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Original Article

Benefits of routine uniportal thoracoscopy during rib fixation in the diagnosis and repair of diaphragmatic injury

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ABSTRACT

Background: The incidence of missed diagnosis of traumatic diaphragmatic injury (TDI) is about 30%. Lower rib fractures may cause TDI. We aimed to present our clinical results of uniportal video-assisted thoracoscopic surgery (VATS) in terms of detecting and repairing TDI, in patients undergoing rib fixation.

Materials and Methods: In this retrospective study, routine uniportal VATS was performed in patients planned to undergo rib fixation due to flail chest and severely displaced rib fractures between January 2021 and January 2023. The results of 11 patients with TDI were investigated.

Results: All patients were male. Eighty-two percent of the patients had blunt type of injury. Most TDIs were detected during VATS (55%). There were 7 left and 4 right TDIs with diaphragmatic defects varying from 2 to 5 cm in size. Two patients had minor omental herniation. Mean number of fractured ribs was 4. Mean duration of operation was 139 minutes. Mean hospital stay was 7 days. Morbidity developed in 1 patient (9%, wound infection).

Conclusions: Routine VATS in patients undergoing SSRF helps detecting and repair TDIs. Its diagnostic benefit in the diagnosis of acute TDI is greatest in patients with multiple rib fractures involving the lower chest wall, although there are no radiographic evidences of TDI.

Keywords: diaphragm injury, uniportal thoracoscopy, rib fracture, trauma

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Introduction

Traumatic diaphragmatic injuries (TDIs) secondary to blunt or penetrating thoraco-abdominal trauma are difficult to diagnose in the acute trauma setting [1]. Despite advances in radiological imaging, it is known that the incidence of missed or delayed diagnosis of TDI is about 30% [2]. The diagnostic yield of chest radiography and ultrasound in the acute TDI is low [3], and computed tomography has a diagnostic yield of 61-72% [4].

Flail chest and severely displaced rib fractures due to trauma are associated with significant morbidity and mortality, it has been shown that the presence of more than three rib fractures in adults may be a marker for associated solid organ injury [5]. Moreover, lower rib fractures are demonstrated to be related with TDI [1,6]. Delayed massive hemothorax due to TDI secondary to lower rib fractures have been reported [7,8].

The use of exploratory video-assisted thoracoscopic surgery (VATS) for the diagnosis and treatment in traumatic patients with intrathoracic injury has been proposed. VATS is shown to be safe and useful approach in selected patients with thoracic trauma [9-11]. In addition, the benefits of VATS in the diagnosis and treatment of TDI are well-demonstrated [12-15].

In our clinic, we provide surgical stabilization of rib fractures (SSRF) for patients with flail chest injuries or severe multiple rib fractures. We adopted to use routine VATS in the management of these patients, as previously advised [1]. By this way, we had the possibility to detect and treat acute TDIs in patients with traumatic chest wall injury. Here in this report, we aimed to present our experience in this topic.

Materials and Methods

We retrospectively reviewed the patients (n = 980) who presented with chest wall trauma to the emergency department from January 2021 to January 2023. Among them, patients with sternal, clavicular, scapular and thoracic vertebral bony fractures; patients with additional extrathoracic traumas; patients with chest wall injury related soft tissue; patients undergoing emergency surgery due to trauma; and patients with simple rib fractures not necessitating SSRF were excluded. Patients with flail chest and severely displaced rib fractures for whom SSRF were planned, were taken into the consideration. Among them, patient who necessitated conversion to thoracotomy due to relevant indications were also excluded, and 11 patients who underwent SSFR and diaphragmatic repair using VATS included into the study. All patients

underwent chest X-ray and computed tomography of the chest at the admittance. Data collected included patient demographics, mechanism of injury, numbers and places of rib fractures, intraoperative findings, length of operation, length of hospital stay, and follow-up results.

VATS was performed using lung isolation with a double lumen endotracheal tube or bronchial blocker placed through a single lumen endotracheal tube. Any previously placed chest tube was removed following the induction of general anesthesia and lung isolation. A 3 cm camera port incision was made anterior to the iliac spine in the 6th or 7th intercostal space, but if the broken ribs were very close to the incision site, a more suitable place was chosen. No CO₂ gas insufflation was used. A 10 mm 30-degree thoracoscope was introduced via a 12 mm port into the pleural space. A sucker was inserted through the same port to aspirate ant fluid and/or blood, then the pleural space, lungs, diaphragm and other structures were carefully inspected. The displaced rib fractures were observed and any potential arterial and/or venous bleeding were cauterized or clipped (Figure 1A). Detected lung lacerations were sutured using a running 3-0 polypropylene suture. In TDI was detected, the port incision was extended to 5 cm (Figure 1B). Any herniated abdominal viscera, if present, were reduced to the abdominal cavity and the repair of the diaphragm was performed using interrupted 0-vicryl sutures (Figure 1C). The repair of the diaphragm was done via uniportal approach (Figure 1D). Then using a separate muscle-sparing incision, approximately 4 to 5 cm in size, SSRF was done by placing plates and screws on the external aspect of the ribs in the submuscular space (Figures 2A,B). Following SSRF, the pleural space was investigated using VATS, a 28 Fr chest tube was placed through the camera port, and the incisions were closed appropriately. All patients were extubated at the operating room. All the operations were performed within the first 2 days following the injury.

Postoperatively, all patients received similar analgesic (intravenous patient-controlled analgesia), antibiotic and bronchodilator treatment. The chest tubes were removed when the lungs were totally expanded without air-leak, and the daily drainage was less than 150 mL. Patients were discharged on the day of chest tube removal or the following day, as appropriate. The follow-up scheduled 2 times in a month during 3 months. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local institutional review board (2023/4022). Individual consent for this study was waived from each patient.

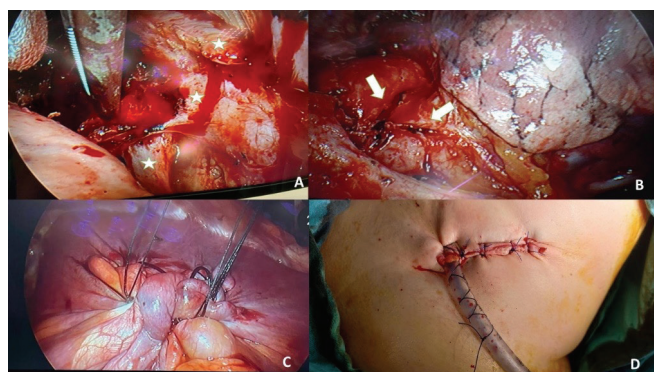


Figure 1. Displaced rib fractures (white stars) and minimal intercostal bleedings (A), injuries in the diaphragm (white arrows) (B), diaphragm after the repair (C), the view of the uniportal VATS approach (D).



Figure 2. Separate muscle-sparing incision for rib fracture repair (A), the view after the fixation of 3 ribs (B).

Results

The characteristics of the patients, data about the injury, and per- and postoperative outcomes were given in table 1. Blunt type injury predominated (82%). All the broken ribs were lower ribs (7th to 12th ribs), as previously defined [6]. Computed tomography of the chest demonstrated TDI in 5 patients (45%). TDIs were detected peroperatively in the remaining 6 patients (55%). Traumatic pneumothorax and hemothorax were detected in 6 patients (3 for each, 55%). Two patients with penetrating type of injury had both pneumothorax and hemothorax. Each patient underwent tube thoracostomy at the admittance to the emergency department. Pulmonary laceration was seen in 2 patients with penetrating trauma, and sutured. In addition, 5 patients (45%) had pulmonary contusion which resolved with appropriate medication. Diaphragmatic defects varied in size from 2 to 5 cm. Only 2 patients had minor herniation (only part of omentum).

Postoperative periods of the patients were uneventful except for a wound infection in a patient with penetrating trauma which resolved with medical treatment (9%). No mortality occurred during the study. Each patient was followed up 3 months postoperatively. A postoperative computed tomography of the chest was routinely taken at the third month which showed no problem related to rib fractures and TDI, then the follow-up was terminated.

Table 1. Characteristics of the patients, data about the injury, and per- and postoperative outcomes.

Age, years (mean, range)	29 (21-41)
Gender	Male (100%)
Type of injury (%)	Blunt (car accident) 6 (55%) Blunt (fall) 3 (27%) Penetrating (knife) 2 (18%)
Side	Left 7 (64%) Right 4 (36%)
Mean number of rib fractures, (range)	4 (3-5)
Duration of surgery (minutes), mean $\pm$ SD	139 $\pm$ 12
Chest tube removal (days), mean $\pm$ SD	6 $\pm$ 1
Postoperative length of stay (days), mean $\pm$ SD	7 $\pm$ 1

Discussion

Jones et al [16] assessed 36 patients with penetrating thoracic trauma using thoracoscope and presented their results in 1981. Then Graeber and Jones [17] outlined the potential applications of VATS after thoracic injury in 1993. Since then, VATS has been used increasingly in selected patients with thoracic injury. This approach was proved to be useful, especially in the detection of TDI. In a series of 42 patients with both blunt and penetrating thoracic injury, VATS revealed 14 TDIs (33%) [10]. Among 13 patients undergoing VATS due to penetrating thoracic injury, TDI was detected in 5 patients (36%) [11].

We operated 11 patients due to flail chest and severely displaced rib fractures, and by using VATS, we repaired diaphragmatic injuries. In 5 patients (45%) computed tomography had already demonstrated TDI, but VATS helped us to detect TDI in the remaining 6 patients (55%). Our result demonstrates that VATS is a useful approach to detect TDI which is not seen radiologically. Similar results have been given in the literature. In the series of Martinez et al [12] consisting of 40 patients, VATS documented TDI in 67% and a sizable hemothorax in 63% of the patients. In a recent study consisting of 22 patients, the missed TDI rate was 18% although patients were evaluated radiologically using chest X-ray, computed tomography of the chest and abdominal ultrasound [15].

In our series, we noted that patients with multiple rib fractures and TDI were more likely to have ribs in-

volving the lower chest wall. All patients in our study had their lower ribs broken (7th to 12th ribs). Similar results have been reported [1,6]. The mechanism of TDI was penetrating injury from the fractured ribs puncturing and tearing the diaphragm [1]. We agree with this proposed mechanism in the development of TDI for patients with blunt type of trauma however, we had 2 patients with penetrating type of injury in our series. Although each patient had 3 broken ribs, we can't be sure that whether TDI developed from penetrating injury from the fractured ribs or from directly to the knife.

The management of rib fractures has changed in the last two decades. Benefits of surgical stabilization in traumatic flail chest has been proven [18] and the popularity of SSRF in patients with severe chest wall injuries increased [19]. Wemeijer et al [20] favored the use of an inspection through thoracotomy or thoracoscopy during SSRF to diagnose missed intrathoracic injuries. The authors investigated 51 patients with thoracotomy or thoracoscopy while SSRF, and 11 patients was found to have TDI (22%). Of them, 3 patients had radiologically demonstrated TDI but the remaining 8 patients had TDI discovered by inspection during surgery.

Since the beginning of 2021, routine VATS inspection of thoracic cavity during SSRF has been performed in our clinic. The same protocol has been used by Powell et al [1]. In their study, they found and repaired TDI in 15 patients with fractures during SSRF using multiportal VATS approach. Multiportal VATS repair of TDI is a preferred approach [12,13]. Uniportal or single-port VATS approach has been recently reported under CO₂ gas insufflation [21,22]. We performed uniportal VATS approach during the repair of TDI in our series. We did not use CO₂ insufflation during the surgery, although it is known to make the uniportal approach easier by flattening of the diaphragm [21,23].

In a recent study, Bui et al [24] performed uniportal VATS during SSRF. They divided their patients into two groups: routine VATS and VATS in selected cases. Among 97 patients in total, they detected 31 incidental traumatic findings (32%), especially retained hemothorax (n = 18) and lung laceration (n = 7). They found 2 cases with TDI, both in routine VATS group. Overall, routine VATS detected insignificantly higher number of incidental finding compared to selected VATS group (23 versus 8 findings, p > 0.05). Beside they also compared

patients undergoing VATS during SSRF and only SSRF, and found out that there were no significant differences between groups in terms of length of hospital and intensive care unit stay, length of operation, ventilator support, and mortality. They concluded that there was no additional risk or increased operative time with performing routine VATS at the time of SSRF.

In conclusion, routine VATS is not associated with increased operative time, length of stay, or mortality in patients undergoing SSRF. It may help detecting incidental traumatic findings. The diagnostic benefit of VATS in the diagnosis of acute TDI is greatest in patients with multiple rib fractures involving the lower chest wall, although there are no radiographic evidences of TDI. But more prospective multi-institutional studies with higher number of patients are needed to determine potential benefits of routine VATS approach in patients undergoing SSRF.

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 SBÜ Şişli Hamidiye Etfal Research and Training Hospital Clinical Research Ethical Committee (no: 4022, Date: 04/07/2023).

Authors' contribution

OD; conceptualized and designed the study, collected, analyzed and interpreted the patient data, wrote the paper, UT; collected the literature data, revised the final version of the manuscript, and co-wrote the paper. All authors read and approved the final manuscript.

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Original Article

VATS versus open thoracotomy in patients with spontaneous pneumothorax: where do we stand?

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ABSTRACT

Background: Spontaneous pneumothorax (SP) can be surgically treated with video-assisted thoracoscopic surgery (VATS) or conventional open thoracotomy (OT), but there are still controversies in the literature concerning the outcome of both procedures. We aim to compare VATS and OT in the treatment of SP, in perioperative and postoperative outcome, as well as to determine which procedure is more cost-effective for both the patients and the health care system.

Materials and Methods: Overall, 136 patients underwent surgery for SP at our institution, out of which 104 met the inclusion criteria of our study. Patients were further divided into two groups, consisting of 56 and 48 patients who underwent VATS and OT, respectively. Data were collected prospectively for 5 years and comparison of the perioperative and postoperative outcome, as well as cost-effectiveness of both procedures was performed.

Results: The VATS group was superior to the OT with shorter duration of surgery (87.77 vs 132.92 min.; $p < 0.05$), reduced length of hospital stay (7.28 vs 9.81 days; $p < 0.05$) and chest drain duration (4.84 vs 5.98 days; $p < 0.05$). There was no statistically significant difference in the recurrence rate, bleeding and postoperative complications. Average cost per patient for VATS was significantly lower than the cost for open thoracotomy (EUR 1504.93 vs EUR 1973.09; $p < 0.05$).

Conclusions: VATS can be implemented as the optimal approach in the treatment of SP given the current clinical, financial and cosmetic advantages. Like other minimally-invasive procedures, VATS has an associated learning curve which, once is surpassed, any complications are less likely to be prevalent and optimum results can be achieved.

Keywords: pneumothorax, thoracotomy, surgery, video-assisted

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Introduction

Pneumothorax ranks high on the list of common medical conditions, thus being a significant global health problem. It may be encountered by physicians in several clinical specialties and the spectrum of its severity may range from the self-limiting to the life-threatening.

Spontaneous pneumothorax (ST) can be classified as either primary (PSP) or secondary (SPS). Primary spontaneous pneumothorax has an estimated incidence of 18-28/100,000 cases per year for men, and 1.2-6/100,000 for women [1-3], while the incidence for SPS is 6.3 and 2 per 100,000 patients, for men and women, respectively. In terms of recurrence, the majority occurs within the first year, and incidence ranges widely from 25% to 50%. Notably, underlying chronic lung diseases, significantly contribute to recurrence [4]. Despite the global prevalence of pneumothorax, there is a noticeable gap in the literature regarding its epidemiology, incidence rate, and disease demographics in the Republic of North Macedonia.

Recent guidelines from the British Thoracic Society (BTS), published on August 8, 2023, underscore a nuanced approach to spontaneous pneumothorax management [5]. While endorsing conservative and ambulatory management for minimally symptomatic or asymptomatic primary spontaneous pneumothorax in adults, the BTS guidelines acknowledge the individualized nature of treatment decisions. Needle aspiration or tube drainage is recommended as initial interventions, with considerations for chemical pleurodesis in select cases. Thoracic surgery is advised as a consideration for the initial treatment in specific scenarios, such as tension pneumothorax or high-risk occupations. Nevertheless, the definitive treatment for spontaneous pneumothorax remains a subject of ongoing debate among thoracic surgeons, with numerous studies contributing to the discourse.

Our study aims to critically evaluate the effectiveness of video-assisted thoracoscopic surgery (VATS) and compare its outcomes with open thoracotomy, adding valuable insights to this dynamic field.

Materials and Methods

This prospective single-center clinical study was conducted for a five-year time period, between 2018 and 2022, at the University Clinic of Thoracic and Vascular surgery in Skopje, North Macedonia, after fulfilling Ethical Committee requirements (03-275, 26.05.2020)

and having written informed consent of the patients. During the time period previously mentioned, a total number of 136 patients were surgically treated for SP, of which 104 met the inclusion criteria and therefore were included in our study. All the surgeries were performed by the same surgical team. Patients were evaluated prior to surgery, as well as after. The timeline for follow-up in evaluation of the clinical data was 1 day post-surgery, the day before the discharge from the hospital and 3 months after the procedure, in order to check for late complications (recurrence).

Our study enrolled patients meeting specific inclusion criteria: individuals aged 18-80 experiencing the first episode of spontaneous pneumothorax (SP) with prolonged air leak or no re-expansion of the lung after non-surgical treatment, as well as those with secondary or recurrent episodes of SP. Conversely, exclusion criteria comprised individuals younger than 18 or older than 80 years, low ejection fraction (< 50%) indicative of cardiac impairment, and those who refused to participate in the study.

Upon meeting inclusion criteria, patients were thoughtfully stratified into two groups, Group A (patients who underwent VATS) and Group B (patients who underwent thoracotomy). For the stratification, several factors were considered such as pneumothorax size (smaller pneumothoraces were treated by VATS), pleural adhesions (in extensive adhesions, OT was preferred) and if the patient expressed a preference for a less invasive approach, VATS was considered (if applicable).

The decision-making process involved a comprehensive evaluation of each patient's unique circumstances, ensuring that the chosen intervention aligned with their clinical profile and personal preferences. This approach aimed to optimize patient outcomes and satisfaction. Subsequently, Group A consisted of 56 patients, and Group B of 48 patients.

Eligible patients with confirmed symptomatic spontaneous pneumothorax underwent comprehensive assessment, including baseline characteristics and symptoms. Comorbidities, such as hypertension and diabetes mellitus, were noted. Clinical evaluation pre- and post-surgery involved standard indicators. Laboratory findings were analyzed before and after the surgical procedure. Imaging techniques (chest radiography and CT) were employed pre-admission, one day before discharge, and three months post-surgery for definitive diagnosis and postoperative evaluation.

All patients underwent general anesthesia with double lumen intubation. Patients were placed on a lateral decubitus position, so that access to the affected hemithorax was provided. Specifically, for patients in Group A, a singular incision, not exceeding 5 cm, was strategically positioned for a port within the 5th intercostal space, complemented by an additional incision for a port in the 7th intercostal space along the mid-axillary line. In Group B, a standard posterolateral open thoracotomy was performed. Selective one lung ventilation was confirmed with the anesthesiologist. For Group A, the ensuing introduction of the thoracoscope facilitated access to the hemithorax, allowing for a detailed examination of the entire thoracic cavity. This visual inspection aimed to identify bullae, discern pleural adhesions, and reveal any associated pathology. Delicate manipulation of lung tissue ensued, utilizing atraumatic instruments, particularly forceps, to ensure precision and minimize tissue trauma. Bullae were subsequently excised using the EndoGia stapler. Thorough inspection was performed in patients from Group B, as well. The excision of abnormal lung tissue was facilitated with linear staplers, and smaller bullae were treated with electrocautery. Both groups underwent mechanical (abrasion) pleurodesis. Pleurectomy was performed in a small number of patients, the indication being recurrent pneumothorax or persistent air leak. Hemostasis was achieved, the pleural cavity was irrigated with warm saline, and a chest tube was inserted.

Statistical Analysis

In evaluating video-assisted thoracoscopic surgery (VATS) versus open thoracotomy (OT), a comprehensive analysis covered key demographic factors and side of pneumothorax. The examination extended to the perioperative and postoperative results. Additionally, assessment of overall costs for VATS and OT patients allowed for a thorough comparison of their cost-effectiveness. The ensuing results will be presented in tables to provide an overview of the comparative outcomes.

Patient data were analyzed using IBM SPSS Statistics 26.0 and expressed as mean $\pm$ SD for quantitative variables, and frequency and percentage for qualitative variables. Descriptive analysis included ratio coefficients, proportions, and cross-tabulations for attributive features. Numerical series were analyzed for central tendency (mean, median) and dispersion (SD, variance). Statistical tests, such as Pearson's chi-square and Fischer's exact tests, assessed associations. Normality and homogeneity checks employed Kolmogorov-Smirnov, Shapiro-Wilk, Levene, and Bartlett's tests. Parametric or non-parametric tests were chosen based on variable

homogeneity and normal/approximately normal distributions. Student's t-test compared means for homogeneous, normally distributed variables; Mann-Whitney test did so for non-parametric scenarios. Testing significance was set at $p < 0.05$, with results presented in figure and tables.

Results

Out of 104 patients surgically treated for SP at our center, 48 (46.20%) underwent open thoracotomy, while 56 (53.8%) underwent video assisted thoracoscopic surgery, as a minimally invasive technique (Figure 1). The mean age of the patients was 47 ± 17 and 45 ± 15 in Group A and Group B, respectively. Subsequently, with $p = 0.553$, there was no statistically significant difference.

For VATS, out of 56 patients, 44 (78.57%) were male and 12 (21.43%) were female. For OT, out of 48 patients, 40 (83.33%) were male and 8 (16.67%) were female. Therefore, the ratio for spontaneous pneumothorax in male to female patients is roughly 4:1, or SP is 4 times more common in men than women. Also, there was no statistically significant difference in the distribution of the variable 'gender' between the OT and VATS group ($p = 0.539$).

A great number of our patients had a history of cigarette smoking. Out of 104 patients included in the study, 55 (52.88%), or more than half, were smokers. In the VATS group, 28 patients out of 56 (26.92% of the total number of patients) had a positive smoking status. At the same time, in the OT group, 27 out of 48 patients (25.96% of the total number of patients) were also smokers, with no statistically significant difference between both groups ($p = 0.524$). 19 smokers in the VATS group had primary pneumothorax (67.86% of smokers in this group), while 15 smokers in the OT group experienced primary pneumothorax (55.56% of smokers in this group).

In the VATS group, out of 56 patients, 16 have HTA (15.38% of all patients evaluated), and 5 have DM (4.81% of all patients evaluated). In the OT group, or Group B, out of 48 patients, 13 have HTA (12.50% of all patients evaluated), and 5 have DM (4.81% of all patients evaluated) (Table 1).

In both groups, the right side of the hemithorax was more frequently affected. That is, out of 104 patients in total, 58 (55.77%) presented with a right-sided pneumothorax. This was established using the imaging methods; chest radiography and CT, preoperatively. Out of 56 patients in the VATS group, 33 (58.93%), presented with a right-sided SP, while 23 (41.07%), with a left-sided SP. When it comes to the 48 patients in the OT group, 25 of them (52.08%), had right-sided pneumothorax. Left-sided SP was noted in 23 (0.48%) patients. (Table 1).

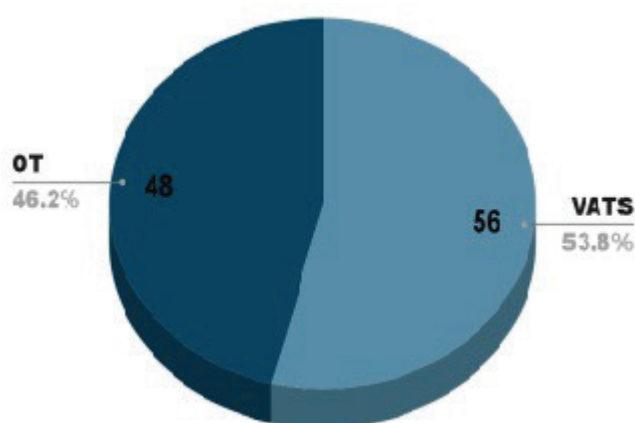


Figure 1. Distribution of patients according to type of surgery.

For patients who underwent open thoracotomy, the intervention lasted significantly longer (average of 132.92 minutes) than the intervention for patients who underwent video-assisted thoracoscopic surgery (average of 87.77 minutes). We observed intraoperative bleeding only in a small number of patients, which is 9 out of the total number of patients (for VATS and OT), or 8.65%. Out of these 9 patients, 3 underwent VATS and 6 open thoracotomy. There was no conversion to thoracotomy from VATS required in any of our cases.

The patients who underwent VATS, had a shorter length of hospital stay (statistically significant), when compared to those who underwent OT. The mean dura-

tion of hospital stay is directly related to the chest drain duration, with the patient being discharged the day following the removal of the chest drain. Therefore, there was also a statistically significant difference in the chest drain duration of both groups, in favor of patients who underwent VATS. The results are shown in table 2.

In terms of complications, we observed air leak, recurrence and ICU admissions. The total number of patients who presented with either one of the complications mentioned, was 23 or 22.12%. Out of 104 patients included in our study, 2 from the VATS group (3.57%) and 3 from the OT group (6.25%) presented with early recurrence of pneumothorax. Late recurrence was the case for 4 patients from the VATS group (7.14%) and 3 from the OT group (6.25%). Although the follow-up in this study was determined to be 3 months after the surgery, no limitation was placed on its duration when investigating for a recurrence and mainly because at our center, patients are referred back to our service if they develop a recurrent pneumothorax at any time following operative intervention. Air leak was also not very common and presented in 2 patients from the VATS group and 4 from the OT group (3.57% and 8.33%, respectively). Also, only 2 patients from the VATS and 3 from the OT group were admitted at the ICU. The results regarding complications following surgery, are also presented in table 2.

Table 1. Distribution of patients according to common comorbidities and side of pneumothorax.

	VATS	OT	Total	P value
Hypertension,	16	13	29	0.866
Diabetes mellitus	5	5	10	0.797
Right sided / left sided	33 (58.92%) / 23 (41.07%)	25 (52.08%) / 23 (47.92%)	58 (55.77%) / 46 (44.23%)	0.483

Table 2. Distribution of patients according to postoperative outcome and complications.

	VATS	OT
LOHS	7.38 ± 4.061(6.29 - 8.46)	9.81 ± 3.993(8.65 - 10.97)
Mean ± SD (95% CI)		
Min.-Max.	2 - 20	4 - 21
LOHS		
Chest drain duration in days	4.84 ± 2.749 (4.10 - 5.58)	5.98 ± 2.058 (5.38 - 6.58)
Mean ± SD (95% CI)		
Min.-Max.	2 - 14	3 - 15
Chest drain duration in days		
Early recurrence	2 (3.57%)	3 (6.25%)
Late recurrence	4 (7.14%)	3 (6.25%)
Air leak	2 (3.57%)	4 (8.33%)
ICU admission	2 (3.57%)	3 (6.25%)

Abbrev.; LOHS: length of hospital stay; ICU: intensive care unit

We estimated the total financial cost per patient for the surgical procedure itself, accompanied by the cost of the hospital stay, as well as the diagnosis and follow-up methods. The average cost (in MKD) per patient for video-assisted thoracoscopic surgical treatment for SP is EUR 1504.15, whereas the average cost for open thoracotomy is EUR 1972.27. The difference of EUR 468.12 is statistically significant, with p being 0.000 ($p < 0.05$).

Discussion

After it was established that there was no statistically significant difference in the demographic and clinical characteristics of the patients between the two groups, VATS and OT, we moved on to the comparison of the two surgical techniques in terms of the duration of surgery. In the current literature, the operating time was reported to be shorter for VATS, the same for both procedures or longer for VATS than for thoracotomy [6-8]. In our study, VATS lasted significantly shorter than OT.

When it comes to intraoperative complications, we observed bleeding (500-700 mL) in 8.65%, which is 3 of the patients who underwent VATS and 6 of those who underwent OT. Unfortunately, the specific vascular involvement or other details of the bleeding events were not delineated in our dataset. This also came in agreement with Laohathai et al [9] who reported that the operative time was longer and there was more blood loss in patients who underwent open thoracotomy. In addition, Vohra et al [10] and Lin et al [6] have demonstrated that VATS results in a shorter duration of surgery and less intraoperative blood loss than open thoracotomy.

There are different views on the postoperative outcome of VATS for the treatment of spontaneous pneumothorax. Although a great number of large studies state that the recurrence rate is higher with VATS [11,12], that was not the case in our study; on the contrary it was lower. This may be attributed to lesser trauma to lung tissue, which may contribute to enhanced tissue healing and a lower likelihood of recurrence. The patient selection criteria (our patients that underwent OT had more extensive pleural adhesions), could also play pivotal roles in the observed lower recurrence rates. We came to the same conclusion when comparing the air leak between both groups. In accordance with our results, several studies report a lower recurrence rate for patients that underwent VATS for the treatment of SP, two of which, providing long term date (up to 53 months). Unfortunately, we were not able to conduct a longer fol-

low-up and collect date for all of our patients, hence the parameter set to 3 months after surgery (in line with the median time to recurrence in a large propensity score analysis) [13]. Extending the follow-up duration for a subset of patients would risk introducing bias.

Often, recurrences are more frequent in patients in whom no blebs or bullae are identified [14]. Also, some evidence suggests that apical lung excision, even in the absence of visible lesion, may reduce SP recurrence [14]. Many authors believe that the recurrence rate is often associated with the surgeons' exposure to the procedure, meaning the efficiency in performing VATS improves over time. In regard to this theory, Waller emphasizes the importance of the learning curve in VATS procedures for pneumothorax [15]. He noted an inversely proportional relationship between recurrence rates and experience in his study population over a seven-year period. While our center has routinely performed video-assisted thoracoscopic surgery in recent years, it was not fully integrated at the inception of this study. Consequently, we anticipate enhanced outcomes over time and in subsequent research, aligning with the trajectory of improved proficiency in VATS procedures.

Our results also show a significantly shorter length of hospital for VATS, when compared to open thoracotomy (7 ± 4 and 9 ± 4 , for VATS and OT, respectively). We witness the same conclusion for the chest drain duration, ranging from 2 to 20 for VATS, and 4 to 21 days for OT. If the stay was prolonged it was mostly due complications and postoperative pain. The length of hospital stay was greatly dependent on the chest drain duration, with the patient being discharged the day following the chest drain removal. To remove the chest drain we considered several factors (criteria), through collecting postoperative data, which consisted of daily assessment of the drainage volume until there was 150-200ml or less (performed every morning), no obvious air leakage and complete re-expansion of the lung determined by chest X-ray. A similar study to ours including 100 consecutive patients [16] also reports a shorter length of hospital stay for VATS than OT, with an average of 3.2 and 12 days, respectively.

Finally, we analyzed the cost-effectiveness of video-assisted thoracoscopic surgery and open thoracotomy. We estimated the total financial cost per patient for the surgical procedure itself, accompanied by the cost of the hospital stay, as well as the diagnosis and follow-up methods. The average cost (in MKD) per patient

for video-assisted thoracoscopic surgical treatment for SP is EUR 1504.15, whereas the average cost for open thoracotomy is EUR 1972.27.

The difference of EUR 468.12 is statistically significant, with p being 0.000 ($p < 0.05$). Therefore, we conclude that the VATS procedure is more cost-effective, as it is significantly cheaper than the OT procedure. This is mainly because, as previously shown, patients that underwent VATS for the treatment of ST had a significantly shorter length of hospital stay, as well as less complications, plus the procedure lasted for a significantly shorter period of time. There are several study reports in accordance with our results [17,18].

One additional study by Fung S et al, conducted in 2021, analyzed the socioeconomic impact of recurrent primary spontaneous pneumothorax [19]. Initially, the primary treatment costs per patient, including hospitalization and surgical material in the VATS group, was higher (EUR 1.360) compared to the OT group (EUR 1.247), and mainly due to the higher cost of surgical materials for VATS (EUR 465 vs. EUR 77). However, due to the low rate of recurrence, overall cost for recurrence treatment was lower in the VATS group (EUR 5.412) than in the OT group (EUR 33.825). This disparity resulted in a considerably lower total management cost per patient in the VATS group (EUR 1.473) compared with the OT group (EUR 1.952), and later increased considerably after addition of the treatment cost for complications (VATS: EUR 1.501 vs. OT: EUR 2.233).

In conclusion, cost may vary according to the clinical center and country, but in our experience, VATS for the treatment of SP seems to be associated with reduced socioeconomic burden for both the patients and the healthcare system. Taking into consideration the other factors, especially the shorter duration of surgery and decreased length of hospital stay, VATS is more cost-effective and a better tolerated procedure for the treatment of spontaneous pneumothorax compared to the open thoracotomy.

Declaration of conflicting interests

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Ethics approval

The study was approved by University Clinic of Thoracic and Vascular surgery in Skopje, North Macedonia Ethical Committee (No: 03-275, Date: 26.05.2020).

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Authors' contribution

NJ; conceived and designed this study, RC,LA; contributed to data collection, analyses and interpretation, DD; contributed to interpretation and revision. All authors have read and approved the final manuscript.

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Original Article

Factors affecting clinical follow-up of patients who had extended resection due to non-small cell lung cancer with vertebral invasion

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ABSTRACT

Background: Chest wall involvement or vertebral invasion can be detected in 8-15% of patients with non-small cell lung cancer. We aimed to evaluate the surgical treatment outcomes and factors affecting overall survival (OS) in those patients who underwent en-bloc resection due to vertebral and chest wall invasion.

Materials and Methods: The study encompassed 15 patients with locally advanced non-small cell lung cancer who underwent anatomical lung resection and various vertebral and/or chest wall resections because of vertebral invasion at our institution between 2007 and 2019. Demographic, clinical, and pathological data of these patients were collected retrospectively and the effects of these factors on surgical outcomes and survival were evaluated.

Results: The mean age of the 15 patients was 59.1 ± 10.2 years. Among the patients, six had adenocarcinoma (40%), five had squamous cell carcinoma (33.3%), one had large cell neuroendocrine carcinoma (6.7%), two had a combination of large cell neuroendocrine and adenocarcinoma (13.3%), and one had pleomorphic cell carcinoma (6.7%). Simultaneous to lung resection, hemi-corpectomy in four patients (26.6%), total vertebrectomy in one patient (6.6%), partial corpectomy in three patients (20.0%), en-bloc transversectomy in five patients (33.3%), hemilaminectomy in two patients (13.3%) were performed. Two patients underwent only vertebra resection, while 13 patients underwent partial rib resection along with the vertebra. The median overall survival (OS) was 26.3 months (14.7-37.8). The postoperative survival rates were 93%, and 33% for 30-day, and 3-year respectively. When comparing OS among histopathological subgroups, no statistically significant difference was observed ($p = 0.473$). The median OS was 9.2 months for patients who underwent only vertebra resection, while it was 26.3 months for those who underwent vertebra and rib resection ($p = 0.534$). Other clinical features such as neoadjuvant treatment status, surgical margin positivity, and presence of recurrence did not exhibit a statistically significant impact on the patients' survival.

Conclusions: En-bloc resection is a treatment alternative that can be successfully applied in patients with primary lung malignancies together with vertebral invasion. Nonetheless, chemotherapy, radiotherapy, or immunotherapy is advised for disease management during the postoperative period.

Keywords: vertebral invasion, non-small cell lung cancer, extended resection

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Introduction

Eighty percent of all lung cancer cases are attributed to non-small cell lung cancer (NSCLC). Approximately 50% of these patients have metastasis. In 8-15% of cases, chest wall involvement (T3) or vertebral invasion (T4) can be detected. Vertebra surgery has been performed by neurosurgeons for many years with the logic of decompression surgery and was not aimed at oncological complete surgery. Special orthopedic spinal surgeons' focus on this field together with thoracic surgeons has led to more radical surgical interventions [1]. This study aimed to assess surgical treatment outcomes and the factors that impact overall survival (OS) in NSCLC patients who underwent en-bloc resection because of vertebral and chest wall invasion.

Materials and Methods

This study included 15 locally advanced patients diagnosed with T3-T4/N0/M0 lung cancer with chest wall and transverse process (T3) and vertebral (T4) invasion between 2007 and 2019 at our clinic. The patients did not exhibit mediastinal lymph node involvement or distant organ metastasis during their invasive staging, and therefore, they were classified as operable according to the International Association for the Study of Lung Cancer (IASLC) 2017 criteria. All surgeries were performed by the same spine and thoracic surgeon. The study excluded patients with distant metastatic involvement in the vertebra and chest wall. The primary objective of the study was to explore the prognostic impacts of resection type, histopathological type, and the utilization of neoadjuvant/adjuvant chemotherapy or radiotherapy on survival outcomes.

All patients underwent preoperative evaluation encompassing cardiac and pulmonary physical examinations, routine blood tests, chest X-rays, fiberoptic bronchoscopy (FOB), and pulmonary function tests (PFTs). In clinical staging, computerized tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) were utilized.

Patients with an FEV1 value above 1.5 liters were deemed appropriate candidates for lobectomy, whereas those with an FEV1 value above 2 liters were considered suitable for pneumonectomy. Patients with an FEV1 value falling within the range of 1.5 to 2 liters (equivalent to less than 80%) underwent a reevaluation that included additional tests such as carbon monoxide diffusing capacity measurement (DLCO), ventilation-perfusion scintigraphy, and cardiopulmonary exercise tests.

Patients with mediastinal lymph nodes that had a short axis longer than 1 cm on chest CT or showed suspicious FDG uptake on PET/CT underwent lymph node sampling and, to rule out metastasis, either endobronchial ultrasound (EBUS) or mediastinoscopy was performed. In each case, guided by neuromonitoring (Medtronic®), anatomical resection of the lung, vertebra, and/or chest wall was carried out through posterolateral thoracotomy or high posterior incision (Paulson-J incision) based on the lesion's location. Anatomical lung resection was performed first in all cases, followed by surgical intervention directed at the vertebra to achieve complete resection. The ethics committee of Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital (CREC 2022/22-44) approved the protocol for the current study. All patients gave written informed consent for surgical treatment and were aware that all information could be used anonymously for scientific purposes only.

Statistical Analyses

Statistical analyses were conducted using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). In descriptive statistics, continuous variables were represented as mean $\pm$ standard deviation, while categorical variables were presented as counts and percentages. Survival analysis was performed using the Kaplan-Meier method and assessed using the log-rank test. Survival times were presented along with the median and 95% confidence intervals (CI). Statistical significance was determined as $p < 0.05$ in all tests.

Results

The average age of the 15 patients, consisting of 12 males and 3 females, was determined to be 59.1 ± 10.2 years. The mean tumor diameter was 46.4 ± 20.7 mm. Among the patients, six had adenocarcinoma (40%), five had squamous cell carcinoma (33.3%), one had large cell neuroendocrine carcinoma (6.7%), two had a combination of large cell neuroendocrine and adenocarcinoma (13.3%), and one had pleomorphic cell carcinoma (6.7%) (Table 1).

The postoperative pathological stages were as follows: T3N0 (Stage 2B) for five patients, T4N0 (Stage 3A) for seven patients, T4N1 (Stage 3A) for two patients, and TxN0 for one patient. The patient who underwent PTx had received a diagnosis of adenocarcinoma (T4N0M0) and had regressed to T3N0 after neoadjuvant chemo-radiotherapy, followed by resection. The final pathology report did not reveal any viable tumor tissue.

Among the patients with T4N1, one had tumor tissue detected in a hilar lymph node, which was not observed in the preoperative evaluation, as there was no FDG uptake in mediastinal tissues on the patient's PET/CT scan. Additionally, due to the lymph node's size being larger than 1 cm, it was evaluated with EBUS, and no tumor tissue was found. In the case of another patient with T4N1, the lymph node containing the observed tumor was surgically removed from the lobectomy material.

In 4 cases, a posterolateral thoracotomy was conducted, while a Paulson incision was performed in 11 patients. The most important indication for making a Poulson incision is the proximity of the lesion to the superior sulcus structures and the depth of invasion. Therefore, it is not a certain level of elevation that determines the shape of the incision, but the depth of invasion. Among the surgical procedures, right upper lobectomy was carried out in 10 cases, left upper lobectomy in three cases, left pneumonectomy in one case, and left lower lobe superior segmentectomy in one case. Besides lung resection, hemi corpectomy in four patients (26.6%), total vertebrectomy in one patient (6.6%), partial corpectomy in three patients (20%), en-bloc trans-

versectomy in five patients (33.3%), hemilaminectomy in two patients (13.3%) were performed. All patients were preoperatively scored for spinal instability using the Neoplastic Spinal Instability Score (SINS), with an average SINS score of 4.93. Furthermore, to achieve complete resection because of local invasion, partial rib excision was conducted in 13 cases. The average number of ribs removed was 3.2 (ranging from 1 to 5 ribs). Instrumentation was applied to include one healthy vertebra below and above in 6 patients. Two patients underwent only vertebra resection, while 13 patients underwent partial rib resection along with the vertebra (Table 1). In the postoperative period, one patient experienced prolonged air leakage, another had cerebrospinal fluid leakage, and one patient developed pneumonia. None of the patients experienced neurological damage. The diagnosis of CSF leaks is usually made by looking at the color of the incoming fluid. Because the examinations to be performed are far from practical and open to complications. The discharge of white fluid in a patient whose drainage is interrupted is considered a void leak, and it usually disappears spontaneously. In our case, it also resolved spontaneously.

Table 1. Demographic and clinical characteristics.

Age (years) mean±sd (min-max)	59.1±10.2 (43.0-78.0)
Gender n (%)	
Male	13 (86.7)
Female	2 (13.3)
Histopathology n (%)	
Adenocarcinoma	6 (40.0)
Squamous cell carcinoma	5 (33.3)
Large cell neuroendocrine carcinoma	1 (6.7)
Pleomorphic cell carcinoma	1 (6.7)
Combined large cell + adenocarcinoma	2 (13.3)
Stage at diagnosis n (%)	
T3N0	4 (26.7)
T4N0	11 (73.3)
Neoadjuvant therapy n (%)	6 (40.0)
Tumor size (mm) mean±sd (min-max)	46.4±20.7 (15.0-100.0)
Incision n (%)	
Posterolateral thoracotomy	4 (26.7)
Paulson	11 (73.3)
Resection n (%)	
Vertebral resection	2 (13.3)
Vertebra + chest wall resection	13 (86.7)
Surgical margin n (%)	
Positive	7 (46.7)
Negative	8 (53.3)
Recurrence n (%)	4 (26.7)
3-year survival n (%)	5 (33.3)
Postoperative mortality (30-day) rate (%)	93
Follow-up time (month) mean±sd (min-max)	31.3±31.4 (0.9-126.5)

Preoperatively, neoadjuvant treatment was administered to six patients, with only chemotherapy (CT) given to two patients and chemotherapy combined with radiation therapy (CRT) given to four patients. Additionally, 14 patients received adjuvant treatment, with CT alone given to three patients and CRT given to 11 patients. The only patient who did not receive adjuvant treatment had postoperative pathology reported as pTx. Among the patients, 4 (26.6%) experienced recurrence, with brain metastasis occurring in two cases, lumbar vertebral metastasis in one case, and contralateral lung and rib metastasis in one case (Table 1). Among the cases with recurrence, three had the histological subtype of adenocarcinoma, and one had a combination of large cell neuroendocrine carcinoma and adenocarcinoma. One of the recurrent patients (Tx) did not receive adjuvant treatment, while the other two did not receive neoadjuvant treatment.

The median OS was 26.3 months (95% CI, 14.7-37.8). The postoperative survival rates at different time intervals were 93%, 33% for 30-day, and 3-year respectively. Among the surviving patients, one had undergone right upper lobectomy, partial resection of the 3rd rib, and T3 transversectomy, with a pathological report indicating T4N1 adenocarcinoma. The other patient had undergone left upper lobectomy, partial resection of the

2nd, 3rd, and 4th ribs, and T3 total vertebrectomy, with a pathological report indicating T3N0 combination of large cell neuroendocrine and adenocarcinoma.

When comparing OS among histopathological subgroups, no statistically significant difference was found ($p = 0.473$). The median OS for each subgroup was as follows: 26.3 months for adenocarcinoma, 15.7 months for squamous cell carcinoma, 4.6 months for large cell neuroendocrine carcinoma, 31.1 months for pleomorphic cell carcinoma, and 58.3 months for the combination of large cell neuroendocrine and adenocarcinoma (Table 2). Out of the 6 patients who received neoadjuvant treatment, 5 (83%) were assessed as T4 in the preoperative evaluation, while 1 (16%) was T3. The median overall survival (OS) was calculated as 22.0 months. Among the 9 patients who did not receive neoadjuvant treatment, 6 (67%) were evaluated as T4 in the preoperative assessment, while 3 (33%) were T3, and the median OS was 31.1 months ($p = 0.307$) (Table 2). Regarding the surgical approach, the median OS was 9.2 months for patients who underwent only vertebra resection, while it was 26.3 months for those who underwent vertebra and rib resection ($p = 0.534$) (Table 2). The comparison of OS based on clinical and pathological characteristics of the patients is presented in table 2.

Table 2. Overall survival analyses of patients according to clinical and pathological characteristics.

	Overall survival (months) 95% CI	P value (Log Rank test)
Histopathology		0.473
Adenocarcinoma	26.3 (15.3-37.2)	
Squamous cell carcinoma	15.7 (0.0-42.3)	
Large cell neuroendocrine carcinoma	4.6 (-)	
Pleomorphic cell carcinoma	31.1 (-)	
Combined large cell + adenocarcinoma	58.3 (-)	
Stage at diagnosis		0.637
T3N0	15.6 (0.0-51.7)	
T4N0	26.3 (16.4-36.2)	
Neoadjuvant therapy		0.307
Yes	22.0 (0.0-48.0)	
No	31.1 (0.0-70.1)	
Resection		0.534
Vertebra	9.2 (-)	
Vertebra+chest wall	26.3 (14.7-37.8)	
Surgical margin		0.153
Positive	22.0 (0.0-66.7)	
Negative	26.3 (7.7-44.8)	
Recurrence		0.462
Yes	17.7 (0.0-38.9)	
No	26.8 (10.1-43.6)	



Figure 1. Preoperative MRI image of en bloc resection and lung carcinoma with vertebral invasion (a), intraoperative image after anterior hemi corpectomy (b), hemicorpectomy with instrumentation placement (c).

Discussion

In patients diagnosed with NSCLC, over 50% are initially found to have distant organ metastasis at the time of diagnosis, whereas only around 15% are confined to the primary site. The axial skeleton is one of the regions where bone metastases are frequently faced with its rich venous webwork clearing out lung, pelvis, and thorax. Several studies have reported vertebral invasion in approximately 8-15% of lung cancer cases [1]. Invasion of the vertebra can occur through direct adjacency or via the Batson plexus hematogenously [2,3]. Vertebral invasion is viewed as a locally advanced stage and is associated with a poor prognosis; however, it is not regarded as an indicator of inoperability. Advances in surgical equipment and the availability of multidisciplinary surgical approaches with spine surgeons have increased the chances of surgical treatment [4]. Nevertheless, metastatic vertebral involvement should be accepted as a systemic disease, and surgery should not be aspired.

On a standard X-ray (direct radiograph), metastatic lesions in the vertebrae from lung cancer are typically observed as lytic lesions. However, it has been noted that for these lesions to become visible on direct radiographs, invasion of nearly 50% of the vertebral body is usually required. For that reason, when there is suspicion of vertebral metastasis, additional imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) is suggested. CT may offer information about the localization and number of metastases; however, it may not always clearly distinguish between infectious and tumoral lesions. Therefore, the combination of CT with radionuclide scanning techniques is recommended [2]. On the other hand, magnetic resonance imaging (MRI) allows for a more detailed evaluation of the relationship and boundaries of the mass with surrounding tissues so provides a clearer picture of the lesion's adjacency and extent.

When evaluating NSCLC by their subtypes, it has been reported that squamous cell carcinoma is the subtype that most frequently invades the vertebrae and has the most aggressive course. It often leads to massive vertebral destruction. Surgery is typically performed as a salvage procedure with a focus on preserving movement and neurological function. In the case of small cell carcinomas, radiotherapy is prioritized due to the tumor's radiosensitivity, and surgery does not have a role [3]. In our study, although the squamous cell carcinoma's median OS was found to be shorter than that of adenocarcinomas, no statistically significant difference was observed among histopathological subgroups. The limited patient population in the study may have hindered the statistical significance of this difference from being reflected in the results.

SINS criteria are the initial evidence-driven guidelines for evaluating instability in spinal metastases, and if the score is 7 or higher, the patient is recommended to be evaluated for surgery [5]. In our cases, the average SINS score was 4.93. Only one patient had vertebral corpus involvement of more than 50%, while in the remaining cases, it was less than 50%. In addition, in the classification of NSCLC according to IASLC 8th edition, T3 is considered as chest wall invasion and T4 is considered as vertebral invasion. There is no specific T classification for isolated transverse process involvement of the vertebra; it is generally considered as T3 [6]. The ribs articulate with the vertebrae through the tuberculum costae to the transverse process and through the costal head to the vertebral corpus. In this study, the involvement of the ribs that included both articulations were classified as T3, and complete removal was interpreted as unblock transversectomy.

Postoperative complications can vary and may include pulmonary complications such as pneumonia, prolonged air leakage, bronchopleural fistula, empyema, chylothorax, hemothorax, surgical site infection, and respiratory failure. Additionally, according to the vertebra resection applied there can be neurological complications such as medulla spinalis injury and neurological sequelae, cerebrospinal fluid leakage, and in cases of superior sulcus tumors, Horner syndrome [7-9]. In our study, three cases experienced pneumonia, prolonged air leakage, and cerebrospinal fluid leakage as complications.

Due to the observed correlation between resection type and prognosis, it is recommended to perform the broadest possible resection and en-bloc excision. A favorable impact is observed on survival in NSCLC with vertebral invasion when complete resection is achieved [8,10]. For cases of NSCLC with vertebral invasion 5-year survival rate of 65% have been reported following complete resection [9]. In our research, the 1-year and 3-year survival rates were 53% and 33% respectively.

In this study, performing chest wall resection along with vertebrae resection prolonged the median OS of the patients compared to patients who underwent only vertebral resection, but there was no statistically significant difference between the groups. The reason why no statistical difference could be demonstrated may be the limited number of patients in this study. However, this result may be a guide for future studies that will be better planned.

Surgical approaches may involve either the Paulson incision or thoracotomy. In the Paulson incision, an incision is made along the line between the posterior edge of the scapula and spinal processes and can extend up to the upper border of the scapula or even to the level of C7. This approach provides visibility of the vertebra, thoracic nerves, posterior chest wall, transverse processes, and brachial plexus roots [11]. In our cases, 4 patients underwent posterolateral thoracotomy, while 11 patients received the Paulson incision.

Koizumi et al [8] have recommended total vertebrectomy when more than 50% of the vertebra is destroyed due to apical chest tumors. For cases with less than 30% involvement, partial vertebrectomy can be considered, but defining clear surgical margins with partial tumor resection can be challenging. Therefore, several studies have suggested that combining complete resection ensuring surgical margin safety with preoperative or postoperative chemoradiotherapy reduces the local recurrence rate and achieves extended survival in patients receiving neoadjuvant or adjuvant treatment [8,9]. However, it's worth noting that neoadjuvant chemoradiotherapy can lead to an increase in tumor invasion depth during the treatment period and may result in the progression of neurological symptoms related to local invasion. Additionally, preoperative radiotherapy has been suggested to potentially reduce bone density and may pose stabilization concerns in post-resection bone instrumentation procedures [4,9]. For this reason, in our cases, we targeted adjuvant radiotherapy rather than preoperative radiotherapy.

The main limitation of our retrospectively designed study is the small number of patients since this surgical method is performed rarely and requires a multidisciplinary approach. Nevertheless, it provides preliminary findings that may guide prospective studies planned with a larger patient population in the future.

In conclusion, patients with primary lung malignancies associated with vertebral invasion have the opportunity for successful surgical intervention through en-bloc resection while preserving safe surgical margins. However, in the postoperative period, chemotherapy, radiotherapy, or immunotherapy is recommended to achieve the control of disease and enhance treatment effectiveness.

Declaration of conflicting interests

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Ethics approval

The study was approved by Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital Ethical Committee (CREC 2022/22-44).

Authors' contribution

BAS,AS; conceived and designed this study, BAS,FM; made the analysis of data, FIU,UAD; made the creation of new software used in the work, VK,OA; have drafted the work, BAS,AS contributed to interpretation and revision. All authors have read and approved the final manuscript.

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Original Article

Tracheobronchial surgical interventions

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ABSTRACT

Background: Surgical treatment is almost always necessary for lesions that cause stenosis or obstruction of the tracheobronchial system. Sleeve resection is a surgical method that ensures airway continuity and reduces the loss of lung tissue by creating a primary anastomosis following the resection of the affected segment.

Materials and Methods: In this study, 65 patients who underwent tracheobronchial sleeve resection and bronchoplasty at the Ankara Atatürk Sanatorium Training and Research Hospital between 1974 and 1997 were retrospectively evaluated. Patient data were obtained from medical records and surgical reports, and compared with the previous studies.

Results: Of the 65 patients, 34 were male and 31 were female (mean age, 32.56 years; range, 5–65 years). Tracheal resection and reconstruction were performed in 25 patients because of stenosis and neoplasm, whereas bronchial sleeve resection and bronchoplasty were performed in 40 patients because of benign neoplasm, bronchial adenoma, bronchial carcinoma, endobronchial foreign body, and bronchial rupture.

Conclusions: Resection of a small bronchial segment instead of pneumonectomy offers a curative treatment alternative for centrally localized, benign endobronchial lesions with low malignancy potential. In bronchial carcinomas, the results obtained from the complete removal of tumor tissue with sleeve lobectomy in a selected group of patients have shown that this surgical method may be an alternative to pneumonectomy. In patients with bronchial cancer, pneumonectomy should not be performed if sleeve lobectomy is possible. The high postoperative quality of life and low mortality and morbidity emphasize the superiority of this surgical method over pneumonectomy.

Keywords: pneumonectomy, bronchial anastomosis, bronchoplasty

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Introduction

The continuity of the trachea and the bronchial tree is vital for survival. The disruption of continuity due to lesions or traumatic rupture within the respiratory transmission system, which is responsible for air conduction, leads to respiratory insufficiency.

Surgical treatment is almost always necessary for lesions that cause stenosis or obstruction of the tracheobronchial system. Sleeve resection is a surgical method that ensures airway continuity and reduces the loss of lung tissue by creating a primary anastomosis following the resection of the affected segment. In 1947, Price Thomas performed the first bronchoplasty on a patient with an adenoma in the right main bronchus and no alternative to pneumonectomy. Thomas performed sleeve resection and primary bronchial anastomosis because the patient was a pilot by profession [1].

With this method, surgical treatment options can be provided to patients considered inoperable because of limited respiratory function, while preserving maximum lung tissue.

Materials and Methods

In this study, 65 patients who underwent tracheobronchial sleeve resection and bronchoplasty at the Ankara Atatürk Sanatoryum Training and Research Hospital between 1974 and 1997 were retrospectively evaluated. Patient data were obtained from medical records and surgical reports, and compared with the previous studies. Our study was carried out following the ethical principles determined by the 1964 Helsinki Declaration and subsequent amendments. Ethical approval for this study was obtained from a relevant institute (1/18, 27.02.2012 Ankara Atatürk Sanatorium Training and Research Hospital).

Statistical Analyses

Statistical analyses were performed using the SPSS version 15 package program. The variables were analyzed using visual (e.g., histograms and probability plots) analytical methods (Kolmogorov-Smirnov test) to determine whether they showed normal distribution. Descriptive analyses were presented as means for normally distributed variables and as medians and interquartile ranges for nonnormally distributed and ordinal variables.

Results

Of the 65 patients, 34 were male and 31 were female (mean age, 32.56 years; range, 5–65 years). Tracheal resection and reconstruction were performed in 25 patients because of stenosis and neoplasm, whereas bronchial

sleeve resection and bronchoplasty were performed in 40 patients because of benign neoplasm, bronchial adenoma, bronchial carcinoma, endobronchial foreign body, and bronchial rupture (Table 1).

Patients were referred based on the underlying pathology, with the most common complaint identified as shortness of breath (Table 2).

Two patients with tracheal tumors were treated with a preliminary diagnosis of asthma for two years before presenting to our clinic.

The most common finding on physical examination was decreased respiratory sounds. Subcutaneous emphysema was observed in 2, 5, and 1 patient with penetrating tracheal injury, traumatic rupture, and tracheal tumor, respectively. Clubbing was identified in 13 patients and flail chest was detected in 2 patients with bronchial rupture. Patients were initially evaluated using posteroanterior and lateral chest X-rays (Table 3).

Table 1. Indications for tracheobronchial sleeve resection and bronchoplasty.

Indication	n
Tracheal stenosis	8
Tracheal neoplasm	14
Bronchial neoplasm	24
Bronchial rupture	12
Endobronchial foreign body	5
Penetrating tracheal injury	2
Total	65

Table 2. Patients' complaints.

Tracheal neoplasm (n=25) and stenosis		Bronchial cancer (n=8)	
Shortness of breath	25	Cough	8
Cough	23	Side pain	4
Bloody sputum	5	Bloody sputum	2
Hoarseness	5	Sputum	6
Wheezing	3	Shortness of breath	2
		Fire	1
Bronchial adenoma (n=15) and benign lesions		Bronchial rupture (n=12)	
Cough	15	Shortness of breath	12
Side pain	9	Side pain	12
Fever	10	Endobronchial foreign body (n=5)	
Sputum	12	Cough	5
Bloody sputum	5	Sputum	2
Shortness of breath	5	Fever	2

Table 3. Radiological findings of the patients (findings detected on chest X-rays).

Tracheal neoplasm and stenosis	(n=25)	Bronchial cancer	(n=8)
Normal	20	Atelectasis	4
Pneumomediastinum	1	Apical mass	2
Upper mediastinal enlargement	4	Mass in the lower zone	1
		Normal	1
Bronchial adenoma and benign lesions	(n=15)	Bronchial rupture	(n=12)
Pneumonia	8	Pneumothorax	8
Atelectasis	6	Hemopneumothorax	4
Normal		Rib fracture	3
Endobronchial foreign body	(n=5)	Subcutaneous emphysema	
Normal	3		
Pneumonia + atelectasis	2		

After chest X-rays, advanced diagnostic methods were applied to patients based on the etiological causes. All patients underwent preoperative bronchoscopy. Patients with tracheal neoplasm or stenosis underwent tracheal laminography, and in one case, an MRI was performed. All patients underwent thoracic computed tomography (CT) scans, except those with acute trauma and endobronchial foreign bodies. After establishing a definitive diagnosis, treatment was performed using surgical methods (Table 4).

Twelve patients who underwent sleeve lobectomy had the most common lesion localization in the right upper lobe (Table 5).

Furthermore, in 12 patients who underwent sleeve resection without lobectomy, the most common sites of involvement were the main and intermediate bronchi (Table 6).

All 8 patients who underwent surgery for bronchial carcinoma had a preoperative histopathological diagnosis. A preoperative histopathological diagnosis was established in 8 of 14 patients (57%) with carcinoid tumors. The histopathological diagnoses are listed in table 7.

Table 4. Surgical methods applied to patients.

	n	%
Tracheal resection and reconstruction	23	35
Primary tracheal anastomosis	2	3
Sleeve lobectomy	12	18
Sleeve resection + cranioplasty	3	5
Bronchotomy + primary anastomosis	3	5
Sleeve resection (without lobectomy)	22	34
Total	65	

Table 5. Lesion localization in patients undergoing sleeve lobectomy.

	n	%
Right upper lobe	7	58
Left upper lobe	2	17
Middle lobe bronchus	2	17
Right lower lobe bronchus	1	8

Table 6. Lesion localization in patients undergoing sleeve resection without lobectomy and bronchotomy + mass excision.

	n	%
Right main bronchus	10	45
Left main bronchus	8	36
Bronchus intermedius	2	9
Left lower lobe bronchus	1	5
Right lower lobe bronchus	1	5

Table 7. Histopathological diagnoses of patients undergoing sleeve resection for tracheal and bronchial neoplasms.

	n
Tracheal Neoplasms	Adenocystic carcinoma
	8
	Epidermoid carcinoma
	1
	Mucoepidermoid carcinoma
	1
Secondary tumors	Invasive fibrous tumor of the trachea
	1
	Plasma cell granuloma
Bronchial neoplasms	1
	Thyroid follicular carcinoma
	1
	Thyroid papillary carcinoma
	1
	Carcinoid tumor
	14
Bronchial neoplasms	Epidermoid carcinoma
	5
	Adenocarcinoma
	2
Bronchial neoplasms	Mucoepidermoid carcinoma
	1
Bronchial neoplasms	Endobronchial hamartoma
	1

Among patients who underwent tracheal surgery, 11 underwent cervical incision, 11 underwent right thoracotomy, and 3 underwent median sternotomy. End-to-end anastomosis was performed in all patients who underwent resection.

Standard posterolateral thoracotomy was performed in all patients who underwent bronchial sleeve resection. The postoperative hospital stay for tracheobronchial sleeve resection was 28 days (7–58 days). Complications occurred in 26.2% (n = 17) of the 65 operated patients. All patients underwent postoperative bronchoscopy performed during follow-up (Table 8).

Table 8. Postoperative complications.

	n	%
Atelectasis	14	22
Wound infection	4	6
Postoperative empyema	2	3
Osteomyelitis	1	2
Tracheoesophageal fistula	1	2
Granulation at the anastomosis line	2	4
Vocal cord paralysis	2	4
Total	26	43

A patient with bronchial carcinoma died on postoperative day 7 because of massive hemoptysis. The mortality rate was 8% in patients who underwent tracheal resection. One patient who underwent tracheal resection died because of postoperative cardiac arrest, and another patient died because of bleeding. Granulation tissue developed at the anastomotic site in two patients and was cleared bronchoscopically. One patient developed tracheoesophageal fistula in the third postoperative month. Reoperation was performed. Two patients developed left vocal cord paralysis.

Two of our patients with traumatic bronchial rupture underwent thoracomyoplasty because of postoperative empyema. In one patient with a right main bronchial rupture, osteomyelitis developed in postoperative month 4, and vertebral resection was performed. Local recurrence or distant metastasis was not observed in any patient with carcinoid tumors.

Discussion

The bronchoplastic technique and sleeve resection, first described by Paulson et al [2], is a conservative surgical method that minimizes the loss of healthy lung tissue. The aim of this study was to preserve normal lung tissue and respiratory function. Resection of a small bronchial segment instead of pneumonectomy offers a curative treatment alternative for centrally localized, benign endobronchial lesions with low malignancy potential. In bronchial carcinomas, the results obtained from the complete removal of tumor tissue with sleeve lobectomy in a selected group of patients have shown that this surgical method may be an alternative to pneumonectomy [3-12,13]. Frist et al [14] reported that the 5-year survival rates in patients with bronchial carcinoma undergoing sleeve lobectomy were as follows: Stage 1, 58% + 25%; Stage 2, 69% ± 18%; and Stage 3, 38% ± 13%. Weisel et al compared the outcomes of sleeve lobectomy in 70 patients (27 patients due to reduced

pulmonary reserve, 43 patients as elective surgery) with the outcomes of pneumonectomy performed in an equal number of patients during the same period and reported no significant difference in the 5-year survival rate between the two groups [14].

There are different ideas regarding the application of preoperative radiotherapy to make surgery more suitable in malignant cases. Jensic et al [15] recommended preoperative radiotherapy followed by sleeve lobectomy after 4–6 weeks. In a sleeve lobectomy series of 115 patients, 62 patients underwent surgery after preoperative radiotherapy of 4,000 rad, with a 5-year survival rate of 33%. Frist et al [14], Lowe et al [16], and Weissberg [17] stated that preoperative radiotherapy poses a risk for anastomosis and contraindicates sleeve resection if there is mediastinal lymph node metastasis. In a study conducted by Jensic [5], the 5-year survival rate was 36% in patients without lymph node metastasis (–), 9.5% in patients with lymph node metastasis (+), and the recurrence rate was 10%. In our study, inadequate pulmonary reserve and localization of the lesion constituted the indication for sleeve resection in patients with bronchial cancer, and none of our patients received preoperative radiotherapy.

For benign endobronchial lesions or those with a low potential for malignancy, sleeve resection is the best surgical method to preserve the distal lung tissue. Patients who may be candidates for sleeve resection should be preoperatively evaluated with bronchoscopy to identify the localization of the lesion and histopathological diagnosis. In malignant cases, CT and positron emission tomography should be used to identify mediastinal and hilar lymph nodes. With appropriate indication and surgical methods, mortality and morbidity are low and the outcomes are excellent. The 5-year survival rate is reported to be between 86% and 100% in various series [16,18]. In this study, 8 (53.3%) of 15 patients who underwent sleeve resection and bronchotomy along with primary anastomosis for benign endobronchial lesions and bronchial adenomas were asymptomatic.

In cases where surgery is indicated for bronchial rupture, the prevailing idea is to perform bronchial anastomosis within the first 24–48 hours [15,19–25]. Therefore, promptly diagnosing the rupture and initiating treatment is crucial. Successful outcomes have been reported with bronchoplastic methods applied in the late period for patients in whom the diagnosis of bron-

chial rupture could not be established early. Nonoyama et al reported a case in which he performed primary bronchial anastomosis for left main bronchial rupture, achieving full expansion of the lung after 9 years [26].

The most common complication after surgery is atelectasis; therefore, respiratory physiotherapy and bronchial hygiene should be carefully monitored. On the first and second days, bronchoscopy is recommended for aspiration and anastomosis control [4,10], whereas some surgeons prefer to avoid bronchoscopy as much as possible [9]. Bronchoscopic control after administering low-dose corticosteroids for 5-8 days to control edema and secretions was recommended [27].

Other complications observed in bronchial sleeve resections include anastomotic insufficiency, stenosis at the anastomotic site, and bronchopleural and bronchovascular fistulas. The routine practice for securing the integrity of the anastomotic site is to wrap it with a pleural or pericardial flap [3,4,9,14,16,28,29]. In this study, we did not observe complications such as anastomotic insufficiency or stenosis at the anastomotic site; however, tracheoesophageal fistula developed in one patient, requiring surgical intervention. Therefore, we evaluated the points to be considered in terms of surgical technique in bronchial sleeve resections based on our experience.

Careful incision and opening of the mediastinal pleura facilitate closure of the anastomosis. Particularly, the meticulous dissection and removal of the peribronchial and surrounding lymph nodes allow for the easy execution of bronchial resection and anastomosis. Before performing bronchial resection, a sling suture should be placed in the anatomical plane proximal and distal to the lesion. These sutures assist in aligning the bronchi in the same plane during anastomosis. After bronchial resection, both the removed segment and the remaining ends should be inspected for lesions, and if necessary, further resection should be performed. The secretion in the distal bronchus should be aspirated with a thin probe, and it must be ensured that no secretion remains. Especially in bronchial adenomas, the thick and viscous distal mucus that has been obstructed for a long time should be aspirated repeatedly with gentle massaging of the lung. Anastomosis should be performed in the same plane, and the sutures of the posterior wall should have knots outside the lumen. There should be no difficulty in resuturing for air leakage from the back. After completion

of the anastomosis, air leakage should be checked using normal saline. The lung should be expanded, and the anatomical condition of the bronchi should be evaluated. Similarly, the pulmonary artery should be examined for any twisting or bending in the lobular expansion position. The mediastinal pleura should be brought over the anastomosis and sutured loosely to allow for air and fluid leakage.

Although the first bronchial sleeve resection was performed in 1947, tracheal resection and reconstruction were rarely reported till the 1960s.

Initially, it was proclaimed that resecting more than two or three tracheal rings would be unsafe. However, in 1970, Grillo successfully performed primary anastomosis after resecting 50% of the trachea [30,31].

The most common indications for tracheal resection and reconstruction are intubation-related strictures, neoplasms and traumas, and rarely tracheomalacia, acquired tracheoesophageal fistula, and congenital anomalies [31]. It provides an excellent chance of cure for benign tumors and tumors with low malignancy potential and a high chance of palliation and cure in squamous cell carcinoma and adenoid cystic carcinoma along with radiotherapy.

In 1990, Grillo reported an operative mortality rate of 5% in 132 patients who underwent tracheal resection and reconstruction for tracheal tumors [32]. In this study, tracheal resection and reconstruction were performed in 9 and 14 patients because of stenosis and neoplasms, respectively. Two patients died during the postoperative period, with the cause of death being innominate vein bleeding in one patient and cardiac arrest in another. Stenosis occurred in the anastomotic line in 2 of the other 23 patients. One of these patients underwent endobronchial stent placement. In one patient operated for adenoid cystic carcinoma, recurrence was observed 5 years later, and endoscopic excision was performed, whereas seven patients are still asymptomatic.

Silk was previously used for anastomosis in tracheal and bronchial resections. When it was observed that silk knots penetrated into the bronchus and formed granulation tissue, the use of absorbable suture materials was attempted. Currently, the technique of anastomosis with synthetic absorbable suture material, with knots left outside using individual sutures, is widely accepted [3,4,9,12,14,33]. In the literature, especially in series

focusing on bronchial rupture, polypropylene has been commonly used for anastomosis [19,24,25,34]. Some doctors even recommend continuous suture technique with polypropylene for anastomosis (25,34). In this study, a synthetic absorbable suture material (polyglactin 910) was used for anastomosis in 90% of the patients.

To conclude, patients with obstructive lesions or ruptures in the trachea and large bronchi should be thoroughly examined clinically, radiologically, and endoscopically. After definitive diagnosis, primary anastomosis should be considered first following tracheal lesion resection. In benign and low-grade malignant endobronchial lesions, the primary goal should be to preserve healthy lung tissue along with lesion resection. In bronchial ruptures, the possibility of elective bronchoplasty should be considered after stabilizing the patient's vital signs and other systemic indicators. In patients with bronchial cancer, pneumonectomy should not be performed if sleeve lobectomy is possible. The high postoperative quality of life and low mortality and morbidity emphasize the superiority of this surgical method over pneumonectomy.

Declaration of conflicting interests

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Ethics approval

The study was approved by Ankara Atatürk Sanatorium Training and Research Hospital Ethical Committee (No: 1/18, 27.02.201)

Authors' contribution

DBK; conceptualized and designed the study, collected, analyzed and interpreted the patient data, wrote the paper, SŞEG; collected the literature data, revised the final version of the manuscript, and co-wrote the paper. All authors read and approved the final manuscript.

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Original Article

Is the double edge closure technique effective against post-thoracotomy pain in the long term?

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ABSTRACT

Background: In this study, we aimed to evaluate the long-term pain and quality of life of patients following the pericostal closure (PC) and double edge closure (EC) techniques.

Materials and Methods: This prospective study was conducted between April 2019 and January 2021 with 60 patients who underwent thoracotomy and surgical resection for non-small cell lung cancer

Results: The median length of stay was 4 days for both the EC and PC groups ($p = 0.608$). Complications occurred in 11 patients (18.3%) overall, including 5 patients in the PC group (16.7%) and 6 patients in the EC group (20%). The complication rate did not differ significantly between the groups ($p = 0.739$). The most common complication was prolonged air leak ($n = 9$, 15%). Mean postoperative pain scores were lower in the EC group than in the PC group on the first 4 days and at 2 weeks ($p < 0.05$). While there was no difference between the two groups in terms of neuropathic pain at 6 months, an analysis of quality of life showed that the PC group experienced more perceived pain.

Conclusions: The EC technique was associated with less thoracotomy pain in the early postoperative period. However, it was not found to affect neuropathic pain in the long term.

Keywords: thoracotomy, pain, double edge technique

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Introduction

Postoperative pain presents a significant challenge that can impede treatment adherence. Specifically, larger incisions made for better exposure tend to increase morbidity [1]. Thoracotomy is recognized as one of the most painful surgical procedures. Although various drugs and surgical techniques have been proposed to alleviate this pain, effective treatment for neurogenic pain remains elusive [2,3]. Consequently, different techniques have been developed to protect intercostal nerves intraoperatively. This study aims to assess the early and long-term pain and quality of life of patients with the double edge closure technique.

Materials and Methods

The study was conducted prospectively between April 2018 and January 2020. It included a total of 60 patients undergoing lung resection for non-small cell lung cancer (NSCLC). Patients with a history of previous chest trauma, those undergoing rethoracotomy, exploratory thoracotomy or surgeries involving video-assisted thoracoscopy, as well as those with thoracic wall resection, were excluded due to the potential for pre-existing intercostal nerve injury. Additionally, patients who developed perioperative rib fractures, those who underwent iatrogenic rib resection, and those with regular opioid or analgesic drug use were also excluded from the study.

The patients' comorbidities were evaluated using the Charlson Comorbidity Index (CCI). Lung cancer staging was conducted according to the IASLC 8th edition staging system.

A posterolateral thoracotomy (preserving the serratus anterior muscle) was performed in all procedures. Incisions measuring approximately 20-30 cm were made in the fifth or sixth intercostal space. Two different surgical techniques were used in the study. In surgeries using the pericostal closure (PC) technique, a Finochietto retractor was placed in the intercostal space during the procedure. At the end of the procedure, two Z-shaped 2/0 polyglycolic acid sutures were passed through the intercostal muscles to close the intercostal space. In the double edge closure (EC) technique, the intercostal muscle tissue was separated from the rib using electrocautery and a dissector. The intercostal vessels and nerve were protected by passing the needle along the posterior surface of the rib. Two or three sutures were used, and a Z suture was applied (Figure 1). No retractor was used during the procedure, and measurements did not show that the procedure significantly increased the total surgical time.

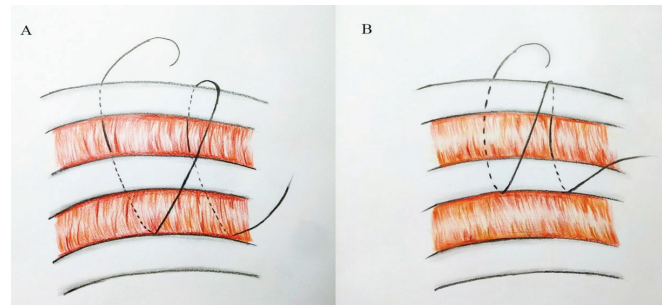


Figure 1. Conventional thoracotomy closure technique (A), double edge thoracotomy closure technique (B).

During the operation, standard opioid and analgesic procedures were applied to all patients by the anesthesia team. Early postoperative monitoring was done in the intensive care unit. After the patients' general conditions stabilized, they were monitored in the inpatient ward.

Patients in both groups received patient-controlled analgesia (PCA) with intravenous pethidine HCl (50 mg bolus and 5 mg with a 15-minute lockout time) for the first 2 postoperative days. Subsequently, pain control was maintained with oral diclofenac potassium 50 mg twice daily and paracetamol 500 mg three times daily. After discharge, all patients continued on the same oral analgesia regimen. Oral analgesia treatment was discontinued in the first postoperative month of the patients included in the study. Analgesic treatments were administered in doses appropriate to the patient's body mass index (BMI). No perioperative or postoperative intercostal blockade was applied to any patient included in the study.

Postoperative pain was evaluated using a visual analog scale (VAS), where a score of 0 indicated no pain and a score of 10 indicated the worst pain ever experienced. Pain levels at rest and during coughing were assessed every 6 hours until postoperative hour 72. Pain assessment with the VAS was repeated at 2 weeks postoperative.

Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scores were assessed at 6 months postoperatively to evaluate chronic neuropathic pain. The LANSS scale has a maximum of 24 points. Patients with a score of 12 or lower were not considered to have neuropathic pain, whereas those with a score above 12 were classified as having neuropathic pain. Quality of life was also assessed at 6 months postoperatively using the SF-36 quality of life scale.

Demographic characteristics, complications, early and long-term pain, operation time, and quality of life were evaluated based on the two different surgical techniques

applied. Postoperative complications occurring in the first 30 days included atelectasis, wound site infection, prolonged air leak (7 days or more), and atrial fibrillation.

Approval for the study was obtained from the local ethics committee of our hospital.

Statistical Analyses

Continuous variables are presented as mean $\pm$ standard deviation, and discrete variables are expressed as frequencies. The demographic and clinical characteristics of the patients were tested for normal distribution using the Kolmogorov-Smirnov test. The t-test was used to calculate the means of these variables, and the chi-square test was used to compare morbidity between these groups. All analyses were performed using SPSS software (version 22; IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered as significant.

Results

Sixty patients, consisting of 17 women (28.3%) and 43 men (71.7%), were included in the study. There were 38 patients (63.3%) with a Charlson Comorbidity Index (CCI) of 1 or higher. The mean age was 61.3 ± 10.23 years, and the mean tumor diameter was 4.32 ± 2.27 cm. Table 1 displays the demographic and histopathological characteristics of the patients. No significant differences were found between the two groups in terms of age, sex,

side of disease, tumor size, and operative time.

The mean duration of chest tube drainage was 3 days, and the median length of hospital stay was 4 days for both the EC and PC groups ($p = 0.608$). Complications occurred in 11 patients (18.3%) within the study. The complication rate was 16.7% ($n = 5$) in the control group and 20% ($n = 6$) in the EC group ($p = 0.739$). The most common complication was a prolonged air leak, observed in 9 patients (15%), followed by atrial fibrillation in 2 patients (3.3%), non-operative hemorrhage in 1 patient (1.6%), wound infection at 1 week postoperative in 1 patient (1.6%), pneumonia in 1 patient (1.6%), and an expansion defect due to atelectasis in 1 patient (1.6%).

Mean postoperative pain scores were significantly lower in the EC group compared to the PC group during the first 4 days and at 2 weeks ($p < 0.05$). Table 2 presents the comparison of postoperative pain scores.

The mean LANSS score for patients in the study was 7.90 ± 6.89 . At 6 months postoperative, the median LANSS score was 5 in the EC group and 7.5 in the PC group ($p > 0.252$). In assessing the quality of life at 6 months, patients in the EC group had a significantly lower body pain score than those in the PC group ($p = 0.026$). No differences were observed in other quality of life indices. Table 3 displays the comparison of postoperative quality-of-life scores.

Table 1. Comparison of patients' demographic and histopathological characteristics.

Variable		PC		EC		p value
		n	%	n	%	
Gender	Male	20	66.7	23	76.7	0.390
	Female	10	33.3	7	23.3	
Age (years), mean $\pm$ SD						0.250
CCI	0	10	33.3	12	40	0.592
	>1	20	66.7	18	60	
Resection	Lobectomy	25	83.3	26	86.7	0.718
	Pneumonectomy	5	16.7	4	13.3	
Stage	1	12	40	12	40	0.792
	2	12	40	10	33.3	
	3	6	20	8	26.7	
Side	Right	12	40	13	43.3	0.793
	Left	18	60	17	56.7	
Histopathology	Adeno ca	16	53.3	13	43.3	0.450
	Squamous cell ca	12	40	12	40	
	Other	2	6.7	5	16.7	

Abbrev.; PC: Pericostal closure group, EC: Double edge closure group, CCI: Charlson comorbidity index, SD: Standard deviation, CA: Cancer

Table 2. Comparison of postoperative pain scores.

Variable	PC	EC	p value
Pain score at rest			
Day 1 (mean $\pm$ SD)	5.65 $\pm$ 1.40	3.53 $\pm$ 1.69	<0.001
Day 2 (mean $\pm$ SD)	4.46 $\pm$ 2.30	3.21 $\pm$ 2.11	0.025
Day 3 (mean $\pm$ SD)	2.70 $\pm$ 1.77	1.81 $\pm$ 1.54	0.043
Day 4 (mean $\pm$ SD)	2.13 $\pm$ 0.96	1.65 $\pm$ 0.74	0.038
Pain score while coughing			
Day 1 (mean $\pm$ SD)	7 $\pm$ 1.48	5.03 $\pm$ 1.79	<0.001
Day 2 (mean $\pm$ SD)	5.83 $\pm$ 2.26	4.58 $\pm$ 2.31	0.050
Day 3 (mean $\pm$ SD)	4.06 $\pm$ 1.96	2.97 $\pm$ 1.98	0.032
Day 4 (mean $\pm$ SD)	3.99 $\pm$ 0.97	3.43 $\pm$ 0.85	0.023
Postoperative week 2 pain score (mean $\pm$ SD)	3.66 $\pm$ 1.29	2.23 $\pm$ 1.27	<0.001

Abbrev.; PC: Pericostal closure group, EC: Double edge closure group

Table 3. Comparison of postoperative pain scores.

Variable	PC	EC	p value
Physical functioning	50	60	0.619
Role limitations due to physical problems	100	100	0.430
Body pain	77.5	55	0.026
Role limitations due to emotional problems	50	100	0.798
Emotional well-being	80	76	0.789
Social functioning	68.7	62.5	0.976
Energy/fatigue	62.5	65	0.947
Global health perception	65	77.5	0.558

Abbrev.; PC: Pericostal closure group, EC: Double edge closure group

Discussion

Although thoracoscopic surgery is increasingly common in the treatment of lung cancer, thoracotomy is still the preferred method for advanced-stage tumors, patients with extensive adhesions, and other cases where greater exposure is required [4]. Post-thoracotomy pain is a common issue for patients and a significant concern for thoracic surgeons. Postoperative pain can lead to complications such as pneumonia and atelectasis due to sputum retention; pulmonary embolism as a result of limited mobility; and hypoxia and cardiac ischemia due to non-adherence to pulmonary physiotherapy [5].

Post-thoracotomy pain is associated with numerous factors, including the duration of surgery, location and length of the incision, intercostal nerve damage, the positioning of the chest tube, chest wall inflammation, as well as psychophysiological and social factors [6]. Increased surgical time due to complications such as bleeding and adhesions also raises the risk of intercostal nerve damage [7], which is one of the primary risk factors for chronic pain.

In half of the patients, post-thoracotomy pain can persist for two years following surgery. Consequently,

various closure techniques for pain prevention have been documented in the literature. These methods include the subcostal suture technique, the double edge suture technique, the intracostal suture technique, and intercostal muscle flap harvesting [7-10]. Cerfolio et al reported in their study that harvesting an intercostal muscle flap before chest wall retraction reduced post-thoracotomy pain and improved spirometric values [11]. Bayram et al found that the intracostal suture technique decreased early postoperative pain while only adding two minutes to the operative time [7].

In 2010, Sakakura et al introduced the edge closure technique as a method to mitigate post-thoracotomy pain [9]. This technique involves the dissection and preservation of the neurovascular bundle on the caudal side of the intercostal space, thereby preventing compression of the intercostal nerve. In our study, we compared 30 patients who underwent the edge closure technique with a control group that received pericostal closure. The comparison was based on VAS pain scores measured both at rest and during coughing. The patients who received the edge closure technique experienced less early postoperative pain,

both at rest and while coughing, and required fewer post-operative analgesics. However, no statistically significant difference was observed between the two groups in terms of chronic neuropathic pain at the 6-month postoperative LANSS assessment. Similar outcomes -significant reductions in acute pain without a significant difference in chronic post-thoracotomy pain -have been noted with other closure techniques [7,8,12,13]. Nonetheless, in our 6-month postoperative quality of life assessment using the SF-36, patients who underwent the edge closure technique reported less body pain, although there was no significant difference in other quality of life dimensions.

A risk of lung herniation has been reported following closure techniques, particularly after the intracostal closure technique [14]. However, lung herniation was not observed as a complication in our study, which is consistent with findings from previous studies. The most common complication we encountered was a prolonged air leak, occurring in 15% of patients. Atrial fibrillation was noted in 3.3% of patients, while non-operative hemorrhage, wound site infection, pneumonia, and atelectasis-related expansion defects each presented in 1.6% of cases. There were no differences in the length of hospital stay or complication rates between the EC and PC groups.

The primary limitation of our study is the subjective nature of pain assessment. Additionally, the small sample size constitutes another limitation. Despite there being no comorbidities within our study group, the use of the VAS for patients with motor or cognitive impairments may also represent a limitation.

In conclusion, the double edge closure technique is a fast, reliable, and effective procedure that does not increase the risk of complications but reduces acute post-thoracotomy pain and allows an earlier return to normal daily life.

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 Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (No: 223/1, date: 08.01.2020).

Authors' contribution

SB; conceptualized and drafted the article, wrote the paper, visualization, CBS,OVY,MSOM,YA,CA; drafted the article, collected and analyzed data, OS,MM; critical review. All authors actively contributed to discussion of the results from the study and reviewed and approved the final version to be released.

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Original Article

Catastrophic injuries caused by tube thoracostomy with trocar: a series of nine cases

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ABSTRACT

Background: Tube thoracostomy is a procedure that is frequently used in thoracic surgical practice. However, in certain circumstances, it may lead to serious complications during or soon after the procedure. Herein, we report a series of tube thoracostomies causing life-threatening intrathoracic and intraabdominal injuries.

Materials and Methods: This case series consisting of nine cases with serious organ and vascular injuries after tube thoracostomy between 2014 and 2021 are presented and the possible causes are discussed. The indications for tube thoracostomy were empyema, COVID pneumonia-related pneumothorax, traumatic pneumothorax, tracheal rupture related-hydropneumothorax during nasogastric tube application, and pleural effusion due to malignancy. A trocar was used in all patients for tube thoracostomy.

Results: Malpositioned thoracic drains included five pulmonary parenchymal lacerations and pulmonary artery, spleen, liver and stomach injuries; one of each.

Conclusions: In the light of these cases, all the procedures and the faults that caused those embarrassing complications have been reviewed honestly. Lessons learned from these events such as avoiding the use of trocars, and CT evaluation before the procedure may also help to prevent such complications in the future.

Keywords: malposition, chest tubes, injuries, tube thoracostomy

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Introduction

Pleural drainage is a procedure dating back to the time of Hippocrates, which is still clinically important with its basic principles [1]. Currently, this procedure continues to be a common surgical intervention in the thoracic surgery field, which is frequently performed in the presence of hemothorax and/or pneumothorax [2]. Various serious complications such as organ laceration, vascular injury, and infection may tend to develop after this procedure and it is important to be aware of these complications to be able to identify the risk factors, which have a significant risk in terms of morbidity and mortality, and to establish preventive strategies.

In this case series consisting of nine cases with serious organ and vascular injuries after tube thoracostomy (TT) between 2014 and 2021 is presented and the possible causes are discussed. This is the first case series of life-minatory complications of chest tube insertion encountered in the PubMed search. Considering the diversity of the cases and their post-complication processes, we believe that they may draw attention to the ones interested in the surgical field.

Materials and Methods

The cases of malpositioned thoracic drains; including five pulmonary parenchymal lacerations and pulmonary artery, spleen, liver, and stomach injuries are listed in table 1.

Results

Case 1 is a 94-year-old female patient with previously known diagnoses of bronchiectasis, type-2 diabetes and

hypertension who was admitted to the emergency department with complaints of chest pain and dyspnea. On the thorax computerized tomography (CT), an image compatible with hydropneumothorax was observed in the right hemithorax. The patient, who already had a history of multiple thoracentesis due to pleural effusion, was consulted by our clinic. In thoracentesis, purulent fluid was aspirated and TT was performed with placement of 28 Fr chest tube to the right hemithorax. At the time of performing TT, she had a hemoptysis in the form of blood-streaked sputum. The chest tube was revised. In control CT, a laceration caused by the malpositioned tube was detected in the posterior segment of the right upper lobe (Figure 1).

Case 2 is a 43-year-old male patient who was admitted to the emergency department with a sudden onset of stabbing chest pain. Since the CT appearance was compatible with pneumothorax, he underwent a TT and his Covid-19 PCR test was positive. Massive air drainage prompted us to take a chest radiograph followed by CT which revealed the chest tube passing throughout the parenchyma of the left upper lobe.

Case 3 is a 72-year-old male patient who was admitted to the emergency room due to an in-vehicle traffic accident and was consulted to us for subcutaneous emphysema. Chest radiograph revealed bilateral pneumothorax and he underwent bilateral TT. CT demonstrated an intraparenchymal position of the chest tube (Figure 2). Due to a prolonged serious air leak, the operation was planned. Extensive adhesions between the lung and chest wall in addition to parenchymal damage were seen.

Table 1. Characteristics of the cases with catastrophic injuries.

No	Primary disease	Indication for TT	Injured structure
1	Bronchiectasis	Empyema	Lung
2	Covid-19 pneumonia	Pneumothorax	Lung
3	In-vehicle traffic accident	Pneumothorax	Lung
4	Tracheal rupture during the misplacement of nasogastric tube	Hydropneumothorax	Lung
5	Synovial sarcoma	Pleural effusion	Lung
6	In-vehicle traffic accident	Hemopneumothorax	Liver
7	In-vehicle traffic accident	Hemopneumothorax	Pulmonary artery
8	Anaplastic oligoastrocytoma	Pleural effusion	Spleen
9	Dehiscence of the diaphragmatic suture following partial resection	Assumed pneumothorax	Stomach

Abbrev.; TT: tube thoracostomy.

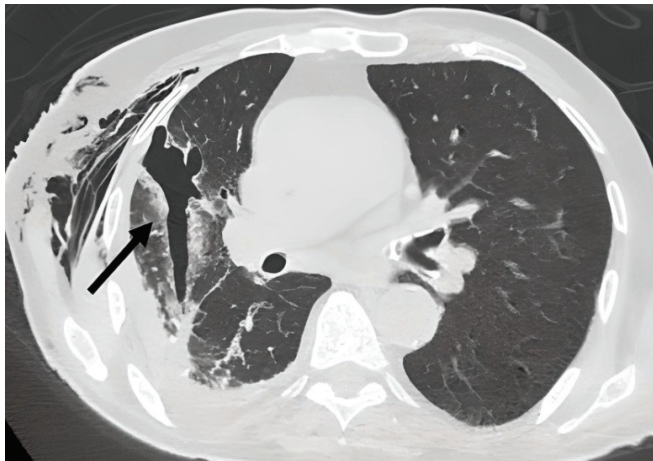


Figure 1. Pulmonary parenchymal laceration in the right upper lobe caused by the chest tube.

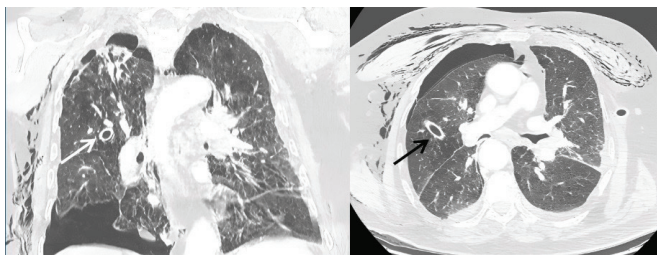


Figure 2. Thorax CT coronal and transverse sections reveal an intraparenchymal thoracic drain located in the right hemithorax and an appearance compatible with the right expansion defect.

Consultation was requested by neurology clinic for a 68-years-old male patient, who underwent thrombectomy due to occlusion in his left middle cerebral artery (MCA) and suffered iatrogenic lung parenchymal injury during insertion of a nasogastric tube (case 4). TT was applied to the patient whose nasogastric tube was seen traversing through the right hemithorax on thorax CT. The fluid is compatible with the enteral nutritional fluid drained from the chest tube due to nasogastric tube feeding. After performing TT, a CT scan showed that the chest tube was passing through the parenchyma of the right lung.

Case 5 is a 22-year-old male patient who was diagnosed with synovial sarcoma and followed up in the medical oncology clinic for chemotherapy and was examined for dyspnea. The chest radiograph showed a homogeneous density filling the right lower zone of the chest (Figure 3a). After sero-hemorrhagic fluid was aspirated by thoracentesis, TT was applied to the right hemithorax. Since there was no drainage, the chest tube was pulled out. Thorax CT revealed a 10x7 cm mass extending to the major fissure in the right lower lobe, which was seen to be penetrated by the chest tube (Figure 3b).

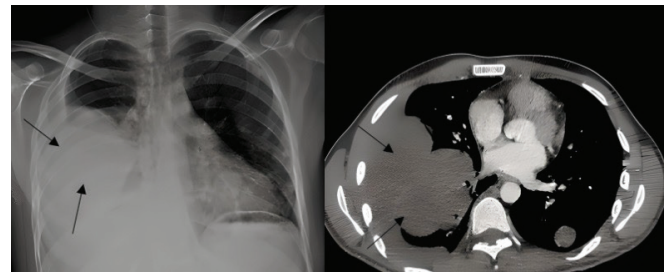


Figure 3. Homogenous density in the middle and lower zones of the right hemithorax (a), and on CT, a 10x7 cm mass extending to the major fissure in the right lower lobe of the right lung, bilateral multiple metastatic foci having the dimensions of up to 2 cm and accompanying minimal pleural effusion (b).

Case 6 is a 53-year-old male patient who was admitted to the emergency service after a traffic accident. On thorax CT, serial rib fractures on the right side, minimal pneumothorax, and hemothorax in the right hemithorax were observed. After a TT was performed there was no oscillation in the underwater sealed drainage system. The control chest radiograph demonstrated the tube in the subdiaphragmatic area (Figure 4a). CT showed that the tube which was inserted from the 8th intercostal space, traversed the entire liver (Figure 4b).

Case 7 is a 24-year-old female patient who was taken to the emergency room after a traffic accident with loss of respiratory sounds. Bilateral TT was applied as the air was aspirated following thoracentesis. Massive air drainage from the right chest tube and expansion defect in the right lung persisted on the control chest X-ray and thorax CT was taken afterward. An apical chest tube was inserted into the right hemithorax in addition to the existing tube. Following the procedure, the patient had 500 mL of sudden hemorrhagic drainage and was urgently taken to the operative room. At the operation, a coagulum-filled parenchymal defect and massive hemorrhage were detected on the anterior surface of the right upper lobe. It was observed that bleeding originated from one of the pulmonary artery branches in the lung parenchyma. The branch of the pulmonary artery branch was primarily repaired and the bleeding was ceased.

Case 8 is a 32-year-old male patient, who was under observation for anaplastic oligoastrocytoma and was consulted to our clinic due to dyspnea. On his CT scan, bilateral pleural effusion was seen, and bilateral TT was performed (Figure 5a). After the procedure, the patient had a sudden hemorrhagic drainage of about 1000 mL. Chest x-ray revealed an appearance compatible with hemothorax was seen in the left hemithorax (Figure 5b). The hypotensive and tachycardic patient was urgently taken to the operating room. On exploration, it was observed that the elevated diaphragm was lacerated and the spleen was lacerated by the chest tube. The patient underwent a splenectomy.

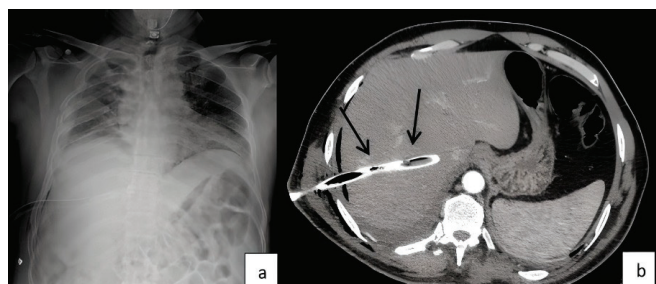


Figure 4. Posteroanterior chest radiograph showed the chest tube located in the subdiaphragmatic area on the right (a), transverse the whole liver on CT (b).

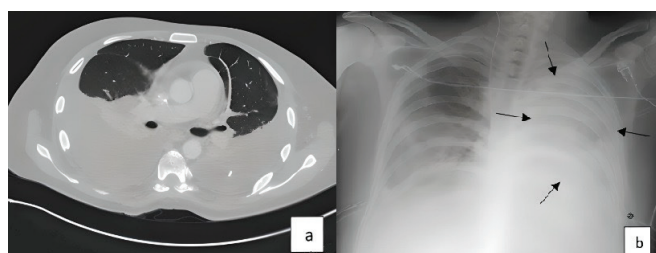


Figure 5. Appearance compatible with bilateral pleural effusion on thorax CT (a), increased opacity in the left hemithorax in the posteroanterior chest X-ray taken urgently after massive hemorrhagic drainage after tube thoracostomy (b).

The last case is a 67-year-old male patient who underwent left lower lobectomy and partial diaphragmatic resection due to the adenosquamous carcinoma of the left lower lung invading hemi-diaphragm. The defect in the diaphragm was primarily repaired with non-absorbable separated sutures. After removing the chest tube on postoperative 2nd day, the patient developed dyspnea. An appearance that could be compatible with hydropneumothorax was seen on the chest X-ray and TT was performed to the left hemithorax. Drainage of gastric content from the thorax tube prompted the surgical team to take a CT (Figure 6) and afterward the patient underwent re-operation in emergent condition. On exploration, a defect in the diaphragm, a part of the stomach and omentum entering into the thoracic cavity, and an iatrogenically injured gastric fundus by the chest tube were observed.

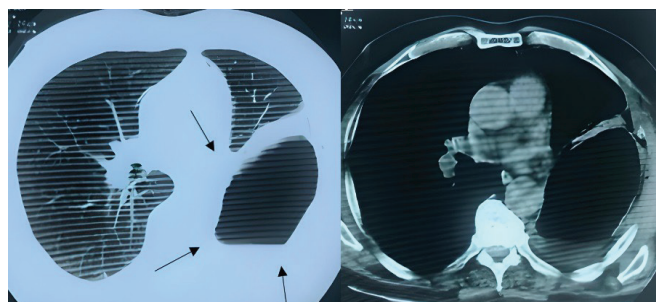


Figure 6. Air-fluid level on thorax CT was misinterpreted as hydro-pneumothorax in the left hemithorax.

Discussion

Tube thoracostomy is a minor surgical intervention frequently performed in the clinical practice of thoracic surgeons with various indications. Complications such as improper localization of the tube, infection, and organ injury may occur during or after the procedure, with malposition being the most common. Thoracic and abdominal organ damage and vascular injury are among the most serious ones for malpositioned TT, which may cause significant morbidity and mortality. There are nine cases in our case series for malpositioned thoracic drains; including five pulmonary parenchymal lacerations and pulmonary artery, spleen, liver, and stomach injuries; one of each.

In these cases, the indications for TT were empyema, COVID pneumonia-related pneumothorax, post-traumatic pneumothorax, and tracheal rupture related hydropneumothorax during nasogastric tube application, and pleural effusion due to malignancy.

In this series, a trocar was used in all patients who underwent tube thoracostomy. We also performed TT without trocar in our clinic. Within the scope of this study, patients who underwent TT in our clinic between 2014 and 2021 were examined retrospectively. As a result of the examination, it was determined that all patients who developed malposition or injury were patients in whom trocars were used. No catastrophic injuries occurred in patients who underwent TT without the use of a trocar. For this reason, although there may be patient groups in which the use of trocars may be relatively safe, such as patients with radiologically proven total pneumothorax, in our clinical practice we recommend that the use of trocars should be avoided, especially in patients with suspicion of pleural adhesion and in whom the lung parenchyma may have become fragile due to underlying diseases or TT will be performed through the lower level ribs (i.e., 9 to 12 ribs). Remérand et al investigated the incidence of chest tube malposition in critically ill patients and reported that the only factor that could be associated with malposition was the use of trocars during tube placement. It is well-known that, presence of the pleural adhesions, reduced lung compliance and underlying parenchymal consolidation may lead to parenchymal injury. In patients with suspected pleural adhesions (thoracotomy, pleurodesis, previous infection/empyema, chest trauma) and parenchymal lesions, it is important to examine the pre-procedural radiological images carefully to determine the

localization, avoiding the use of trocars and to explore pleural space digitally. In patients with a history of malignancy, similar appearance of mass and pleural effusion on plain radiographs may be misleading.

In a study in which TTs were applied in trauma resuscitation centers, the chest tubes causing pulmonary parenchymal injuries were detected in 11% of the cases [4], while 10 (9%) were reported in 106 TTs who were examined with CT in another study [3]. In the presented case series, there are five parenchymal injuries among all the 2,691 TT procedures (0.19%) between 2014 and 2021, either performed in emergent conditions or not.

The patient whose pulmonary artery was injured was the most catastrophic TT procedure among our case series. The number of TT cases resulting in pulmonary artery injury is quite limited in the literature and only 11 cases were reported in the PubMed field [5-15].

In our three cases with extrathoracic organ damages, one had a liver injury, another had a spleen injury, and the third had a stomach injury. It can be said that, if TT was performed through the lower level ribs (i.e., 9 to 12 ribs) by trocar technique, the risk of diaphragmatic and/or intraabdominal organ injury will be quite high. In the literature, various cases that developed liver injury; of which two of them were treated by embolization of the liver. Whereas major hemorrhage and/or hemodynamic instability in patients with liver injury, surgical exploration is often indicated [16-19]. Spleen laceration after TT often requires splenectomy. Although it is encountered rarely, hemoperitoneum and hemorrhagic shock may also occur in spleen injury [20].

In our case with the stomach injury, the patient developed a dehiscence of the diaphragmatic sutures in the early postoperative period after which the stomach was displaced towards the thoracic cavity. The appearance on the tomography mimicked hydropnomothorax. Some cases in which gastrothorax mimics pneumothorax have also been reported in the literature [21-22]. In partial resection of the diaphragm, a nasogastric tube should be inserted in the early postoperative period to reduce the tension in the diaphragm, unlike in the present case.

In conclusion, although TT is widely used as a life-saving surgical intervention, it also bears its risks in terms of various complications. Being familiar with the causes of these complications and discussing them is important in developing preventive strategies. Lessons learned over 7 years from these embarrassing complications led us to get some take of messages as follows:

First, if possible, the patient should be evaluated with chest CT before TT to avoid malposition and/or organ injury. However, in some cases, a CT scan is not possible because the patient is unstable, or because frequent measurements are wanted to track the progress of a bleed. In these situations, bedside sonography can also be used.

Second, the use of trocars during the procedure increases the risk of complications. The use of a trocar allows rapid drainage with a smaller incision, while the sharp trocar tip may lead to injury. Avoiding the use of trocars in patients can prevent the occurrence of complications.

Lastly, if there is still doubt about the indication or on which point to insert the tube into the chest cavity, to find the right way, one should not hesitate to get a second opinion, especially from a senior specialist.

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Informed consent and Ethical approval

Written informed consent was obtained from all participants or their legally authorized representatives. Ethics Committee approval was waived.

Availability of data

The dataset of the research presented in this article is under record. Corresponding author can be contacted to reach the required data network.

Authors' contribution

GKO; design, conceptualization, writing the paper, DG; design, conceptualization, collecting and processing data, UC; designed the research, conceptualization and supervision, AO,TIA,AGE,KT; supervision, co-writing, review and editing.

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Original Article

Results of surgery after neoadjuvant treatment for non-small cell lung cancer

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ABSTRACT

Background: In locally advanced non-small cell lung cancer, survival rates achieved only by surgical treatment are unfortunately lower than expected. It's believed that survival rates can be raised by multimodal therapies including surgery. The purpose of the study is to analyse the results of surgical treatment in patients who underwent surgical resection after neoadjuvant treatment due to locally advanced non-small cell lung cancer.

Materials and Methods: The patients who underwent lobectomy or pneumonectomy after neoadjuvant chemotherapy and/or radiotherapy due to locally advanced non-small cell lung cancer were included in this study. The patients were divided into two groups according to oncological treatment indication. Group A included patients who received neoadjuvant therapy due to T disease and group B due to N2 disease. The surgical interventions, pathological results, postoperative complications, mortality, recurrence, 5-year disease-free survival, and overall survival were analysed.

Results: 154 patients were included in the study. 142 were men and 12 were women with a mean age of 57.7 ± 16.97 (between 35 and 77). Ninety-six patients received induction therapy due to T disease, and 58 patients due to N2 disease. Pneumonectomy was performed on 41 patients, lobectomy was performed on 113 patients (18 bronchial sleeve resection). Histopathologic results revealed squamous cell carcinoma in 96 (62.3%), adenocarcinoma in 52 (33.8) and large cell carcinoma in 6 (3.9%) patients. A complete response to neoadjuvant treatment was achieved in 19 (Group A, n = 15, group B, n = 4) patients. Postoperative pathologic results showed mediastinal lymph node metastasis in 13 (13.6%) patients in group A and, in 28 (48.3%) patients in group B, which is statistically significant. Prolonged air leak was the most common complication in both groups. Operative mortality was observed in 4 (2.6%) patients. In 82 patients 47 in group A and 35 in group B recurrence or metastasis were detected during the follow-up. 5-year disease-free survival rate was 43.2% in group A and 38.4% in group B. Five- year survival rate was 46.1% in group A and 38% in group B.

Conclusions: The patients who achieved a histopathologic complete response following induction therapy had statistically significantly better disease-free and overall survival rates. Pathologically proven lymph node metastasis increased the rate of recurrence or metastasis significantly ($p = 0.01$). The disease-free and overall survival rate decreased significantly ($p = 0.0001$, $p = 0.0001$). It is deducible in light of these findings that patients who received neoadjuvant treatment for N2 achieved better disease-free survival and overall survival.

Keywords: lung cancer, induction therapy, lung resection

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Introduction

Non-small cell lung cancer (NSCLC) accounts for 80-85% of all lung cancers, and the treatment method that provides the best local control and survival is surgical resection [1]. Only about 20% of non-small cell lung carcinomas can be treated surgically when diagnosed, and approximately one-third are diagnosed at a locally advanced stage (stage III) [2]. Stage III covers a heterogeneous patient group. For this reason, its treatment is the most controversial group and there is still no standardized approach to definitive treatment. Locally advanced stage patients are tried to be made candidates for surgical treatment by reducing the tumor volume with neoadjuvant chemotherapy and/or radiotherapy (induction therapy) or by clearing the lymph nodes of the disease [3].

The aim of this study was to evaluate the results by analyzing the pathological diagnosis, surgical resection method, operative mortality, postoperative complications, recurrence or metastasis status, disease-free survival, and overall survival in NSCLC cases that underwent surgical resection after induction therapy.

Materials and Methods

Patients who underwent surgical intervention after induction therapy for T or N2 in locally advanced NSCLC patients between January 2010 and December 2015 were included in the study. Patients' gender, age, neoadjuvant treatment method, surgical methods, histopathological results, postoperative complications, mortality, recurrence or metastasis status, disease-free, and overall survival effects were determined. The results were revised by the new TNM staging system (according to 8th). Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital Ethics Committee approval was received for this study. (2017/3770).

The patients were divided into two groups according to oncological treatment indication. Group A included patients who received neoadjuvant therapy due to T disease such as pleural invasion, vascular invasion, superior sulcus tumors, and group B due to N2 disease.

All patients were evaluated with PET/CT before and 4 weeks after neoadjuvant treatment. EBUS and cervical mediastinoscopy were performed for invasive mediastinal staging, and Thorax CT and PET/CT were used in patients where this could not be performed. A 75% decrease in metabolic activity on PET/CT was considered as a response.

Results

During this period, a total of 905 patients underwent surgery for NSCLC, and 154 patients who were decided on induction treatment at the thorax council due to locally

advanced stage and subsequently underwent lung resection were included in the study. Among these, 96 patients received induction therapy due to T disease, and 58 patients due to N2 disease. 142 (92.2%) of the patients were male, 12 (7.8%) were female, and the average age was 57.7 ± 16.97 (range 35-77). As a histopathological diagnostic method, bronchoscopy was performed in 77 (50%) of the patients and TTNAB was performed in 77 (50%). Squamous cell carcinoma was detected in 96 (62.3%) patients, adenocarcinoma in 52 (33.8%) patients, and large cell carcinoma in 6 (3.9%) patients.

Before induction treatment, mediastinal staging was performed with EBUS in 5 (5.2%) patients in Group A. Histopathological N2 was not detected. In this group, EBUS was performed in 4 (4.2%) patients and mediastinoscopy was performed in 3 (3.1%) patients for mediastinal staging after induction treatment. Before induction therapy, EBUS was performed in 17 (29.3%) patients, mediastinoscopy in 4 (6.9%) patients, and EBUS and mediastinoscopy in one (1.7%) patient for invasive mediastinal staging in Group B. While 20 of them were reported as malignant, 2 of them received induction treatment because their PET/CT findings were predicted to be false negative. When we examined the invasive mediastinal staging after induction therapy in this group of patients, no invasive procedure was performed in 33 (56.9%) patients, EBUS in 9 (15.5%), mediastinoscopy in 7 (12.1%), and EBUS and mediastinoscopy in 9 (15.5%) patients.

Of those who received induction treatment due to T, 75 (78.1%) received chemotherapy, seven (7.3%) received radiotherapy, and 14 (14.6%) received chemoradiotherapy. When we look at the dose of chemotherapy applied, 47 (49.0%) patients were administered less than 4 cycles of chemotherapy, while 42 (43.8%) patients were administered 4 or more cycles of chemotherapy. While radiotherapy was applied to 21 (21.9%) of the patients who received induction treatment due to T, when we examined the radiotherapy dose of the patients, we found that four (4.2%) patients received radiotherapy of 50 Gray or less, and 17 (17.7%) patients received radiotherapy above 50 Gray. The diagnosis of malignancy in this group was obtained by bronchoscopy in 51 (53.2%) patients before induction therapy, and by TTIAB in 45 (46.9%) patients.

Of those who received induction treatment due to N2, 55 (94.8%) received chemotherapy and 3 (5.2%) received chemoradiotherapy. When we look at the dose of chemotherapy applied, 32 (55.2%) patients were administered less than 4 cycles of chemotherapy, while 26 (44.8%) patients were administered 4 or more cycles of chemotherapy. When we examined the radiotherapy dose in patients who received induction therapy due to N2, one (1.7%) patient received radiotherapy at 50 Gray

or less, while two (3.4%) patients received radiotherapy above 50 Gray. The diagnosis was obtained by bronchoscopy in 26 (44.8%) of the patients in this group, while the TTIAB method was used in 32 (55.2%).

Lobectomy was performed in 113 (73.4%) of the patients. The most common operation was right upper lobectomy in 43 patients and left upper lobectomy in 33 patients. Bilobectomy inferior was performed in 12 patients, left lower lobectomy in 11, right lower lobectomy in eight, bilobectomy superior in five and middle lobectomy in one patient. Bronchial sleeve resection was

performed in 18 (11.7%) of the patients, and pneumonectomy was performed in 41 (26.6%) (27 left, 14 right).

The most common additional procedure performed along with lung resection was pericardial resection in 57 patients. Chest wall resection was performed in 10 patients, and pericardial and chest wall resection was performed together in 3 patients. In one patient, partial resection of the superior vena cava was performed along with pericardial resection, and in another patient, partial resection of the diaphragm with pericardial resection and primary repair of the diaphragm was performed (Table 1).

Table 1. Demographic and clinical data of those who received induction therapy due to T and N2.

	Group A n(%)	Group B n(%)
Gender		
Female	7(7.3)	5(8.6)
Male	89(92.7)	53(91.4)
Histopathologic diagnosis method		
Bronchoscopy	51(53.1)	26(44.8)
TTFNAB	45(46.9)	32(55.2)
Histopathologic results		
Squamous cell carcinoma	65(66.3)	31(53.4)
Adenocarcinoma	28(28.6)	24(41.4)
Large cell carcinoma	3(5.1)	3(5.2)
Invasive mediastinal staging method		
Before induction	5(5.2)	22(37.9)
EBUS	5(5.2)	17(29.3)
Mediastinoscopy	-	4(6.9)
EBUS + mediastinoscopy	-	1(1.7)
Induction treatment		
Chemotherapy	89(92.8)	58(100)
4 cycles or less chemotherapy	47(49)	32(55.2)
More than 4 cycles of chemotherapy	42(43.8)	26(44.8)
Radiotherapy	21(21.9)	3(5.2)
Radiotherapy at 50 Gray and below	4(4.2)	1(1.7)
Radiotherapy more than 50 Gray	17(17.7)	2(3.4)
Chemoradiotherapy	14(14.7)	3(5.2)
Invasive mediastinal staging method		
After induction	14(14.6)	25(43.1)
EBUS	7(7.3)	9(15.5)
Mediastinoscopy	4(4.2)	7(12.1)
EBUS + mediastinoscopy	3(3.1)	9(15.5)
Resections		
Lobectomy	69(71.9)	44(75.9)
Pneumonectomy	27(28.1)	14(24.1)
Additional surgical procedures		
Bronchial sleeve	14(14.6)	4(6.9)
Pericardium resection	41(42.7)	16(27.6)
Chest wall resection	7(7.3)	3(5.2)
Pericardium and chest wall resection	2(2.1)	1(1.7)
Pericardium and SVC partial resection	1(1)	
Pericardium and diaphragm partial resection	1(1)	

Postoperatively in Group A, there were 15 patients reported as histopathological Tx. No lymph node metastasis was detected in 68 patients and N1 positivity was detected in 15 patients. While 5 of the patients had only N2 positivity, 8 patients had both N1 and N2 positivity. In Group B, there were 4 patients reported as histopathological Tx, and no lymph node metastasis was detected in 22 patients. 8 patients had N1 positivity, 13 had only N2 positivity, and 15 patients had both N1 and N2 positivity. When the postoperative N status was examined, the most detected N status in both groups was N0, but the presence of postoperative N2 was higher in the group receiving induction therapy due to N2 and this difference was statistically significant ($p = 0.0001$).

According to these evaluations, 19 (12.3%) of all our cases had a complete response and were classified as Tx. Additionally, there was a regression in the tumor in 41 (26.6%) cases and they were classified as T1. 62 (40.3%) of the cases were included in the T2 group, which was the largest group. Additionally, 21 (13.6%) cases were evaluated as T3 and 11 (7.1%) as T4.

When the histopathological lymph node status was examined after surgery, 90 (58.4%) were evaluated as N0, 23 (14.9%) as N1, and 41 (26.7%) as N2. While 18 (11.6%) of the patients in the N2 group had only N2, 23 (14.9%) had both N1 and N2 lymph node metastases (Table 2).

Adjuvant treatment was given to 89 (57.8%) of the patients. The most frequently applied adjuvant treatment was chemotherapy in 63 (40.9%) patients. Additionally, 3 (1.9%) patients received radiotherapy and 23 (14.9%) patients received chemoradiotherapy.

During the follow-up, no complications were observed in 87 (56.5%) patients, while complications were observed in 67 (43.5%) patients (Table 3).

Table 2. Postoperative histopathologic results.

	Group A n(%)	Group B n(%)
T results		
Tx (Complete response)	15(15.6)	4(6.9)
T1	23(23.9)	18(31.1)
T2	34(35.4)	28(48.2)
T3	15(25.6)	6(10.3)
T4	9(9.5)	2(3.5)
N results		
N0	68(70.8)	22(37.9)
N1	15(15.6)	8(13.8)
N2	5(5.2)	13(22.4)
N1+N2	8(8.4)	15(25.9)

Table 3. Postoperative complications.

Prolonged air leakage	42(27.3)
Expansion defect	14(9.1)
Atelectasis	15(9.7)
Pneumonia	10(6.5)
Pulmonary embolism	1(0.6)
Early period bronchopleural fistula	3(1.8)
Rethoracotomy due to hemorrhage	7(4.5)
Early period bronchopleural fistula + empyema	3(1.8)
Chylothorax	3(1.8)
Wound infection	1(0.6)

When the postoperative complications that developed during the follow-up of the patients were examined, it was observed that gender and age group were not statistically significant. When pneumonectomy compared to lobectomy, the presence of a bronchoplastic procedure caused a statistically significant higher rate of postoperative complications. The type, dose, and indication of induction treatment were not a statistically significant factor in postoperative complications. Postoperative complications were detected in 43 (44.8%) patients who received induction therapy due to T and in 24 (41.4%) patients who received induction therapy due to N2, and there was no statistically significant difference between the two groups ($p = 0.73$). Additionally, it was determined that the histopathological type of the tumor and postoperative T and N status were not statistically significant factors in postoperative complications.

Operative mortality occurred in four (2.6%) patients, two patients in each age group, and there was no statistically significant difference. Operative mortality was statistically significantly higher in female gender ($p = 0.03$). In addition, it was determined that the presence of lobectomy, pneumonectomy, bronchoplasty, and the type and dose of induction therapy did not statistically affect operative mortality. Operative mortality was detected in two (2.1%) patients who received induction therapy due to T and in two (3.4%) patients who received induction therapy due to N2 which was not statistically significant ($p = 0.62$).

Although recurrence or metastasis was detected in 47 (49%) patients who received induction therapy due to T and 35 (60.3%) patients who received induction therapy due to N2, there was no statistically significant difference between the two groups ($p = 0.18$). However, the patients who received induction radiotherapy doses above 50 Gray had a lower rate of recurrence or metastasis than others, and this was statistically significant

($p = 0.04$). In addition, a higher rate of recurrence or metastasis was detected in patients whose tumor histopathological type was reported as adenocarcinoma compared to others, and this was statistically significant ($p = 0.01$). When we examined the effect of the postoperative T group, it was found that as the T of the tumor increased, a higher rate of recurrence or metastasis was detected, as expected, and this was statistically significant ($p = 0.01$). Additionally, postoperative lymph node metastasis is similar; It was observed that as the lymph node metastasis positivity group increased, more relapses or metastases were detected and this was statistically significant ($p = 0.01$).

The best 5-year survival rate, 94.7%, was found in the Tx group, where no viable tumor was detected postoperatively and was evaluated as a complete response to induction therapy. In the others, 5-year survival rates were found to be 40.4% in the T1 group, 31.6% in T2, 21.4% in T3 and 51.9% in T4. Postoperative T status was found to have a statistically significant effect on survival ($p = 0.004$). Figure 1 shows the analysis of the effect of postoperative T status on survival.

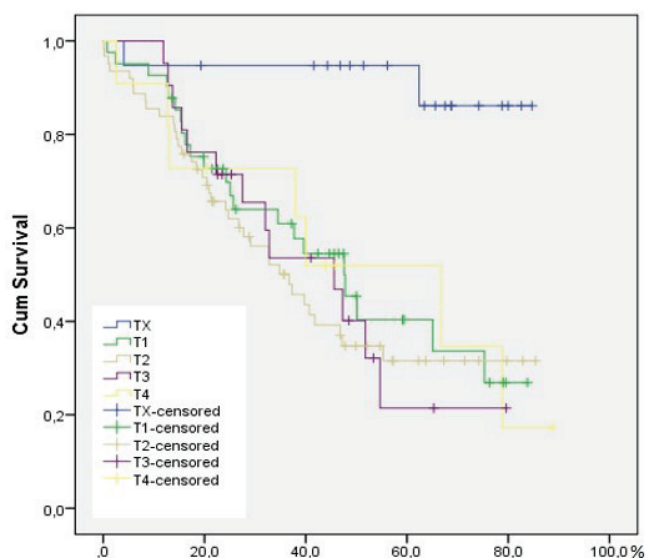


Figure 1. Analysis of the effect of postoperative T status on survival.

When we look at the effect of lymph node metastasis on survival, there was a 5-year survival rate of 51.2% in the N0 group. Hilar lymph node metastasis (N1) was detected in 48.4%, and mediastinal lymph node metastasis (N2) in 51.1%. In the N1+N2 group, 5-year survival was not determined. The effect of postoperative N status on 5-year survival was found to be statistically significant ($p = 0.0001$).

The effect of the postoperative T and N status of the patients on disease-free survival, as expected, was; that as the

T factor and the lymph node metastasis group increased, the disease-free survival was worse and this was statistically significant ($p = 0.008$, $p = 0.0001$ respectively).

During the average 37.7 ± 23.3 (0.1-88.7) month follow-up of all patients, no recurrence or metastasis was detected in 72 (50%) patients. While 17 (11%) of them lived with recurrence or metastasis, 65 (42.2%) had mortality after recurrence or metastasis. When the factors affecting the development of recurrence or metastasis were examined, it was observed that no statistically significant difference was found in terms of age group, gender, operation type, presence of bronchoplasty, induction therapy indication group, type and chemotherapy dose.

When the study was completed, 73 (47.4%) of the patients were alive (56 patients without disease, 17 patients with recurrence or metastasis) and 81 (52.6%) patients were dead (65 patients due to recurrence or metastasis and 16 patients due to reasons other than disease). After an average follow-up of 37.7 ± 23.3 (0.1-88.7) months, the 5-year survival rate of the patients was 43.1%. Median survival was found to be 47.3 months and average survival time was 51.1 months.

The 5-year survival rate was 46.1% in those treated for T and 38% in those treated for N2, and there was no statistically significant difference between the two groups ($p = 0.28$). Although the 5-year survival rate was higher in women compared to men, in those who underwent pneumonectomy compared to lobectomy, and in those who did not undergo bronchoplastic procedure compared to those who did not, no statistically significant difference was detected. Figure 2 shows the disease-free survival analysis with the neoadjuvant treatment group.

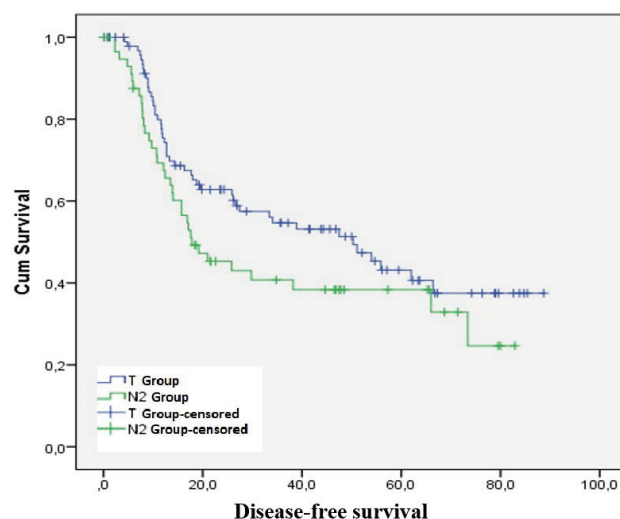


Figure 2. Disease-free survival analysis with neoadjuvant treatment group.

When the effect of the histopathological type of the tumor on disease-free survival was considered, large cell carcinoma had a 5-year disease-free survival rate of 83.3%. 5-year disease-free survival was found to be 45% in squamous cell carcinoma and 28.1% in adenocarcinoma, and the difference between the two was statistically significant ($p = 0.04$).

The type of induction therapy, its dose, and additional surgical procedures in groups no significance on survival was detected. When the effect of adjuvant treatment on recurrence or metastasis was considered, a lower rate of relapse or metastasis was present in those who did not receive adjuvant treatment, while the highest rate of relapse or metastasis was detected in the group receiving chemoradiotherapy as adjuvant treatment, and this was statistically significant ($p = 0.007$).

The 5-year survival rate was 51.5% in patients who did not receive adjuvant treatment and 16.9% who received adjuvant chemoradiotherapy, and the difference was statistically significant ($p = 0.004$).

Statistical Analysis

SPSS 24 Package Program was used in this retrospective study. Comparative analyses of the groups were made using "Fisher's Exact Test" and "Pearson Chi-Square test". The "Kaplan-Meier" method was used in survival analyses. Statistical analyses were performed using the "log-rank" method for survival comparisons between groups. $P < 0.05$ was considered significant.

Discussion

Long-term survival in non-small cell lung cancer is determined by multiple factors [2]. The most important determinants are tumor stage, determined by tumor size (T), lymph node metastasis (N), and distant metastasis (M) [4]. While surgical resection is recommended as the first treatment option for best survival in early-stage NSCLC, multimodal treatment options are used in locally advanced NSCLC [2]. Induction treatments are preferred in locally advanced NSCLC because they reduce tumor size, increase the likelihood of complete resection, and prevent micrometastases [5,6]. Although studies have not definitively shown that neoadjuvant treatment increases survival, neoadjuvant treatment is preferred by many clinicians because non-surgical oncological treatment does not provide the desired success in locally advanced NSCLC patients, postoperative adjuvant treatment is poorly tolerated by the patient, and most patients cannot complete the treatment [7,8].

Pneumonectomy accounts for 10-25% of lung resections performed for non-small cell lung cancer [9,10]. It has been reported that the rate of pneumonectomy increases in post-neoadjuvant surgeries [10]. In addition to pneumonectomy being a disease in itself, the importance of sleeve resections has increased due to the higher mortality rate and the higher probability of postoperative major complications. Stamatis et al commented that, while the lobectomy rate was 66%, bronchial sleeve lobectomy was performed in 14% in their series [10]. Lobectomy was performed in 113 (73.4%) patients in our study, and 18 of them underwent bronchial sleeve lobectomy. These rates show a similar correlation to large series. The presence of a bronchoplastic procedure did not have a statistically significant effect on recurrence or metastasis, disease-free survival and overall survival. However, it was determined that postoperative complications were observed in 13 (72.2%) of 18 patients who underwent bronchoplastic procedures and this was statistically significant ($p = 0.01$). Similarly, while no statistically significant effect was detected on recurrence or metastasis, disease-free survival and overall survival in patients who underwent lobectomy, postoperative complications were detected in 57 (50.4%) of those who underwent lobectomy and in 10 (24.4%) of those who underwent pneumonectomy and were statistically significant ($p = 0.005$). The rate was lower in our study after pneumonectomy. However, while more major complications such as bronchopleural fistula were observed after pneumonectomy, more minor complications such as expansion defect and prolonged air leakage were observed in the presence of lobectomy or bronchoplasty.

Neoadjuvant treatment can be applied as chemotherapy, radiotherapy, or chemoradiation, depending on the indication. Kirn et al primarily recommend chemotherapy as induction therapy in N2 patients with locally advanced NSCLC. In their study, they found that induction chemotherapy increased survival compared to radiotherapy in N2 patients [11]. Westeel et al in their French intergroup study, examined the induction chemotherapy dose and the timing of chemotherapy in 528 patients. In this study, patients who received 2 cycles of chemotherapy and 4 cycles of chemotherapy preoperatively were examined. Additionally, patients who received all 4 cycles of chemotherapy before surgery, 2 cycles before surgery, and 2 cycles after surgery were compared. At the end of this study, it was

observed that the chemotherapy dose did not make a difference in terms of effectiveness, timing, survival and morbidity [12]. In the study by Sonett et al, among 40 patients, it was found that preoperative radiotherapy applied to patients over 45 Gray increased postoperative complications, but there was no difference in terms of operative mortality, recurrence or metastasis, and survival [13]. In our study, no statistically significant effect of the type of induction treatment was detected on operative mortality, postoperative complications, recurrence or metastasis, disease-free survival and overall survival.

In the review written by Candela et al for mediastinal evaluation after induction therapy, it was determined that thorax CT, PET-CT and remediastinoscopy had a false negative rate of up to 20%. Better results have been obtained with needle biopsy methods such as EBUS and EUS. It has been determined that mediastinoscopy is the most reliable method for mediastinal staging and the false negative rate increases in the case of remediastinoscopy. For this reason, it has been suggested that the initial evaluation should be made with needle methods such as EBUS or EUS, and that mediastinoscopy would be more appropriate for re-evaluation after induction treatment [14]. In our study, the methods used in mediastinal invasive staging were in line with the literature. While EBUS was used more before induction treatment, the rate of mediastinoscopy increased after induction treatment. As expected, post-treatment invasive mediastinal staging was used at a statistically significantly higher rate in those who received induction therapy due to N2 ($p = 0.001$).

In a study, 57% of the patients who underwent lung resection after induction therapy were found to have squamous cell carcinoma, 32% to adenocarcinoma, and 11% to large cell carcinoma. Similarly, in our study, squamous cell carcinoma was detected at a higher rate. In their study, it was stated that the histopathological type of the tumor did not have a statistically significant effect on survival, but the presence of squamous cell carcinoma was a better prognostic factor [15]. In our study, it was found that a higher rate of recurrence or metastasis developed in adenocarcinomas and this was statistically significant ($p = 0.01$). However, no statistically significant effect of the histopathological type of the tumor on operative mortality and survival was detected. When we examined the effect of histopathological type on disease-free survival, the 5-year disease-free survival rates were

found to be 45% in squamous cell carcinoma, 28.1% in adenocarcinoma and 83.3% in large cell carcinoma. The highest 5-year disease survival rate was found in large cell carcinoma and the lowest in adenocarcinoma, and the difference was statistically significant ($p = 0.04$).

Junker et al and Cyjon et al's studies evaluated the effect of pathological T status on survival in patients who underwent lung resection after induction therapy. Junker et al grouped the patients with the best response rate to induction therapy as grade I and, those with the lowest response rate as grade III and compared the 3-year survival of the patients. As a result of the Junker study, a 3-year survival rate of 56% in grade I and 11% in grade III was obtained, and it was determined that the response rate to treatment had a statistically significant effect on survival [16,17]. Cyjon et al divided tumors into groups according to tumor size and made a second tumor size classification, using 4 centimeters (cm) as a limit, as under 4 cm and over 4 cm. In their study, survival decreased as tumor size increased, and the median survival time for tumors less than 4 cm was calculated as 17 months, and for tumors larger than 4 cm, the median survival time was calculated as 14 months, and a statistically significant difference was found between the two groups [17]. When literature data are examined, the complete response rate to induction therapy varies between 5-15%. It has been determined that a complete response to treatment is a very important factor in terms of survival. In the study conducted by Mouillet et al, 5-year survival was found to be 80.1% in patients with a pathological complete response, while it was 44.8% in those without a complete response, and a statistically significant difference was detected ($p < 0.0001$) [18]. In our study, when we examined the effect of postoperative T status on disease-free survival, the highest 5-year disease-free survival was in the Tx group with 74.4%. Although the 5-year disease-free survival rate was lower as the group of postoperative T status increased, the 5-year disease-free survival of the T3 group was lower than the T4 group. Postoperative T status was found to have a statistically significant effect on disease-free survival ($p = 0.008$). When we examined the effect of postoperative T status on overall survival, the highest 5-year overall survival rate was in the Tx group with 94.7%. It was determined that postoperative T status had a statistically significant effect on the overall survival of the patients ($p = 0.004$). It was determined that induction therapy had a statistically significant effect on both disease-free survival and overall survival, especially in cases of complete response. Although both overall survival

and disease-free survival rates decreased as the postoperative T factor increased, it was observed that the rate in the T4 group was higher than the T3 group in both parameters.

In the study by Yoshino et al, although the 5-year overall survival rate was 35% in patients with only N2 positivity, this rate was stated to be 13% in N1+N2 positivity [19]. As expected, it was observed that as the lymph node metastasis group increased, the survival rate decreased and the worst group was the N1+N2 group. In the literature, the 5-year survival rate of patients who underwent lung resection after induction chemotherapy in case of mediastinal lymph node positivity detected by mediastinoscopy is given as 30-40% [20]. In our study, although 5-year overall survival was not observed in patients with hilar and mediastinal lymph node positivity, others had a 5-year overall survival rate of up to 50%. In the study conducted by Sause et al, the 3-year survival rate of patients in whom lymph node metastasis was not detected in the mediastinal lymph nodes by radiological evaluation and mediastinoscopy, but in whom mediastinal lymph node metastasis was detected in the pathological examination of resection samples, was found to be approximately 50% [21].

Decker et al argued that adjuvant chemotherapy is more effective than radiotherapy in reducing the risk of distant metastasis. However, in patients with positive surgical margins and a high risk of local recurrence, simultaneous chemoradiation was recommended before adjuvant chemotherapy [22]. In our study, a 41.5% rate of recurrence or metastasis was detected in those who did not receive adjuvant treatment and this rate was found to be 82.6% in those receiving chemoradiotherapy. It was thought that this was because patients with a higher postoperative stage needed adjuvant treatment, and as the stage increased, the need for multimodality treatment in adjuvant treatment increased.

In conclusion, it was determined that, patients who responded well to neoadjuvant treatment and whose stage regressed after treatment had better survival outcomes after surgery. We believe that after neoadjuvant treatment with an experienced team, all surgical interventions, including pneumonectomy and bronchoplastic procedures, can be performed with acceptable mortality, morbidity and complication rates.

Declaration of conflicting interests

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Ethics approval

This study was approved by Health Sciences University, Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital Ethics Committee (2017/3770).

Authors' contribution

TY; Concept, design, literature search, data acquisition, writing the article AU; data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review, SY,ÖS,SG; supervision, manuscript review.

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Case Report

A case of congenital total pericardial agenesis mimicking pneumothorax findings

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ABSTRACT

Congenital pericardial agenesis has been reported as usually asymptomatic cases, operated on for other reasons and found incidentally or in autopsy reports. Herein, we present a case of congenital total pericardial agenesis mimicking the findings of pneumothorax and incidentally detected in a uniportal video-assisted thoracic surgery (VATS). Total agenesis of the pericardium, which is very rare and usually asymptomatic, has a very good prognosis and does not require additional treatment unless it causes complications. It may mimic pneumothorax findings.

Keywords: pericardial agenesis, uniportal VATS, pneumothorax, congenital

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Introduction

Congenital agenesis of the pericardium is a very rare cardiac pathology [1,2]. It develops as a defect in the form of partial or total absence of the pericardium as a result of the defective separation of the pleura and pericardium joining in the midline, with an incidence of $<1/10,000$ [3,4]. Two cases and one case were reported in two large autopsy series of 13,000 and 14,000 patients [4,5]. The diagnosis of this anomaly, which is mostly asymptomatic, is usually made during autopsy or surgical intervention. Therefore, the true incidence is not known. The male gender is dominant, and the male-female ratio is 3:1. Familial transmission is rare [6,7].

This congenital defect manifests with complete or partial pericardial agenesis. A left-side pericardial defect is detected 70% more frequently, a right-side defect is detected in 14% of cases, and a complete bilateral pericardial defect is detected in 7-9% of cases [5,8,9]. The prognosis of total pericardial agenesis is better without mechanical complications [10]. A case of incidentally detected complete pericardial agenesis mimicking the radiological findings of pneumothorax is presented in this study.

Case Report

A 27-year-old man presented to our clinic with complaints of shortness of breath and chest pain. A chest X-ray showed a pneumothorax line on the left. The air-fluid level in the costodiaphragmatic sinus was pushed to the left diaphragm, with enlarged intercostal distances on the left and left retraction of the heart. Figures 1a,b shows the preoperative and postoperative chest X-ray. Left posterior lower lobe and lingula bulla, pneumothorax, and minimal pleural effusion were observed on computed tomography of the thorax. Cardiac herniation with a complete deviation of the heart to the left was considered (Figure 2). The patient's smoking history was 10 packs/year. No pathology was detected in blood biochemistry and laboratory tests. The pulse was 70/min, with normal sinus rhythm on ECG. The arterial blood pressure was measured as 120/70 mmHg. No additional disease was determined in the patient's past or family history. Surgery was recommended for the patient, who underwent tube thoracostomy and was found to have a giant bulla with no lung expansion. Wedge resection of the posterior lower lobe and lingula bullae (bulla resection) was performed with left uniportal video-assisted thoracic surgery (VATS). The exploration of the intraoperative thoracic organs showed an absence of pericardium (Figure 3). The opinion of the perioperative cardiovascular surgery team was received, and additional intervention was not considered. Congenital cardiopulmonary pathology was not detected in this case, which was detected incidentally, except for congenital bullae. The patient, who did not develop

postoperative complications, was discharged on the 5th day. The retrospective findings included EF: 65%, PAP: 28 mmHg, and the absence of pericardium in the right and left heart. Other cardiac evaluations and parameters were normal on the echocardiogram performed at the postoperative 3rd-month follow-up. The patient has been followed up without problems in the 6th postoperative year. Written informed consent was obtained from the patient for the publication of his data.

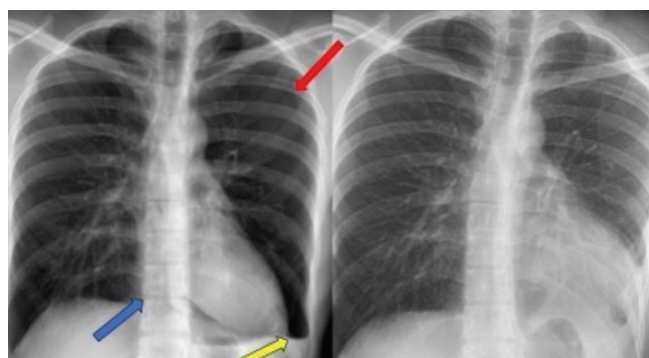


Figure 1. Preoperative chest X-ray showing enlarged intercostal spaces (red arrow), mediastinal shift (blue arrow), air-fluid level (yellow arrow) (a), postoperative chest X-ray showing mediastinal shift (b).

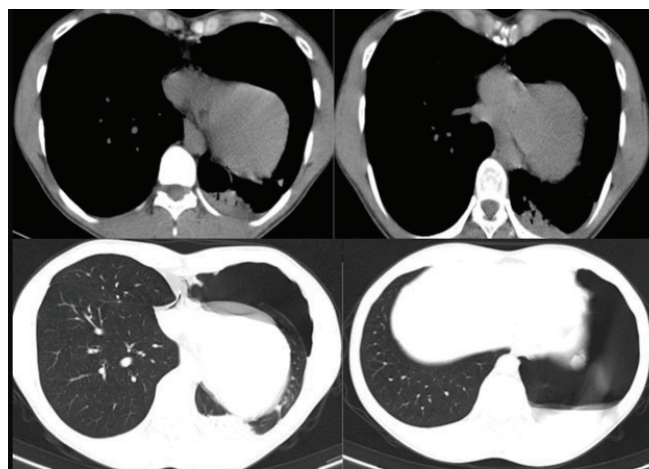


Figure 2. Thorax CT images showing the complete deviation of the heart.

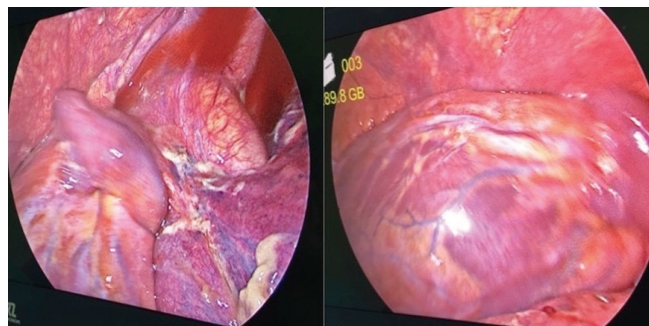


Figure 3. Operative images showing the absence of pericardium.

Discussion

The congenital absence of the pericardium is a rare malformation, characterized by the absence of the fibrous membrane surrounding the heart. Inadequate blood supply to the pleuropericardium causes defective development of the pleuropericardial membranes because of early atrophy of the left main cardiac vein, causing pericardial insufficiency [8]. The absence of pericardium on the left side is the most common (70%), and the complete bilateral absence of pericardium (7-9%) is rare [5,8]. Although congenital pericardial agenesis is reported as an isolated pathology, it can be detected together with other congenital cardiac and pulmonary anomalies in 30% of cases [10]. No congenital cardiopulmonary pathologies other than congenital bullae were observed in our case, and isolated complete absence of the pericardium was detected.

Pericardial agenesis is usually asymptomatic and can be detected incidentally in autopsies or cardiothoracic operations. Rarely, clinical manifestations such as stabbing chest pain, shortness of breath, palpitations, and dizziness have been reported [8]. We think that the complete pericardial agenesis detected in this case was asymptomatic and the complaints of dyspnea and chest pain were related to acute pneumothorax. Only the left side was evaluated with VATS after the absence of pericardium on the left side and the absence of pericardium on both sides was detected on the postoperative echocardiogram. The retrospective re-evaluation with computed tomography of the thorax supported the findings. Therefore, the case was evaluated as complete pericardial agenesis. Right bundle branch block with sinus bradycardia, prominent P waves, and weak R waves have been reported on ECG in patients with pericardial agenesis [11]. A case with T-wave changes has also been reported [12]. The ECG was in normal sinus rhythm, and no pathological changes were detected, in our case.

Atelectasis may develop in pneumothorax because of the collapse of the lung, with possible retraction of the heart to the same side. There is an indication for emergency intervention because it presents a serious life-threatening situation. Ipsilateral retraction of the heart because of pulmonary atelectasis was interpreted as a sign of pneumothorax, and pericardial pathology was not considered, in our case. Although the lung was expanded with tube thoracostomy, no improvement in the cardiac shift was observed. In such pleural patholo-

gies, if no improvement occurs in cardiac shift despite the expansion of the lung with the necessary intervention, the rare condition of pericardial agenesis should be considered.

The prognosis of complete pericardial agenesis without mechanical complications is very good. However, tricuspid regurgitation because of cardiac herniation, stretching of the chordae, myocardial strangulation, ischemia, atrial septal defect, mitral valve prolapse, and sudden death have been reported in the partial absence of pericardium [1,13-15]. The prognosis was good in our case, and the patient has been followed for 6 years without any problems.

In conclusion, no pathognomonic finding exists on clinical, radiological, ECG, and echocardiogram examination for the diagnosis of total agenesis of the pericardium, which is rare and usually asymptomatic. As long as complete pericardial agenesis does not cause any complications, it should be followed without the need for additional surgical intervention. Notably, it may mimic pneumothorax findings.

Declaration of conflicting interests

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Authors' contributions

HU; Data curation, formal analysis, project administration, resources, writing, review and editing, MA, NE,MRÇ; resources, co-writing, review, editing.

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Case Report

Video-assisted thoracoscopic surgery for a giant mediastinal teratoma in a pediatric patient

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ABSTRACT

Mediastinal teratomas are tumors originating from the primitive germ streak. The primary treatment for these tumors is surgery, traditionally performed through thoracotomy or sternotomy. Video-Assisted Thoracic Surgery (VATS) procedures have been increasingly employed in adult patients. However, the utilization of the VATS approach in pediatric patients remains limited worldwide. Furthermore, the presence of teratomas in the anterior mediastinum poses a challenge for VATS surgery in pediatric patients, as it involves delicate anatomical structures such as the heart, vena cava, and aorta. Here we present the case of a symptomatic pediatric patient weighing 35 kilograms who presented with respiratory distress. The patient had a mass measuring 7.5 cm in diameter with indistinct borders with the pericardium. The patient underwent a successful complete surgery using the VATS technique. VATS is a reliable surgical approach for mediastinal teratoma surgery in pediatric patients, provided the surgeon has adequate experience.

Keywords: mediastinal teratoma, mature teratoma, pediatric surgery, teratoma, video-assisted thoracic surgery

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Introduction

Teratomas are tumors that may arise from more than one primitive germ cell layer. They commonly occur in the sacrococcygeal region, as well as other locations such as the ovaries, head and neck, mediastinum, testes, and central nervous system. Mediastinal teratomas usually lack specific clinical signs and are often asymptomatic. However, when symptoms do arise, they typically include chest pain, fever, cough, and hemoptysis. The primary treatment for these tumors is surgery [1].

Video-Assisted Thoracic Surgery (VATS) has become a standard surgical approach for the diagnosis and treatment of various disease groups among adults. However, its utilization in pediatric patients remains limited worldwide. This limitation stems from factors such as the anatomical structure of the pediatric chest, limited space, challenges with intubation (single lumen/double lumen), and the lack of specialized closed surgical instruments for pediatric patients, and insufficient experience in this population [2].

Furthermore, the localization of teratomas in the anterior and superior mediastinum presents an additional challenge in pediatric patients due to their proximity to critical anatomical structures, including the heart, vena cava, aorta, innominate vein, and phrenic nerve [2-4].

Case Report

A 13-year-old male patient, who had been followed up for growth retardation, presented to another medical center with a persistent cough that had been ongoing for the past month without improvement despite treatment. During the physical examination, the patient's height was measured at 137 cm, and he weighed 35 kg, leaving him below the 3rd percentile and indicating growth and developmental retardation. As a result of visualizing a well-defined opacity in the right mediastinal area on the posteroanterior chest X-ray (Figure 1), a contrast-enhanced chest CT scan was conducted.

The CT scan revealed a mass measuring 75x36x47 mm in size, located in the prevascular area of the anterior mediastinum. This mass contained fluid, fat, soft tissue density, and calcification (Figure 1). To further assess the mass's relationship with the mediastinal structures, a contrast-enhanced chest MRI was performed. The borders of the mass with the pericardium were not clearly distinguishable, raising suspicions of a germ cell tumor.

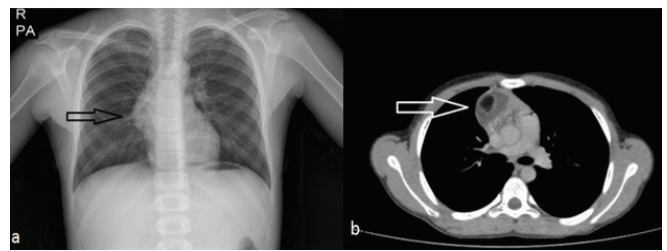


Figure 1. The view of mediastinal mass in lung x-ray (arrow) (a), mediastinal teratoma in Thorax CT scan (arrow) (b).

Based on the initial findings, the patient was referred to our center for surgical treatment. The blood tests showed no abnormalities, and the AFP and beta-HCG levels were within the normal range. Considering the possibility of a gonadal primary tumor, scrotal and abdominal ultrasound examinations were conducted, which revealed no gonadal lesion.

Given the unclear borders of the lesion with the pericardium and its diameter of 7.5 cm, the family was informed about the high likelihood of requiring conversion to thoracotomy or sternotomy during the surgery.

The patient was placed in the supine position, and intubation was successfully achieved using a size 28 double-lumen left intubation tube. To access the thoracic cavity, a mini camera port was created through the right anterior axillary 7th intercostal space. A 5-mm-diameter optical camera system with a 30-degree view angle was employed. Within the anterior mediastinum, a well-defined encapsulated mass displaying adhesions with the thymus and mediastinal structures was observed (Figure 2). During the surgery, it was determined that the wing of the mass could be separated from the pericardium through blunt dissection. As a result, a second port entrance was created in the right mid-axillary line at the 4th intercostal space to facilitate the dissection process. The mass was dissected from the surrounding tissues using an ultrasonic energy device. Once the lesion was completely resected, the camera port was enlarged, and the mass was removed en-bloc in an endobag (Figure 2). During the procedure, no carbon dioxide (CO₂) was used. The operative time was 93 minutes, and the estimated blood loss was 110 cc. Macroscopically, the mass was observed to contain sebum, fat, hair, and cartilage tissues (Figure 3). Following the removal of the mass, a 16F chest drain was inserted into the right hemithorax and the operation ended. No complications arose during the surgery.

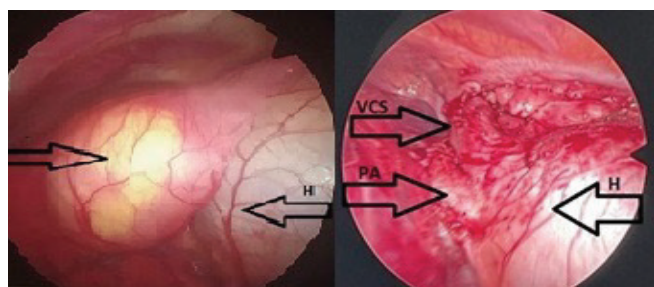


Figure 2. The location of teratoma during surgery; T; teratoma, H; Heart (arrow) (a), mediastinal space after resection of the teratoma (Abbrev.: VCS; vena cava superior, PA; pulmonary artery, H; heart) (arrow) (b).

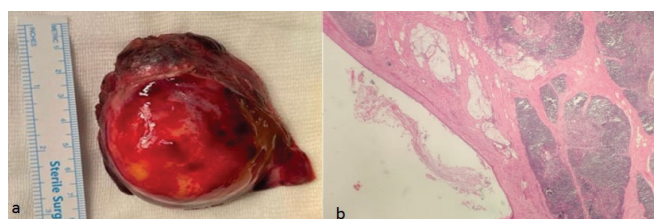


Figure 3. Macroscopic view of the tumor (a), microscopic view of the tumor; Squamous epithelium, skin layers (ectoderm), muscular and fat tissue (mesoderm), salivary glands (endoderm) in hematoxylin eosin stain (b).

The patient, postoperatively extubated and transferred to the intensive care unit, demonstrated a good general condition with stable vital signs and consciousness. No air or fluid drainage was observed from the chest tube. Furthermore, the patient did not exhibit diaphragm elevation and was subsequently transferred to the ward where he was mobilized.

During the ward follow-up, the patient remained free of complications. On the third postoperative day, the patient was discharged after the removal of the chest drain. The chest X-ray taken on the 15th day after discharge was insignificant.

The results of the pathological examination indicated a mature teratoma with typical hyperplasia and multiple cysts (Figure 3). No additional treatment was deemed necessary, and the patient was placed under regular follow-up. Written informed consent was obtained from the parents for the publication of his data.

Discussion

Mediastinal teratomas account for 5-10% of all mediastinal tumors. They originate from vascular potential stem cells during the development of thymus tissue in embryonic life and consist of multiple germ layers. These tumors do not show a clear gender distribution. The highest incidence is observed in the age group of 20-40 [5,6].

Mediastinal teratomas often do not cause specific symptoms and are typically asymptomatic. However, symptomatic patients commonly present with chest pain, dyspnea, and hemoptysis. The presence of symptoms is considered by some authors as a relative contraindication for minimally invasive surgery [7].

Chest X-ray is often the initial diagnostic modality, but the main diagnostic tool is a chest CT scan [7].

Surgery is the primary treatment for mediastinal teratomas. The conventional surgical approaches include sternotomy and thoracotomy. VATS is increasingly preferred due to its minimally invasive nature, better cosmetic outcomes, shorter length of hospital stay, and potential to reduce complications such as scoliosis and muscle development defects, which can occur in up to 10% of pediatric patients undergoing thoracotomy. However, VATS is not yet considered a standard surgical approach for pediatric mediastinal tumors [8].

Performing VATS surgery for mediastinal teratomas in pediatric patients presents two primary technical challenges. The first challenge relates to the patient's characteristics. Pediatric patients, due to their anatomically limited thoracic space, elliptical thorax shape, absence of specialized closed surgical instruments for their size, and lack of surgical experience, cannot be intubated with double-lumen tubes if they weigh less than 30 kg [3,4,7]. The second challenge is associated with the location of the teratomas in the anterior and superior mediastinum. These tumors are localized close to critical anatomical structures such as the heart, vena cava, innominate vein, and phrenic nerve, making the surgical procedure more complex and increasing the risk of major complications. Although there are limited studies available in the literature on this subject, both in pediatric and adult patients, it appears that the location of mediastinal teratomas poses significant challenges [4].

The literature contains various opinions regarding the eligibility of patients for the VATS approach. Suspected invasion or presenting symptoms are considered relative contraindications. Furthermore, there is a suggestion that patients with a tumor diameter exceeding 5 cm may not be suitable candidates for VATS. However, it is important to note that these recommendations are primarily based on studies conducted with adult patients, and there is a lack of specific recommendations for pediatric patients [4,7].

The largest study we found in the literature focusing on adult patients included 108 patients and accumulated data over 26 years. Remarkably, only 22 out of 108 adult patients with mediastinal teratoma underwent VATS surgery. Another study from China, spanning 10 years and involving a total of 28 adult patients, reported the largest series of patients who underwent teratoma surgery using minimally invasive techniques. These limited publications emphasize the rarity and complexity of such surgeries, even among adult patients [1,7].

There is a lack of serial studies specifically focusing on isolated mediastinal teratomas in pediatric patients. Sato et al. reported a pediatric VATS series involving 31 patients with tumors located in various mediastinal compartments, out of which only 6 patients underwent surgery for teratoma over a period of 23 years [4]. Similarly, in the study by Da et al., which included 137 patients with mediastinal tumors, the lowest rate of VATS utilization was observed in cases of anterior mediastinal masses upon careful evaluation of the article. Specifically, in that study, VATS surgery was performed on only 5 out of 18 children with teratoma [9].

Complete resection is recommended in teratoma surgery, although there are articles in the literature suggesting that incomplete surgeries have no impact on survival [7].

Although our patient exhibited dyspnea at admission and showed signs of pericardial invasion on MRI, along with a tumor diameter of 7.5 cm, we decided to proceed with VATS surgery based on our experience and interest with pediatric patients, despite these relative contraindications [10,11].

In conclusion, it is important to emphasize that there are no absolute contraindications for the removal of anterior mediastinal masses/teratomas using VATS. We believe that a practical approach is to begin the surgery with VATS and assess the situation intraoperatively before deciding whether to convert to open surgery. This allows for flexibility and ensures that the most appropriate surgical technique is chosen based on the patient's specific condition.

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Authors' contributions

OFD; organized the article, wrote the paper, FTB, YDKJ; contributed to the data collection MŞ, ÇG, HM; revised the the article. All authors revised the manuscript. The authors read and approved the final manuscript.

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Images in Thoracic Surgery

Pneumothorax or pseudopneumothorax?

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Here a 91-year-old male patient is presented who complained of left chest pain and shortness of breath after a percutaneous vertebral facet blockage. He has been treated for congestive heart failure for years. The initial AP chest x-ray was performed bedside, showing a curved sharp lucent line very convincing for a left sided iatrogenic pneumothorax (Figure 1a). However on auscultation, the lung sounds were similar at both apical regions. Then a PA chest X-ray was performed at the radiology unit which showed no evidence of pneumothorax (Figure 1b). We concluded that skinfold in the elderly patient mimicked pneumothorax which is known as Mach band effect [1].

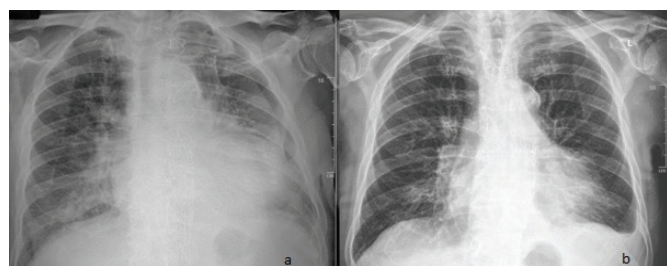


Figure 1. Skin fold mimicking a left sided pneumothorax (AP projection) (a), PA chest X-ray showing no evidence of pneumothorax (b).

We recommend to all our colleagues that chest x-rays be taken in an upright position, PA projection, and clinical evaluation should be performed to eliminate an unnecessary

chest tube insertion. Written informed consent was obtained from the patient for the publication of his data.

Keywords: invasive procedures, diagnostic imaging, pneumothorax

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Authors' contribution

TY, BO; design, review, editing and co-writing the paper equally.

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Letter to the Editor

Non-intubated thoracic surgery programs: “just another brick in the wall”

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Dear Editor,

The history of surgery is studded by innovations; but great improvements have often been initially opposed due to consolidated experiences and traditions. On the other hand, history is plenty of meteors and technical speculations fueled by exasperating personalisms miserably shipwrecked on the rock of unequivocal evidences.

However, innovations represent undoubtful milestones in surgery with the aim to achieve applicability, reproducibility and, at least, a real benefit for patients. In this scenario, non-intubated thoracic surgery (NITS) techniques stand as new strategies in the wide portfolio of patients’ tailored approaches and pathways, such as minimally invasive surgery (video-assisted and robotic) and perioperative optimization programs [1].

Although one-lung ventilation (OLV) surgery still guarantees an unavoidable safety profile (stable operating field, airways control, titration of proper ventilation volumes), it is associated with detrimental related complications, such as iatrogenic airway injuries, laryngeal spasms, ventilator-induced lung injury, high risk of mechanical ventilation dependence or weaning issues in high-risk patients (COPD, reduced pulmonary functional reserves, neuropathies), as well as intraoperative ventilation-perfusion mismatches [2].

Furthermore, the need to resort to intraoperative rescue maneuvers, such as the adoption of positive pressures on the non-dependent lung or the need for intraoperative forced lung re-expansions could predispose to

an early parenchymal staple-line oozing and the onset of air-leaks in the immediate postoperative period. Finally, ventilation exclusion represents a predisposing factor for atelectasis, sublobar air-trapping and cardiovascular events as the results of transient intraoperative pulmonary hypoxic vasoconstriction. In this context, the benefits of a spontaneous breathing would appear rather obvious by guaranteeing a physiological approach and preserving intact muscle tone, functional residual capacity and mucociliary clearance [3]. But what are the limits of a NITS approach? But above all, is it an innovation for the surgeon or for the patient?

Unfortunately, we still have to come to terms with the past. Since the ancillary works by Pompeo et al [4], thoracic surgery scientific communities have rather limited its adoption only to mere diagnostic or minor parenchymal resections [5]. Nowadays, the first limit to the implementation of NITS programs still appears to be the lack of cultural transition from historical eligibility criteria, as in high-risk patients. This inexorably follows a discrepancy between theoretical advantages and daily clinical practice.

The multicenter INFINITY study [6] clearly offered an objective picture of an alarming and emblematic “leitmotiv” cyclically reappearing in the history of surgery. About one-fifth of the enrolled Centers reported lack of confidence with regional anesthesiological techniques for such approach and, in 42% of cases, the non-implementation of NITS was attributed to a putative surgical unsafety. This resulted into NITS indications’ restriction only to minor diagnostic procedures and for the treatment

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of pneumothorax in patients with high comorbidity or poor respiratory performance; while, only a small number of Departments intentionally resorted to NITS for fit for surgery patients. Although postoperative advantages were undeniable, main doubts were raised upon the management of the airways in emergency, the onset of intraoperative hemodynamic instability, the failure to resolve cough reflex, patients' cooperation and increased operating times. Moreover, additional issues raised from lack of standardization in analgesedation procedures and high incidences of ineffective intraoperative analgesia (up to 42% of cases). However, the need for a stable operating field requires technical compromises, such as the control of the cough reflex by airways anesthetic aerosolization and intraoperative vagal infiltration [7].

Facing with such ambiguous scenario and discordant literature evidences, an adjunctive element for general reticence arises from intraoperative management of life-threatening complications requiring conversion to one-lung ventilation, the need to deepen anaesthesia and the introduction of a double-lumen tracheal tube or bronchial blocker in such precarious setting, promoting a new concept of spontaneous ventilation with double-lumen intubation and short relaxation techniques [8]. But, is it only a mere compromise strategy? Probably a pre-announced failure to set aside peculiar aspects and rationale of NITS itself.

Moreover, in the context of a heterogeneous literature, geographical disparities are undeniable, as most evidences come from Eastern countries, while a generalized skepticism still claims debate in the Western ones.

In a large retrospective study, Hung et al [9] reported NITS in a cohort of 1.205 lung cancer patients. 426 were anatomical resections (lobectomies and segmentectomies). Post-operative complication rates were modest (2% air leak, 0.2% arrhythmias, 0.3% haemothorax) and intubation conversion was required in 2% of cases due to mediastinal movement or instability of the operative field. At the multivariate analysis, the Authors reported a BMI of 25 kg/m² or more and anatomical resections as risk factor for OLV conversion.

Guo et al [10], comparing 48 non-intubated video-assisted thoracic surgery (NiVATS) with 92 OLV-segmentectomies, reported no significant differences in intra- and perioperative complications. Similarly, Liu et al [11] have clearly demonstrated an undeniable safety profile of NITS procedures for anatomical parenchymal surgery

with an overall conversion rate of 7%, mainly due to unexpected pleural adhesions, mediastinal movements and the onset of hypercapnia or refractory hypoxemia.

However, taking into account technical and anaesthesiological issues, why to start a NITS program? Are there more risks or benefits? The answers seem quite far from an exhaustive definition, although the "NITS theory" would not significantly differ from "NITS practice". But, it would be a mistake to consider NITS as the latest evolution of minimally invasive thoracic surgery.

Regarding patients' outcome, surgery translates into a transient state of immunosuppression [12]. NITS would seem to reduced post-operative IL-6, TNF-alpha and C-reactive protein serum titers and these peculiar aspects should be priorities when facing oncological surgery. Recent studies have demonstrated both overall survival and disease-free survival were significantly better after NITS than OLV-surgery [8,13].

In conclusions, NITS is a modern approach claiming dignity into clinical practice. A complementary and non-exclusive opportunity among several innovations in the modern thoracic surgery.

NITS is "just another brick in the wall".

Keywords: non-intubated thoracic surgery, pulmonary resections, lobectomy

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Authors' contributions

MB,FM; organized the article, contributed to the data collection, co-wrote the paper, revised the article. The authors read and approved the final manuscript.

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Appendix A. Editorial comment

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I enjoyed reading your letter to the editor on non-intubated thoracic surgery (NITS), written with a scientific and philosophical approach in this issue of CTS. While drawing attention to the high skepticism and distancing from this approach among thoracic surgeons, the advantages and disadvantages of the procedure are clearly stated. NITS, which has been recently introduced in our country, has only been used in a few thoracic surgery centers and in small pleural and pulmonary procedures. This is not only because the application is new for us. The incomplete evaluation of data from large series and, of course, surgical conservatism are other reasons. Although the 10th, 11th and 13th literatures clearly point out the reliability of NITS, in my opinion, what is needed for widespread application is knowledge and time. Whether NITS will

be just another brick in the wall in a limited sense or a surgical-anesthesiologic roof in a new and inclusive sense will be determined by evaluating the results of large series. I believe that this letter to the editor will broaden the horizons of the readers of our journal.

Keywords: non-intubated thoracic surgery, pulmonary resections, lobectomy

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Appendix B. Editorial comment

 **Burçin Çelik*, MD**

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The authors wrote a philosophical article about non-intubated thoracic surgery (NITS) techniques in this issue of CTS. Let's remember when VATS was first introduced for lung cancer. When VATS operations were first introduced at congresses and meetings, some questioned its feasibility. A lot of surgeons said, "Is this possible? Lung cancer surgery is open, why do we need closed surgery?". Those who made these comments at that time were not wrong, because preoperative imaging methods (PET-CT, thorax CT) were not used sufficiently. As a result, preoperative metastatic lymph nodes and metastatic nodules in the lung parenchyma could not be adequately detected, thus the staging of the disease was inaccurate. In open surgery, even the smallest nodules can be palpated and evaluated with peroperative frozen section.

Another justifiable reason is that both the inadequacy of surgical instruments and the technology and variety of staplers used in minimally invasive surgery are not as good as they are today. As a result, the risk of perioperative complications will be high in forced surgeries performed with inadequate instruments and devices. Why put patients at this risk?

Now let's look at today, VATS is easily applied in almost every clinic, even in some clinics all operations are performed with minimally invasive surgery. This is because the preoperative staging methods are almost perfect, and the surgical instruments and staplers are being improved with new features every day. In addition, the surgeons, especially young surgeons, are improving their skills and abilities in minimally invasive surgery every day by using technology.

This is how NITS will be in the future and NITS is just a "brick" as the authors state. With the continuous advancement of technology and artificial intelligence, the potential innovations and developments in this field are boundless.

Keywords: non-intubated thoracic surgery, pulmonary resections, lobectomy

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