strategies.

Declaration of conflicting interests

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Ethics approval

This study was approved by the Ethics Committee of Memorial Atasehir Hospital (No: 23.04.2026/27)

Authors' contribution

CC: Concept, design, data collection, statistical analysis, writing, and critical review. HFB: Design, supervision, and critical review. All authors read and approved the final version of the manuscript.

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Original Article

Predicting talc pleurodesis outcomes: insights from early systemic inflammatory biomarkers and machine learning analysis

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ABSTRACT

Background: This study aimed to investigate the predictive value of early post-procedural systemic inflammatory biomarkers and baseline pleural fluid parameters in determining the clinical success of talc pleurodesis using a machine learning-based framework.

Materials and Methods: Data from 51 evaluable patients who underwent talc pleurodesis between June 2019 and April 2026 were retrospectively analyzed. Clinical success was defined as the absence of recurrence at the 1-month follow-up. Baseline pleural fluid parameters and post-procedural 2-hour systemic inflammatory markers were recorded. Features were analyzed using a regularized LASSO (L1) logistic regression model under stratified 5-fold cross-validation and visualized via global TreeSHAP analysis. Unsupervised k-means clustering was additionally implemented to identify distinct patient stratification trajectories based on inflammatory kinetics.

Results: The overall success rate was 68.6% (n = 35). Although acute post-procedural shifts occurred across traditional systemic markers, univariate analyses demonstrated no linear differentiation between outcomes. However, in the LASSO multivariate framework, baseline intrapleural total protein emerged as the strongest independent predictor of success, validated by robust AUC and TreeSHAP configurations. Unsupervised k-means clustering successfully stratified patients into distinct phenotypes, revealing that a regulated, stable inflammatory kinetic profile yields significantly superior clinical efficacy compared to an unmitigated hyper-inflammatory surge.

Conclusions: While early systemic inflammatory markers lack standalone linear predictive capacity, machine learning uncovers critical non-linear prognostic phenotypes based on acute biomarker kinetics. Baseline intrapleural total protein remains a robust local predictor, highlighting that a pre-existing exudative microenvironment, coupled with a regulated systemic inflammatory response, dictates talc pleurodesis success.

Keywords: pleurodesis, inflammation, talc, stress, physiological

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Introduction

Chemical pleurodesis is a well-established therapeutic modality aimed at obliterating the pleural space by inducing an acute inflammatory reaction via various sclerosing agents. This intervention is clinically indicated for the management of prolonged air leaks, recurrent spontaneous pneumothorax, and malignant pleural effusions. Talc (purified, asbestos-free magnesium silicate hydroxide, $\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$) is the most frequently chosen sclerosing agent because it is effective, inexpensive, commonly available, and associated with minimal side effects in most studies, particularly when graded large-particle formulations are utilized to prevent systemic dissemination [1,2]. Intrapleural administration can be performed via a pleural catheter, single-port medical thoracoscopy, or video-assisted thoracoscopic surgery (VATS).

Despite its long-standing clinical utilization, granular data fully elucidating the precise mechanisms of action of sclerosing agents remain scarce [3]. Intrapleural administration of talc triggers a robust inflammatory cascade characterized by a significant upregulation of interleukin-8 (IL-8) production [4]. IL-8 has been postulated to play a pivotal role in driving the chemotaxis of neutrophils and monocytes into the intrapleural space [5]. Talc particles activate both the visceral and parietal mesothelium. The resulting inflammatory cascade can be bifurcated into local and systemic responses. The systemic inflammatory response can be quantified by monitoring serum total white blood cell (WBC) counts, neutrophil, lymphocyte, and monocyte profiles, alongside the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) levels [6]. However, the low specificity of these parameters poses a significant challenge in quantitatively evaluating inflammatory activity, thereby limiting their predictive value regarding pleurodesis success [7]. Consequently, current research is focused on identifying a specific indicator to precisely determine the intensity of the induced inflammatory activity within the pleural space. The objective of this study was to evaluate the early systemic inflammatory response following talc pleurodesis and to investigate its direct correlation with pleurodesis efficacy.

Material and Methods

Patient selection and study design

A retrospective cohort analysis was conducted on 58

consecutive patients who underwent talc pleurodesis at our clinic between June 2019 and April 2026. Clinical indications for the procedure included recurrent symptomatic malignant pleural effusion, recurrent spontaneous pneumothorax, and prolonged air leak.

Comprehensive data points were extracted from institutional medical records, including demographic characteristics, oncological treatment histories, and relevant comorbidities. Documented procedural and laboratory variables comprised the number of pre-procedural thoracenteses, as well as baseline serum albumin and pleural fluid characteristics including lactate dehydrogenase (LDH), albumin (Alb), glucose, total protein, pH, and cytological findings. To monitor early cellular dynamics, peripheral venous blood profiles specifically platelet (PLT) counts, white blood cell (WBC) counts, absolute neutrophil counts, and absolute lymphocyte counts were collected at baseline (pre-procedure) and 2 hours post-procedure. Systemic inflammatory dynamics were quantified using the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII), which was calculated using the standard formula: $\text{SII} = \text{Platelets} \times \text{neutrophils} / \text{lymphocytes}$.

Pleurodesis protocol and clinical technique

Following definitive procedural indication, a standardized intrapleural protocol was executed. Local analgesia was initiated via the administration of 400 mg prilocaine hydrochloride dissolved in 50 mL of normal saline through the existing chest tube. Subsequently, 4 g of purified talc (Steritalc® F4, Novatech, La Ciotat, France) was completely dissolved in normal saline and instilled into the pleural cavity via the chest drain, followed immediately by a 50 mL saline flush to clear the lumen, after which the chest tube was securely clamped.

To maximize the homogeneity of talc distribution across both pleural surfaces, patients underwent a strict, sequential positional rotation schedule every 30 minutes during the clamping period, traversing the supine, right/left lateral decubitus, prone, Trendelenburg, and reverse Trendelenburg positions. To safeguard the integrity of the acute localized inflammatory reaction essential for successful pleurodesis, systemic nonsteroidal anti-inflammatory drugs (NSAIDs) were strictly avoided; post-procedural analgesia and pain management were restricted to intravenous tramadol HCl and paracetamol.

Peripheral venous blood samples were obtained exactly 2 hours after the completion of talc instillation. The chest tube was unclamped 4 hours post-procedure, and subsequent chest tube removal was performed based on clinical stabilization, daily drainage volumes, or the resolution of air leaks.

Response evaluation criteria

Therapeutic efficacy was evaluated 30 days post-procedure utilizing the Paladine criteria adapted for patients treated for spontaneous pneumothorax. Clinical response was categorized into three tiers: Complete Response (CR), defined as total symptom resolution with no radiological recurrence; Partial Response (PR), characterized by minimal, stable fluid not requiring therapeutic intervention; and No Response (NR), defined as symptomatic re-accumulation necessitating recurrent thoracentesis or auxiliary interventions. For binary clinical modeling, CR and PR cases were collectively designated as successful pleurodesis, while NR cases were defined as pleurodesis failure.

This study received ethical approval from the Institutional Non-Interventional Clinical Research Ethics Committee of the Gazi University (Approval No: E-77082166-604.01-1537754, Date: 12/05/2026) 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 and Machine Learning Validation

Statistical analyses were performed using IBM SPSS version 26.0 and Python version 3.9. Data normality was assessed via the Kolmogorov-Smirnov test. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) based on distribution, and compared using the independent Student's t-test, Mann-Whitney U test, paired t-test, or Wilcoxon signed-rank test as appropriate. Categorical variables were presented as frequencies with percentages and analyzed via Chi-square or Fisher's exact tests. To identify distinct patient subgroups based on systemic inflammatory kinetics, unsupervised k-means clustering was implemented, with the optimal cluster count determined by the elbow method and clinical interpretability. Predictive

modeling was conducted in strict accordance with the updated TRIPOD+AI statement. To prevent multicollinearity and overfitting under small-sample constraints, parameters were feature-selected using a regularized LASSO (L1) logistic regression model under stratified 5-fold cross-validation. Retained features were then transitioned into standard multivariate logistic regression to compute exact Odds Ratios (OR), 95% Confidence Intervals (CI), and definitive p-values. Model performance was evaluated using Accuracy, F1-Score, and Receiver Operating Characteristic (ROC) curve analysis for Area Under the Curve (AUC). Model interpretability was established via global TreeSHAP analysis. A two-tailed $p < 0.05$ indicated statistical significance.

Results

Baseline clinical and pathological characteristics

Of the 58 patients who underwent talc pleurodesis during the study period, 7 were excluded due to loss to follow-up or early mortality within the first month. Consequently, the final analyzed cohort consisted of 51 patients, including 33 (64.7%) males and 18 (35.3%) females, with a median age of 62.0 years (range: 24.0-85.0 years). The primary indications for pleurodesis were malignancy-associated pleural effusion ($n = 47$, 92.2%) and spontaneous pneumothorax ($n = 4$, 7.8%). Among the oncological cases, lung cancer was present in 24 (47.1%) patients and malignant pleural mesothelioma in 3 (5.9%). Positive pleural fluid cytology was documented in 23 (45.1%) patients. Comprehensive demographic and clinical baseline characteristics are detailed in Table 1.

Among the 51 fully evaluated patients, successful pleurodesis was achieved in 35 (68.6%), comprising 28 (54.9%) complete and 7 (13.7%) partial responses. No major procedure-related complications, including wound infections, pleural empyema, acute respiratory failure, or direct perioperative mortality, were observed within the evaluated cohort.

Dynamics of systemic inflammatory parameters

Complete blood count parameters measured immediately prior to talc pleurodesis and at the 2-hour post-procedural mark including WBC counts, platelet counts, absolute neutrophil counts, absolute lymphocyte counts, NLR, and PLR are detailed in Table 2.

Table 1. Characteristics of patients.

Characteristics	All (n = 51)	Successful pleurodesis (n = 35)	Failed pleurodesis (n = 16)	p-value
Age, years	62.0 (range 24.0-85.0)	61.0 (range 24.0-85.0)	64.0 (range 31.0-77.0)	0.11
Gender, (%)				0.29
Male	33 (64.7)	21 (60.0)	12 (75.0)	
Female	18 (35.3)	14 (40.0)	4 (25.0)	
Primary cancer, (%)				0.85
Lung	24 (47.1)	17 (48.6)	7 (43.7)	
Mesothelioma	3 (5.9)	2 (5.7)	1 (6.3)	
Others	24 (47.1)	16 (45.7)	8 (50.0)	
Previous chemotherapy, (%)	32 (62.7)	20 (57.1)	12 (75.0)	0.81
Previous thoracentesis, number	1.6±0.8	1.6±0.9	1.7±0.7	0.47
Positive pleura fluid cytology, %	23 (45.1)	15 (42.9)	8 (50.0)	0.62

Table 2. Complete blood count parameters and systemic inflammatory markers sampled before talc pleurodesis and at 2 hours post-procedure.

Characteristics	Before pleurodesis	2nd h after pleurodesis	p-value
WBC count, per mm ³	8.6±3.2	8.4±3.5	0.61
Neutrophil count, per mm ³	5.9±2.3	6.2±3.3	0.43
Lymphocyte count, per mm ³	1.1±0.5	0.9±0.5	<0.001
Platelet count, per mm ³	296.7±127.7	272.0±108.4	0.01
NLR	6.4±4.5	8.1±5.8	0.03
PLR	303.2±224.6	375.5±335.9	0.03
SII	1838.4±1641.2	2175.3±2091.8	0.053

Abbrev.: NLR; neutrophil-to-lymphocyte ratio, PLR; platelet-to-lymphocyte ratio, WBC; white blood cell, SII; Systemic Immune-Inflammation Index

A comparative evaluation of the acute systemic inflammatory response demonstrated that peripheral platelet counts ($p = 0.01$) and absolute lymphocyte counts ($p < 0.001$) significantly decreased 2 hours after the procedure. Conversely, a significant post-procedural elevation was observed in systemically calculated indices, with both PLR ($p = 0.03$) and NLR ($p = 0.03$) values increasing significantly.

Traditional predictors of pleurodesis outcomes

Pleural fluid biomarkers and acute post-procedural systemic inflammatory parameters stratified by definitive therapeutic outcomes are summarized in Table 3. Regarding baseline parameters, both Pleural Total Protein ($p = 0.019$) and Pleural Albumin ($p = 0.035$) demonstrated statistically significant differentiation between the groups, exhibiting markedly elevated baseline concentrations in patients who achieved successful pleurodesis.

Due to the inherent biological collinearity between pleural protein components, Pleural Total Protein was selected as the primary biochemical surrogate for further single-marker diagnostic optimization. A receiver operating characteristic (ROC) curve analysis revealed

that a Pleural Total Protein cut-off value of 4.01 g/dL predicted final talc pleurodesis success with a sensitivity of 62.9% and a specificity of 62.5% (Figure 1).

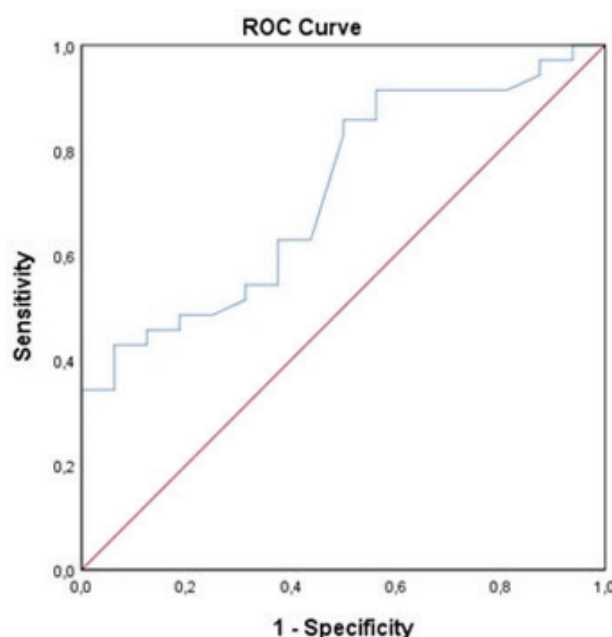


Figure 1. Receiver operating characteristic (ROC) curve of baseline pleural fluid total protein levels for predicting talc pleurodesis success (AUC = 0.72, $p = 0.01$; 95% CI: 0.57-0.86).

Table 3. Comparative analysis of complete blood count, pleural fluid, and systemic inflammatory parameters based on the outcome of talc pleurodesis.

Characteristics	Successful pleurodesis (n=35)	Failed pleurodesis (n=16)	p-value
WBC count change, per mm ³	-0.3±3.4	0.2±3.1	0.927
Platelet count change, per mm ³	-21.4±66.3	-27.5±64.7	0.529
Lymphocyte count change, per mm ³	-0.1±0.3	-0.2±0.3	0.235
Neutrophil count change, per mm ³	0.1±3.1	0.8±3.0	0.434
NLR before pleurodesis	5.9±4.5	7.1±4.9	0.350
NLR 2 h after pleurodesis	6.6±3.6	10.4±6.6	0.071
NLR change	0.6±4.9	3.2±5.5	0.264
PLR before pleurodesis	304.6±242.6	278.7±189.1	0.429
PLR 2 h after pleurodesis	349.0±278.8	325.9±178.6	0.839
PLR change	44.4±136.3	47.2±139.2	0.598
Serum albumin, g/dL	3.31±0.5	3.05±0.54	0.095
Pleural fluid protein, g/dL	4.42±0.9	3.4±0.9	0.019
Pleural fluid albumin, g/dL	2.6±0.5	2.2±0.6	0.035
Pleural fluid pH	7.36±0.10	7.39±0.15	0.437
Pleural fluid LDH, U/L	236.0 (range 84.0-4773.0)	371.0 (range 115.0-5766.0)	0.435
Pleural fluid glucose, mg/dL	116.8±66.7	102.9±49.8	0.484
SII before pleurodesis	1754.3±1671.4	1999.8±1775.3	0.761
SII 2 h after pleurodesis	1791.1±1005.7	2551.8±2174.0	0.570

Abbrev.: NLR; neutrophil-to-lymphocyte ratio, PLR; platelet-to-lymphocyte ratio, WBC; white blood cell, SII; Systemic Immune-Inflammation Index

Conversely, dynamic peripheral blood indices and cellular kinetic phases yielded no statistically significant differences between the success and failure groups. Specifically, standalone homogeneity across clinical outcomes was observed for net changes in leukocyte, lymphocyte, and platelet counts, delta NLR, PLR metrics, and the 2-hour systemic immune-inflammation index (SII), with 2-hour post-procedural NLR demonstrating only a marginal downward trend ($p = 0.071$).

Advanced machine learning validation and clinical modeling (TRIPOD+AI framework)

To address the limitations of conventional univariate statistics, evaluate the cumulative and non-linear predictive capabilities of these clinical, biochemical, and inflammatory variables, and fully isolate hidden independent interactions, an advanced machine learning framework was deployed in strict accordance with the updated TRIPOD+AI guidelines.

1. Strategic layered benchmarking and algorithm selection rationales

To mimic real-world clinical decision-making pathways and evaluate feature groups systematically, the evaluable cohort ($n = 51$) was analyzed using a stratified 5-fold cross-validation scheme across three distinct,

pre-defined strategic feature layers (comprehensively detailed in Table 4).

Model 1 (Clinical baseline layer): Included exclusively non-invasive bedside demographics and initial clinical burden indices, namely age and the number of prior thoracenteses.

Model 2 (Isolated laboratory layer): Comprised baseline pleural fluid biochemistry including lactate dehydrogenase (LDH), albumin, glucose, total protein, pH, and cytology alongside pre-procedural and 2-hour post-procedural peripheral blood counts (WBC, platelets, neutrophils, lymphocytes) and dynamic inflammatory kinetic metrics (Baseline NLR, 2nd-hour NLR, NLR gradient, and the 2nd-hour NLR/baseline NLR ratio).

Model 3 (Combined full-stack ensemble layer): Integrated all clinical, biochemical, and early acute systemic inflammatory phases comprehensively (The complete combined features of Model 1 and Model 2).

To identify the optimal mathematical fit for each data architecture, diverse algorithms including logistic regression, random forest, and XGBoost were independently trained and benchmarked within each model layer. In this competitive framework, Model 1 (Clinical layer) achieved a peak area under the curve

(AUC) of 0.624 via random forest, which excelled at capturing non-linear interactions within sparse metrics. For Model 2 (Isolated Laboratory Layer), Logistic regression emerged as the top-performing algorithm with a standalone AUC of 0.629. The full integration of all parameters (Model 3) achieved the highest overall predictive performance across the entire study, where regularized logistic regression demonstrated the most robust and stable calibration, reaching a peak AUC of 0.648. Conversely, complex gradient-boosted tree architectures like XGBoost underperformed under these small-sample constraints due to a high susceptibility to overfitting. The comparative discriminatory power of these optimized layered strategic configurations is visually demonstrated in the multi-model ROC curve analysis (Figure 2).

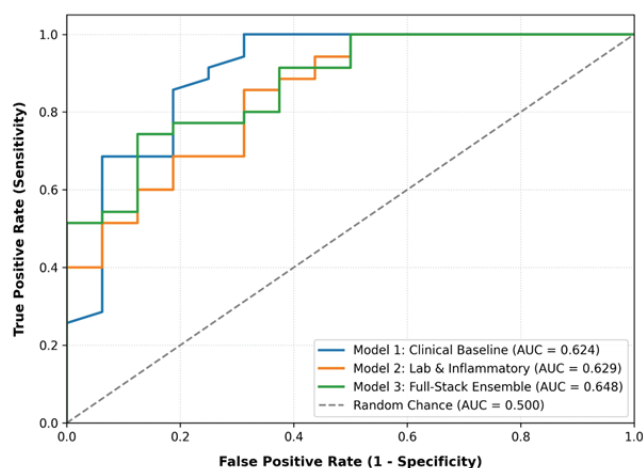


Figure 2. Layered predictive models and ROC curve analyses compliant with TRIPOD+AI reporting framework. Comparative evaluation of model performance in predicting talc pleurodesis success: Model 1 (Clinical Baseline; AUC = 0.624), Model 2 (Lab & Inflammatory parameters; AUC = 0.629), and Model 3 (Full-Stack Ensemble; AUC = 0.648). The dashed diagonal line indicates baseline random classification performance (AUC = 0.500). (AUC: Area Under the Curve).

2. Feature regularization and hybrid two-stage modeling

To overcome the potential risks of overfitting and multicollinearity inherent to traditional multivariate regression in a small sample size, and to isolate the independent biological drivers without prior arbitrary p-value restrictions, a regularized LASSO (Least Absolute Shrinkage and Selection Operator - L1) logistic regression model was utilized. An initial 18-feature matrix encompassing demographics, baseline pleural biochemistry, and peri-proce-

dural inflammatory metrics was constructed. Missing data points were managed using feature-specific median imputation to prevent target leakage. Feature selection was performed using LASSO regularization ($C = 0.5$), which shrank the coefficients of 12 non-contributing variables to absolute zero: number of prior thoracenteses, baseline NLR, pleural pH, pleural albumin, 2nd-hour NLR/Baseline NLR ratio, NLR Gradient, baseline WBC, 2nd-hour WBC, 2nd-hour neutrophils, 2nd-hour lymphocytes, baseline platelets, and 2nd-hour platelets. Conversely, LASSO isolated 6 predictors with non-zero coefficients: Pleural Total Protein (+0.7614), age (-0.5161), 2nd-hour NLR (-0.4121), baseline lymphocytes (-0.0711), serum albumin (+0.0126), and baseline neutrophils (-0.0120). These 6 optimized features were subsequently entered into a multivariate logistic regression model to calculate the final clinical coefficients. The hybrid model was evaluated using both whole-cohort optimization and Stratified 5-Fold Cross-Validation to assess out-of-fold (OOF) generalizability (Table 5). While internal optimization yielded a peak AUC of 0.852 and an accuracy of 78.4%, the cross-validated pipeline demonstrated a stable mean OOF AUC of 0.702 and a mean accuracy of 64.7%. The cross-validated metrics aligned within the baseline 95% confidence intervals (F1-Score: 0.741, Sensitivity: 74.3%, positive predictive value [PPV]: 74.8%), confirming model stability. However, due to sample size constraints, the mean OOF specificity settled at 45.0%.

Within this final regularized clinical configuration, Pleural Total Protein was confirmed as a significant independent positive predictor of pleurodesis success (OR = 3.192, 95% CI: 1.093-9.326, $p = 0.034$). Conversely, among the remaining features retained by the regularized framework, advanced age (OR = 0.938, 95% CI: 0.878-1.002, $p = 0.056$) and the 2nd-hour post-procedural NLR (OR = 0.827, 95% CI: 0.672-1.018, $p = 0.073$) demonstrated notable negative trends, showing an inverse biological direction toward clinical success despite falling just outside the conventional alpha threshold (Table 6).

3. Explainable AI and feature hierarchy

To unravel the "black-box" nature of the algorithmic framework and provide transparent clinical interpretability, a global TreeSHAP (Shapley Additive exPlanations) analysis was performed on the optimized final model (Figure 3).

Table 4. Comprehensive feature layer architecture and multi-algorithm benchmarking matrix.

Classification layer / model stage	Included parameters and features	Logistic Regression (AUC)	Random Forest (AUC)	XGBoost (AUC)
Model 1 (Clinical baseline)	Age, number of prior thoracenteses	0.579	0.624	0.564
Model 2 (Laboratory and inflammation)	Pleural fluid: LDH, albumin, glucose, total protein, pH, cytology Peripheral blood (Baseline and post-2h): WBC, platelets, neutrophils, lymphocytes Inflammatory kinetics: NLR, 2nd-hour NLR, NLR gradient, 2nd-hour/baseline NLR ratio	0.629	0.557	0.619
Model 3 (Full-stack ensemble)	All comprehensive clinical, biochemical, and early acute systemic inflammatory parameters combined (Complete features of Model 1 + Model 2)	0.648	0.621	0.596

Abbrev. : AUC, Area Under the Receiver Operating Characteristic Curve; LDH, Lactate Dehydrogenase; NLR, Neutrophil-to-Lymphocyte Ratio; WBC, White Blood Cell; XGBoost, eXtreme Gradient Boosting. Bold values indicate the highest predictive performance within each specific model layer.

Table 5. Whole-cohort optimization vs. stratified 5-fold cross-validated performance of the hybrid two-stage model.

Performance metric	Whole-cohort optimization value	95% Confidence Interval (CI)	Mean Cross-validated (OOF) value	95% Confidence Interval (OOF-CI)
AUC-ROC	0.852	[0.739-0.965]	0.702	[0.576-0.829]
Overall accuracy	78.4%	[64.7%-88.7%]	64.7%	[50.8%-78.6%]
F1-Score	0.853	[0.741-0.926]	0.741	[0.632-0.850]
Sensitivity	82.9%	[66.4%-93.4%]	74.3%	[59.4%-89.1%]
Specificity	68.8%	[41.3%-89.0%]	45.0%	[20.1%-69.9%]
Positive predictive value	85.3%	[68.9%-95.1%]	74.8%	[63.4%-86.1%]
Negative predictive value	64.7%	[38.3%-85.8%]	45.0%	[24.8%-65.2%]

Abbrev.: AUC-ROC, Area Under the Receiver Operating Characteristic Curve; CI, Confidence Interval; F1-Score, Harmonic mean of Precision and Recall; LASSO, Least Absolute Shrinkage and Selection Operator; NLR, Neutrophil-to-Lymphocyte Ratio; NPV, Negative Predictive Value; PPV, Positive Predictive Value (Precision); OOF, Out-Of-Fold.

Table 6. Univariate and multivariate logistic regression profiles of the final LASSO-selected predictors.

	Univariate analysis			Multivariate analysis		
LASSO-Selected feature	OR	95% CI	p-value	OR	95% CI	p-value
Pleural total protein	2.685	[1.318-5.467]	0.006	3.192	[1.093-9.326]	0.034
2nd-hour NLR	0.857	[0.753-0.976]	0.020	0.827	[0.672-1.018]	0.073
Age	0.966	[0.921-1.013]	0.150	0.938	[0.878-1.002]	0.056
Baseline neutrophils	1.000	[1.000-1.000]	0.283	1.000	[1.000-1.000]	0.671
Serum albumin	2.832	[0.817-9.820]	0.101	1.079	[0.166-6.991]	0.937
Baseline lymphocytes	1.000	[0.999-1.001]	0.975	0.999	[0.997-1.001]	0.234

Abbrev.: CI, Confidence Interval, LASSO; Least Absolute Shrinkage and Selection Operator, NLR; Neutrophil-to-Lymphocyte Ratio, OR; Odds Ratio.

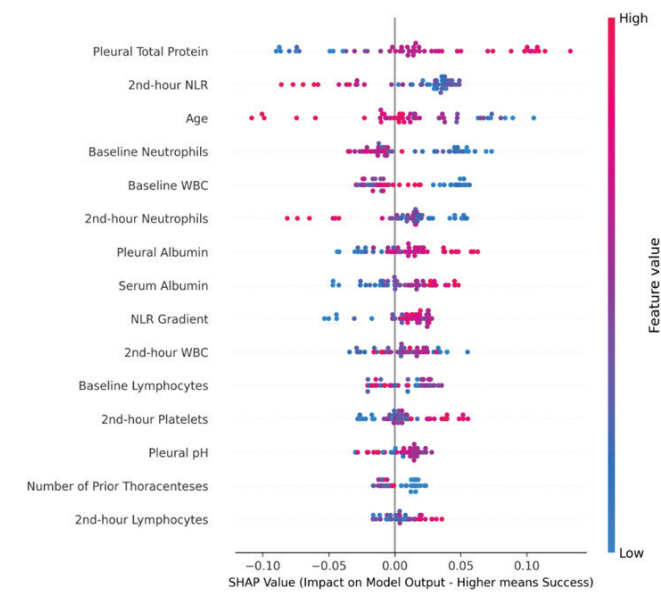


Figure 3. Global TreeSHAP summary plot for talc pleurodesis success prediction. Features are ranked vertically by predictive importance. Each dot represents a patient (red: high value, blue: low value). Right of the baseline indicates a positive impact on success, while the left indicates a negative impact. (NLR: Neutrophil-to-Lymphocyte Ratio, SHAP: Shapley Additive exPlanations).

Hierarchical ranking of the features demonstrated that Pleural Total Protein exerted the most profound global impact on model decisions, where elevated levels (red dots) heavily drove the model output toward pleurodesis success. Notably, the 2nd-hour NLR emerged as the second most critical determinant in the hierarchy. Lower 2nd-hour NLR values (blue dots) were tightly clustered on the positive SHAP axis. Conversely, advanced age and elevated baseline neutrophils negatively impacted the probability of success.

4. Unsupervised patient stratification: k-means clustering analysis

To look beyond supervised predictive classifications and structurally identify natural, distinct patient sub-populations based entirely on post-procedural systemic inflammatory behaviors, an unsupervised k-means clustering analysis was executed. The algorithm mathematically stratified the evaluable cohort (n = 51) into two discrete biological trajectories: Cluster 0 (n = 14) and Cluster 1 (n = 37). Profile analysis of these clusters revealed that Cluster 0 represented a Hyper-inflammatory phenotype, characterized by a profound escalation in the 2-hour post-procedural neutrophil-to-lymphocyte ratio (mean

2.h NLR: 13.82) accompanied by marked acute leukocytosis. Conversely, Cluster 1 represented a regulated/mild phenotype, exhibiting highly stable and well-controlled systemic biomarker kinetics with a significantly lower 2-hour post-procedural NLR (mean 2.h NLR: 5.53). When these unsupervised, laboratory-driven mathematical clusters were crossed with definitive clinical outcomes, a highly significant correlation was observed. In the regulated/mild phenotype (Cluster 1), the definitive clinical pleurodesis success rate was exceptionally high at 78.38% (29 of 37 patients). In stark contrast, the hyper-inflammatory phenotype (Cluster 0) yielded a significantly lower clinical success rate of only 42.86% (6 of 14 patients), with the majority of these patients (57.14%, n = 8) presenting with definitive non-response/treatment failure. Cross-tabulation mapping and subsequent statistical evaluation confirmed that this unsupervised phenotypic distribution was significantly associated with final clinical outcomes (p = 0.021; Figure 4).

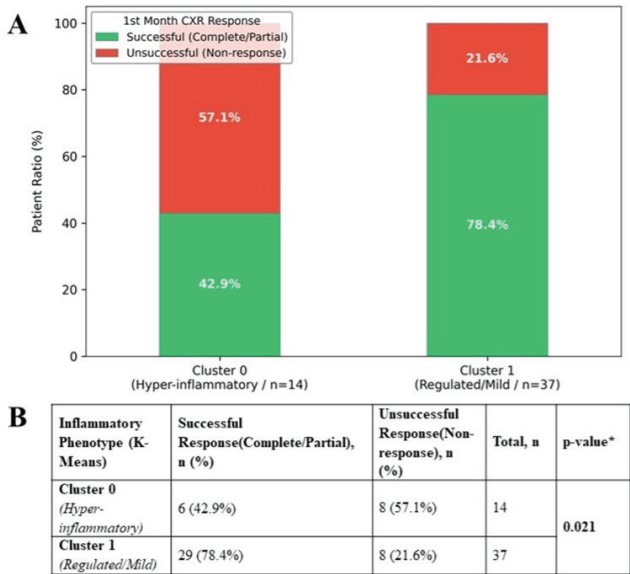


Figure 4. Panel (A) provides a stacked bar chart illustrating the marked diagnostic superiority of the regulated inflammatory response (Cluster 1) over the hyper-inflammatory surge (Cluster 0) for predicting clinical success in talc pleurodesis. Panel (B) presents the cross-tabulation mapping and corresponding Fisher's exact test (p = 0.021) for both k-means derived subgroups.

Discussion

While the exact mechanism of chemical pleurodesis remains unclear, talc instillation is known to trigger a robust histiocytic and granulomatous foreign-body reaction within the pleural space [3]. Mesothelial cells orchestrate this cascade by secreting mediators like in-

terleukin-8 (IL-8), monocyte chemoattractant protein-1 (MCP-1), and transforming growth factor-beta (TGF- β) [8]. IL-8 acts as a potent chemokine that induces intrapleural neutrophil recruitment, serving as a critical mediator of the local inflammatory response. Consequently, this study investigated the relationship between the early systemic inflammatory trajectory and the clinical success of talc pleurodesis.

Chemical pleurodesis with talc is frequently performed to obliterate the pleural space, thereby alleviating dyspnea and improving patient comfort. A meta-analysis of 18 studies utilizing sterile talc reported pleurodesis success rates between 76% and 82% [9]. In our study, the success rate was 68.6%, which is lower than the reported literature. This discrepancy may be attributed to our sample size limitations as a single-center study.

Habal et al. evaluated local and systemic inflammatory parameters in 114 patients with recurrent malignant pleural effusion undergoing talc pleurodesis [7]. When comparing the successful ($n = 98$, 86.0%) and unsuccessful ($n = 16$, 14.0%) groups, they reported that serum leukocyte counts began rising after the 12th hour in both cohorts. However, leukocyte levels were significantly higher in the successful group during peak periods between the 36th and 60th hours ($p_{36.h} = 0.002$, $p_{48.h} = 0.0001$, $p_{60.h} = 0.0001$). In pleural fluid analysis using flow cytometry, a marked decrease in lymphocyte percentage and a prominent increase in granulocyte percentage were observed, though no statistically significant difference was reported between the two groups. Similarly, Mercer et al. reported the outcomes of 285 patients undergoing talc pleurodesis for malignant pleural effusion, noting an overall success rate of 81.4% (232/285) at the third month [10]. Regarding serum leukocyte dynamics, the difference in leukocyte elevation between the successful (2.35×10^9 /L, SD: 2.94, 95% CI: 1.92-2.78) and unsuccessful (1.79×10^9 /L, SD: 2.44, 95% CI: 1.00-2.58) groups was not statistically significant. However, leukocyte levels increased significantly in both groups when comparing day 0 to day 1 post-procedure ($p < 0.001$ for both). In our study, although an increase in leukocyte and granulocyte counts was observed in peripheral venous blood samples at the 2nd hour, it did not reach statistical significance. Evaluated alongside the literature, these findings suggest that early-phase alterations in leukocyte and granulocyte

counts lack the capacity to independently predict pleurodesis success. Furthermore, while a significant decline in lymphocyte counts was observed consistent with previous reports, it displayed no meaningful association with ultimate clinical outcomes.

In addition to acute inflammation, fibrotic mechanisms play a vital role in establishing effective pleurodesis [3]. Platelets are core components of the coagulation cascade; notably, an inverse relationship between fibrinolytic activity and pleurodesis success has previously been demonstrated via d-dimer measurements [11]. Furthermore, direct intrapleural instillation of TGF- β , a potent pro-fibrotic cytokine, has been shown to induce pleurodesis at a faster rate than talc in rabbit and sheep models [12,13]. Platelets contain 40 to 100 times more TGF- β than other circulating cells and are estimated to source approximately 45% of baseline plasma TGF- β levels [14-16]. Collectively, these insights underscore the impact of platelets on the fibrotic-fibrinolytic equilibrium during the pleurodesis cascade. However, literature regarding platelet count dynamics in patients undergoing talc pleurodesis remains virtually non-existent. In our cohort, while a significant post-procedural decline in serum platelet counts was observed, this alteration exhibited no direct statistical association with ultimate pleurodesis success.

The peripheral blood NLR is a well-established marker of immune-inflammatory dynamics and a cost-effective parameter for assessing clinical severity [17,18]. Furthermore, early alterations (<6 hours) in neutrophil and lymphocyte counts following acute physiological stress position these cellular indices as timelier biomarkers compared to traditional laboratory parameters like total white blood cell (WBC) count and C-reactive protein (CRP) [17]. Zablockis et al. evaluated systemic inflammatory responses and pleurodesis outcomes in 96 patients utilizing non-graded talc, graded talc, bleomycin, or mitoxantrone [6]. In their study, which achieved successful pleurodesis in 81 patients (84.4%; comprising 39.6% complete and 44.8% partial responses), systemic inflammatory markers were assessed using 24-hour post-procedural serum samples. Their findings indicated that serum NLR levels elevated uniformly across all therapeutic agents at the 24th hour. Moreover, comparative analyses between the successful and unsuccessful pleurodesis cohorts demonstrated

that baseline NLR, 24-hour post-procedural NLR, and longitudinal NLR dynamics failed to predict ultimate pleurodesis success. Consistent with the literature, our results demonstrate that 2nd-hour serum NLR levels increased significantly as an indicator of acute inflammation. This early evaluation captures the immediate neuroendocrine-driven immune cell redistribution before delayed systemic cascades fully manifest. According to the kinetic model described by Dhabhar et al., acute stress triggers a time-dependent cellular shift within 30 to >120 minutes, wherein lymphocytes traffic out of the blood into target tissues while neutrophils exhibit sustained mobilization [19]. Therefore, the 2nd-hour NLR captures a dynamic window of this leukocyte redistribution, minimizing confounding by subsequent secondary processes. However, while conventional univariate analysis failed to establish a direct relationship between this acute NLR shift and pleurodesis success, this clinical signal was successfully isolated through our two-stage hybrid AI approach by capturing the synergistic variance among features. Within this regularized framework, post-procedural 2nd-hour NLR emerged as the second most critical determinant. Our explainable AI (TreeSHAP) analysis illuminated this mechanism, revealing that lower 2nd-hour NLR values were associated with positive SHAP values. Clinically, this suggests that a controlled, non-exaggerated early systemic response following talc insufflation is a prerequisite for successful pleurodesis maturation. Our unsupervised k-means clustering further supports this model; patients with a well-controlled inflammatory profile yielded substantially higher success rates than those experiencing a post-procedural hyper-inflammatory surge. Biologically, this highlights an 'optimal inflammatory window', suggesting that while a baseline exudative environment primes the pleura for fusion, an unmitigated early systemic storm may trigger local tissue degradation and excessive exudation that mechanically hinders stable fibrin bridge organization.

Both thrombocytosis and lymphopenia are intrinsically linked to the severity of systemic inflammation, and the PLR provides a composite biomarker integrating both hematological indices [17]. The prognostic utility of PLR has been extensively investigated in various inflammatory conditions, including its combined use with NLR to evaluate disease activity in rheuma-

tological disorders [20]. However, studies exploring the relationship between PLR and talc pleurodesis efficacy remain absent. In our cohort, although 2nd-hour post-procedural PLR levels increased significantly, they failed to independently predict pleurodesis success.

The Systemic Immune-Inflammation Index (SII) was first defined by Hu et al. in 2014 and is calculated using the formula of (Platelets x Neutrophils) / Lymphocytes [21]. These peripheral blood cells play pivotal roles in numerous inflammatory cascades. Consequently, SII has emerged as a prognostic biomarker across various diseases, particularly in malignancies and cardiovascular disorders. However, its clinical utility as a standalone parameter remains limited due to threshold uncertainties and study heterogeneities [17]. To date, no published data directly link SII with talc pleurodesis outcomes. Our data revealed a significant post-procedural elevation in 2nd-hour SII levels. Nevertheless, when stratified by clinical response, no statistically meaningful association was found between SII and ultimate pleurodesis success.

The relationship between pleural fluid characteristics and talc pleurodesis success remains controversial in the literature. Ferreiro et al. evaluated the pleural fluid analysis of 36 patients undergoing talc pleurodesis for malignant pleural effusion achieving success in 26 patients (72.2%) and reported no significant differences between the successful and unsuccessful groups regarding pleural fluid pH, glucose, total protein, albumin, or lactate dehydrogenase (LDH) levels [22]. Conversely, Ukale et al. evaluated 89 patients with malignant pleural effusion undergoing pleurodesis with either talc (n = 48) or mepacrine/quinacrine (n = 41), achieving an overall success rate of 91.0% (n = 81) [23]. In their post-procedural pleural fluid analysis, glucose levels were significantly higher in the successful group (5.34 ± 2.57 vs 3.06 ± 1.54 , $p = 0.05$), whereas no meaningful difference was noted in pH values (7.52 ± 0.35 vs 7.64 ± 0.58 , $p = 0.52$). However, their statistical evaluations were limited to univariate comparisons without accounting for potential confounding variables through multivariate regression models, thereby restricting strong causal inferences. Although published data are limited, an exudative pleural fluid profile typically reflects a

more pronounced local inflammatory state within the pleural space [24]. In our cohort, baseline pleural fluid protein was validated as the strongest independent positive predictor of pleurodesis success in both univariate analysis ($p = 0.006$) and the LASSO-optimized multivariate final model ($p = 0.034$). Specifically, an increase in baseline pleural fluid protein levels elevated the odds of pleurodesis success by 3.192-fold in the multivariate matrix. This parameter also occupied the apex of the SHAP hierarchy, where higher values clearly demonstrated that pre-existing, local exudative/inflammatory activity within the intrapleural space primes the pleural environment for the subsequent talc-induced granulomatous reaction, thereby directly driving clinical success. Consequently, this study provides an innovative, AI-driven framework that enables clinicians to predict patient-specific pleurodesis outcomes by evaluating the baseline pleural fluid protein profile prior to the procedure, a clinical insight that warrants further validation through prospective trials.

Limitations of the study

Our study is subject to several limitations that warrant consideration. First, its retrospective nature inherently introduces potential selection biases. Second, it was conducted as a single-center study with a relatively small sample size ($n = 51$). However, this sample limitation was mathematically addressed by utilizing the regularized LASSO (L1) penalization method to shrink 12 noise-generating variables to zero. Furthermore, since whole-cohort optimization inherently carries an overfitting risk in small datasets, a Stratified 5-Fold Cross-Validation framework was implemented to determine the true out-of-fold (OOF) performance and establish realistic generalizability boundaries. Third, because some patients had received various oncological treatments prior to the procedure, a complete standardization of oncological therapies could not be achieved. Despite these limitations, confirming the validity of our machine learning-based findings through prospective, multi-center studies with larger patient cohorts remains of paramount importance.

In conclusion, while conventional univariate analyses suggest early systemic inflammatory parameters lack linear predictive capacity, our machine learning frame-

work successfully identifies distinct prognostic phenotypes based on acute biomarker kinetics. Specifically, a regulated, stable inflammatory profile significantly outperforms an unmitigated hyper-inflammatory surge in predicting clinical efficacy, while baseline intrapleural total protein remains the strongest independent positive predictor. Utilizing this explainable AI methodology provides clinicians with a powerful framework for patient-specific pleurodesis outcomes, though future prospective trials remain essential for validation.

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 Institutional Non-Interventional Clinical Research Ethics Committee of the Gazi University (Approval No: E-77082166-604.01-1537754, Date: 12/05/2026).

Authors' contribution

IT: Conceptualization, methodology, formal analysis, writing - original draft, project administration. EV: Data curation, investigation, resources. AKT: Data curation, visualization, software. ICK: Supervision, validation, critical review. MS: Formal analysis, software, writing - review & editing. AC: Conceptualization, supervision, validation, critical review. All authors read and approved the final manuscript.

Use of Generative AI and AI-assisted technologies in the writing process

The authors disclose that a Generative Artificial Intelligence (GenAI) tool was utilized solely as a supplementary aid to enhance the language, grammar, and formatting of the manuscript. The study hypothesis, scientific content, statistical/data analysis, and conclusions were independently conceived, validated, and authored entirely by the human researchers. The authors maintain full and ultimate responsibility for the accuracy, originality, and integrity of the work.

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Review

Environmental microplastic exposure and lung cancer: emerging evidence and a thoracic surgery perspective

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ABSTRACT

In modern times, microplastics are common environmental contaminants that are of increasing importance for human health. Ingestion has been traditionally regarded as the dominant route of exposure. However, inhalation of airborne microplastics represents a direct and biologically relevant exposure route to the respiratory system. Increasing evidence, both experimental and review-based, suggests that inhaled microplastics may become trapped in lung tissue, remain there for long periods of time, generate oxidative stress and chronic inflammation, and disrupt normal cellular function in the lungs. These pathophysiological mechanisms may be directly involved in the development of lung cancer. From the perspective of thoracic surgery, exposure to microplastics can influence the epidemiology of lung cancer, tumor biology, perioperative risk, and future surgical decision making. Identification of these novel relationships could place thoracic surgeons at the intersection of surgical oncology and environmental health. This article aims to increase public awareness of environmental microplastic exposure and the possible link between microplastic exposure and lung cancer based on published peer-reviewed research. The purpose is to evaluate the potential impact of microplastics on thoracic surgery procedures and to alert thoracic surgeons about the possibility of an increase in lung cancer cases due to microplastics in the near future.

Keywords: microplastic, environmental, lung cancer, thoracic surgery

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Introduction

Plastics are used widely in our society, but most of the plastic waste ends up in landfills and in the environment. Their degradation into submillimeter fragments, known as microplastics, is an emerging concern due to potential adverse effects on the environment and human health. Microplastics are airborne, inhalable by humans, and their detrimental effects on the respiratory system are being studied [1]. Beyond its environmental importance, microplastic exposure may have implications for the practice of thoracic surgery, particularly its potential impact on lung cancer epidemiology, tumor biology, and postoperative outcomes. In addition to the environmental and respiratory health concerns, the possible clinical implications of microplastic exposure remain largely unknown in surgical disciplines. The purpose of this paper is to raise public awareness of exposure to environmental microplastics and the potential association of microplastic exposure with lung cancer based on peer-reviewed published research. It aims to evaluate the potential consequences for thoracic surgical procedures, to alert thoracic surgeons to the possible emergence of microplastic lung carcinomas in the near future, and to highlight the active role of thoracic surgery.

Based on microplastic particle characterization, the most abundant particles found in lung tissue were polypropylene and polyethylene. These polymers are the most common types of plastics in production; they can be found, among others, in banknotes, food packaging, automobile parts, and in the packaging of snacks and candies [1]. In recent years, microplastics have been detected in the air, both indoors and outdoors. Indoor environments tend to have more fibers than outdoor environments. The manufacture of clothing often uses natural fibers treated with chemicals such as flame retardants and dyed, which may affect their biodegradability. The type of polymers found in the lungs is likely related to indoor exposures because most city dwellers spend more time indoors than outdoors. The main causes include dust settling and reentering the atmosphere, industrial emissions, plastic material degradation in the environment, and synthetic textile products. Because of their small size, irregular shape, and low density, microplastic particles, especially those in fibrous

form, may possess aerodynamic properties that allow them to deeply penetrate the pulmonary system. Microplastics are used extensively in daily human activities. They may enter the lungs by the respiratory pathway, accumulate around the primary lesion, and ultimately become caught by the expanding tissue of the tumor. Because of the enhanced permeability and retention effect, microplastics can concurrently enter the bloodstream through the digestive system, travel to the lungs, and then infiltrate tumors. The significant variation in microplastic particle size may be caused by these two primary mechanisms [1,2].

Experimental and observational studies have shown that inhaled microplastics can reach the lower respiratory tract, where physiological clearance processes are somewhat less effective [3]. The persistence of these particles within lung tissue raises concerns regarding cumulative accumulation and long-term respiratory health effects, especially in cases of long-term, low-dose exposure. Microplastics can settle in different areas of the respiratory system based on their size, shape, and surface characteristics. The bronchiolar and alveolar regions are more readily penetrated by smaller microplastics and nanoscale plastic particles. It is reasonable to anticipate higher particle retention in these regions. Data from experimental exposure studies support the hypothesis that microplastics may generate persistent particle-tissue interactions and stay in lung tissue for extended periods of time. Because of this persistence, alveolar epithelial cells, which are crucial for maintaining immunological homeostasis and the integrity of the pulmonary barrier, may be more vulnerable to cellular stress reactions. The size of microplastics appears to have a major impact on the phagocytic efficiency of alveolar macrophages. The impact of microplastics on alveolar macrophage function is still not entirely understood [3].

An increasing number of experimental studies have shown that inhaled microplastics can induce oxidative stress, inflammatory responses, and epithelial damage in lung tissue. Studies carried out both *in vitro* and *in vivo* after microplastic exposure consistently show elevated production of reactive oxygen species, activation of inflammatory signaling pathways, and enhanced

release of pro-inflammatory mediators [2,3]. These biological responses may disrupt the epithelial barrier's ability to function and jeopardize proper pulmonary homeostasis. Review-based evaluations show that micro and nanoplastics can interact with intracellular signaling pathways involved in tissue remodeling, immunological regulation, and cellular stress responses. Additionally, they might physically damage blood vessels, which could lead to inflammation and stress. Additionally, microplastics can lower the energy supply and disrupt respiratory processes. The effect on human health depends on the level of exposure to concentration. Microplastics usually affect the neurological system, excretory system, gastrointestinal tract, internal organs, respiratory tract, and placenta. Inhaling these microscopic particles could lead to their accumulation in the respiratory system, raising worries about respiratory issues and inflammation. Therefore, future studies on microplastics should look more closely at people's inhalation exposure levels, assessing both the level of exposure and any potential effects on respiratory health. Additionally, it will be critical to evaluate the biological mechanisms by which microplastics may affect respiratory health, considering factors such as toxicity, inflammation, and potential long-term consequences on various respiratory and cardiovascular organ systems. It is recognized that air microplastics pose risks to human health and the environment since they are a major source of particles that humans and other organisms consume and inhale. Environmental particle exposure is associated with long-term lung pathology through significant mechanisms, such as inflammation and chronic oxidative stress, which are known causes of pulmonary disease [4,5].

The increasing amount of data suggests that exposure to microplastics may play a physiologically plausible but indirect role in carcinogenic processes. Chronic inflammation caused by persistent particle buildup can establish a tumor-promoting environment with oxidative DNA damage, impaired DNA repair processes, and dysregulated cell proliferation [6]. Some of the most well-known markers of the development of cancer are these mechanisms. Additionally, by serving as carriers for co-occurring ambient pollutants or chemical additives, microplastics may intensify local detrimental and

genotoxic effects within lung tissue. The significance of particle exposure in the development of lung cancer is emphasized in reviews that focus on the relationship between airborne particulate matter and lung cancer. Microplastics have several physical characteristics with recognized carcinogenic particles, including their small size, surface reactivity, and capacity to induce persistent inflammatory reactions [7]. Current mechanistic insights provide a physiologically solid framework that stimulates further investigation, even if there is currently limited direct epidemiological evidence linking breathing microplastics to lung cancer.

With over 2 million fatalities reported in 2021, lung cancer is the most common cancer in the world and the primary cause of cancer-related mortality [8]. Growing global air pollution, especially in low- and middle-income countries, continues to contribute to high mortality from lung cancer and other respiratory diseases, even if incidence and death have decreased in wealthier nations [8]. Only around 10% of the more than 450 million tons of plastic generated annually worldwide is recycled, and estimates indicate that by 2050, the amount of plastic garbage entering the environment could surpass 30 million tons [8]. The existence of microplastics in soil and even the environment has drawn more attention in the last ten years. Especially considering the ability of plastic particles to be carried by atmospheric processes. Additionally, aquatic pollution makes it easier for plastics to enter food webs, where detrimental impacts have been shown at several trophic levels [8,9].

Due to their greater ability to penetrate, smaller particles are more dangerous. Particulate matter with a size of 2.5 has been shown to cause or hasten the development of cancer by directly damaging DNA in lung tissue and generating pro-inflammatory proteins. Clinical and experimental studies have shown that both smokers and non-smokers have a significantly higher incidence of lung cancer in urban areas with particulate matter pollution.[8] In light of ongoing climate change and the expansion of global economic activity and its associated environmental impacts, lung illnesses, including lung cancer, are predicted to remain a major public health concern for many years to come [8,10].

Outdoor microplastic concentrations are lower than

indoor ones, and barometric pressure, humidity, wind, and location all affect the abundance of particular polymer particle sizes and shapes [8]. This suggests that microplastic intake is more common in offices and among other employees, as well as among those who work with polymers. According to research, air quality and exposure to ambient microplastics are significantly influenced by the type, quantity, and quality of room ventilation [8]. Concerns over patients being exposed to microplastics during surgery or medication infusions have also surfaced recently. According to a recent study, commercially available saline and glucose infusions frequently contain nanoparticles of different synthetic polymers, polypropylene, and polystyrene, which may have detrimental effects on patients [8,11].

In order to assess the available data and apply environmental discoveries to medical research, it is essential to understand the analytical techniques utilized to identify and characterize microplastics. The validity, comparability, and clinical importance of published data are directly impacted by the advanced spectroscopic and imaging techniques used to detect microplastics in human lung tissue. Because surgically removed lung tissues may provide valuable biological material for assessing long-term environmental exposure, standardized and reproducible detection techniques are particularly important for thoracic surgery research. There are numerous techniques for identifying plastic in the environment and living things. The most widely used approach and the gold standard is Fourier Transform Infrared Spectroscopy (FTIR). The micro-FTIR technique allows for the evaluation of individual spectral bands thanks to focal arrays, which in turn translates into greater efficiency [8,12,13]. FTIR is often used in conjunction with Raman spectroscopy (RS), which is based on Raman scattering radiation, because of the restrictions on particle size. A variety of qualitative sample analysis services are provided by RS. In contrast, Micro-Raman spectroscopy (MRS) enables the evaluation of micrometer-sized items by focusing the laser on a small research area. According to MRS, enhanced stimulated Raman spectroscopy (SRS) with increased efficiency was achieved [8,14-16]. The laser-assisted direct infrared (LDIR) imaging technique has a noticeably quicker measurement time [8,17]. Optical photothermal infrared spectroscopy (O-PTIR)

is another method that uses spectroscopy. By monitoring infrared absorption during thermal expansions of the material caused by an infrared laser, a Quantum Cascade Laser approach that uses IR and Raman spectroscopy enables highly effective qualitative assessment of particles [8,18]. Using fluorescent dyes for optical microscopic inspection is another method for evaluating microplastics. It is a reasonably priced approach, but because of the size of the particles and the presence of pollutants in the sample, it gives relatively low accuracy and necessitates labor-intensive sample and particle preparation [8,19]. The energy-dispersive X-ray scanning electron microscope (SEM) is another microscopy-based technique. Although it is one of the more difficult, costly, and low-throughput methods, it offers the capacity to evaluate the surface and elemental composition of particular particles [8,20]. Atomic force microscopy and infrared spectroscopy are combined to create the AFM-IR, a technique used for in situ microplastic analysis in tissue and water samples [8,21]. Mass spectrometry has a narrow range of evaluations. Mass spectrometry and chromatography of evaporated sample material are combined in pyrolysis-gas chromatography mass spectrometry (Py-GC-MS) [8,22,23]. Thermogravimetric analysis of microplastics (TGA), a technique based on detecting the mass loss of a sample during heating at a regulated pace, also uses the sample's thermal breakdown [8,24].

According to Zhu et al.'s study, lung tissue had the greatest microplastic concentrations, with almost 14 particles per gram and sizes ranging from 20 μm to 100 μm , with Polyvinyl chloride being the most common kind of polymer [8,25]. Given that it is impossible to totally remove all aggregated particles from lung tissue and that chronic inflammation encourages the growth of malignancies, such as liver or lung cancer, the data show that even brief exposure to MNP may have long-term effects [6,8,26]. The detrimental effects of cigarette smoke, dust, and microplastics on animal respiratory systems have been documented, and micro- and nano-plastic particles have been found in commercially available cigarettes. When combined, cigarette smoke and microplastics showed the anticipated increased harmful effects on BEAS-2B cells, including oxidative stress, genotoxicity, anchorage-independent growth, invasiveness, and a reduced oxidative stress response

[8,27]. According to research, exposure to micro- and nanoplastics can cause oxidative stress, trigger cellular repair mechanisms, and mechanically harm organelles, interfering with several metabolic processes. Lung epithelial cells and other tissues have shown carcinogenic effects from both short- and long-term exposure [8].

Exposure to environmental contaminants is a major etiological factor in the development of lung cancer, according to numerous academic studies. Some literature has examined and documented the connections between lung cancer-causing variables and other contaminants, specifically microplastics, passive smoking, polycyclic aromatic hydrocarbons, radon, asbestos, cadmium, nickel, and pesticides [7,28].

Lung cancer has been identified as directly related to deteriorating ambient air quality, indoor pollutants, and occupational exposure. Outdoor PM_{2.5} exposure affects all human groups and is a significant carcinogen. Indoor passive smoking is also a major source of exposure. Asbestos exposure has also been identified as a high carcinogen. Priority should be given to innovative approaches to improving air quality, while simultaneously avoiding long-term exposure to pollutants. The long-term health consequences of air pollutants should be systematically investigated. The contributions of environmental factors to lung cancer need to be documented through comprehensive epidemiological studies from a public health perspective and shared with the public [7].

Smokers are vulnerable to microplastics, as they have been detected in 99% of cigarette filters. Findings have shown that microplastics are present in biological samples such as feces (100%), lung tissue (88%), blood (77%), and placenta (75%), indicating systemic human exposure to microplastics. Improper disposal of cigarette waste is a major contributor to microplastic pollution [27]. Cigarette filters are made of cellulose acetate, a type of plastic that is not biodegradable. Improper disposal of cigarette butts causes microplastic pollution. Studies have shown that cigarette butts contain heavy metals and toxic substances and can release chemicals into the environment, negatively impacting aquatic life and ecosystems [27,29].

Hospitals have a significant environmental impact due to waste generation. The increasing volume of medical waste is a major problem. Due to plastic waste, mi-

croplastics constitute a significant portion of medical waste. In addition to being widely used in daily life, plastics are an essential component of medical equipment. Many medical devices used in regular hospitals are either plastic-made or come in plastic packaging. In a study investigating microplastics in surgical environments, it was found that the abundance of environmental microplastics is highest during operating room working hours, and the most abundant polymer types are polyethylene terephthalate and polypropylene [30,31]. Further concerns about perioperative exposure are brought up by the existence of airborne microplastics in operating room settings. During surgical procedures, dispersed particle matter may rise due to surgical activity, staff mobility, and the heavy usage of synthetic materials. Surgical personnel and susceptible patients should be investigated for repeated exposure to airborne microplastics, even if the clinical significance is still unknown. Future elements of environmentally conscious surgical practice could include monitoring the composition of airborne particulate matter, evaluating the use of disposable materials, and optimizing operating room ventilation systems.

Discussing the possible effects of lung cancer growth linked to exposure to environmental microplastics on thoracic surgery practice is critical at this point. The biggest risk factor for lung cancer is still cigarette smoking. However, current beliefs on the origin of lung cancer may need to be reevaluated if long-term exposure to environmental microplastics is demonstrated to contribute to carcinogenesis. This change may contribute to the explanation of lung cancer in nonsmokers. Therefore, while assessing patients, thoracic surgeons may need to take into account occupational, environmental, and other exposure profiles in addition to smoking history.

Microplastic exposure may potentially affect the surgical patient profile and the biology of tumors. If lung cancers appear at a younger age, have different histological subgroups, and have more lesions in the periphery, surgical strategies may need to be altered. In this case, the importance of parenchyma-sparing procedures such as segmentectomy and sublobar resections may increase. Minimally invasive surgical techniques, such as video-assisted and robotic-assisted thoracic surgery, may become increasingly crucial in the treatment of these patients.

If microplastic exposure is determined to be a high-risk factor, new screening techniques may be considered for populations residing in high-risk areas, specific occupational groups, and individuals with substantial indoor exposure. Thoracic surgeons may take an active role in developing screening programs, standardizing surgical criteria, and developing algorithms for managing pulmonary nodules. Microplastic-induced microvascular damage, fibrotic changes, and chronic inflammation in lung tissue may affect the risk of prolonged air leakage, total postoperative complication rates, and postoperative recovery. In this case, more comprehensive preoperative pulmonary function assessments and individualized risk stratification may be necessary. The development of biomarkers to quantify the quantity of microplastics in lung tissue, microplastic analysis of surgical specimens, and the integration of environmental exposure data into the assessment of resection margins are possible long-term research avenues.

From the perspective of thoracic surgery, confirmation of a causal relationship between lung cancer development and exposure to environmental microplastics may lead to a substantial shift in clinical practice, including patient selection, surgical techniques, diagnostic approaches, and interdisciplinary collaboration. Large scale, long-term epidemiological studies that combine environmental exposure data with clinical outcomes are essential to clarify this connection. The lack of such data is now a significant limitation. However, the amount of microplastics in human lung tissue may be quantified thanks to advancements in analytical techniques, opening up new possibilities for exposure biomarkers and risk assessment.

By giving access to human lung tissue, thoracic surgery makes it possible to examine long-term environmental exposure inside the target organ. Surgically removed lung tissue may enable direct evaluation of long-term particle accumulation within the pulmonary parenchyma, in contrast to blood or bronchoalveolar lavage samples. In order to detect compounds that have accumulated in the respiratory system over decades, surgically removed samples can be essential biological

archives. The creation of new biomarkers may be made possible by routine examination of the microplastic burden in excised lung tissue. In this situation, thoracic surgeons may play a crucial role in both environmental illness surveillance and treatment. Thoracic surgeons' professional roles may gradually change as environmental factors of lung illness become more widely recognized. Surgeons may become more involved in interdisciplinary collaborations combining pulmonology, environmental science, epidemiology, and public health by acting as observers of environmental pathology in addition to providing technical intervention.

Long-term exposure to inhaled microplastics can alter the biomechanical properties and tissue flexibility of the lung parenchyma, which is important for thoracic surgery, in addition to their carcinogenic consequences. Therefore, recognizing environmental exposure as a possible modulator of lung tissue quality may become more important in preoperative risk assessment and surgical planning. Changes in local immunological dynamics may affect lymphatic dissemination patterns, tumor invasiveness, and sensitivity to systemic medications used following surgery, according to surgical oncology. Future research examining resected lung specimens may shed light on the connection between ambient particle load and histopathological features. Together, these results and projections suggest that exposure to ambient microplastics should be taken into account as both an ecological concern and a possible risk factor for the development of postoperative disease. These advancements have the potential to change thoracic surgery from its current role in lung diseases to a proactive area that includes research initiatives, environmental risk assessment, surgical procedures, and participation in all of these processes.

There are studies in the literature that indicate microplastic involvement in the lungs and that this issue is very closely related to thoracic surgery, meaning that this topic should not be considered speculation.

In an autopsy study, Amato-Lourenço et al. found microplastics in human lung tissues. They found fibers ($n = 4$) and polymeric particles ($n = 33$) in 13 out of 20 tissue samples, with fibers ranging from 8.12 to 16.8

μm and all polymeric particles smaller than $5.5 \mu\text{m}$. Following inhalation, these contaminants' varied properties were linked to detrimental health effects [1].

In the first study by Jenner et al., which reported the presence of microplastics in human lung tissue samples using μFTIR spectroscopy, the microplastic concentration in the obtained samples was significantly higher than in empty samples, supporting environmental exposure through human respiration. This study emphasized the detection of microplastics as small as $4 \mu\text{m}$ and even $>2 \text{ mm}$. This finding provides significant information regarding the presence of microplastics in human lung tissues. In this study, 39 microparticles were detected in 11 out of 13 lung tissue samples, and the average microparticle/tissue ratio was reported as 1.42 ± 1.50 [13].

In the study conducted by Liu et al., evidence was presented that metals and microplastics complexes accumulate in human lung adenocarcinoma tissues and are associated with poor clinical outcomes. This study used a multi-technique approach on tissue samples, including laser direct infrared imaging, pyrolysis-gas chromatography-mass spectrometry, inductively coupled plasma mass spectrometry, and Single-cell RNA sequencing, and identified 34 different microplastic species in lung tissues. Transcriptome-level sequencing and The Cancer Genome Atlas validation revealed that metal-microplastic complex accumulation activates pro-tumorigenic pathways [2].

Ernhofer et al. emphasized that polystyrene micro and nanoplastic particles did not significantly affect the malignant behavior of cancer cells, but these small particles could promote malignant characteristics, mostly in normal lung cells, by causing DNA damage, oxidative stress, migration, and mitogenic pathways [32].

Studies on microplastics in operating room settings are quite rare. In their study, Field et al. found that polyethylene terephthalate, polypropylene, polyethylene, and nylon were the most common polymer types found in operating rooms. They were unable to detect microplastics outside of operating room hours. These results indicate that this new route of contamination through surgery represents a potentially new exposure route for humans [30].

In a study on microplastic concentration in lung tissue conducted by Wang et al., lung tissue samples were taken from 12 non-smoking patients to evaluate the characteristics of microparticles in human lung tissues using an Agilent 8700 laser infrared imaging spectrometer and scanning electron microscope. They detected 108 microparticles encompassing 12 types in the lung tissue samples. The microparticles in the lung tissues consisted of polypropylene, polyethylene terephthalate, and polystyrene, and a correlation was found between microplastic exposure and certain blood test indicators. This correlation was noted as positive with platelets, thrombocytocrit, and fibrinogen [33].

These findings suggest that linking environmental microplastic exposure to lung cancer and the aforementioned claims regarding thoracic surgery practices are a more serious matter than mere speculation.

In conclusion, there is evidence to support the hypothesis that oxidative stress, persistent inflammation, epithelial and DNA damage caused by inhaled microplastics may result in lung cancer. Even if a causal relationship has not yet been conclusively shown, the consistency of mechanistic findings highlights the necessity for improved preventive measures and collaborative research efforts. In addition to highlighting the significance of integrating environmental health perspectives into future thoracic surgery diagnostic, therapeutic, and preventive approaches, this review aims to increase awareness of environmental microplastic exposure. Furthermore, beyond the environmental impacts of microplastic exposure, it is conceivable that it could alter the epidemiology, tumor biology, and postoperative outcomes of lung cancer, potentially affecting future thoracic surgery practices.

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Case Report

Late-onset right main bronchus erosion and penetration developing on the basis of chronic fungal infection (*Aspergillus*) originating from a central venous port: a rare case report

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ABSTRACT

Currently, the increase in the population of patients with malignancies has led to a rise in the use of chemotherapeutic treatments. Due to the thrombophlebitic effects of chemotherapeutic agents, temporarily established vascular access routes gradually lose their functionality. Therefore, clinicians increasingly prefer central venous port placement in this patient group. Central venous port placement offers advantages such as multi-drug administration, rapid fluid resuscitation, administration of chemotherapeutic agents, and parenteral nutrition. However, since it is an invasive procedure, various complications can occur in both the early and late stages. Early complications include carotid artery injury, catheter malposition, hydrothorax, pneumothorax, air embolism, tracheobronchial injury, and nerve damage. Late complications include infections, thrombophlebitis, and, in rare cases, catheter malpositioning. In this report, we aimed to present the management of a complicated catheter-related complication in a patient who underwent central venous port placement for radical chemotherapy due to pancreatic malignancy and was subsequently diagnosed with mediastinal aspergilloma during follow-up. After antifungal therapy, follow-up evaluation revealed erosion of the right main bronchus by the port catheter, resulting in penetration of the catheter into the bronchial lumen.

Keywords: late catheter-related complication, mediastinal aspergilloma, tracheobronchial penetration

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Introduction

Central venous port placement is an invasive procedure widely used for various indications in the monitoring and treatment of critically ill patients. It is associated with a range of complications that require clinical management and can be broadly categorized into early and late complications. Early complications occur during catheter insertion and include vascular, pulmonary, and cardiac events, as well as catheter malposition. Delayed complications include catheter dysfunction and infections. Among delayed complications, infections are particularly noteworthy. Central venous catheter-related infections may lead to sepsis, shock, and even death. These infections are associated with biofilm formation on the venous catheter, with *Staphylococcus aureus* and *Staphylococcus epidermidis* being the most common pathogens [1,2].

When risk factors for vascular migration are evaluated, increased intrathoracic pressure due to positive-pressure ventilation, physical movements, sneezing, weightlifting, or coughing appears to be prominent. Vascular complications include arterial and venous injuries as well as hematoma formation. Vascular injuries are most frequently observed during femoral vein procedures and least commonly during subclavian vein access. It is thought that after guidewire placement, the dilator or catheter may damage the vessel wall, leading to bending of the guidewire and subsequent advancement toward the vessel wall [2].

In this case, no acute tracheobronchial injury was observed in the immediate post-catheterization period; rather, the complication developed because of the synergistic effect of chronic erosion of the bronchial wall by the distal tip of the port catheter and tissue necrosis caused by a superimposed invasive fungal infection (aspergilloma).

Tracheobronchial perforation is described in the literature as an early complication of catheterization, whereas delayed tracheobronchial perforation has been reported in only a few cases. To our knowledge, tracheobronchial perforation following port-related mediastinal aspergilloma has not been previously reported in the literature.

Case Report

A 58-year-old male patient with pancreatic malignancy had a chemotherapy port placed via the jugular vein 9

months prior. The patient was referred by the medical oncology department due to a newly developed area of suspicious increased metabolic activity along the right main bronchus walls at the level of the main carina on PET/CT imaging (SUVmax: 7.5) (Figure 1). The patient was asymptomatic, with laboratory findings revealing a white blood cell count of $3.21 \times 10^3/\mu\text{L}$ and a C-reactive protein level of 5.26 mg/dL.



Figure 1. PET/CT image demonstrating a newly developed area of suspicious increased metabolic activity along the right main bronchus wall at the level of the main carina (SUVmax: 7.5) (black arrow).

Due to suspicious imaging findings suggestive of an endobronchial lesion in a patient with malignancy, bronchoscopy was performed under general anesthesia. At the level of the main carina, a white, soft tissue lesion eroding the bronchial mucosa was identified at the origin of the right bronchial system, and biopsy specimens were obtained and sent for histopathological examination. In addition, a bronchoalveolar lavage sample from the right bronchial system was collected for further analysis. Fungal spores and hyphae were observed in both specimens, with *Aspergillus* species reported as the predominant organism. The biopsy specimens were also submitted for tissue culture, which yielded growth of *Haemophilus parainfluenzae*.

After seven weeks of antifungal therapy, the patient was re-evaluated with follow-up bronchoscopy under general anesthesia. During the procedure, the distal tip of the chemotherapy port catheter was observed to penetrate the mucosa and enter the right bronchial system (Figure 2). The site of penetration corresponded to the mucosal

area where fungal growth had been identified during the previous bronchoscopy. The bronchoscopy was terminated, and a postoperative chest CT scan was subsequently performed (Figure 3). Imaging revealed the catheter component of the port within the right main bronchus. No pneumothorax or hemothorax was observed.

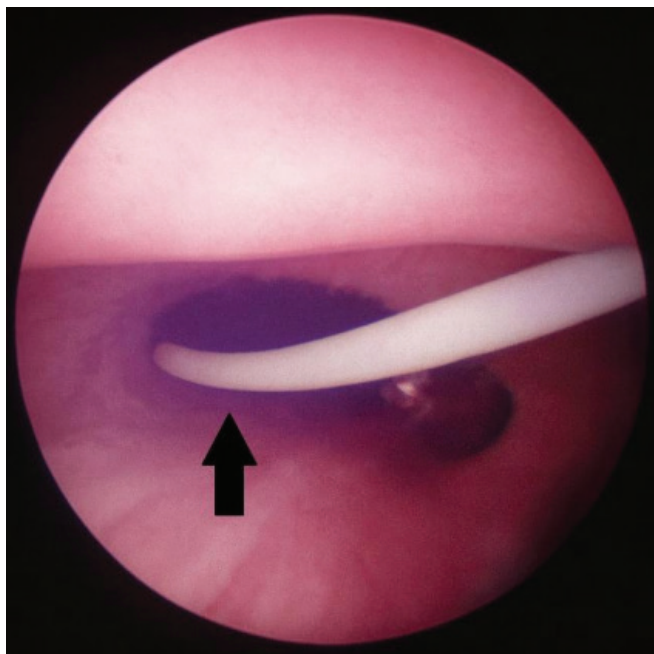


Figure 2. Bronchoscopic view showing the distal tip of the chemotherapy port catheter entering the bronchial system from above the carina and advancing within the right intermediate bronchus (black arrow).

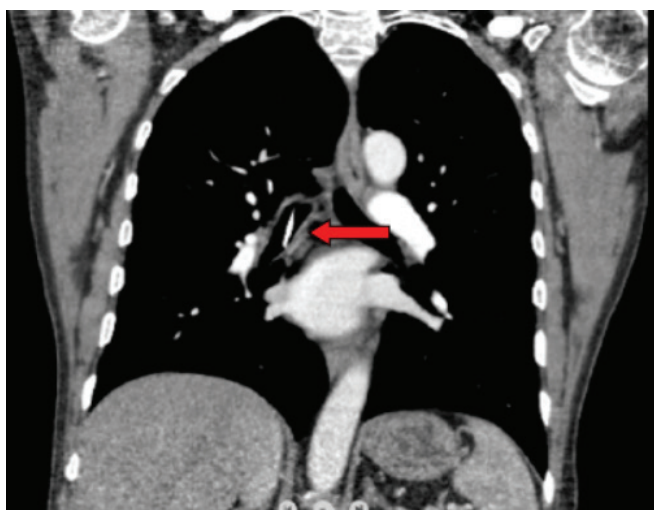


Figure 3. Mediastinal chest CT section demonstrating the chemotherapy port catheter eroding the bronchial wall and extending into the right bronchial system (red arrow).

Interventional radiology and cardiovascular surgery departments were consulted, and surgical removal of

the chemotherapy port under general anesthesia was decided. The patient was taken to the operating room with the involvement of these teams. During catheter removal, the patient was placed in the Trendelenburg position to prevent air embolism, and bronchoscopic access to the bronchial system was achieved through the endotracheal tube. To minimize the risk of endobronchial bleeding during catheter withdrawal, a bronchial blocker was introduced through the endotracheal tube and the balloon was inflated. While the right main bronchus was monitored bronchoscopically, the surgical field was prepared in a sterile manner, and the chemotherapy port was removed via surgical incisions.

The patient was extubated and transferred to the ward with stable vital signs and no perioperative complications. Postoperative posteroanterior chest radiography revealed no complications (Figure 4). After five days of clinical, laboratory, and radiological follow-up, the patient was discharged. Written informed consent was obtained from the patient for the use of the medical data in academic studies.

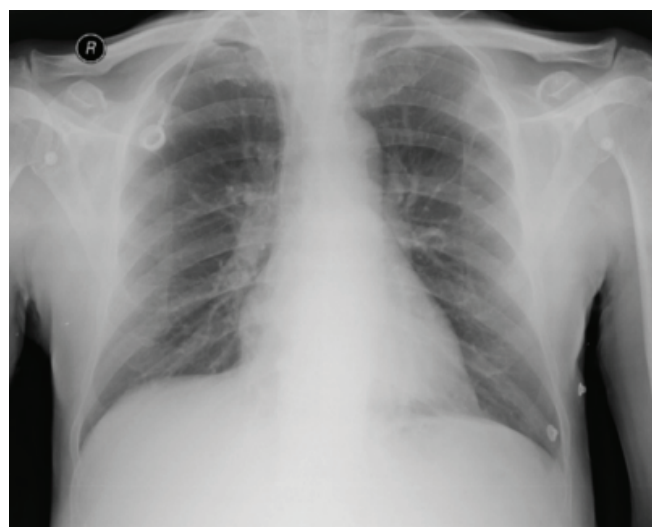


Figure 4. The postoperative control posteroanterior (PA) chest radiograph was evaluated, and no acute pulmonary complications were observed.

Discussion

Central venous catheterization is indicated in patients requiring long-term intravenous therapy or the simultaneous use of multiple agents. These indications include the administration of multiple drugs, fluid replacement, safe infusion of chemotherapeutic agents and the provision

of total parenteral nutrition. The physician may decide to place a central venous catheter after evaluating the patient's clinical condition and treatment requirements [3].

The subclavian vein, internal jugular vein, and femoral vein can be used for central venous catheterization. The subclavian vein is frequently preferred for catheterization due to its lower risk of thrombosis, lower incidence of infection and relatively low rates of mechanical complications compared to other central venous access sites [4].

It has been observed that the rate of acute complications that may arise during ultrasound-guided central venous catheterization is lower compared to catheterization performed blindly [5]. Some of the possible complications include cardiac, mechanical, thrombotic, infectious, and pulmonary complications.

Among acute cardiac complications, arrhythmias are prominent, and this condition is most often associated with the guidewire contacting the right atrium. Fluoroscopy-assisted guidewire placement can help prevent vascular injury [6]. When vascular injury develops, most hematomas can be spontaneously resolved; however, in some cases, if progression or abscess formation occurs, evaluation should be performed with thoracic computed tomography, and drainage should be applied if hemothorax or empyema is detected [7].

Pulmonary complications include pneumothorax, pneumomediastinum, chylothorax, tracheobronchial injury, and air embolism [8]. Numerous catheter attempts and the use of an inappropriately sized catheter can increase the risk of pneumothorax. Tracheobronchial injuries can occur because of needle contact with the trachea or bronchus during vascular access attempts via guidewire [9]. Imaging methods that can aid in the diagnosis of pulmonary complications are plain radiography and CT scans.

In patients receiving mechanical ventilator support, small perforations in the endotracheal or tracheostomy cuff can lead to significant air leakage, requiring tube replacement. Especially in patients exposed to high airway pressure, holes under the cuff can cause pneumomediastinum or subcutaneous emphysema [10].

Air embolism can occur during catheter placement or irrigation. The negative intrathoracic pressure cre-

ated during catheter placement can lead to air entry into the vessel. Massive air embolism can cause hypoxia. To prevent this, the patient should be placed in the Trendelenburg position, and all catheter access points should be closed. If air embolism is suspected, high-flow oxygen therapy should be administered [5,11].

In the management of these complications, simple catheter removal is theoretically considered an undesirable method as it can lead to venous air embolism or uncontrollable bleeding in the airway [12].

Early tracheobronchial perforation usually occurs within the first few days following an iatrogenic procedure and is mostly associated with technical errors, excessive mechanical trauma, or direct damage to the tracheal or bronchial walls during the procedure (e.g., intubation, bronchoscopy, central venous catheterization, etc.). Late tracheal perforation refers to cases where symptoms appear weeks or even months later; in these cases, processes such as tissue ischemia, chronic compression, or infection are more prominent than direct trauma [13].

Central and peripheral catheter insertions can cause tracheobronchial perforation through mechanisms such as indirect compression of the trachea or bronchus, or excessive compression of adjacent tissues. Incorrect positioning of catheter tips, especially with long-term use, increases the risk of chronic compression on the tracheobronchial wall and subsequent tissue erosion [14]. Major factors that increase the risk of developing late-stage tracheobronchial perforation include long-term steroid use, existing infections, malnutrition, diabetes, and other immunosuppressive conditions.

Fungal tracheobronchitis is a fungal infection that invades the trachea and bronchi, more common in immunocompromised patients. These infections can directly target the tracheobronchial mucosa, leading to tissue necrosis. Although rare, the literature reports that ulcerative or pseudomembranous forms of fungal involvement are associated with subcutaneous emphysema and tracheobronchial perforation by disrupting the wall integrity [15].

The angiotropic property of *Aspergillus* species allows for direct tissue and vascular invasion. Particularly in immunosuppressed individuals, this leads to mucosal necrosis and erosion of the bronchial wall. It has been reported

that fungal infection creates a "second hit" effect on top of the mechanical damage caused by the catheter itself [15].

In a study on port catheter migrations, migration was observed in 7 patients (incidence rate 2.3%) in a group of 298 patients [16]. Literature reviews show that tracheobronchial injuries can occur in the acute phase during central venous catheterization [17]. However, the damage observed in our case report did not develop in the acute phase during the central venous catheterization procedure but occurred due to erosion of the distal end of the port catheter in the wall and fungal infection in the chronic phase. Fungal organisms are rarely pathogenic in healthy individuals; however, they can become pathogenic in immunosuppressed groups, as in our patient. [18].

Our case of right main bronchus perforation that developed in the late period following central venous catheterization adds a new pathophysiological link to the known spectrum of complications of this procedure based on current literature. Especially its late onset suggests that the case may involve a more complex mechanism related to catheter placement, mechanical pressure, infectious processes, or individual patient factors. In this respect, the presented case points to a rare but clinically significant complication in the literature and provides a unique contribution to the literature by raising awareness about long-term follow-up of central venous catheterization.

In conclusion, central venous access procedures are among the frequently performed invasive procedures in hospitals. These procedures also carry complications, and detailed evaluation and information gathering are crucial for developing a management plan for these complications. Especially in patients with accompanying comorbidities, complex catheterization procedures may require a multidisciplinary approach. As presented in our case report, early detection of tracheobronchial perforation, a late complication of central venous catheterization, is as vital for the patient as its prevention. Since perforation occurring during port catheter use can lead to sudden respiratory symptoms, allergic reactions, and potentially fatal complications if left undetected, close clinical monitoring and careful evaluation of these patients are critical. While it is not possible to completely prevent complications, their prevention should be one of the clinician's primary goals.

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Authors' contribution

NO: Conceptualization, data curation, visualization, and writing - original draft. DH: Investigation, surgical procedure, data curation, and writing - review and editing. TUK: Literature search, resources, and writing - review and editing. EA: Conceptualization, supervision, validation, critical revision, and final approval. All authors read and approved the final version of the manuscript.

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Case Report

Management of intraoperative breast implant injury during sternal metastasectomy and chest wall reconstruction: a surgical challenge

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ABSTRACT

Breast cancer is the most common malignancy in women, and the concept of oligometastasis supports local treatment in selected cases. Bone is the most frequent metastatic site, while isolated sternal involvement is uncommon. However, prior implant-based breast reconstruction introduces additional technical challenges, including the risk of intraoperative implant injury. A 40-year-old woman with a history of bilateral mastectomy and implant-based reconstruction presented with an isolated lytic metastasis of the sternal corpus 14 months after initial treatment. She underwent subtotal sternal resection with en bloc removal of adjacent costochondral segments, followed by chest wall reconstruction using titanium bars and costal clips. Intraoperatively, implant injury was detected and managed through the same incision with immediate replacement in collaboration with plastic surgery. The postoperative course was uneventful, and the patient was discharged on postoperative day three without complications. Isolated sternal metastasis from breast cancer is rare and may be amenable to surgical resection in selected patients. Although prior implant-based reconstruction increases technical complexity, sternal metastasectomy and chest wall reconstruction can be safely performed with careful planning and multidisciplinary management, even in the setting of intraoperative implant injury.

Keywords: breast cancer, sternum, metastasis, breast implants, thoracic wall, reconstructive surgical procedures

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Introduction

Breast cancer is the most frequently diagnosed malignancy in women worldwide and remains a leading cause of cancer-related mortality. Although metastatic breast cancer is generally considered a systemic and incurable disease, the concept of oligometastatic disease, first described by Hellman and Weichselbaum [1], has challenged this paradigm. Bone is the most common site of distant metastasis in breast cancer, with the sternum representing an uncommon but clinically significant location [2]. Several retrospective studies suggest that surgical resection of isolated or limited metastases in breast cancer may improve survival in carefully selected patients [3,4]. However, previous bilateral mastectomy with implant-based reconstruction introduces unique surgical challenges. The presence of breast prostheses may complicate exposure and increase the risk of intraoperative implant injury. Reports addressing sternal metastasectomy in patients with pre-existing breast implants are extremely limited in the literature.

This report highlights the oncologic rationale for isolated sternal metastasectomy and addresses the critical technical considerations required when operating in the presence of indwelling breast prostheses.

Case Report

A 40-year-old female patient underwent bilateral mastectomy and right axillary lymph node dissection with simultaneous implant-based bilateral breast reconstruction 14 months earlier, following neoadjuvant chemotherapy for triple-negative breast cancer. Adjuvant radiotherapy was administered in the postoperative period. During follow-up, a painful swelling over the sternum prompted thoracic computed tomography, which revealed a lytic lesion in the sternal corpus. On positron emission tomography–computed tomography (PET/CT), a newly developed lytic lesion was identified at the midline of the sternum with a maximum standardized uptake value (SUVmax) of 10.83 (Figure 1).

The patient was referred to our clinic by the oncology department for evaluation regarding metastasectomy. As the lesion was considered an isolated and resectable sternal metastasis, sternal resection and reconstruction were planned. Following a vertical midline incision of approxi-

mately 10 cm, the pectoralis major muscle was dissected, and the sternum along with the adjacent costochondral structures was mobilized. The proximal two-thirds of the sternal body together with the bilateral second, third, and fourth costochondral segments were resected en bloc. After resection, anterior chest wall stabilization was achieved using two titanium bars and four titanium costal clips (Figure 2). During placement of a clip at the left third costochondral region, injury to the existing breast implant was noted. Through the same surgical field, the deformed implant was removed, and after adequate irrigation and surgical field preparation, a new implant of the same size was placed in coordination with the plastic surgery team. The postoperative course was uneventful, and postoperative chest radiography demonstrated the titanium bars in proper position with no evidence of procedure-related complications (Figure 3). Accordingly, the patient was discharged on postoperative day three without any complications. Written informed consent for both participation and publication was obtained from the patient.

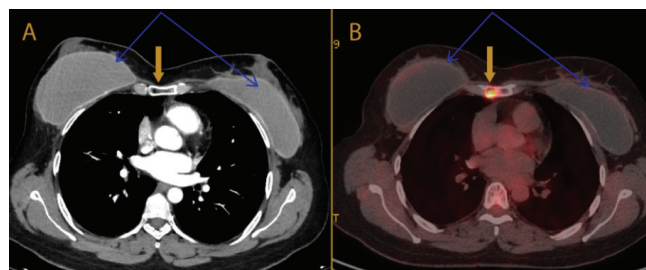


Figure 1. Thoracic CT (A) and PET/CT (B) showing a lytic lesion in the sternal body (yellow arrow) and bilateral breast implants (blue arrow).

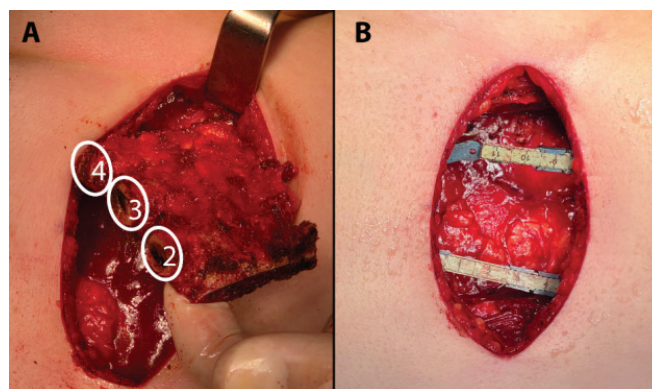


Figure 2. The proximal two-thirds of the sternal body together with the bilateral second, third, and fourth costochondral segments were resected en bloc (A). After resection, anterior chest wall stabilization was achieved using two titanium bars and four titanium costal clips (B).

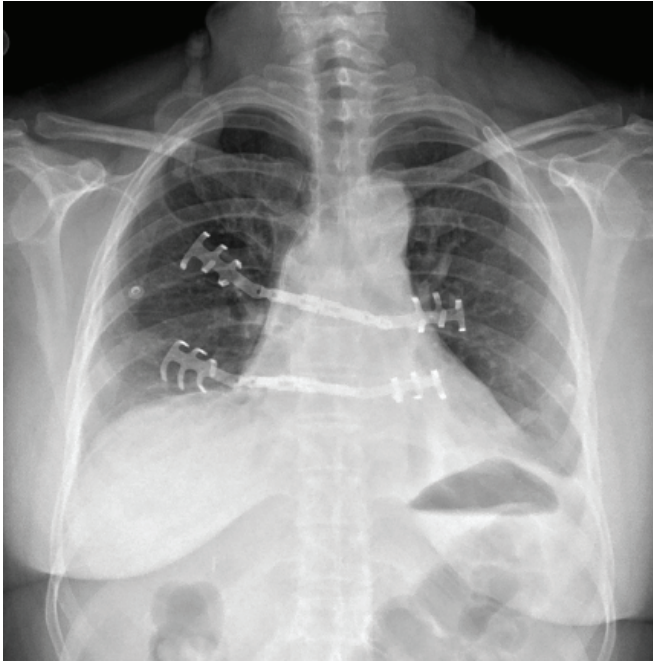


Figure 3. Postoperative chest radiography demonstrated the titanium bars in proper position.

Discussion

Isolated sternal metastasis from breast cancer is an uncommon clinical presentation but has been described in the literature as a distinct subgroup of metastatic disease. Early case series demonstrated that aggressive surgical resection is technically feasible and can be performed with acceptable morbidity in selected patients. More recent retrospective analyses further suggest that partial or total sternal resection, when combined with appropriate chest wall reconstruction techniques, may provide favorable long-term local control and potentially improved survival outcomes in carefully selected cases [4,5]. In our case, reconstruction was performed using transverse titanium plates, which provided a solid structural framework for the large anterior chest wall defect, ensuring sufficient rigidity and stability while preserving respiratory mechanics [6].

Against this background, improved survival rates in breast cancer have made it necessary to offer breast reconstructive procedures to enhance quality of life and self-esteem. Implant-based breast reconstruction is the most utilized reconstructive approach following mastectomy; however, it is associated with a considerable risk of major complications and prosthesis failure,

which may in turn complicate subsequent surgical interventions. Surgeons should be aware of possible implant injury and evaluate implant integrity intraoperatively [7]. In the study by Coombs et al. evaluating patients with preexisting breast implants who underwent cardiothoracic surgery or electrophysiologic procedures, postoperative implant-related complications within one year were reported in approximately 8%, 29%, and 5% of patients undergoing minimally invasive cardiac surgery (MICS), median sternotomy, and electrophysiologic procedures, respectively. Although the intraoperative implant rupture rate was higher in the MICS cohort, in 92% of cases the implant was safely manipulated through the original incision used for its placement [8]. These findings highlight the potential technical challenges posed by preexisting breast implants during thoracic procedures. In our case, the presence of bilateral breast implants posed a technical challenge during the mobilization of the costochondral structures and placement of clips through a limited incision. Despite prior bilateral implant-based reconstruction and adjuvant radiotherapy, the procedure was successfully completed with coordinated plastic surgery involvement. The implant damage was recognized intraoperatively at an early stage, and a new implant was inserted during the same session through the same operative field, without postoperative implant-related complications. Sternal resection and reconstruction performed without removal of the breast implant, using gentle and careful retraction and enlarging the surgical incision when necessary, may allow preservation of the integrity of the fibrous capsule and reduce the risk of postoperative incisional or prosthesis-related complications.

In conclusion, isolated sternal metastasis from breast cancer is an uncommon presentation in which surgical resection may be considered in carefully selected patients. However, prior implant-based breast reconstruction adds technical complexity to thoracic procedures. This case suggests that, with careful surgical planning and multidisciplinary collaboration, sternal metastasectomy and chest wall reconstruction can be safely performed despite intraoperative breast implant injury.

Declaration of conflicting interests

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Authors' contribution

KNK: Conceptualization, data curation, formal analysis, methodology, visualization, writing - original draft. SO: Data curation, formal analysis, visualization, writing - review and editing. SK: Conceptualization, methodology, project administration, supervision, writing - review and editing. All authors read and approved the final version of the manuscript.

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Case Report

Single-port left lower lobe common basal segmentectomy: the first experience in robotic surgery in Türkiye

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ABSTRACT

Robotic thoracic surgery has evolved as an advanced minimally invasive approach that provides enhanced dexterity, three-dimensional visualization, and improved ergonomics compared with video-assisted thoracoscopic surgery. The dedicated da Vinci SP platform represents a further development in robotic surgery, enabling true single-port access and potentially reducing surgical trauma while maintaining the benefits of minimally invasive surgery. We present the first thoracic surgical case in Türkiye performed using the Intuitive Surgical da Vinci SP system: a single-port robot-assisted left lower lobe common basal segmentectomy with mediastinal lymph node dissection. A 51-year-old female non-smoker was found to have a 13-mm centrally located pulmonary nodule that remained stable during follow-up but demonstrated moderate metabolic activity on positron emission tomography. Owing to its proximity to the segmental bronchus, wedge resection was not feasible, and anatomical segmentectomy was planned. The procedure was successfully completed using the da Vinci SP platform with systematic lymph node dissection and indocyanine green-guided identification of the intersegmental plane. The postoperative course was uneventful, with chest tube removal on postoperative day 1 and discharge on postoperative day 3. Final pathology revealed sclerosing pneumocytoma. This case demonstrates the feasibility of anatomical segmentectomy using the dedicated da Vinci SP system and highlights its potential technical advantages in the management of centrally located indeterminate pulmonary nodules.

Keywords: robotic-assisted thoracic surgery, single-port robotic surgery, pulmonary segmentectomy

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Introduction

Video-assisted thoracoscopic surgery (VATS) has revolutionized thoracic surgery over the past three decades by reducing surgical trauma, facilitating faster recovery, and improving postoperative outcomes compared with open thoracotomy [1]. Initially, VATS was performed using a three-port approach, with one port dedicated to the camera and two working ports for surgical instruments. This technique demonstrated clear advantages over open surgery, including reduced postoperative pain, shorter hospital stays, preservation of pulmonary function, and improved cosmetic outcomes.

The evolution from multiportal to uniportal VATS initially involved minor procedures; however, its indications subsequently expanded to include anatomical lung resections [2]. In parallel, robotic-assisted thoracic surgery (RATS) gained popularity because of its enhanced precision and ergonomics compared with VATS. Its advantages, including high-definition three-dimensional visualization and wristed instruments, facilitate meticulous dissection and effective lymphadenectomy [3].

Nevertheless, the conventional robotic approach typically requires multiple ports. To further minimize surgical trauma, many centers adopted the uniportal approach [4]. Several reports have demonstrated the technical feasibility of uniportal robotic-assisted thoracic surgery (U-RATS) using the da Vinci Xi platform. However, because the Xi system was not originally designed for uniportal access, technical challenges such as limited instrument triangulation and internal arm collisions may be encountered.

In contrast, the da Vinci SP system was specifically developed for single-port surgery. Its unique design allows triangulation of multiple instruments through a single access port, minimizes internal arm collisions, and incorporates a wristed camera that facilitates complex thoracic procedures [5].

Segmentectomy has been shown to provide oncological outcomes comparable to lobectomy in selected patients with early-stage lung cancer and also represents a valuable parenchyma-sparing option for benign lesions that are unsuitable for wedge resection [6,7]. Herein, we present a case of single-port robot-assisted common basal segmentectomy performed using the da Vinci SP platform for an indeterminate pulmonary nodule that was anatomically unsuitable for wedge resection.

Case Report

A 51-year-old woman with no history of smoking or prior malignancy was found to have a 13-mm pulmonary nodule located in the common basal segment of the left lower lobe on computed tomography (CT). During radiological follow-up, the lesion remained stable (Figure 1). Surgical intervention was indicated because the lesion persisted despite antibiotic therapy, and positron emission tomography revealed a maximum standardized uptake value (SUVmax) of 4.1.

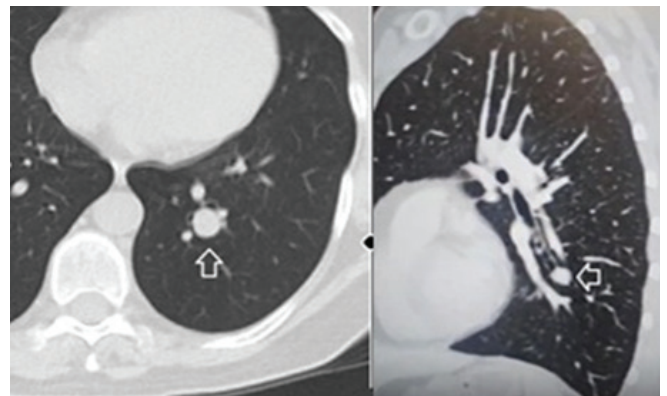


Figure 1. Preoperative chest CT scan demonstrating a 13-mm solid nodule located in the left lower lobe (arrow).

Preoperative evaluation, including echocardiography and pulmonary function tests, revealed no significant abnormalities. Owing to the lesion's central location and its proximity to the segmental bronchus, wedge resection was considered unsuitable. Therefore, a left lower lobe common basal segmentectomy was planned.

Preparation of the single-port robotic system and docking

A 3.5-cm incision was made in the seventh left intercostal space. To optimize exposure, maintain diaphragmatic position, and facilitate instrument mobility, the diaphragm was sutured to the skin (Figure 2a). A large access port (2.7-7 cm) with a wound protector was inserted, and CO₂ insufflation was initiated at a flow rate of 7 L/min (Figure 2b).

The robotic cart was positioned posterior to the patient, and docking was performed (Figure 2c). The procedure was initiated with the camera in the "below" position. A Maryland bipolar forceps and two Cadiee forceps were used as the working instruments (Figure 2d).

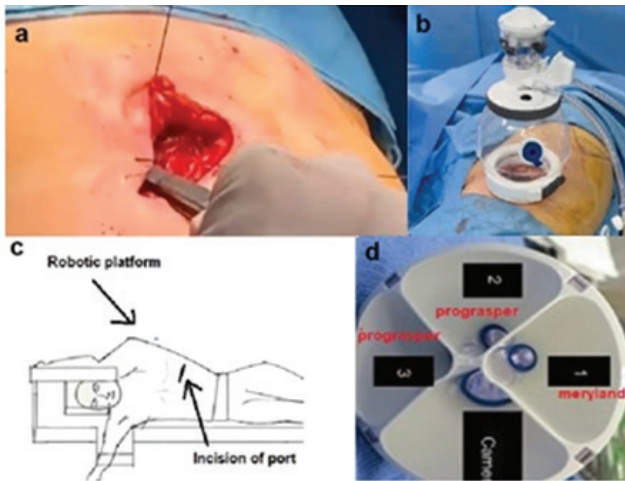


Figure 2. Fixation of the diaphragm to the skin with sutures (a), placement of the large access port and initiation of CO₂ insufflation (b), docking configuration of the da Vinci SP platform (c), arrangement of the camera and robotic instruments (d).

Surgical technique

The operation commenced with division of the inferior pulmonary ligament and dissection of station 9 lymph nodes. Attention was then directed to the hilum, where the inferior pulmonary vein and subsequently the common basal vein were carefully dissected and exposed. The interlobar fissure was subsequently developed to identify and isolate the arterial branches supplying the basal segments. Station 11 lymph node dissection was performed, followed by completion of the anterior fissure. Then the common basal segment artery was stapled (Figures 3a,b).

During stapler application, one robotic arm was temporarily withdrawn to optimize instrument positioning and facilitate safe stapler deployment. The common basal vein and bronchus were divided using an endoscopic stapler. Although stapler insertion through the assistant port may be technically challenging, the use of a 12-mm ROSI port (Robotic operative suction and irrigation) provided adequate access, as the gray cap of the access port allows 270° rotation, thereby facilitating stapler positioning (Figure 3c).

Indocyanine green (ICG) fluorescence imaging was performed after intravenous administration of 0.5 mg/kg ICG. The intersegmental plane between the preserved and devascularized lung parenchyma became clearly visible approximately 100 seconds after injection and was subsequently divided (Figure 3d).

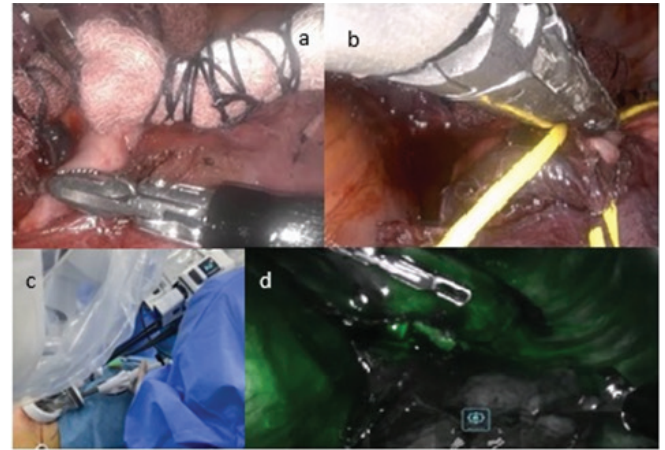


Figure 3. Dissection of the common basal artery (a), stapling of the common basal artery (b), introduction of staplers through the access port (c), indocyanine green (ICG) fluorescence imaging for delineation of the intersegmental plane (d).

After specimen retrieval, meticulous hemostasis was achieved, intercostal nerve blocks were performed, and a chest tube was placed. Examination of the specimen confirmed that the lesion was located within the resected segment (Figure 4). Docking time was 15 minutes, and console time was 2 hours and 10 minutes. Estimated blood loss was 125 mL.



Figure 4. Resected segment demonstrating adequate tumor-free surgical margins.

Postoperative course

The postoperative course was uneventful. The chest tube was removed on postoperative day 1, and the patient was discharged on postoperative day 3. Final pathologi-

cal examination revealed a sclerosing pneumocytoma with a surgical margin of 3 mm. A total of six lymph nodes from stations 7, 10, and 11 were harvested, and no nodal involvement was identified. No postoperative complications occurred. At the 3-month follow-up, the patient remained well, with no evidence of recurrence or other complications.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

Robotic thoracic surgery was developed to overcome some of the limitations of video-assisted thoracoscopic surgery (VATS), including restricted instrument maneuverability and two-dimensional visualization. More recently, uniportal robotic-assisted thoracic surgery (URATS) has emerged as an attractive minimally invasive approach that combines the benefits of robotic technology with the reduced surgical trauma associated with a single incision [8-10].

Unlike the da Vinci Xi platform, which was adapted for uniportal procedures, the da Vinci SP system was specifically designed for single-port surgery. Its architecture allows triangulation of multiple instruments through a single access port while minimizing internal arm collisions. In addition, the wristed camera and flexible instrument deployment facilitate complex dissections and may expand the applicability of single-port robotic surgery to advanced thoracic procedures [5].

In the present case, a centrally located lesion involving the common basal segment of the left lower lobe precluded wedge resection. Therefore, anatomical segmentectomy was preferred to achieve complete resection while preserving functional lung parenchyma. Single-port robotic common basal segmentectomy enabled both definitive diagnosis and treatment in a single session, with minimal surgical trauma and an uneventful postoperative course.

Surgical resection remains the gold standard treatment for patients with early-stage and selected locally advanced non-small cell lung cancer (NSCLC), offering the best chance for cure when complete resection is achieved [9-12]. In this context, segmentectomy has

been shown to provide oncological outcomes comparable to lobectomy in appropriately selected patients, without compromising survival or recurrence rates [13].

In recent years, an increasing number of small pulmonary nodules have been detected through lung cancer screening programs and widespread use of chest imaging during the COVID-19 pandemic [14,15]. Although many of these lesions are suspected to be malignant, a proportion are ultimately diagnosed as benign entities, including sclerosing pneumocytoma. In such cases, parenchyma-sparing anatomical resections may provide both definitive diagnosis and treatment while preserving pulmonary function. Furthermore, single-port robotic surgery is an effective option for these cases.

Declaration of conflicting interests

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Authors' contribution

TC: Conceptualization, methodology, surgical procedure, data curation, writing - original draft. CST: Conceptualization, supervision, validation, writing - review and editing. All authors read and approved the final version of the manuscript.

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Case Report

Presternal elastofibroma: an unusual anterior chest wall presentation following median sternotomy

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ABSTRACT

Elastofibroma is an uncommon benign soft-tissue lesion that most frequently arises in the subscapular region of elderly patients. It predominantly affects females, and occurrences outside the periscapular region are exceedingly rare and may pose a diagnostic challenge. A 59-year-old man presented with a progressively enlarging, palpable, and painful mass in the preternal region. Physical examination revealed a firm, fixed lesion beneath a previous sternotomy scar. Ultrasonography demonstrated a vascularized soft-tissue mass, while thoracic computed tomography showed a solid lesion adjacent to the sternum. Because malignancy could not be ruled out, complete surgical excision was performed. Histopathological evaluation established the diagnosis of elastofibroma. The postoperative course was uneventful, and no recurrence was detected during follow-up. Presternal elastofibroma is an exceptionally rare entity. In the present case, chronic mechanical irritation related to a malpositioned sternal wire may have contributed to lesion development, highlighting the importance of considering elastofibroma in the differential diagnosis of unusual anterior chest wall masses.

Keywords: elastofibroma dorsi, chest wall, preternal mass, sternotomy, soft tissue neoplasms

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Introduction

Elastofibroma is a benign soft-tissue lesion that typically arises in the subscapular region in middle-aged to elderly individuals. It is characterized by slow growth, absence of a true capsule, and poorly defined margins. Although etiopathogenesis remains poorly understood, several mechanisms have been proposed. The most widely accepted hypothesis suggests that repetitive mechanical stress and microtrauma induce reactive hyperproliferation of elastic and collagen fibers [1]. Histopathologically, elastofibroma is an unencapsulated lesion composed of dense collagen bundles and thickened, fragmented elastic fibers arranged haphazardly among fibroblasts and adipocytes. While its borders may be partially discernible, they are typically irregular. Although the subscapular region is a classic location, atypical localizations have been reported rarely [2,3]. In this report, we present the clinical, radiological, and histopathological features of an elastofibroma located in the presternal region. We also discuss a potential etiopathogenetic mechanism involving chronic microtrauma from a sternal wire, in light of the existing literature.

Case Report

A 59-year-old man presented with a palpable mass in the presternal region that had been present for approximately one year and had progressively increased in size over recent months. His medical history included coronary artery bypass grafting and aortic-mitral valve replacement in 2005, left knee prosthesis surgery, hypertension, and coronary artery disease. On physical examination, a midline sternotomy scar was noted, along with a subcutaneous nodular lesion at the level of the manubriosternal junction measuring approximately 1.5-2 cm in diameter. The lesion was well-circumscribed, firm and elastic in consistency, fixed to the deep plane, and non-mobile. No erythema, local warmth, or ulceration of the overlying skin was observed. Ultrasonographic examination demonstrated a 15 × 14 mm nonspecific hypoechoic lesion with lobulated contours in the subcutaneous tissue, showing marked vascularity on Doppler imaging; therefore, a tissue diagnosis was recommended. Non-contrast thoracic computed tomography revealed a nodular soft-tissue density lesion measuring approximately 17 mm at the same level, accompanied by reticulonodular in-

creased density in the surrounding subcutaneous tissue. No osseous erosion or invasion was identified (Figures 1,2). Given the atypical location and vascularity, malignancy could not be excluded, and surgical excision was planned. A 4-5 cm skin incision was made along the previous sternotomy scar. Following dissection through the skin and subcutaneous tissue, the mass was identified within the adipose tissue. A malpositioned sternal closure wire extending anteriorly into the lesion was observed. The lesion was dissected free and excised en bloc, and the twisted end of the sternal wire was bent back and repositioned (Figure 3). There were no intra-operative or perioperative complications. Gross examination revealed a 1.5 cm mass within a 4 × 5 cm specimen, with cystic areas containing fibrinoid material. Histopathological examination revealed an acellular, dense collagen matrix with thick, fragmented, eosinophilic elastic fibers interspersed throughout. Globules arranged linearly along these fibers were observed. Islands of mature lipocytes (fat deposits) were detected between the fibroelastic stroma. Immunohistochemical analysis demonstrated characteristic elastic fibers highlighted by Verhoeff-Van Gieson staining, confirming the diagnosis of elastofibroma. Postoperatively, the patient developed a wound seroma, which was managed with daily dressing changes without the need for surgical revision. Vital signs remained stable throughout the hospitalization. Anticoagulation therapy was carefully monitored, with warfarin dosage adjusted according to INR values and subcutaneous enoxaparin administered until a therapeutic INR level (>2.0) was achieved. The patient was subsequently discharged without any further complications. At 1-year follow-up, no recurrence was observed. Written informed consent for publication of the case report was obtained from the patient.

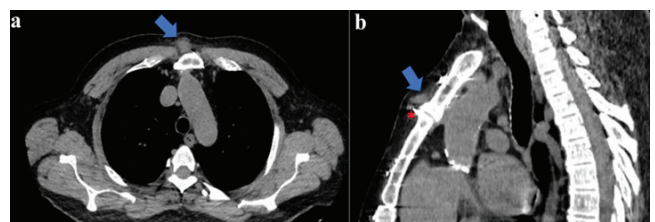


Figure 1. Axial (a) and sagittal (b) scans of chest computed tomography show a 17 mm, well-circumscribed soft tissue mass in the presternal region (arrow) and a malpositioned sternal wire (asterisk).

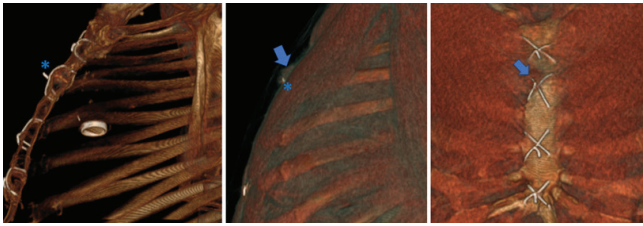


Figure 2. Three-dimensional volume-rendered CT reconstruction showing a malpositioned sternal wire (asterisk) and soft tissue mass (arrow).

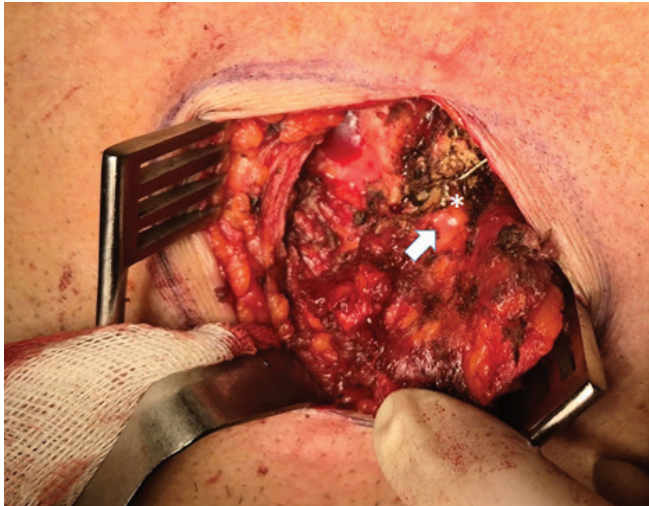


Figure 3. Intraoperative photograph demonstrating the malpositioned sternal wire (asterisk) and the associated presteral mass (arrow).

Discussion

This case highlights an unusual presternal localization of elastofibroma, presenting as an anterior chest wall mass adjacent to a sternotomy site. Elastofibroma dorsi typically occurs in individuals over 50 years of age, most commonly between the sixth and seventh decades, and shows a female predominance. It is classically located between the inferior angle of the scapula and the thoracic wall. Occurrence in male patients and outside the periscapular region is considerably less common [3]. In this regard, our case is atypical in both patient demographics and lesion location. The etiology of elastofibroma is thought to involve repetitive mechanical stress and microtrauma, possibly in combination with genetic predisposition. Recent studies have also demonstrated cytogenetic abnormalities and clonal fibroblastic proliferation, suggesting that elastofibroma represents a lesion with intermediate features between reactive and neoplastic processes [1]. In the present case, the lesion developed in close association with a malpositioned

sternal wire. We hypothesize that chronic microtrauma induced by the wire, which was exacerbated by respiratory motion and cardiac pulsation, may have triggered localized fibroelastic proliferation, analogous to the friction-related mechanism described in classical periscapular elastofibroma.

Radiological evaluation of elastofibroma typically involves ultrasonography, CT, and MRI. Classic imaging findings include a heterogeneous soft-tissue mass with attenuation similar to skeletal muscle and interspersed fatty streaks, producing a layered or striated appearance [4,5]. However, in atypical locations, these characteristic features may be absent. In our case, imaging findings were non-specific, and malignancy could not be excluded, necessitating surgical excision. In the differential diagnosis of the lesion, a vascularized soft-tissue malignancy was considered the most likely possibility. The painful nature of the lesion, its fixation to the surrounding tissues, and the marked vascularity observed on Doppler ultrasonography initially raised suspicion for a soft-tissue malignancy. Computed tomography findings further supported the presence of a soft-tissue mass. Granulation tissue associated with a malpositioned sternal wire was also included in the differential diagnosis. Other considerations included benign soft-tissue neoplasms, such as desmoid tumors and fibromas. As a definitive radiological diagnosis could not be established, histopathological examination was performed for definitive diagnosis.

Histopathological examination remains the gold standard for diagnosis, with characteristic findings including dense collagen bundles, fragmented elastic fibers, and interspersed adipose tissue. Special stains such as Verhoeff-Van Gieson are essential for confirming the diagnosis and excluding malignancy [6]. Although conservative management may be appropriate for asymptomatic lesions in typical locations, surgical excision is recommended in symptomatic cases or when malignancy cannot be ruled out. Recurrence after complete excision is exceedingly rare, consistent with the favorable outcome observed in our patient.

In conclusion, although elastofibroma is most commonly encountered in the periscapular region, fixed presternal lesions are usually regarded as potentially

malignant. Therefore, complete surgical excision is often preferred to establish a definitive diagnosis and provide treatment. In our case, histopathological evaluation of a lesion that had been excised under the presumptive diagnosis of malignancy revealed an elastofibroma. Elastofibroma should be considered in the differential diagnosis of anterior chest wall masses in patients with a history of sternotomy, particularly when sternal closure wires are present. Awareness of this rare presentation may help avoid misdiagnosis and guide appropriate management.

Declaration of conflicting interests

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Authors' contribution

SSO,FOT: contributed to the conceptualization and design of the study. GA,AC,MS: involved in data curation, formal analysis, and the acquisition of clinical resources. SSO,FOT,GA: drafted the initial manuscript. AC,MS: critically revised the manuscript for important intellectual content. All authors contributed to the visualization of clinical data, read and approved the final version of the manuscript, and agree to be accountable for all aspects of the work.

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Case Report

Staged reconstruction of thoracic ectopia cordis with complete sternal aplasia: a case report

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ABSTRACT

Ectopia cordis is a rare and frequently fatal congenital anomaly characterized by partial or complete displacement of the heart outside the thoracic cavity due to defective midline fusion during embryogenesis. Surgical management remains challenging because of the associated cardiac and chest wall defects. A 37-week gestational age neonate presented with thoracic ectopia cordis, atrial septal defect, pericardial defect, and complete sternal aplasia. On day 29 of life, after hemodynamic stabilization and multidisciplinary operative planning, the patient underwent combined cardiovascular and reconstructive surgery. Following cardiac repositioning into the thoracic cavity and pericardial reconstruction using a bovine pericardial patch, chest wall reconstruction was performed with bipedicle fasciocutaneous flaps harvested from the pectoral region. Initial postoperative recovery was complicated by suture line necrosis, which required surgical debridement and Z-plasty reconstruction. Subsequent patch exposure was successfully managed with patch excision, flap release, medial advancement, repeat Z-plasty reconstruction, and wound dressings. Wound cultures demonstrated no significant bacterial growth. Complete secondary healing was achieved without additional complications. Thoracic ectopia cordis requires individualized multidisciplinary management and careful staged reconstruction. Bipedicle fasciocutaneous flaps provided reliable soft tissue coverage and allowed successful reconstruction following postoperative wound complications. Flexible reconstructive strategies and close postoperative monitoring may improve outcomes in these complex patients.

Keywords: ectopia cordis, chest wall reconstruction, surgical flaps, sternal aplasia

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Introduction

Ectopia cordis is a rare and often fatal congenital anomaly characterized by the partial or complete displacement of the heart outside the thoracic cavity, posing significant neonatal challenges [1]. This condition results from incomplete fusion of the anterior chest wall during embryogenesis, typically between the sixth and eighth weeks of gestation, leading to aberrant extra-thoracic positioning of the heart [2]. With an incidence of 5.5 to 7.9 per million live births, ectopia cordis remains an uncommon but critical congenital defect.

The severity of this condition varies; it is classified into cervical, cervicothoracic, thoracoabdominal, and abdominal subtypes, each requiring distinct management strategies. Ectopia cordis is frequently associated with additional anomalies, notably Cantrell's pentalogy, which includes diaphragmatic hernia, omphalocele, sternal and pericardial defects, and congenital heart disease. The absence of pericardial protection further increases vulnerability to trauma and infection [2]. When the heart protrudes through the chest wall above the diaphragm, it is classified as extrathoracic ectopia cordis, one of the most severe forms of the anomaly. Prognosis is generally poor, particularly in thoracic ectopia cordis, emphasizing the need for immediate intervention [3].

Surgical reconstruction primarily involves repositioning the heart and covering the chest wall defect; however, because of the high mortality associated with this condition, successful surgical correction remains uncommon [4]. Single-stage thoracoabdominal repairs have demonstrated feasibility, reducing the need for multiple interventions. Given the complexity of ectopia cordis, surgical approaches must be tailored to the severity of the presentation and associated anomalies to optimize survival [3].

Although successful repairs have been reported, long-term outcomes and quality of life remain underexplored due to the rarity of this condition [3]. Large-scale studies and clinical trials are limited, posing challenges in developing standardized management guidelines. Future research should focus on refining surgical techniques and evaluating individualized approaches based on severity and associated anomalies [3].

Case Report

We present the case of a 37-week gestational age neonate diagnosed with ectopia cordis, characterized by the heart apex positioned outside the thoracic cavity (Figure 1). At birth, the infant exhibited bradycardia

and respiratory distress, requiring positive pressure ventilation, endotracheal intubation, and admission to the neonatal intensive care unit (NICU) with synchronized intermittent mandatory ventilation. Intravenous ampicillin and gentamicin therapy was initiated, and the exposed cardiac tissue was covered with saline-soaked dressings. No other congenital anomalies were immediately noted.



Figure 1. Preoperative clinical presentation of the neonate with thoracic ectopia cordis. The apex of the heart is exposed through a midline anterior chest wall defect, without sternal coverage.

Echocardiography revealed an atrial septal defect with a left-to-right shunt, a 2 mm patent ductus arteriosus, and an open ductus venosus. Additional findings included aplasia cutis, retrognathia, and a high-arched palate. Thoracic computed tomography (CT) demonstrated complete sternal aplasia with intact bilateral clavicles and ribs, together with a 2 cm anterior thoracic wall defect through which the cardiac apex herniated. Dextrocardia was also noted.

On day 29 of life, after hemodynamic stabilization, completion of diagnostic evaluations, and multidisciplinary operative planning, the patient underwent a combined cardiovascular and plastic surgery procedure. During the preoperative period, the exposed cardiac tissue was managed with saline-soaked dressings to maintain tissue hydration. Antibiotic ointments and advanced wound coverings were intentionally avoided because of concerns regarding possible local reactions and irritation over the exposed cardiac structures. For infection prophylaxis, intravenous ampicillin and gentamicin therapy was initiated and continued throughout the surgical procedures

and postoperative period. The cardiovascular surgery team repaired the pericardial defect with a bovine pericardial patch (4 x 6 cm, 0.1-0.5 mm in thickness) and repositioned the heart apex within the thoracic cavity. Cardiopulmonary bypass was not required during the procedure. Simultaneously, chest wall reconstruction was performed using 15 x 15 cm bipediced fasciocutaneous flaps harvested from the pectoral region (Figure 2). Flap donor sites were closed primarily, and two surgical drains were placed (Figure 3).

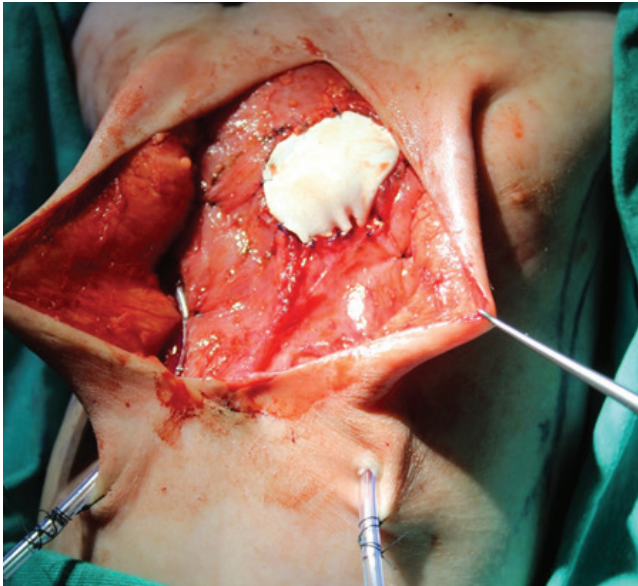


Figure 2. The heart was repositioned within the thoracic cavity, and the pericardial defect was reconstructed using a bovine pericardial patch. Bipediced fasciocutaneous flaps, harvested from the pectoral region, were advanced to cover the anterior thoracic defect.



Figure 3. Immediate postoperative appearance showing complete soft-tissue coverage of the anterior chest wall and bilateral closed-suction drain placement.

On day 35 of life, necrosis along the inferior suture line was noted, requiring a second surgical intervention. The necrotic tissue was debrided, and Z-plasty was performed for wound closure. On day 49 of life, erythema developed at the flap junction, and further evaluation revealed patch exposure localized to the flap suture line (Figure 4). Wound culture demonstrated no significant bacterial growth. The bovine pericardial patch was excised, and the inflamed area was trimmed. To improve wound closure, previously elevated bipediced fasciocutaneous flaps were released via lateral thoracic incisions, advanced medially, and approximated at the midline using new Z-plasty flaps. Donor sites were treated with epidermal growth factor-based wound dressings (Figure 5).

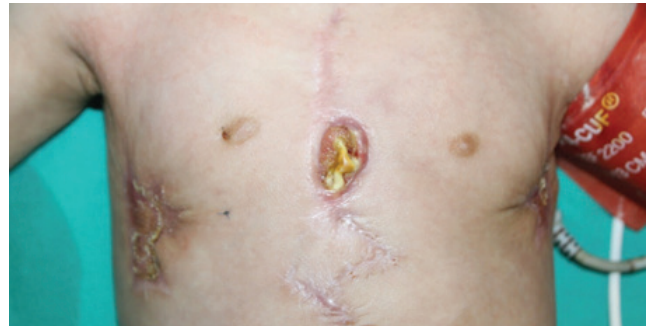


Figure 4. On day 49 of life, erythema appeared at the flap junction, and further evaluation revealed exposure of the bovine pericardial patch.



Figure 5. Final reconstructive procedure. The exposed bovine pericardial patch was excised, and the inflamed tissue was debrided. Previously elevated bipediced fasciocutaneous flaps were released from the lateral thoracic region, advanced toward the midline, and reapproximated using new Z-plasty flaps to reinforce closure. Donor sites were treated with epidermal growth factor-based wound dressings.

By day 64 of life, the dressings were removed, demonstrating complete secondary wound healing without additional complications (Figure 6). The patient remained hospitalized for an additional 10 days and was discharged in stable condition. Postoperative follow-up continued for 2 months, during which no recurrent wound complications, signs of infection, hemodynamic instability, or additional cardiac complications were observed. After the second postoperative month, the patient did not return for further follow-up at our institution. To the best of our knowledge, no mortality was reported during the available follow-up period.



Figure 6. On day 64 of life, the dressings at the flap donor sites were removed, showing complete secondary healing with no further complications.

Discussion

Managing ectopia cordis requires a multidisciplinary approach involving neonatology, cardiothoracic surgery, and reconstructive surgery to optimize outcomes. Both our case and the existing literature demonstrate that successful cardiac and chest wall repair may be achieved in infancy, particularly in thoracic and thoracoabdominal forms of ectopia cordis [3]. Initial management focuses on protecting the exposed heart from trauma, dehydration,

and infection while addressing associated anomalies such as omphalocele [5]. When immediate surgical correction is not feasible, sterile dressings and protective barriers remain essential for temporary management.

Surgical decision-making depends on the type and severity of the defect, associated anomalies, and overall patient stability. Surgical correction remains the definitive treatment [2]. Although successful single-stage repairs have been reported, staged reconstruction may be necessary to allow adequate tissue adaptation and to prevent hemodynamic compromise [1,3,5]. Premature closure of the thoracic cavity may result in compression of the heart and great vessels, necessitating alternative reconstructive strategies such as subcutaneous pockets, tissue expansion, or staged soft tissue advancement [3]. In patients with complete or near-complete sternal aplasia, achieving durable chest wall coverage remains particularly challenging because of limited local tissue availability and increased wound tension. In our patient, postoperative wound complications were likely related to increased tension at the midline closure rather than prosthetic infection, as wound cultures demonstrated no significant bacterial growth.

In the present case, bipedicle fasciocutaneous flaps harvested from the pectoral region were preferred because they provided reliable vascularity, adequate soft tissue coverage, and preservation of thoracic wall compliance without muscle sacrifice. However, postoperative wound complications developed, including suture line necrosis followed by patch exposure. Management of prosthetic exposure in neonatal chest wall reconstruction remains challenging because wound closure and preservation of chest wall stability must be achieved simultaneously. Therefore, a staged reconstructive approach was preferred in our patient. Debridement, excision of the patch, flap release, medial advancement, and repeat Z-plasty reconstruction allowed preservation of chest wall integrity while achieving successful wound closure.

Recent surgical advances have improved the management of ectopia cordis. Extracorporeal membrane oxygenation (ECMO) has been used in infants developing cardiac failure following repair [3]. Additionally, three-dimensional printing technologies may facilitate preoperative planning and improve chest wall reconstruction accuracy. Alloplastic materials, including synthetic meshes and bioabsorbable plates, may provide structural support and improve long-term

reconstructive outcomes. Mohan et al. emphasized the importance of stable soft tissue coverage in pediatric chest wall reconstruction, particularly in patients requiring prosthetic support [4]. In our case, a soft tissue-based reconstructive approach was preferred because it provided adequate chest wall coverage while preserving thoracic compliance during the neonatal period.

Future research should focus on refining surgical techniques, exploring novel biomaterials, and developing individualized reconstructive strategies for these complex patients. Advanced imaging modalities, including fetal MRI, may improve prenatal diagnosis and facilitate earlier multidisciplinary planning. Long-term follow-up studies remain necessary to better evaluate cardiac function, respiratory mechanics, chest wall development, and quality of life in surviving patients [3]. In selected patients with significant intracardiac anomalies, additional palliative procedures such as Blalock-Taussig shunting or pulmonary artery banding may also be required [6].

Ectopia cordis remains one of the most challenging congenital thoracic anomalies and requires individualized surgical planning. The successful staged reconstruction of our patient with complete sternal aplasia highlights the importance of flexible reconstructive strategies and multidisciplinary management. Continued advances in neonatal care, biomaterials, and reconstructive techniques will be essential for improving survival and long-term outcomes in these patients.

This report has several limitations. The patient was lost to follow-up after two months, precluding assessment of long-term chest wall growth, respiratory mechanics, prosthetic durability, and developmental outcomes. Furthermore, because this is a single case report, conclusions regarding the superiority of this reconstructive strategy cannot be generalized.

In conclusion, ectopia cordis remains a rare and challenging congenital anomaly associated with high morbidity and mortality. Successful management requires individualized multidisciplinary planning involving neonatal intensive care, cardiovascular surgery, and reconstructive surgery teams. In our case, bipedicle fasciocutaneous flaps provided effective chest wall coverage following cardiac repositioning and allowed successful reconstruction after postoperative wound complications. Careful postoperative monitoring and staged reconstructive management are critical for preserving thoracic stability and optimizing clinical outcomes in these complex patients.

Declaration of conflicting interests

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Authors' contribution

AUY,EG: Surgical procedure, conceptualization, methodology, writing - original draft. OB: Cardiovascular surgery procedure, data curation, writing - review and editing. All authors read, critically revised, and approved the final version of the manuscript.

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Case Report

Simultaneous robotic right middle lobectomy and thymectomy via a single-docking, supine approach: a strategic 5-port solution

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ABSTRACT

The management of synchronous mediastinal and pulmonary pathologies presents a significant technical challenge, often requiring staged operations, intraoperative patient repositioning, or system re-docking. We report a case of a 67-year-old man with active myasthenia gravis and a synchronous right middle lobe pulmonary nodule who successfully underwent simultaneous robotic total thymectomy and right middle lobectomy during a single session. This single-docking robotic strategy maximizes the robotic system's ergonomic advantages, eliminates the risks of repeated anesthesia in neurologically vulnerable patients, and offers an efficient alternative for multi-compartment thoracic resections.

Keywords: lobectomy, myasthenia gravis, robotic surgical procedures, thymectomy, synchronous neoplasms

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Introduction

Robot-assisted thoracic surgery (RATS) has considerably expanded the scope of minimally invasive thoracic procedures [1]. Nevertheless, the simultaneous treatment of mediastinal and pulmonary pathologies remains technically challenging because these operations often require different patient positions, port configurations, or re-docking of the robotic system. As a result, combined procedures are frequently associated with increased operative complexity, prolonged anesthesia time, and higher resource utilization.

We present a rare case of a patient with myasthenia gravis (MG) and a synchronous hypermetabolic right middle lobe pulmonary nodule who underwent simultaneous robotic total thymectomy and right middle lobectomy during a single operative session. This approach demonstrates a practical and efficient strategy for multi-compartment thoracic surgery while preserving the ergonomic advantages of the robotic platform and avoiding intraoperative realignment of the system.

The presented case is one of the few reported cases of simultaneous robotic total thymectomy and anatomical pulmonary lobectomy performed through a single docking strategy, without patient repositioning, using a modified periareolar thymectomy port configuration.

Case Report

A 67-year-old man with active MG was referred to our thoracic surgery department for evaluation of synchronous thymic tissue and a PET-positive right middle lobe pulmonary nodule. The patient was receiving pyridostigmine and corticosteroid therapy and had completed a preoperative course of intravenous immunoglobulin treatment. His medical history was significant for coronary artery disease requiring coronary stenting and a remote history of lymphoma diagnosed following mediastinoscopic lymph node biopsy. Thorax computed tomography demonstrated a 9-mm right middle lobe nodule, while PET/CT showed mild FDG uptake, raising suspicion for early-stage primary lung cancer (Figure 1). Bronchoscopy revealed no endobronchial abnormality, and pulmonary function testing confirmed adequate reserve for anatomical lung resection. Finally, the patient was scheduled for simultaneous thymectomy and right middle lobectomy.

The operation was performed in a near-supine position with minimal table tilt. Initially, robotic total thymectomy was completed using a right-sided

periareolar approach with robotic arms positioned through ports 1, 2, and 3 (Figure 2).

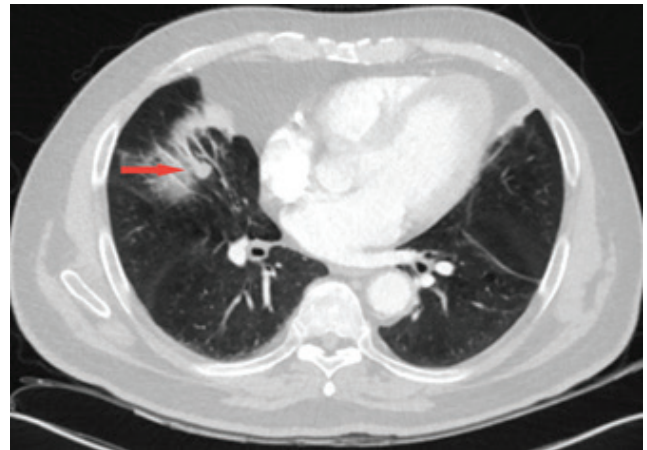


Figure 1. Preoperative chest computed tomography demonstrating a middle lobe pulmonary nodule (arrow).

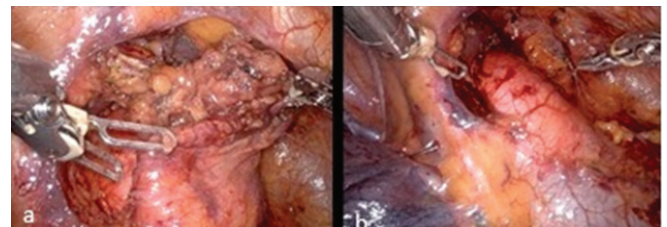


Figure 2. Division of the thymic veins during robotic thymectomy (a), operative view of the anterior mediastinal cavity following thymectomy (b).

During the thymectomy phase via the right hemithorax approach, the right lung was collapsed with the aid of carbon dioxide insufflation maintained at a pressure of 8-10 cmH₂O. The mediastinal pleura was then dissected in a caudal-to-cranial direction, extending up to the junction of the superior vena cava and the brachiocephalic vein. At this stage, gas insufflation facilitates retrosternal and prepericardial dissection by creating a controlled pneumomediastinum. The thymic veins were carefully isolated, divided at their drainage point into the brachiocephalic vein, and secured using titanium clips. Dissection was continued until the left mediastinal pleura was reached, achieving a complete total thymectomy. The resected thymus was placed in an endobag and extracted through the port incision.

Following completion of the thymectomy, the port configuration was adapted for the pulmonary resection phase without patient repositioning or robotic re-docking. A fourth robotic port was added and the robotic setup was reconfigured without re-docking. The lobectomy phase was performed with Arm 4 in port 1, Arm 1 in port 2, the camera arm (Arm 2) in port 3,

and Arm 3 in the newly created fourth port (Figure 3). This configuration provided a more favorable working geometry for hilar dissection and pulmonary resection while maintaining the advantages of a single-docking approach. Consequently, the lobectomy was performed using robotic arms 4, 1, 2 and 3, together with a dedicated assistant port (Figure 4).

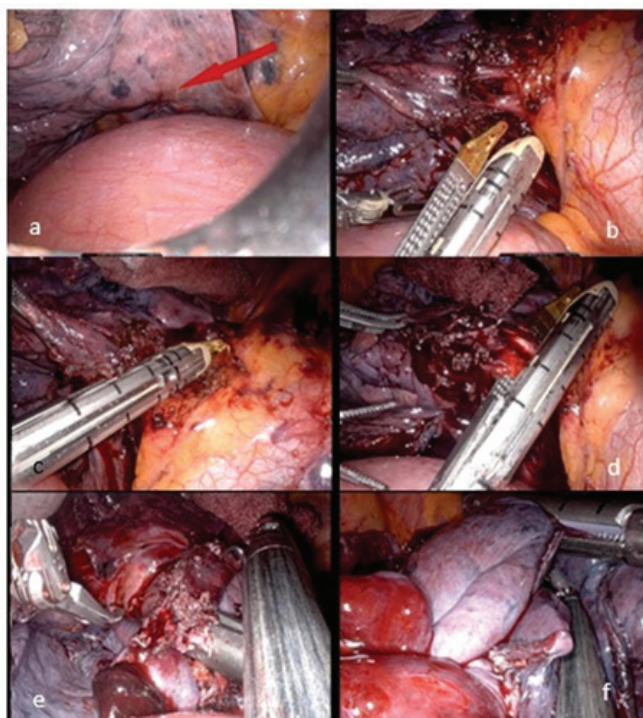


Figure 3. Middle lobe pulmonary nodule causing visceral pleural retraction (arrow) (a), division of the middle lobe pulmonary vein, demonstrating separate venous drainage of the two segments (b), stapled division of the middle lobe pulmonary vein (c), stapled division of the middle lobe bronchus (d), stapled division of the middle lobe pulmonary artery (e), division of the horizontal fissure using an endoscopic stapler (f).

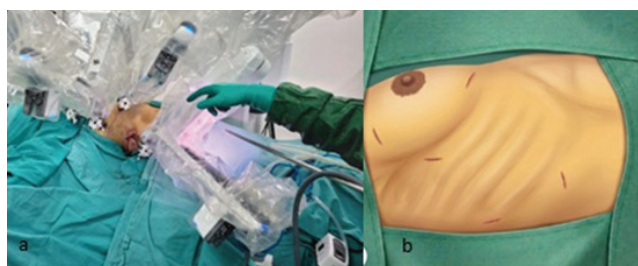


Figure 4. Robotic arm positioning and docking configuration (a), schematic illustration of the 5-port incision sites (b).

This modification enabled seamless transition from total thymectomy to right middle lobectomy and systematic lymph node dissection while maintaining a single docking strategy throughout the procedure.

During the right middle lobectomy phase, the mediastinal pleura was incised to expose the hilum of the middle lobe under continued carbon dioxide insufflation. The middle lobe veins were observed to drain independently as segmental branches and were subsequently divided through the assistant port using an endoscopic vascular stapler. Immediately proximal to the venous anatomy, the middle lobe bronchus was isolated and divided with a stapler, followed by the dissection and vascular stapler closure of the middle lobe artery. Due to an incomplete horizontal fissure, the resection was completed by creating the fissure line using mechanical staplers. Finally, systematic mediastinal and hilar lymphadenectomy was performed, which included the clearance of stations 4 (lower paratracheal), 10 (hilar), and 12 (lobar) lymph nodes. The resected middle lobe was placed in an endobag and extracted through the assistant port, which had been widened via skin incision extension.

The total operative time was 270 minutes, which included a docking time of 20 minutes and a total robotic console time of 220 minutes. The console phase was divided into 70 minutes for the thymectomy and 150 minutes for the right middle lobectomy. The estimated blood loss was minimal, remaining well below 50 mL throughout the entire procedure.

The postoperative course was uneventful. The chest tube was removed on postoperative day four, and the patient was discharged without any complications (Figure 5). Final histopathological examination revealed invasive adenocarcinoma with 1 cm in greater dimension in the right middle lobe with negative resection margins and no lymph node metastasis (pT1aN0). Histological evaluation of the thymectomy specimen confirmed thymic tissue without evidence of thymoma or malignancy. Written informed consent was obtained from the patient for the use of the medical data in academic studies.

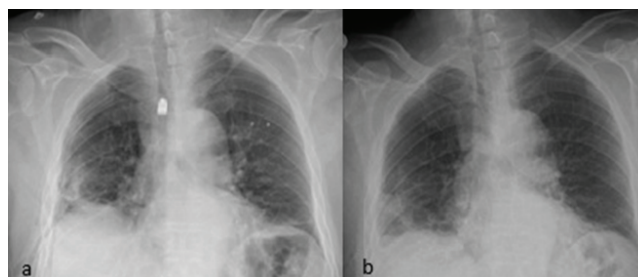


Figure 5. Chest radiograph on postoperative day 1 (a), chest radiograph obtained before hospital discharge (b).

Discussion

Traditionally, managing synchronous mediastinal and pulmonary pathologies required either staged procedures or highly invasive approaches like a median sternotomy. Today, however, addressing multiple intrathoracic lesions within a single session has become significantly more feasible and manageable through minimally invasive surgery (Video-assisted thoracic surgery - VATS, and RATS) bypassing the extensive trauma associated with open surgery. This evolution in minimally invasive techniques allows surgeons to confidently execute complex, multi-compartment procedures in one continuous operation.

For patients with active MG, this single-stage approach offers a distinct clinical advantage. By consolidating the treatment, it spares the patient from the cumulative risks of repeated general anesthesia and preserves vital postoperative respiratory function by minimizing overall surgical effects on cardiopulmonary function.

Most existing reports on combined resections involve intraoperative repositioning or robotic re-docking, maneuvers that inevitably prolong anesthesia time and disrupt the surgical workflow [2-4].

Okazaki et al described the robotic resection of a posterior mediastinal dumbbell tumor performed with the patient in the prone position [2]. Although such positioning can facilitate surgical exposure, prone position may introduce additional challenges in airway management intraoperatively. This position may also complicate an urgent conversion to open surgery (thoracotomy or sternotomy), as repositioning the patient can be both time-consuming and technically demanding. In contrast, our patient remained in a supine position with a slight lateral tilt throughout the procedure. We believe that this approach not only provided favorable cardiopulmonary conditions for a patient with MG but also allowed the surgical team to convert to the lateral decubitus position or proceed directly to open surgery, if necessary, without repositioning the patient or changing the operating table setup.

The case report reported by Luzzi et al demonstrated that thoughtful robotic planning can simplify complex multi-site procedures [3]. They successfully performed a combined robotic thymectomy and transaxillary thyroidectomy by rotating the robotic platform by only 30° after completing the first procedure, thereby avoiding complete system re-docking. Rather than being merely

a technical adjustment, this strategy optimized the use of disposable instruments and contributed to a faster postoperative recovery. Their experience reflects the same principle of our approach. Instead of dismantling and rebuilding the robotic setup between procedures, careful optimization of robot positioning can improve workflow, reduce unnecessary operative steps, and make complex multi-compartment thoracic resections more efficient for both the surgical team and the patient.

Zhang et al further highlighted the technical challenges of multi-compartment robotic surgery by reporting the simultaneous resection of a left-sided anterior mediastinal tumor and a right-sided lower thoracic paravertebral mass through the same four port incisions on the right side of the chest [4]. Although they successfully utilized a single-sided approach with the patient positioned in a left lateral decubitus position throughout, the completely opposite orientations of the two lesions within the right hemithorax required a two-step docking strategy. After completing the posterior paravertebral resection, they had to undock the robotic system, rotate the operating table 180° counterclockwise while keeping the patient in the same decubitus position, and re-dock the system from the ventral side to access the anterior mediastinum. While their technique avoided additional incisions, the need for undocking, table rotation, and re-docking inevitably increases logistical complexity and prolongs both operative and anesthesia times. In contrast, our single-docking strategy for synchronous thymectomy and right middle lobectomy required neither undocking nor operating table manipulation.

In another published case report, simultaneous robotic surgical procedures involving cardiac surgery and lobectomy were documented. The initial approach was performed via a minithoracotomy for the cardiac procedure in the supine position. Following the completion of the cardiac phase, the robotic arms were removed for the lobectomy; the patient was then repositioned into the lateral decubitus position, and robotic docking was established using four ports to perform a right upper lobectomy. The total operative time was reported as 10 hours [5].

In our approach, these limitations were overcome by placing the patient in a supine position with a modest 15-degree right-sided elevation. This configuration provided sufficient exposure for both the anterior mediastinum and the right hemithorax, eliminating the need for repositioning for RATS. The operative sequence

was intentionally designed to perform the thymectomy first. This served as a strategic safety measure: by securing the mediastinal clearance while the patient was in the optimal position for thymectomy, we preserved the flexibility to convert to a lateral decubitus position should technical difficulties arise during the lobectomy.

Previously, a simultaneous VATS sleeve lobectomy and thymectomy was described by Xie et al [6]. In that particular case, the surgical team first performed the right upper bronchial sleeve lobectomy in a lateral decubitus position, after which the patient had to be completely repositioned to access the mediastinum for the thymectomy phase. Even within the versatile domain of VATS, where the surgeon typically has a broad range of manual manipulation, a formal intraoperative patient repositioning was still deemed necessary, which stands in sharp contrast to our single-position, single-docking strategy. This highlights a critical reality in multi-compartment thoracic surgery: the chosen surgical trajectory and overall approach must adapt dynamically based on which specific pulmonary lobe or mediastinal compartment harbors the pathology.

From an anatomical perspective, the right middle lobe is exceptionally well-suited for this near-supine approach. Its anterior location and favorable hilar orientation allow for a dissection trajectory that closely resembles subxiphoid or anterior thoracoscopic perspectives [7]. Similar to the approach used in the presented case, simultaneous resections may not be appropriate for posterior or superior pulmonary pathologies, such as left-sided resections or lower lobe tumors requiring extensive posterior mobilization, where a standard lateral decubitus position remains mandatory for optimal exposure.

Approaching right-sided pulmonary resections alongside anterior mediastinal surgery through a single incision and a single patient position provides favorable ergonomics and optimal alignment for endoscopic instruments. Indeed, case reports in the literature have demonstrated that simultaneous thymectomy and lobectomy with VATS can be successfully completed via a subxiphoid approach without requiring intraoperative patient repositioning [8]. However, to the best of our knowledge, simultaneous lobectomy and thymectomy performed completely via robot-assisted thoracic surgery (RATS) has not yet been reported.

When evaluating our operative metrics, the docking time in the present case was comparable to existing literature data [9, 10]. Although our total console and

overall surgical times were longer than those reported for isolated procedures, this discrepancy remains highly acceptable given that our data reflect the cumulative duration of two major resections performed back-to-back.

This technique represents a significant refinement in minimally invasive thoracic surgery. By avoiding the mechanical and logistical delays of re-docking or table manipulation, this single-docking approach maximizes the ergonomic advantages of the robotic platform. For carefully selected patients, this method offers a seamless, efficient, and oncologically sound alternative for concomitant mediastinal and pulmonary resections, ensuring high surgical precision while minimizing perioperative risk.

Declaration of conflicting interests

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Authors' contribution

HY,AC: Surgical procedure, conceptualization, methodology, writing - original draft. TS,MAT,SK,ES: Data curation, visualization, writing - review and editing. All authors read and approved the final version of the manuscript.

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Case Report

Primary mediastinal small round cell tumor suggestive of Ewing's sarcoma associated with pneumothorax: a case report

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ABSTRACT

Ewing's sarcoma (ES) is a rare form of malignancy that commonly affects the bone. Extraskelatal ES (EES) accounts for 20% of ES cases. The mediastinum is an exceedingly rare primary site of EES and presents with non-specific symptoms that may mimic several other thoracic pathologies. We describe a suspected case of primary mediastinal ES presenting with pneumothorax in a 17-year-old female who presented with chronic cough, dyspnea, and chest pain. The patient had been commenced on empirical treatment for tuberculosis (a common diagnosis in our sub-region) for six weeks before presentation to our facility, due to a lack of improvement in symptoms. Chest computed tomography scan revealed a huge anterior mediastinal mass extending into the left hemithorax with pneumothorax on the right. She underwent a transthoracic percutaneous biopsy, and histological analysis revealed a monomorphic small-round-cell morphology, suggestive of primary mediastinal Ewing's sarcoma.

Keywords: mediastinal neoplasms, Ewing's sarcoma, pneumothorax, neuroectodermal tumors, extraskelatal

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Introduction

Ewing's sarcoma (ES) is a rare aggressive tumor postulated to be of neuroectodermal or mesenchymal origin with a slight male predominance. It has a higher incidence in Whites than in people of African and Asian descent, with peak incidence seen between the ages of 10 and 19 years. ES commonly affects the bones and rarely the extra-skeletal soft tissues. There is a paucity of data on the exact incidence of ES in Sub-Saharan Africa [1].

Extraskeletal ES (EES) has an incidence of 0.4/1,000,000 and represents about 20% of ES cases. EES has a bimodal distribution with peak incidence in individuals < 5years and > 35years old. EES, unlike ES of the bone, shows no predilection for biological sex and race. The upper thigh, buttocks, upper arm, and shoulders are the most common sites of EES [2]. The mediastinum is an exceedingly rare primary site of EES and thus presents a diagnostic dilemma due to nonspecific symptoms that may suggest commoner diseases such as Tuberculosis (TB) in high TB-burden countries [3]. We report a presumed case of primary mediastinal ES with a distinctive presentation of pneumothorax and review the literature.

Case Report

A 17-year-old female presented to the emergency department of our tertiary referral center with a three-month history of persistent cough, a two-month history of progressive shortness of breath, and right-sided chest pain of one-week duration, which worsened a day before her presentation. The cough was productive of whitish sputum, but there was no hemoptysis. There was a history of unintentional weight loss in the preceding month. She had been commenced on anti-tuberculosis (TB) drugs (isoniazid, rifampin, pyrazinamide, and ethambutol) empirically at a peripheral center, six weeks before her presentation. Her family denied a history of malignancy.

On examination, she had a temperature of 37.0 °C, blood pressure of 110/70 mmHg, heart rate of 120 beats/min, respiratory rate of 46 breaths/min, oxygen saturation of 98% in room air, and grade III digital clubbing. Chest examination revealed trachea deviation to the right, stony dull percussion note, and absent breath sounds on the left hemithorax. There was no significant peripheral lymphadenopathy, hepatosplenomegaly, or jaundice.

Chest X-ray showed an ill-defined homogenous opacity in the left hemithorax with a mass-induced mediastinal shift to the right, where a pneumothorax was also seen (Figure 1).

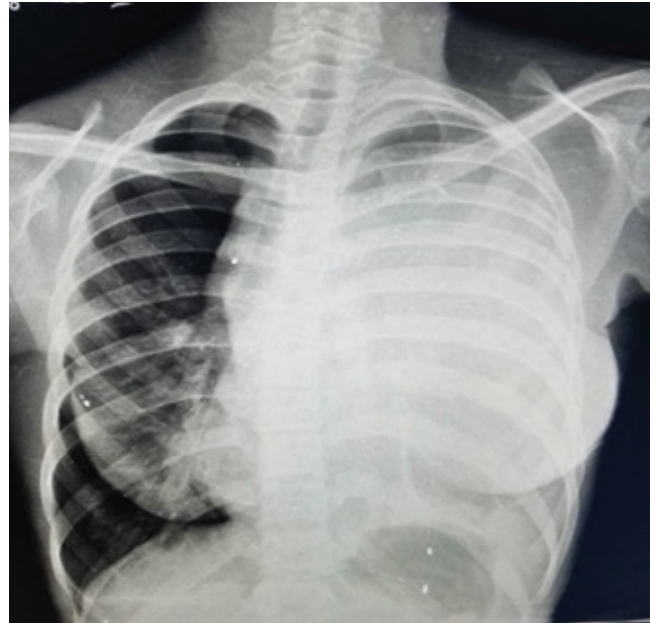


Figure 1. Plain chest radiograph showing a dense, homogeneous opacity throughout the left hemithorax with a massive mediastinal shift to the right, accompanied by a right-sided pneumothorax.

Chest CT scan showed a huge mixed-density anterior mediastinal mass measuring 17.3 x 16.4 x 12.6 cm with irregular margins and areas of necrosis extending into the left hemithorax. The mass occupies almost the entire left hemithorax with associated compression atelectasis of the left lung. It encases the arch of the aorta, superior vena cava, main pulmonary artery, and the descending thoracic aorta. It is adherent to the left side of the pericardium. Right-sided pneumothorax can also be seen (Figures 2a-d). No area of calcification, mediastinal lymphadenopathy, pleural effusion or hepatic metastasis noted.

Laboratory evaluation revealed a markedly elevated erythrocyte sedimentation rate (95 mm/hr). Total leucocyte count was $6.3 \times 10^9/L$, packed cell volume of 30%, serum urea: 3.8 mmol/L, creatinine: 75.4 $\mu\text{mol/L}$, and serum electrolytes were within normal limits. Sputum evaluation was negative for acid-fast bacilli, mycobacterium tuberculosis was not detected on GeneXpert, and cytology was negative for malignancy.

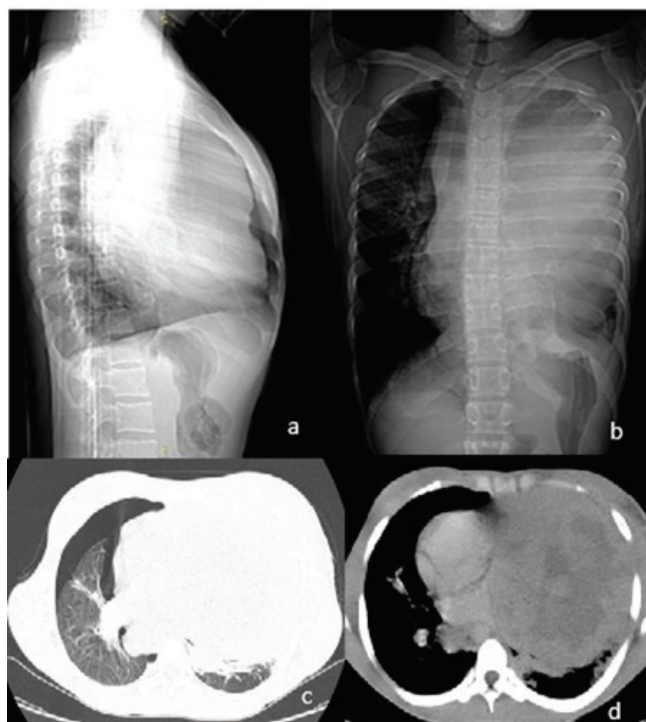


Figure 2. Chest CT scan showing a huge mixed-density anterior mediastinal mass measuring 17.3 x 16.4 x 12.6 cm with irregular margins and areas of necrosis extending into the left hemithorax. The mass occupies almost the entire left hemithorax with associated compression atelectasis of the left lung. It encases the arch of the aorta, superior vena cava, main pulmonary artery, and the descending thoracic aorta. It is adherent to the left side of the pericardium, and a right-sided pneumothorax can also be seen (a-d).

She had a closed thoracostomy tube drainage for the right-sided pneumothorax and symptomatic treatment. Anti-TB medications were discontinued following the results of laboratory investigations, and she underwent a trans-thoracic percutaneous Tru-cut biopsy of the mediastinal tumor. She was discharged after 7 days of admission following improvement of symptoms and was adequately counseled to see the next scheduled specialist clinic with the histology report.

Histological sections showed sheets of monotonous primitive small round blue cells with a high nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, some irregular nuclear contours with fine stippled chromatin, inconspicuous nucleoli, and scanty cytoplasm with an indistinct membrane. No mitotic activity or areas of necrosis or hemorrhage were seen; features highly consistent with a small round-cell malignancy, such as Ewing's sarcoma (Figure 3).

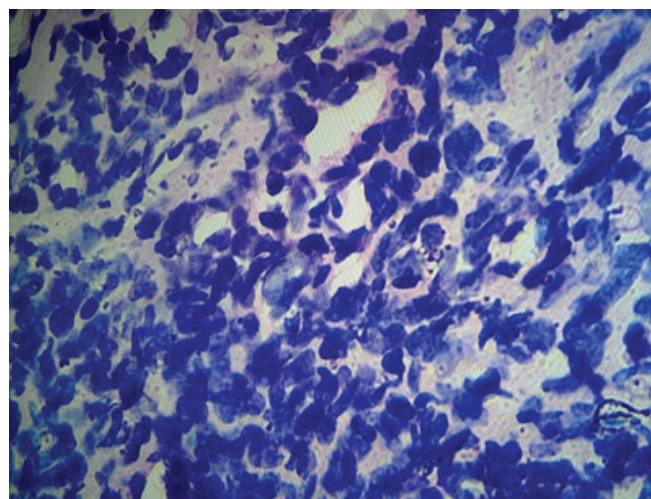


Figure 3. Hematoxylin and eosin staining of the tumor showing small round blue cells with enlarged nuclei, fine stippled chromatin, inconspicuous nucleoli, and scanty clear to eosinophilic cytoplasm with indistinct membrane. Features consistent with classical Ewing's sarcoma (H&E, ×400).

Unfortunately, our patient only re-presented after four weeks of initial discharge with worsening of her symptoms, as her parent had attributed her illness to a “spiritual attack”, which stems from a magico-religious thought system of disease causation that is not uncommon in our sub-region [4]. In a sad turn of events, our patient succumbed to her illness within 2 days of re-presentation to the clinic. A deceased patient's permission form was signed by the patient's next of kin for the publication of this case report.

Discussion

ES typically has a rapid growth pattern with most patients harboring micro-metastasis at presentation. Clinical manifestation of primary mediastinal ES is highly variable with non-specific symptoms, this in addition to its very low incidence, poses a diagnostic dilemma. Patients with mediastinal ES can present with cough, wheezing, and chest tightness when the tumor compresses the trachea. Pleural invasion with resultant effusion or pneumothorax, as in this index case, as well as invasion of intercostal nerves, may cause chest pain and dyspnea. Invasion of the pericardium may present with pericardial effusion, while compression of the heart or great vessels can lead to mediastinal shift and superior vena cava syndrome [3, 5].

Imaging plays a vital role in the management of EES. Although CT scan features are non-specific, they remain

vital for assessing tumor size and resectability. Commonly seen features include a slightly hypodense soft tissue mass with areas of cystic degeneration on non-contrast CT, while contrast-enhanced medium demonstrates a mass with a mixed-density pattern. Calcification is seen in 10% of cases. Pleural effusion, pneumothorax, and pericardial effusion are manifestations of invasion of nearby structures that may be seen [6-8].

Histopathological analysis is required to confirm the diagnosis of EES. The histological picture of EES consists of a large number of uniform small round cells with a high nuclear-to-cytoplasmic ratio and scanty clear to eosinophilic cytoplasm [9].

Immunohistochemistry (IHC) is an indispensable tool in the diagnosis of ES. Positive staining for Cluster of differentiation 99 (CD99), Friend leukemia integration 1 (FLI-1), and NKX2 are currently acceptable markers for diagnosis of ES on IHC. Additionally, genetic testing is helpful for definitive diagnosis, and the presence of EWS-FLI1 fusion gene defines ES on genetic testing [9-11].

What makes this case particularly unique is the rare clinical presentation of a primary mediastinal tumor skewed to the left co-occurring with a contralateral pneumothorax and resultant paradoxical mediastinal deviation. In classic physiology, a right-sided pneumothorax exerts a positive pressure effect that shifts mediastinal structures toward the left hemithorax. However, in our patient, physical and radiological examinations revealed a severe tracheal and mediastinal shift to the right. This paradoxical finding is explained by the massive volume and dominant compressive force of the left-sided anterior mediastinal mass, which completely overwhelmed the contralateral pressure of the right pneumothorax. Such a presentation can easily mislead clinicians, especially in resource-limited settings where symptoms might be misattributed solely to common infectious pathologies like tuberculosis.

A major limitation of this report is the lack of immunohistochemical (IHC) confirmation and molecular or genetic testing (such as detecting the EWSR1-FLI1 fusion gene), which are vital to establish a definitive diagnosis of Ewing's sarcoma. Due to an inadequate tissue block from the initial biopsy, coupled with the

patient's late re-presentation and rapid demise, these ancillary studies could not be completed. Consequently, a broad differential diagnosis for small round blue cell tumors of the mediastinum must be considered. This includes lymphoma, embryonal rhabdomyosarcoma, neuroblastoma, poorly differentiated synovial sarcoma, and newer entities like BCOR or CIC-rearranged sarcomas [12]. While the cytomorphological features were highly suggestive of extraskeletal Ewing's sarcoma, the diagnosis remains presumptive rather than definitive.

Early diagnosis and treatment can improve the prognosis of EES. Treatment involves a combination of systemic chemotherapy and local control either by surgery or radiotherapy. Generally, induction with multidrug chemotherapy is given before local control. Surgery is the preferred method of local control for resectable tumors, as the long-term outcome when radiotherapy is used alone is less favorable, even though ES is radiosensitive [13,14]. Autologous stem cell therapy has also been used in the management of EES [9].

Our literature search identified six documented cases of primary mediastinal ES. Three of the cases were in males and 3 females; the ages ranged from 15 to 66 years. As in our case, the anterior mediastinum was the primary site of the tumor in 3 cases; 2 were located in the posterior mediastinum, and 1 involved both the anterior and posterior mediastinum. Cough was present in 3 out of 4 cases involving the anterior mediastinum, a finding fairly consistent with this index case, while pain was the predominant symptom in the posterior mediastinal tumors. There was an associated pleural effusion in 3 of the 6 cases, and 1 of the 3 cases with pleural effusion had pericardial effusion in addition. Notably, our case is distinguished by the presence of a primary mediastinal small round cell tumor complicated by pneumothorax, a finding we believe is unprecedented in prior case reports. At a minimum, all cases were diagnosed using histology, while 5 included further IHC testing and 3 involved genetic studies. Four of the six patients had surgery as their primary treatment [3,5,7-9,15].

In Table 1, we summarize the management and outcome of six cases of primary mediastinal ES previously reported in the literature.

Table 1. Management and outcome of some previously reported cases of primary mediastinal Ewing's sarcoma.

Study/ Year	Age/ Sex	Presenting complaints	CT scan Features		Method of Diagnosis	Treatment	Outcome
			Primary Site	Description			
Li X et al. [3] 2023	15/F	Cough Wheezing	Anterior mediastinum	15.7x11.7x10.5 cm moderately heterogenous enhancing mass with multiple mediastinal nodes and invading left lung with ipsilateral pleural effusion	Histology + IHC + Genetic testing	Chemotherapy	Follow-up
Su C et al. [5] 2024	32/M	Chest pain Back pain	Posterior mediastinum	4x4x3 cm well-defined mass with heterogenous density	Histology + IHC + Genetic testing	Surgery	Follow-up
Halefoglu AM et al. [7] 2012	19/F	Pain in the left upper arm	Posterior mediastinum	16x15x15cm heterogenous mass with smooth edges extending to the left hemithorax and supraclavicular region, plus contralateral mediastinal shift	Histology + IHC	Surgery	N/A
Cui M et al. [8] 2023	66/M	Chest tightness	Anterior mediastinum	Giant cystic and solid mass with moderate enhancement and enlarged mediastinal nodes. Invasion of SVC, Pericardium with pericardial effusion, and right lung with ipsilateral pleural effusion	Histology + IHC	Surgery	Metastatic pericardial effusion re-appeared two months after surgery. Death
Calvituro A et al. [9] 2023	30/F	Cough Dyspnea	Anterior mediastinum	Well-defined solid mass extending to the left hemithorax compressing the superior lung lobe and contralateral mediastinal dislocation	Histology + IHC + Genetic studies	Surgery + adjuvant chemotherapy + autologous stem cell transplant	Relapse after a few months of surgery. On follow-up after adjuvant therapy.
Ata F et al. [15] 2021	16/M	Cough Dyspnea	Anterior and posterior mediastinum	18cm mediastinal mass extending to the left hemithorax with ipsilateral pleural effusion and contralateral basal nodule and mediastinal shift	Histology	N/A	N/A

Abbrev.: M: Male, F: Female, CT: Computed tomography, IHC: Immunohistochemistry, N/A: Not applicable (i.e.: details not provided by publishing authors).

In conclusion, primary mediastinal tumors consistent with Ewing's sarcoma are rare, aggressive malignancies that pose significant diagnostic challenges. This case highlights a highly unusual presentation characterized by a contralateral pneumothorax and paradoxical mediastinal shift. In high-burden regions, such presentations can mask underlying malignancies and lead to empirical tuberculosis treatment, delaying diagnosis. Although the lack of immunohistochemical and molecular confirmation in this case limits a

definitive diagnosis, clinicians should maintain a high index of suspicion for small round cell malignancies when evaluating massive mediastinal tumors with atypical intrathoracic pressure dynamics.

Declaration of conflicting interests

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Authors' contribution

POA, RU were responsible for the initial assessment, the request, and the interpretation of radiological findings. POA, HIA contributed to the biopsy and closed tube thoracotomy procedures. AAD was responsible for the histological analysis. POA, HIA, and AAD were responsible for drafting the manuscript. RU and HIA oversaw the literature review and prepared the figures. All authors have reviewed and approved the final manuscript.

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Case Series

Surgical management of complex esophageal perforations: a case series with early and delayed presentations

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ABSTRACT

Esophageal perforation from sharp trauma, including ingested foreign bodies, carries significant morbidity and mortality. This retrospective case series describes our experience with early surgical management across seven heterogeneous cases. We reviewed the records of seven patients with esophageal perforation admitted to our center between July 2015 and January 2022. Etiologies included impacted disc batteries ($n = 3$), a penetrating syringe needle, an ingested nail, a firearm injury, and false intubation. Data on presentation, surgical intervention, and outcomes were collected. The series included five children (10 months to 4 years) and two adults (aged 23 and 43 years). Surgical approaches varied by injury location and included cervicotomy, thoracotomy, and laparotomy for feeding tube placement. Six patients survived with eventual resumption of oral intake, though recovery was prolonged in delayed presentations. One mortality occurred from an unrecognized aorto-esophageal fistula following disc battery extraction. In this small, heterogeneous case series, early surgical intervention facilitated foreign body removal, mediastinal drainage, primary repair, and enteral access, contributing to favorable outcomes in most patients. Delayed diagnosis, particularly of aorto-esophageal fistula, remains a critical risk factor for mortality.

Keywords: foreign body impaction, esophageal perforation, false intubation, aorto-esophageal fistula, disc battery ingestion

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Introduction

Overall mortality from esophageal tears remains high, ranging from 20% to 50% despite advanced technology in therapeutic strategies and management [1-4]. Impaction of a foreign body in the esophagus is an important thoracic and gastrointestinal emergency with a risk of morbidity and potential mortality either from perforation or sepsis [5]. Mucosal ischemia and ulceration due to prolonged foreign body impaction in the esophagus represent a morbid complication [6].

The narrowest part of the esophagus is the first part at the level of cricopharyngeus, where the cricopharyngeal muscle plays a role to shorten the diameter of the lumen. This anatomical feature led Jackson to name this constricted area the pass of "Bal-el Mandeb" or the "gate of tears" [7].

In this article, we illustrate seven different case scenarios of esophageal perforation resulting from penetrating ingested foreign bodies, a firearm injury, and iatrogenic false intubation. In all seven cases, early surgical intervention provided a safe and effective approach for foreign body removal and complication management, which successfully minimized morbidity, mortality, and the duration of hospitalization.

Case Reports

A retrospective review was conducted of all patients admitted to our center with esophageal perforation between July 2015 and January 2022. Seven patients were identified: five children and two adults (4 males, 3 females), aged 10 months to 45 years. The pediatric age range was 10 months to 4 years, while adult ages were 23 and 45 years.

Presenting symptoms included throat pain, dysphagia, excessive salivation, gagging, regurgitation, and pleural collection on chest radiographs. Routine posteroanterior (PA) and lateral chest radiographs were obtained on arrival. Multi-slice computed tomography (MSCT) of the chest was ordered after failed endoscopic extraction, when a dangerous complication was suspected, or when pleural effusion was present on initial radiograph.

Postoperative courses varied markedly. One mortality occurred (secondary to aorto-esophageal fistula); the remaining six patients survived. Table 1 shows a brief summary of the cases.

Written informed consent was waived by the Medical Ethics Committee of our institution due to the retrospective nature of the study, use of anonymized data, and minimal risk to patients. However, we informed all participants during the telephone follow-up and obtained their verbal informed consent.

Cases 1, 2 and 3: impacted disc battery ingestion

Case 1

A 15-month-old male child presented with a rounded foreign body impacted in the upper esophagus of unknown nature and duration. A chest radiograph revealed rounded foreign body shadow with double edges suggesting disc battery (Figures 1a,b). The patient was prepared for esophagoscopy which revealed markedly inflamed hyperemic, and easily bleeding mucosa at the suspected site of the foreign body. It was neither possible to extract the foreign body nor to clearly visualize it as it was covered with extensive food particles. Therefore, open surgical extraction was planned.

A left half collar cervical incision was performed upon which we found remarkable adhesions around the esophagus. Intraoperative fluoroscopy was used to perfectly locate the foreign body, and a small incision was made in the esophageal wall. The foreign body was confirmed to be a disc battery, that was deeply impacted in and firmly adherent to the esophageal wall. It was covered by granulation tissue and extracted under fluoroscopic guidance. The wound was closed in layers leaving a rubber drain.

Oral feeding was initiated on the fourth postoperative day alongside temporary parenteral nutrition. There was a minimal, transient salivary leak, however, oral feeding was safely continued, the fistula closed spontaneously within a week, and the patient was discharged in good condition on the tenth postoperative day.

Case 2

A 10-month-old female child presented with a history of a disc battery ingestion that occurred more than 10 hours prior while playing with her toys. She was referred to us after failure of multiple esophagoscopy trials of extraction outside our center. A chest radiography and CT was ordered, which revealed distal migration of disc battery to the cardia accompanied by a right pleural effusion, highly indicative of perforation (Figures 1c,d).

Table 1. Summary of complex cases of esophageal perforations.

No	Age/ Sex	Etiology	Injury-to- Diagnosis	Diagnosis-to- Surgery	Mediasti- nitis	Surgical Ap- proach	Hospital Stay (days)	Time to Full Oral Intake	Outcome / Long-term Follow-up
1	15 mo/M	Impacted disc battery (failed endoscopy)	> 15 hours	Urgent (after failed endos- copy)	No	Left cervico- tomy + es- ophagotomy + fluoroscopy	10	Minimal oral intake at POD 4; fistula closed and full intake within 1 week	Survived; discharged POD 10; no long-term data reported
2	10 mo/F	Impacted disc battery (failed multiple en- doscopies)	>10 hours (ingestion to presenta- tion)	Within 24 hours of referral (after CT)	Yes (right pleural effusion, perfora- tion)	Right thoracot- omy + repair (2 tears) + gastrostomy	16	2 weeks post- operatively	Survived; full oral intake at 2 weeks; no long-term data reported
3	2 yr/F	Impacted disc battery (with hematemesis)	>22 hours	Urgent (after esophagos- copy)	No (but had aorto-es- ophageal fistula)	Rigid es- ophagoscopy + extraction	5	Started POD 3	Died on POD 5 from massive hematemesis secondary to aorto-esophage- al fistula
4	4 yr/M	Ingested sy- ringe needle penetrating aortic arch	Acute (<24 hours from ingestion)	Urgent (after CT confirma- tion)	No	Left posterolat- eral thoracot- omy + aortic purse-string + endoscopic removal	4	48 hours post- operatively	Survived; dis- charged POD 4; no long-term data reported
5	3 yr/M	Ingested 10 cm penetrat- ing nail	Acute (<24 hours from ingestion)	Immediately (after imag- ing)	No	Right lateral thoracotomy + primary repair	5	POD 3	Survived; dis- charged POD 5; no long-term data reported
6	23 yr/M	Firearm inju- ry to thoracic esophagus	2 days (food parti- cles noted in chest drain on POD 2)	Urgent (same day after CT diagnosis)	Yes (diffuse pyogenic mem- brane and food debris)	Right thora- cotomy + primary repair + intercostal muscle flap + gastrostomy	45	Full at 40 days post- operatively (slight leak- age at 2 weeks)	Survived; full oral intake at 40 days; no long-term data reported
7	43 yr/F	False in- tubation (iatrogenic, delayed)	>21 days (presented 3 weeks post-thy- roidecto- my)	Urgent (same day of pres- entation)	Yes (huge medi- astinal abscess with barium/ food)	Right thora- cotomy + drainage/ decortication + jejunostomy (duodenal perforation)	60	Light at 1 month; full at ~2 months (by discharge)	Survived; discharged at 2 months; no long-term data reported

Abbrev.: POD, postoperative day; M, male; F, female; yr, years; mo, months.

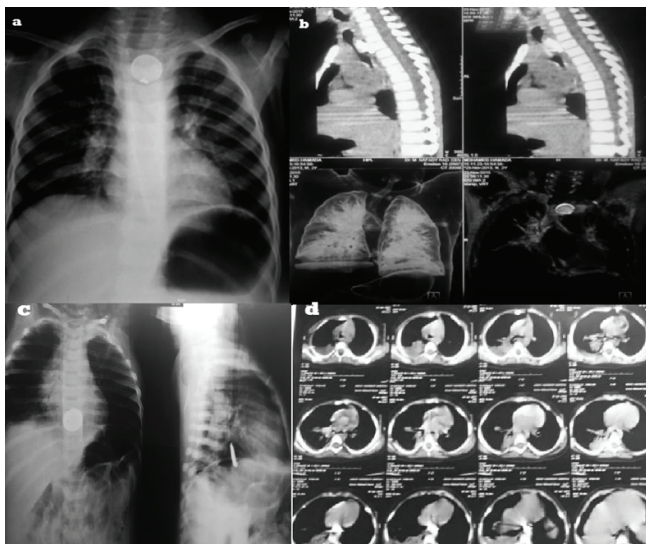


Figure 1. Chest X-ray and MSCT chest of Case 1 showing a rounded foreign body shadow with double edges suggesting disc battery in the upper part of thoracic esophagus (a,b), chest X-ray of Case 2 showing rounded foreign body shadow with double edges suggesting disc battery at the level of the cardia (c), MSCT of case 2 revealed the disc battery into the cardia with right pleural effusion; mostly due to perforation (d).

The patient was planned for surgical extraction and repair of the esophageal perforation. A right thoracotomy was performed, with ligation of azygous vein for better exploration of thoracic esophagus. The disc battery was extracted, and the tear in distal part of thoracic esophagus was repaired by two layers of interrupted 3/0 polyglactin 910 sutures with meticulous insertion of intercostal tube close to the perforation site. As there was another tear in cervical part of esophagus, the patient was returned to supine position and another cervical collar incision was made and the tear repaired by a single layer of 3/0 polyglactin 910 sutures. Finally, an upper laparotomy incision was made to place a feeding gastrostomy tube for secure enteral nutrition.

Intravenous fluids were initiated postoperatively and gradual enteral feeding via gastrostomy was initiated after 48 hours. Oral fluids commenced one week after surgery with minimal leakage via chest tube, until complete oral intake two weeks postoperatively.

Case 3

A 2-year-old female child presented with repetitive chest infection and hematemesis. Upon examination and radiographic evaluation, there was a rounded

impacted foreign body in the lower part of cervical esophagus, mostly disc battery. The patient experienced intermittent, severe attacks of hematemesis, which caused her hemoglobin level to drop sharply from 10.1 g/dL to 6.0 g/dL after each episode.

The patient was planned for rigid esophagoscopy. Under general anesthesia with endotracheal tube in place, the disc battery was successfully extracted with evident slight resistance during extraction which reflects its long-standing impaction into the esophageal wall.

Oral feeding was suspended for 48 hours, after that light fluids were initiated on the third postoperative day. Two days later, the patient developed massive hematemesis and melena. The patient died 2 days later from another massive attack of hematemesis, shock and cardiovascular collapse.

Case 4: ingested syringe needle penetrating the left subclavian artery

A 4-year-old male child presented with a history of foreign body ingestion (a syringe needle). Chest radiographs were performed, and it revealed a metallic foreign body in the upper chest. The chest radiography and CT revealed a metallic needle in the esophagus penetrating its wall into the lumen of the aortic arch to the left subclavian artery, so the patient was scheduled for open surgical extraction (Figures 2a,b).

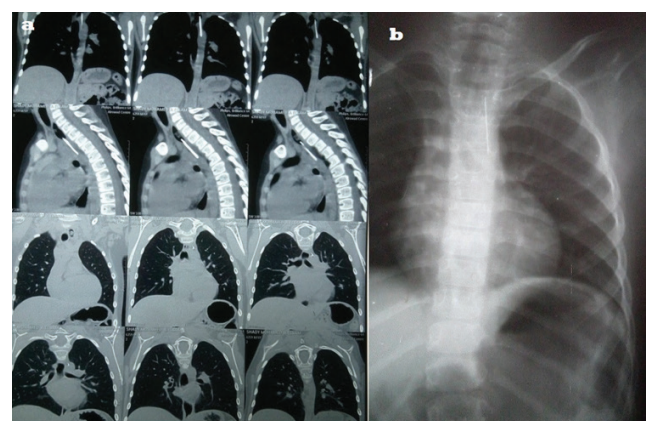


Figure 2. MSCT of Case 4 showing a metallic needle in the esophagus penetrating its wall into the lumen of the aortic arch (a), PA chest X-ray of the same case showing a metallic foreign body in the upper chest (b).

A limited left posterolateral thoracotomy was performed. The aortic arch and the left subclavian were

encircled, a purse string suture was placed around the site of entry of the syringe into the aorta, the foreign body was removed by endoscopy, and the purse string suture was securely tied.

Oral feeding started 48 hours postoperatively, and the patient was discharged on the fourth postoperative day.

Case 5: ingested 10 cm nail

A 3-year-old male child presented with a history of foreign body ingestion (a carpenter's nail). The nail was large and with multiple curvatures and appeared to be penetrating the wall in chest radiograph and CT so open extraction was planned (Figure 3a).

A right lateral thoracotomy was performed, and the site of penetration was revealed after opening of the mediastinal pleura and exposure of the thoracic esophagus, and the penetrating nail was visualized and removed (Figures 3b,c). The esophagus was repaired by three simple interrupted 3/0 polyglactin 910 sutures.

Postoperatively, oral feeding was started on the third day and patient was discharged on the fifth postoperative day.

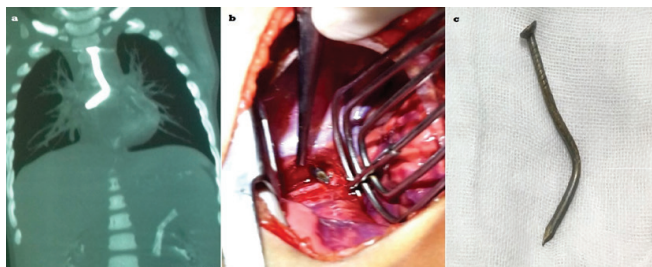


Figure 3. Chest x-ray of Case 5 showing a large, curved nail and appeared to be penetrating (a), intraoperative nail extraction (b), the nail displayed after extraction (c).

Case 6: firearm injury to the thoracic esophagus

A 23-year-old male presented with a gunshot wound to the chest, with an entry wound at the left supraclavicular area and a retained bullet located below the right scapula. On evaluation, he was hemodynamically stable with right hemopneumothorax so right intercostal tube inserted and 500 mL of blood was drained. On the second day after admission, food particles were noticed in the chest drain so chest CT with a water-soluble contrast medium was ordered that revealed perforation in the upper part of thoracic esophagus about 4.7 cm opposite to the third intercostal space. The patient was planned for urgent surgery (Figures 4a-d).

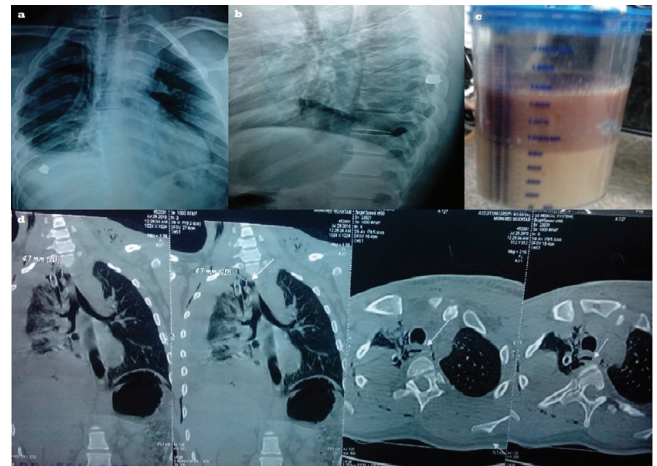


Figure 4. PA and lateral chest X-ray of Case 6 showing retained bullet on right chest with right intercostal tube (a,b), chest drain fluid showing empyema with residual food debris (c), MSCT demonstrating a perforation in the upper part of thoracic esophagus about 4.7 cm opposite to third intercostal space (d).

A right lateral periscapular thoracotomy incision was performed, and the chest was entered through the fourth intercostal space. Before entering the chest, the bullet was extracted below the inferior angle of right scapula. After opening the chest (pleural cavity), intraoperative evaluation revealed a diffuse pyogenic membrane covering the right lung and the mediastinum with food debris in the right thoracic cavity, and about 5 cm esophageal tear. The tear was repaired by 3/0 polyglactin 910 sutures reinforced by vascularized intercostal muscle flap, and the mediastinum irrigated with saline. A wide bore right chest drain was placed, and thoracotomy was closed in layers in a standard fashion. The patient then placed in supine position and mini laparotomy incision was made for placement of feeding gastrostomy.

Postoperatively, nothing per mouth and parenteral nutrition were started immediately. Feeding through gastrostomy tube started on the third postoperative day. Two weeks later, the patient was allowed to begin slight oral intake of light fluids increasing gradually over the days and that associated with slight leakage from chest tube. The patient allowed full oral intake after 40 days postoperatively, and the subsequent course was uneventful.

Case 7: sharp esophageal injury due to false intubation

A 43-year-old female patient was referred to our department in septic shock, with a history of a total

thyroidectomy performed 3 weeks prior. On evaluation, she was hemodynamically unstable with septic shock and tender rigid abdomen, sweaty, tachycardia and hypotension which required infusion of 60 ng/kg/min of norepinephrine. Additionally, there was a right chest drain showing food particles and empyema. Radiological evaluation showed a large tear in the cervical part of the esophagus with remarkable leakage, as well as huge cervical abscess extending into the superior mediastinum. Barium swallow and chest MSCT demonstrated massive leakage from the proximal cervical esophagus into the superior posterior mediastinum (Figures 5a-d) and her laboratory studies revealed WBCs count: 65,000/ μ L, together with hypoproteinemia and impairment of renal function. Urgent exploration of the esophagus via right thoracotomy incision was indicated.

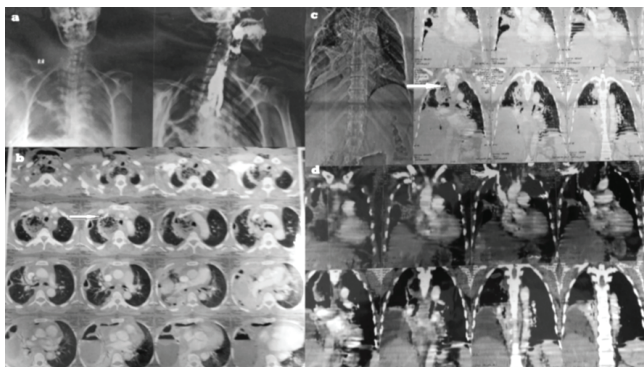


Figure 5. Barium swallow of Case 7 showing a remarkable leakage from the cervical part of the esophagus (a), MSCT showing perforation in the upper part of thoracic esophagus with huge posterior mediastinal abscess (b-d), note that the white arrows in panels b and c indicate the boundaries of the mediastinal abscess.

Intraoperative evaluation revealed there was a huge mediastinal abscess with contamination with food particles and barium contrast material. Mediastinal drainage and irrigation were done together with decortication of the right lung. Two wide-bore right chest drains were placed, and thoracotomy was closed in layers in a standard fashion. The patient was then placed in supine position, and upper mini laparotomy incision was made for placement of feeding gastrostomy, but surprisingly we found large perforated duodenal ulcer (stress ulcer) which was repaired by omental patch (Graham's patch), in addition to peritonitis so feeding jejunostomy was the choice and abdominal drains were placed.

Postoperative course of the patient was remarkably slow due to the long-standing perforation more than 21 days and the subsequent toxemia. Parenteral nutrition was initiated immediately postoperatively together with feeding through jejunostomy tube. Significant leakage from cervical tear into thoracic drains continued postoperatively which started to decline 3 weeks postoperatively. Light oral fluids started one month after surgery. Leakage around jejunostomy tube added further impedance to the postoperative course. Upper endoscopy was performed to assess the perforation and possibility of stenting of upper esophageal tear. Upper endoscopy revealed inability to place a stent as the tear was very proximal. The duodenal ulcer was found to be completely healed. Continuation of feeding via jejunostomy and nasogastric tube continued. After 2 months postoperatively, the patient started light oral fluids and the patient was discharged.

Discussion

The esophagus is often intimidating to the surgeons, an organ that needs to be negotiated carefully and meticulously. Long care and hospital stay, and possibly bad outcome make the surgeons cast it aside.

Most foreign bodies (80-90%) will pass spontaneously through the normal pathway of gastrointestinal tract in about one week without causing any noticed complications; however, 10-20% will need endoscopic removal and nearly 1% will need surgery [8].

Foreign body impaction usually presents acutely with a clear history of ingestion especially for adult patients who might have diffuse chest pain, heaviness, sensation of nausea, vomiting or even choking, sometimes vague foreign body sensation, and neck or throat pain. On the other hand, children may have vague history of refusal of feeding, crying or even vomiting [8].

Removal of a foreign body from the esophagus is mandatory, as its impaction leads to mucosal ulceration, inflammation and subsequently morbid complication such as lung abscess, empyema, mediastinitis, perforation and even a fistula between aorta and esophagus [9]. If endoscopic extraction fails, surgery is the treatment of choice. Different surgical approaches can be performed according to the location of the foreign body which might be cervicotomy, thoracotomy or gastrostomy [9].

Contemporary non-operative and minimally invasive alternatives

In recent years, the management of esophageal perforations has evolved significantly with the introduction of endoscopic and minimally invasive techniques. Covered self-expanding metal stents (cSEMS) have emerged as an effective treatment option, particularly for iatrogenic perforations and contained leaks, with a pooled sealing rate of 86.1% (95% CI: 80.2–92.0%) and stent-related mortality of 7.4% (95% CI: 3.5–11.4%) reported in a recent meta-analysis [10]. Endoscopic vacuum therapy (EVT) is another promising organ-preserving approach, based on negative pressure wound therapy, with reported success rates of 89% in multicenter cohorts [11]. The VACStent, a novel device combining a fully covered stent with an integrated EVT sponge has shown an 80% leak healing rate with no mortality in early multicenter studies [12]. Both esophageal stenting and EVT show high efficacy in sealing esophageal defects, with stenting achieving 86.1% success and EVT demonstrating 89.6% success in sensitivity analyses [10]. These advancements have expanded the therapeutic armamentarium, allowing non-operative management (NOM) to be offered to stable patients with early presentation, contained esophageal disruption, and minimal contamination of surrounding spaces [13].

Rationale for open surgical approach in our series

Despite these advances, open surgery remains the cornerstone of management for specific clinical scenarios [13]. In our series of seven cases, operative intervention was chosen based on patient-specific factors that precluded endoscopic or minimally invasive alternatives:

In our case series, esophageal trauma resulted from various etiologies; disc battery ingestion, sharp foreign body, firearm injury and false intubation.

For cases 1 and 2, esophageal injury resulted from neglected disc battery ingestion which led to caustic effect and required surgical intervention to remove the disc battery which was deeply and firmly impacted in esophageal wall and to repair the tears resulting from esophagoscopy manipulations. Endoscopic stenting or EVT would not have addressed the need for

foreign body removal, and the presence of extensive local inflammation made these modalities unsuitable. Furthermore, disc batteries in the esophagus are an indication for emergent surgery when they are irretrievable or close to vital structures [13].

In both cases, surgery provided; a) safe extraction of foreign body, b) primary repair of esophageal perforation, c) effective drainage, and d) placement of a port for enteral feeding as in 2nd case.

In case number 3 and 4, we have 2 different types of esophageal trauma and complication. In case number 3, there was neglected disc battery ingestion, presenting with hematemesis, which should have raised suspicion about aorto-esophageal fistula according to previous records [14,15]. But, unfortunately in our situation that was overlooked, and the battery extracted which was followed later on by massive hematemesis and hemodynamic collapse on the 2nd postoperative day. A similar case resulting in patient death due to an aorto-esophageal fistula was also reported in the recent literature [16,17].

Rarely, the diagnosis of aorto-esophageal fistula is known before massive hematemesis occurred. Chiari's triad of chest pain and sentinel hematemesis followed by rapidly massive hematemesis at a variable interval of time, which is a characteristic feature of aorto-esophageal fistula that mentioned in the literature [18], is rarely observed in fistulas resulting from impacted foreign bodies. Sudden death from an aorto-esophageal fistula due to an impacted ingested foreign body is also reported in the literature [16,19].

In our second case of aorto-esophageal fistula (case number 4), the lesson was learnt and as chest CT demonstrated penetration of the needle into the aortic arch, left posterolateral thoracotomy was performed and we controlled the perforation of the aortic arch before removal of foreign body. Endoscopic removal or stenting would have been dangerous, as manipulation could dislodge the needle and precipitate exsanguination.

The above terrible cases of esophageal perforation from foreign body ingestion suggest a public health problem in the region with improvement for intervention to prevent.

The thoracic surgeons should have low threshold to demand chest CT for every case of foreign body

impaction in the esophagus even if it looks simple, because it may reveal a complication that not be evident in plain chest radiograph only. Using MSCT chest facilitate shorten the study time and add accuracy to diagnosis as it is considered a useful diagnostic tool with high sensitivity for esophageal foreign body [20,21].

Penetrating trauma to esophagus is uncommon mostly due to its protected position even in busy urban trauma center [22-25]. However, perforation from instrumentation is the commonest such as those occurring during esophagoscopy, and esophageal dilation, frequent use of upper endoscopy, and gastroscopy. The commonest area of perforation occurring during an endoscopic examination is at the level of the cricopharyngeus [26].

Traumatic endotracheal intubation can be another cause of esophageal perforation which occurred just below the cricopharyngeus muscle, generally in the posterior midline at Lannier's triangle (the weakest area where the mucosa is supported only by fascia) [27], and that is what happened in one of our cases.

Selective or conservative management versus mandatory exploration or surgical intervention is still a point of debate in case of penetrating trauma to esophagus [24,28,29].

In all our cases, surgery was the mainstay and immediate management of choice. Because, first, early surgical intervention provides a safe and effective management of cases of esophageal perforation as it provides a tool for adequate mediastinal drainage, irrigation and thus relief of toxemia. Second, surgery allows accurate and meticulous placement of chest tube to drain the perforation site. Third, primary repair of esophageal tear which is effective in early hours of perforation preventing the further complication to occur such as mediastinitis, lung abscess, and empyema which is fatal if not urgently managed. Fourth, in delayed esophageal perforations, repair of tears is very debatable, for some surgeons, they see it ineffective due to edematous edges, inflamed tissues and inflamed mediastinum [30]. For us, we adopt repair for every case of esophageal perforation even delayed perforation either by direct suturing alone or plus augmentation by vascularized tissue. In our opinion, it is associated with decrease fistula size and hence its output and shorter recovery period which coincides with

the findings of Wang et al [31]. Lastly, it provides a port for enteral feeding such as gastrostomy or jejunostomy to improve healing.

Surgery in delayed esophageal perforations doesn't necessarily mean repair of esophageal tear. In our serial cases we performed esophageal repair in late perforations in two cases; that of firearm injury to the esophagus and that of impacted disc battery. Non operative management was not selected, as it associated with failure and high mortality especially if the perforation associated with pleural effusion, mediastinitis and contrast extravasation on chest CT. This coincides with opinion of Merchea et al and Mavroudis et al [32, 33].

Postoperative care and surgical nutrition are backbone for success of surgery. In contrast to some authors [23,28], who prefer use of total parenteral nutrition (TPN), we adopt the use of enteral nutrition through gastrostomy tube and that was the opinion of Madiba et al and Muckart et al [24] not only to improve healing, but also to prevent complication from long use of total parenteral nutrition [25,34].

Limitations of the study

Systematic, long-term follow-up beyond hospital discharge was not available for all patients. Outcome data are therefore limited to the immediate postoperative period and, where reported, time to full oral intake. Late complications such as esophageal stricture, dysphagia, or recurrent fistula cannot be excluded.

In conclusion, esophageal perforation remains an exceptionally challenging surgical emergency carrying high risks of morbidity. In this retrospective series of seven patients with diverse etiologies, early surgical intervention achieved survival in six patients. Delayed perforation and aorto-esophageal fistula carry high mortality. Surgery remains the cornerstone of management and was associated with favorable outcomes in most patients, with three key principles: drainage, primary repair (when feasible), and establishment of enteral feeding access. Finally, these cases underscore a critical public health issue in our region, highlighting the urgent need for enhanced parental awareness and regulatory actions to prevent accidental disc battery ingestions in children.

Declaration of conflicting interests

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Authors' contribution

MEA: Conceptualization, methodology, surgical procedure, data curation, writing - original draft. MAN: Data curation, visualization, formal analysis, writing - review and editing. All authors read, critically revised, and approved the final version of the manuscript.

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