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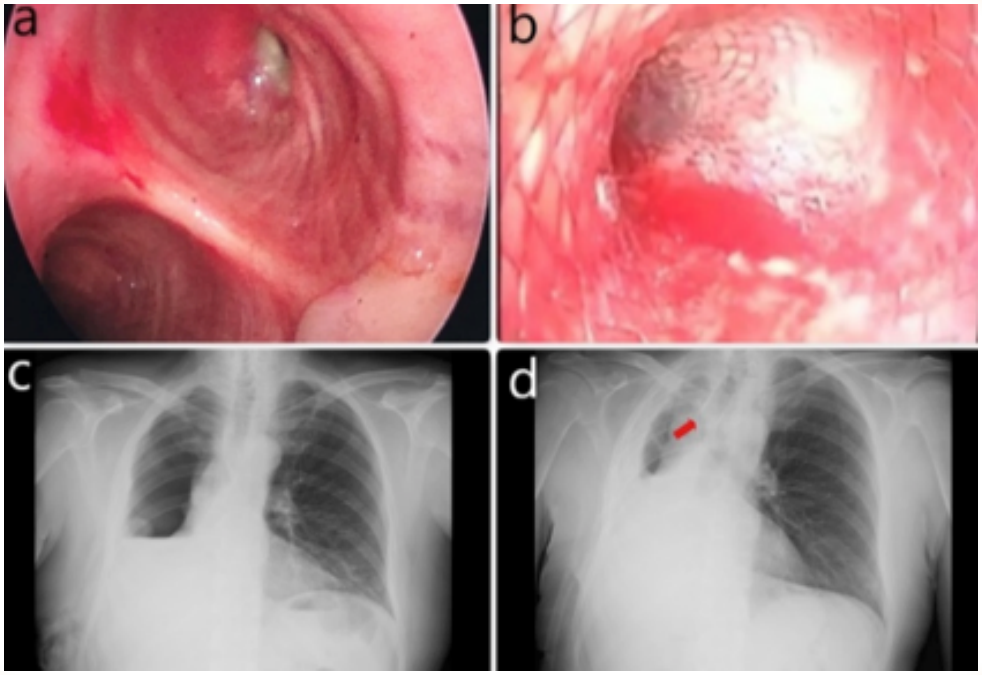
CURRENT THORACIC SURGERY



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Original Article

Reason based analysis of totally implantable venous access port explanted oncology patients: a single-center study

Hüseyin Ulaş Çınar*

Department of Thoracic Surgery, Biruni University Medical Faculty, Istanbul, Turkey

ABSTRACT

Background: Explantation of totally implantable venous access port (TIVAP) is of great importance as it may interrupt treatment in oncology patients. The aim of this study is to determine the reasons of TIVAP explantation, the relationship between TIVAP in situ time and early explantation for these reasons, and also to analyze the effect of increasing experience over time on these results.

Materials and Methods: Patients who underwent TIVAP explantation between 2014 and 2020 were retrospectively reviewed. Demographic characteristics of the patients, indications for TIVAP implantation and explantation, the TIVAPs' in situ time, early explantation rate and post-explant complications were investigated. The results obtained were compared in two time periods (January 2014-June 2017 and July 2017-December 2020).

Results: A total of 90 patients were analyzed. The mean age was 58.7 ± 10.2. While TIVAP implantation was most frequently performed for digestive tract cancers (73%), the most common cause of TIVAP explantation was an infection (53.3%). In patients with TIVAP explant due to infection, mean TIVAP in situ time (73 days) was significantly shorter compared to other reasons ($p < 0.001$). In contrast, the early explantation rate due to infection was only 16.6%. Hematoma was the most common post-explant complications, with a total complication rate of 13%. In the time, it was determined that explantations secondary to complications, early explantations and post-explant complications decreased, while TIVAP in situ time increased.

Conclusions: Infection is the reason of more than half of TIVAP explantations. Although infection significantly decreases the TIVAP survival, it rarely causes early explantation. It is important that TIVAP-related processes are performed in multidisciplinary centers and with experienced staff.

Keywords: venous port, explantation, infection, chemotherapy, cancer

Corresponding Author*: Hüseyin Ulaş Çınar, MD. Medicana International Samsun Hastanesi, Göğüs Cerrahisi Bölümü, 55080, Canik, Samsun, Turkey.
E-mail: ulscnr@yahoo.com.tr
Phone: +90 5065044784
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Introduction

Total implantable venous access port (TIVAP; also called port in brief) plays a major role in improving the quality of life and safety of patients, as that allow long-term intravenous access for chemotherapy, antibiotherapy, blood transfusion and nutritional products, and offers the advantage of obtaining venous blood samples without having to repeatedly puncture the vein [1,2]. Because the port is placed subcutaneously, it doesn't restrict daily activities by affecting the range of motion and is less prone to infections than non-totally implantable catheter [3]. Due to these characteristics, TIVAP has become an ideal tool for long-term treatments, especially cancer treatment, and is being used with increasing frequency [4].

Despite its benefits, TIVAP is also not entirely free from complications. TIVAP, which may be associated with early (hemothorax, pneumothorax, injury to major blood vessels, air embolism, cardiac arrhythmia, catheter misplacement, etc.) and late (infections, venous thrombosis, extravasation of cytotoxic drugs, mechanical dysfunction of the catheter, port-inversion, skin necrosis, etc.) complications, may need to be explanted for various reasons [5,6]. Otherwise, complicated TIVAP left in situ may cause more serious clinical consequences [7]. Apart from complications, patients may also want TIVAP removed or it can be explanted because this is no longer needed [5,6]. However, this TIVAP explantation is of great importance as it may cause delay or interruption of treatment in patients who continue to need chemotherapy. It is also known that the complications that cause TIVAP explantation are closely related to the increased labor and costs of the health system [3].

The aim of this study is to determine the reasons of TIVAP explantation, the relationship between TIVAP in situ time and early explantation for these reasons, and also to analyze the effect of increasing experience over time on these results in oncology patients.

Materials and Methods

Study design

After obtaining approval from the Local Ethics Committee for Non-Interventional Clinical Studies (protocol number: 2022-49-7164-E), a retrospective cohort study was conducted at a level II private healthcare facility. Informed consent was obtained from all patients.

Study population

For the study population, patients over the age of 18 who underwent TIVAP explantation by a single surgeon in the thoracic surgery department between January 2014 and December 2020 were examined. The selection flow diagram for the study population according to the eligibility criteria is shown in figure 1.

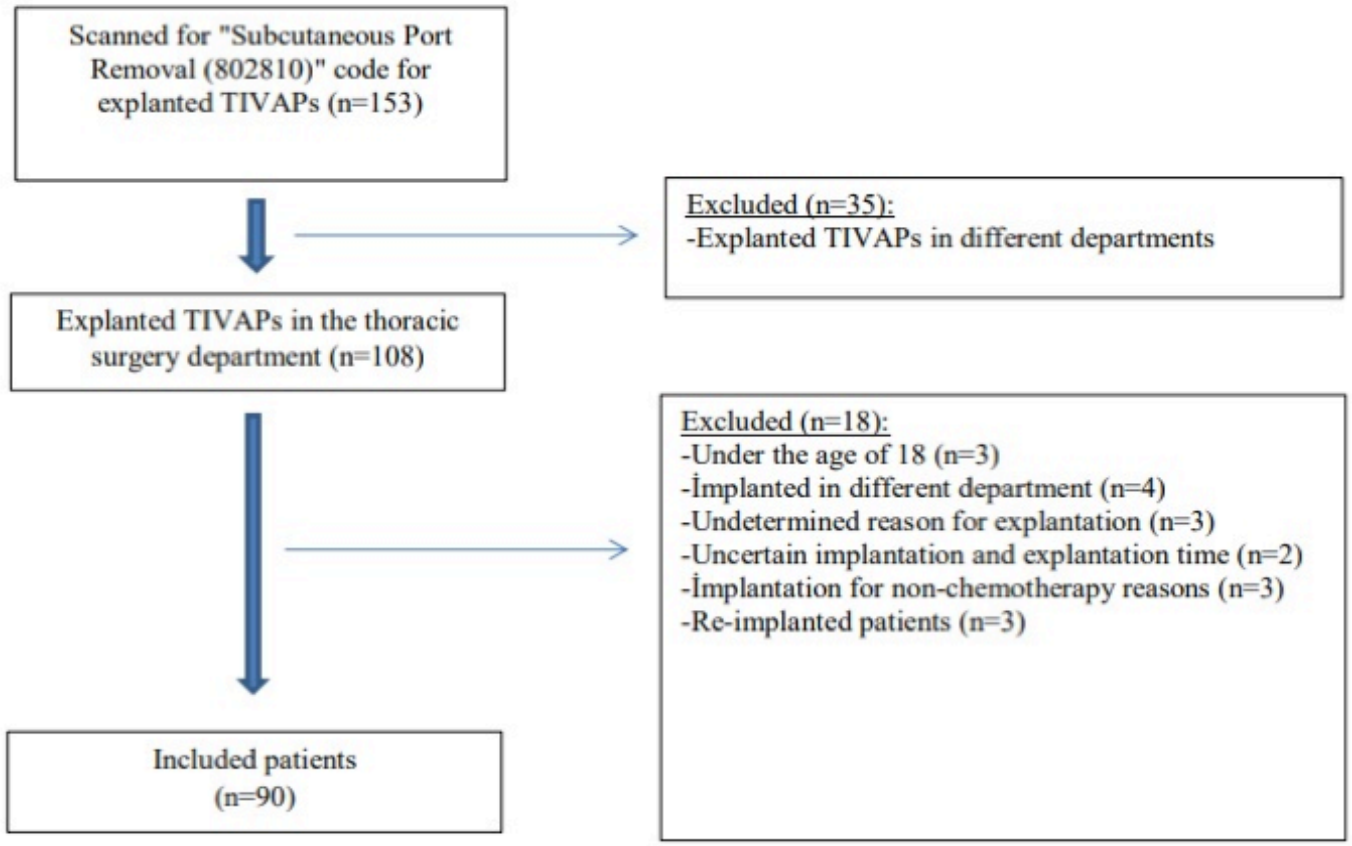

Figure 1. Flow diagram decipting study population selection.

Variables, outcomes

For each patient included in the study, data at explantation such as age, gender, BMI (Body Mass Index), indication for TIVAP explantation, microbiological data, the TIVAP in situ time, CRP (C-reactive protein) level, WBC (white blood cell) count, early explantation rate were obtained. In addition, diabetes mellitus, hypoalbuminemia, leukopenia and thrombocytopenia during implantation, TIVAP implantation indication, TIVAP implantation status, implanted TIVAP brands and post-explant complications were recorded. Primary outcomes were the reasons and frequencies of explantation of TIVAP. Secondary outcomes were the effects of explantation reasons on the TIVAP in situ time, infection parameters during explantation, reason-based early TIVAP explantation rates, and the change in outcomes in two time periods (January 2014 - June 2017 and July 2017 - December 2020).

Data collection

Data of patients who underwent TIVAP explantation were obtained from patient files and the online hospital documentation system. For this purpose, procedure reports codenamed "subcutaneous port removal", anamnesis notes of the relevant patient, epicrisis reports, constantly updated nurse clinical observation notes or consultation records were reviewed in detail.

Definitions

The reason for explantation was determined as infection in cases with fever in the clinical course before the removal procedure, with signs of stiffness, redness, tenderness, and pain on the implantation site or in cases where pathogenic microorganisms grew in one of the cultures (blood, catheter or exudate culture) taken in order to detect the fever focus (without an obvious source in another region) [7]. At the same time, the frequencies of isolated pathogens were determined in the culture studies of these cases. Dysfunctional ports were evaluated as thrombosis if they had a clinical (edema at upper extremity, swelling or pain at neck) and diagnostic (doppler sonography or thorax computerized tomography scan with contrast enhancement) findings [7]. Dysfunction was defined as dislocation, disconnection/breakage of TIVAP elements, displacement of the catheter tip towards the contralateral subclavian vein or internal jugular vein, extravasation of administered drugs, despite washing with heparinized saline solution, inability to aspirate or infuse fluids. In patients whose chemotherapy was ended, the reason for explantation was recorded as end of treatment. TIVAP explantation secondary to perforation of the skin over the reservoir without signs of infection was defined as skin dehiscence, and TIVAP explantation due to subjective ailments such as discomfort, pain, difficulty in moving the neck or shoulder, and aesthetic problems was defined as patient request. The TIVAP in situ time was defined as the number of catheter days from implantation to explantation [1], and explantation of the TIVAP within 30 days after implantation was defined as early explantation [8]. For biochemical parameters, WBC <3.500 cells/μL was defined as leukopenia, platelet count <150.000/μL was defined as thrombocytopenia, serum albumin level <3.5 mg/dL was defined as hypoalbuminemia [9]. For implantation status, patients who were hospitalized in any service during port placement were designated as inpatients, while the patients who admitted to the thoracic surgery outpatient clinic for port placement, were discharged on the same day after the procedure and did not receive any service admissions were designated as outpatients [10].

Perioperative management

In our hospital, TIVAPs are applied when long-term intravenous transportation is required for chemotherapy and blood transfusions. After oncology and hematology patients are referred from the relevant department for TIVAP implantation according to chemotherapy protocols, implantation is performed by a thoracic surgeon or cardiovascular surgeon. Attention is paid to the fact that the explantation process is also carried out by the same surgeon that performs the implantation process.

All TIVAP implantations were performed in the operating room by creating a subcutaneous pocket on the pectoral muscle through a 3 cm skin incision, under local anesthesia (10-20 mL bupivacaine 0.5%) and moderate sedation with titrated midazolam. Neither prophylactic antibiotics nor routine anti-coagulation therapy was administered [1]. Single-lumen port catheters with a diameter of 8 or 8.5 fr (Secureport®, Plan 1 Health Srl. Amaro, Udine, Italy; PowerPort®, Bard Access Systems, Inc. Salt Lake City, Utah, USA; Celsite®, Braun Medical, Boulogne Cedex, France) were applied to all patients. In most cases, the right subclavian vein was preferred with the seldinger technique as the catheterization site. However, in the presence of mastectomy or radiation scarring, the left subclavian vein, and in case of technical failure, ultrasound-guided internal jugular vein was used for implantation [13]. After implanta-

tion, the catheter was flushed with normal saline, the reservoir was filled with diluted heparin, and no antibiotic locks were used. After the procedure, radiographic imaging was performed under fluoroscopy to check the position of the catheter tip in the superior vena cava.

Patients were re-evaluated one week after TIVAP implantation for control of the operative site. After each infusion and every four weeks after chemotherapy treatment is finished, the port was flushed with heparinized normal saline (500 U heparin in 10 cc normal saline). Care and dressings of TIVAPs were managed according to guidelines for the prevention of intravascular catheter-associated infections [11]. Wound infection of the patients was evaluated according to the Surgical Site Infection Prevention Guidelines criteria [12]. The port area was evaluated for infection during each dressing, and wound swabs and blood steam cultures were taken for definitive diagnosis in suspicious cases. While superficial/local wound infections are treated with appropriate antimicrobials, debridement and abscess drainage, in case of port or catheter dehiscence due to wound infection or systemic infection secondary to catheter infection, explantation of TIVAPs were considered [2]. Patients whose catheters were occluded due to thrombosis and who did not respond to the anti-coagulant treatment were also considered for TIVAP explantation.

TIVAP explantation

The explantation procedure was performed under local anesthesia, from the previous incision, with sterile conditions. During TIVAP explantation, the pseudocapsule consisting of fibrous tissue around the port and the catheter was released with blunt and sharp dissections and then opened with a scalpel. Adhesions in the radio-opaque catheter lock area connecting the port and the catheter were cut with a scalpel to ensure full mobilization of the device, and the port and catheter were removed together. After TIVAP was completely explanted, the remaining pieces of fibrous connective tissue in the subcutaneous area were removed. Then, the subcutaneous tissues were sutured with absorbable 3/0 polyglactin (Vicryl; Ethicon, Somerville, New Jersey) and the skin tissue was sutured with 2/0 polypropylene (Prolene; Ethicon, Somerville, New Jersey). Finally, the sterile dressing was applied with a pressure bandage on the formed pocket. Antibiotic prophylaxis was not given for the explantation procedure either.

Statistical Analysis

Descriptive statistics were expressed as frequency, percentage. Categorical variables were analyzed by Pearson chi-square and Fischer exact or Pearson Chi-Square tests. The normality of numeric variables was tested with the Shapiro Wilk test. Mean differences between two groups with normally distributed will be compared by Student's t-test, whereas the Mann–Whitney U test will be applied for comparisons of the abnormally distributed data. Kruskal-Wallis test (post hoc test: Bonferroni corrected Mann Whitney U test) is a non-parametric statistical test that evaluates whether two or more samples are drawn from the same distribution. All statistical analyses were performed by using SPSS (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) 21.0 package program. $P < 0.05$ were considered as statistically significant.

Results

Demographic and clinical characteristics of patients

A total of 90 patients undergoing TIVAP explantation were analyzed for the study. The mean age was 58.7 ± 10.2 years (range, 32-77 years), 51% of the patients were male, 49% were female, and the median BMI was 28.7 kg/m2. Most patients did not have diabetes mellitus (86.7%), hypoalbuminemia (95.6%), leukopenia (96.7%), thrombocytopenia (91.1%) at the time of implantation. It was determined that implantation was performed due to the main digestive tract cancers (73%) [colo-rectal cancer (60%) and gastro-esophageal cancer (13%)]. The majority of patients (73.3%) had TIVAPs placed as outpatients. The distribution of explanted TIVAP brands differed (Table 1).

Reasons for TIVAP explantation & isolated microorganisms

The most common reason of TIVAP explantation (53.3%) was an infection. This was followed by the end of the treatment program (17.8%) (Table 2). Wound cultures, blood cultures, or catheter tip cultures were obtained from all patients with TIVAP-associated infections for further microbiological testing. Evidence of bacterial or fungal growth was found in 36 of 48 patients (75%) with infection due to TIVAP explantation. The most common (16.7%) isolated pathogen in cultures was Staphylococcus Aureus. It was determined that the most common (37.5%) isolated pathogens as a group were members of the Gram-positive cocci family. It was determined that these were followed by Gram-negative bacilli (20.8%). Identified pathogens are shown in table 3. In addition, it was determined that the catheter tip and blood culture results were positive with the same microorganisms in 9 cases.

Table 1. Demographic and clinical characteristics of patients who underwent TIVAP explantation (n=90).

Variable	n (%)
Age, year	
<65	68 (75.6)
≥ 65	22 (24.4)
Sex	
Male	46 (51.1)
Female	44 (48.9)
BMI, kg/m^2	
<18.5	2 (2.2)
≥ 18.5 to <25	60 (66.7)
≥ 25.0 to <30.0	20 (22.2)
≥ 30.0 to < 99.9	8 (8.9)
Diabetes Mellitus	
Yes	12 (13.3)
No	78 (86.7)
Hypoalbuminemia	
Yes	4 (4.4)
No	86 (95.6)
Leukopenia	
Yes	3 (3.3)
No	87 (96.7)
Thrombocytopenia	
Yes	8 (8.9)
No	82 (91.1)
Indication for TIVAP implantation	
Colo-rectal cancer	54 (60)
Gastro-esophageal cancer	12 (13.3)
Breast-thorax cancer	12 (13.3)
Head and neck cancer	6 (6.7)
Others	6 (6.7)
TIVAP implantaititon status	
İnpatient	24 (26.7)
Outpatient	66 (73.3)
TIVAP brand	
Celsite®	14 (15.6)
PowerPort®	30 (33.3)
Secureport®	46 (51.1)

Abbrev.: BMI; body mass index, TIVAP; totally implantable venous access port.

Table 2. Reasons for TIVAP explantation.

Variables	n (%)
Infection	48 (53.3)
Thrombosis	10 (11.1)
Dysfunction	6 (6.7)
Skin dehiscence	6 (6.7)
Patient request	4 (4.4)
End of treatment	16 (17.8)

Abbrev.: TIVAP; totally implantable venous access port.

Table 3. Microorganisms isolated from patients undergoing TIVAP explantation due to infection.

Microorganism	n (%)
Gram-positive cocci	18 (37.5)
Staphylococcus aureus	8 (16.7)
Staphylococcus epidermidis	4 (8.3)
Staphylococcus hominis	4 (8.3)
Enterococcus faecium	2 (4.2)
Gram-negative bacilli	10 (20.8)
Klebsiella pneumonia	4 (8.3)
Stenotrophomonas maltophilia	4 (8.3)
Acinetobacter	2 (4.2)
Fungi	8 (16.6)
Candida albicans	6 (12.5)
Candida parapsilosis	2 (4.1)

Abbrev.: TIVAP; totally implantable venous access port.

TIVAP in situ time, infection parameters and early explantation

The mean TIVAP in situ time was 215.2 ± 330 days (range, 5-1351 days) in all patients included in the study. It was found that the mean TIVAP in situ time was 73 days in patients who underwent TIVAP explantation due to infection, which was significantly shorter compared to patients who underwent TIVAP explantation for other reasons ($p < 0.001$, Kruskal-Wallis test) (Table 4). In addition, these patients had significantly higher CRP levels during explantation compared to other reasons ($p = 0.002$, Kruskal-Wallis test) (Table 4). Although only 16.6% of patients who underwent TIVAP explantation due to infection had the port removed in the early period, the majority of patients (66%) who underwent TIVAP explantation due to technical reasons causing dysfunction [displacement of the catheter towards the contralateral subclavian vein or internal jugular vein (n = 2, 2.2%), hematoma (n = 2, 2.2%), kinking of the catheter (n = 1, 1.1%), extravasation (n = 1, 1.1%)] were performed in the early period ($p = 0.003$, Exact Chi Square test) (Table 4).

Table 4. Analysis of TIVAP in situ time, infection parameters and early explantation according to TIVAP explantation reasons.

Reasons for TIVAP explantation	TIVAP in situ time, day, mean (min-max)	P[a]	WBC at explantation, (×10^3/uL), mean (min-max)	P[a]	CRP at explantation, (mg/dl), mean (min-max)	P[a]	Early explantation (n/%)	P[b]
Infection	73.11 (6 -240)	<0.001*	7.78 (1.60 - 17.01)	0.878	8.49 (0.08-25.14	0.002*	8 (16.6)	0.003*
Thrombosis	117.24 (19-237)		7.22 (3.66 - 13.30)		5.42 (0.31 23.43)		4 (40)	
Dysfunction	97.43 (2 -268)		6.83 (5 - 10.36)		0.84 (0.41 1.47)		4 (66.6)	
Skin dehiscence	368 (163 -760)		7.56 (5.52 - 10.40)		2.51 (0.14 5.06)		0 (0)	
Patient request	229.18 (194 -264)		7.44 (5.27 - 9.60)		0.65 (0.14 1.16)		0 (0)	
End of treatment	686.34 (98 -1351)		5.48 (3.26 - 12.25)		0.60 (0.04 1.16)		0 (0)	

*Abbrev.: CRP: C-reactive protein; TIVAP: totally implantable venous access port; WBC: white blood cell count; * indicates significant differences.*
[a] p value obtained using the Kruskall Wallis H test; [b] p value obtained using the Exact Chi Square test.

Post-explant complications

Peroperative complications were observed in 12 (13.3%) of 90 patients who underwent TIVAP explantation. Among these, hemorrhage and hematoma occurred at the incision site in 6 patients, transection of the catheter in 3 patients, and wound dehiscence in 3 patients. Surgical revision was required in five patients (four patients with bleeding/hematoma, one patient with wound dehiscence). Three transected catheters were removed by interventional radiology. In 10 patients, venous access incision opened, further dissection and traction were required to mobilize the catheter since the catheter could not be easily removed. However, none of the patients required venotomy to mobilize the catheter.

Comparison of results in two time periods

When the results of the study were analyzed in two time periods (49 explantation procedures were performed in the first period and 41 in the second period), it was determined that the explantations secondary to complications de-creased, and the explantations due to the end of the treat-ment and patient request increased in the next 3-year peri-od. In addition, in the second period, it was determined that TIVAP in situ time increased and early explantations and post-explant complications decreased (Table 5).

Table 5. Comparison of TIVAP explantation reasons and TIVAP in situ time over two time periods.

Variables	2014-2017 Median (min-max) /n(%)	2017-2020 Median (min-max) /n(%)
Infection	30 (62.5)	18 (37.5)
Thrombosis	6 (60)	4 (40)
Dysfunction	5 (83.4)	1 (16.6)
Skin dehiscence	4 (66.6)	2 (33.4)
Patient request	0 (0)	4 (100)
End of treatment	4 (25)	12 (75)
TIVAP in situ time	81 (5 -1192)	150 (11- 1351)
Early explantation	10 (62.5)	6 (37.5)
Post-explant complications	8 (66.6)	4 (33.4)

Abbrev.: TIVAP; totally implantable venous access port.

Discussion

In this study, in which a reason-based analysis of oncology patients who underwent TIVAP explantation was performed, attention is drawn to 3 main findings. The first one is that infection is the most common cause of TIVAP explantation. The second one is that the factor that shortens TIVAP in situ time the most among explantation causes is infection. On the other hand, the

rate of early TIVAP explantation due to infection is low. The third and the last one is that TIVAP in situ time increases with increasing experience over time, while the frequency of early TIVAP explantation decreases.

As with all medical devices, the ideal expectation from TIVAP in cancer patients is that it can be processed smoothly from the moment its implanted to the end of the treatment [8]. However, TIVAP may be associated with various complications during its stay in the body. A number of studies have shown that TIVAPs are complicated in a wide range of 1.6-28% [13]. Complications such as infection and vein thrombosis usually render TIVAP unusable and removal of TIVAP becomes inevitable. Otherwise, some undesirable consequences may be encountered, such as progression of the infection to severe sepsis or septic shock, or dissemination of vein thrombosis leading to superior vena cava syndrome [14]. However, TIVAPs do not have to be removed only when they are complicated. Explantation can also be performed for some patient-related reasons such as the end of the chemotherapy or (although not recommended) aesthetic concern [14]. In conclusion, the infection has been shown to be the main reason for TIVAPs explantation in many studies [7,14]. In the series of Biacchi et al [15], the percentage of patients whose TIVAPs were explanted because the therapeutic program ended was only 12%, while the remaining 88% consisted of patients whose TIVAPs were explanted due to various side effects and complications. In this series, infection was reported as the most common reason of TIVAP explantation with a rate of 47%. In another series, the percentage of patients whose ports were removed because the treatment program was ended was 15%, while the most common cause of port removal was infection with a rate of 53% [14]. In our study, the most common reason of explantation was infection with a rate of 53%, while explantation due to end of treatment was in the second place with a rate of 17%, and the results are consistent with the literature. In this context, as a subjective impression, it can be said that these infections may be related to the inappropriate daily use of TIVAP (i.e., no flushing of the device, especially after administering artificial nutrition).

TIVAP-associated infections have been reported to be associated with internal lumen contamination following repeated puncture of the port chamber from the outside during blood collection, washing, or delivery of biological materials [6]. For these reasons, coagulase-negative staphylococci and S. aureus, which are among the natural members of the skin flora, are the most frequently isolated pathogens in port-acquired infections [6]. In addition, recently, gram-negative bacilli, Pseudomonas aeruginosa, and fungi have also begun to be isolated with increasing frequency [6]. In this study, S. aureus and coagulase-negative staphylococci were the most frequently isolated pathogens in patients who underwent TIVAP explantation due to infection, consistent with the results of the literature. Gram-negative bacilli and fungi followed them as a group.

TIVAPs are known to be medical devices with a long lifespan of up to 12 years [15]. In the case of TIVAP-associated infection, our approach is to remove it if there is no response to medical treatment and, if necessary, to insert a new port from the opposite side. In this study, it was determined that the TIVAP in situ time in patients who underwent TIVAP explantation due to infection was significantly shorter compared to patients who underwent TIVAP explantation for other reasons. This may be due to TIVAP explantation as soon as possible after detection of TIVAP-associated infection. Otherwise, it is known that TIVAP-associated infection can result in high mortality and morbidity [14]. On the other hand, it may also mean that, TIVAP explantation is not performed quickly (as in infection) in case of non-infectious complications. In support of this practice, it is recommended to try various 'rescue therapy' methods first for such complications, and to remove TIVAPs only when they are not necessary or non-functional [16]. As a result, it is understandable that there is such a difference between the duration of the port stay in the body in terms of reasons of TIVAP explantation.

In the study, it was determined that the early TIVAP explantation rate was low (15%). The most important reason for this may be that TIVAP explantation rate due to infection (the most common reason) is very low (16.6%) in the early period. Various studies have identified some factors that increase the risk of TIVAP-related infections in the early period. These factors are listed as presence of hematological malignancy, hypoalbuminemia, leukopenia, thrombocytopenia, high INR, diabetes mellitus, inpatient port placement, and port placement in the neonatal and infant period [9,17-20]. The fact that the listed risk factors were absent or very few in our patient group indicates that the risk of TIVAP-related infections in these patients is low in the early

period. In addition, it has been shown that up to 50% of early period TIVAP-associated infections can be prevented with the implementation of various multimodal programs that include the education of healthcare providers and patients [21]. Similar programs, which are increasingly being implemented in our hospital, may also have contributed to the low rate of TIVAP explantation due to an infection in the early period.

In general, TIVAP explantations are considered minor surgical interventions. In a limited number of studies in the literature, it has been reported that the rate of peroperative complications associated with this procedure ranged from 2.6% to 16% [7,22]. In addition, it has been reported that TIVAPs may not be easily removed due to infection, fibrous sheath reaction, fixation to the vessel wall, dense adherent calcifications, post-thrombotic adhesions, long catheter length and a long stay in the body, and even if the catheter fragment is retained, this can have serious consequences, including death, following embolization to the heart or pulmonary arteries [7,22,23]. Therefore, it has been mentioned that interventional radiology may be needed at any time during the procedure, and even open surgery (venotomy, sternotomy, etc.) may be required in cases with high explantation difficulty [22]. In this study, the peroperative complication rate associated with the explantation of TIVAP was 13%, which is comparable to the reported complication rates. The main complication for these cases was post-procedure bleeding/hematoma. In addition, interventional radiology was required for three transected catheters during the procedure, and advanced surgical dissection was required for 10 patients whose catheters could not be removed despite severe traction. In order to reduce these peroperative complications, it is recommended not to use polyurethane catheters, especially for protocols that require long-term implantation [24], and to use electric blades that cannot penetrate the catheter material, instead of a regular scalpel during explantation [7].

The importance of education and increased practice of healthcare providers in the prevention of complications associated with catheter implantation has been noted in various guidelines [11,21]. It has been clearly shown that the inadequacy and inexperience of the nurses and ambulatory staff responsible for the care of central venous catheters are closely related to the increase in catheter-related infection and thrombosis [25]. Accordingly, the multimodal programs (education of home health nurses, oncology nurses and ambulatory staff) implemented in our hospital may have also had an effect on the decrease in TIVAP explantation rates due to infection and thrombosis over time [7]. In the study, it is thought that the reason why the in situ time of TIVAPs placed in the second period is longer than in the first period, is that the rates of TIVAP explantation due to this infection and thrombosis decrease over time. Again, in the periodic comparison, a decrease was found in the rate of early TIVAP explantation in the second period. The reason for this is thought to be the decrease in the rates of technical complications (dysfunction, etc.) that cause TIVAP explantation, mostly in the first 30 days. The decrease in these technical complications over time also shows us that physicians have a learning curve for the implantation process [1]. We can see another effect of this learning curve in the reduction of post-explant complications over time. Supporting our results, in a study by D'Souza et al [1], it was shown that the incidence of both complications and infections decreased significantly in the second study period, and attention was drawn to the learning curve of healthcare staff.

This study has several limitations. Firstly, the study is a single-center, non-randomized, retrospective study with relatively small sample size. Secondly, the study consisted of patients with different underlying malignancies and the use of different brands of catheters, therefore different chemotherapeutic regimens and variations in material quality may have affected outcomes, complications that may cause explantation, and the TIVAP in situ time. Thirdly, since a retrospective database was used over a 6-year period in the study, a detailed analysis of the changes in the patient care that was improved over time could not be performed. Finally, most of the TIVAPs in the study were inserted into the subclavian vein, and only a few were inserted into the internal jugular vein. The bias of these data may affect the observational results. Prospective studies with more controlled patient enrollment will help to eliminate these limitations in the future. Besides, the strength of our study is that all patients were operated on by the same surgeon in the same hospital using the same surgical technique.

In conclusion, infection is the cause of more than half of TIVAP explantations, which may interrupt chemotherapy in oncology patients. Pathogens isolated in cultures of infected patients are predominantly natural members of the skin flora. Although infection is the fac-

tor that most significantly decreases TIVAP survival, it rarely causes TIVAP explantation in the early period. In addition, it is important that processes such as TIVAP implantation, care and explantation (although it may seem like simple medical processes) are carried out in multidisciplinary centers and by experienced staff, as better outcomes are closely related to interdisciplinary collaboration, training of healthcare providers and increasing experience over time.

Declaration of conflicting interests

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Ethics approval

Approval was obtained from the Local Ethics Committee for Non-Interventional Clinical Studies of Biruni University (protocol number: 2022-49-7164-E).

Authors' contribution

HUÇ; conceptualized and designed the study, collected and analyzed data, revised the final version of the manuscript and wrote the paper.

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Original Article

Preoperative assessment and outcomes of general thoracic surgery approaches during COVID-19 pandemics

Seray Hazer*, Necati Solak, Leyla Nesrin Üstün Acar, Funda İncekara, Koray Aydoğdu, Pınar Bıçakçıoğlu, Göktürk Fındık, Selim Şakir Erkmen Gülhan

Department of Thoracic Surgery, Health Sciences University, Atatürk Chest Disease and Thoracic Surgery Research and Training Hospital, Ankara, Turkey

ABSTRACT

Background: COVID-19, a novel coronavirus affecting the respiratory system, was diagnosed in China in December 2019. With the pandemic, many new changes had to be made in thoracic surgery clinics.

Materials and Methods: The patients who underwent surgery at Thoracic Surgery Department between March 11, 2020, and October 11, 2020, during the COVID-19 pandemic were evaluated retrospectively. The precautions and new preoperative procedures in our thoracic surgery clinics were analyzed retrospectively.

Results: A total of 1177 patients were treated in thoracic surgery clinics, 299 underwent surgery under general anesthesia during the pandemic, and 948 patients were excluded. Common complications were prolonged air leakage and pleural effusion, and complications occurred in 16.4% of the patients. The mortality rate was 1%. One of the patients with bullae excision due to prolonged air leakage (with COPD) was diagnosed on the fifth postoperative day, another with right pneumonectomy had radiological findings compatible with COVID-19 on the fourth postoperative day, despite negative PCR results four times, and the third patient with thymoma who underwent extended thymectomy without any COVID-19 findings were deceased.

Conclusions: Considering that COVID-19 increases mortality due to increased inflammation and pulmonary involvement, COVID-19 infection co-occurring surgical interventions of the lung will adversely affect the patient's prognosis and cause an increase in transmission. While caution should always be exercised in all surgical procedures in the pandemic, more severe precautions should be taken in thoracic surgery operations. Implementing comprehensive protective measures such as preoperative PCR test, thorax CT before surgery, quarantine, and disinfection are essential to control nosocomial infection.

Keywords: COVID-19, thoracic surgery, pandemics

Corresponding Author*: Seray Hazer, MD. Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim Araştırma Hastanesi, Göğüs Cerrahisi Kliniği, Pınarbaşı Mah. Sanatoryum Cad. 06280, Keçiören, Ankara, Turkey.
E-mail: drserayhazer@gmail.com Phone: +90 5052942974
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Introduction

The first case of Coronavirus was reported in 1960 and was known as a common cold clinic, which was not fatal until 2002 [1]. In 2003, Coronavirus caused SARS (Severe Acute Respiratory Syndrome) with fatal pneumonia that affected many countries and caused more than 1000 people to die. In 2012, MERS (Middle East Respiratory Syndrome) caused a second epidemic with high mortality pneumonia and showed its effect in many countries. In December 2019, the first COVID-19 (Corona Virus Disease ID- 2019) findings were reported to the World Health Organization (WHO) as a new coronavirus pneumonia agent from Wuhan, China. COVID-19 has lower mortality compared to SARS and MERS (2.3%, 9.5%, and 34.4%, respectively), but it caused an epidemic worldwide in a short time due to its ability to spread much faster than the others [2]. The incubation period is about 1-14 days, primarily symptoms in 2-7 days [3].

COVID-19 pandemic is a significant global health threat and has affected all aspects of the healthcare system. Healthcare professionals had to change their daily practice to adapt to this unexpected situation. In the healthcare services provided during the pandemic period with the principle of "First, Do No Harm- Primum non-nocere" the benefit-harm assessment for patients and measures should be taken to minimize the viral exposure of healthcare workers and other patients. Regulations such as predicting and managing the risks of perioperative complications, postponing elective surgeries, and using the intensive care capacity effectively gained importance in this process. Due to the long process of the COVID-19 disease, its long incubation period (1-14 days), and its asymptomatic cases with a frequency of 30-40%, preoperative selection and evaluation of patients to undergo surgery are difficult. The current preoperative evaluation and preparation approach in thoracic surgery clinics during the COVID-19 pandemic process will be discussed in our article.

Materials and Methods

The patients who underwent surgery at Atatürk Chest Disease and Thoracic Surgery Research and Training Hospital, Thoracic Surgery Department, between March 11, 2020, and October 11, 2020, during the COVID-19 pandemic were evaluated retrospectively. Patient demographics, surgical procedures, complications, COVID-19 symptoms, PCR test results, radiologic assessments, and outcomes were evaluated. Procedures like tube thoracostomy for pleural effusion or pneumothorax, closed pleural biopsies, local biopsies, and bronchoscopies that do not require general anesthesia or operating room usage were excluded.

Surgical activity changed significantly during the pandemic. Selection criteria for surgical patients are also described according to pandemic pace. In our hospital, in the first fifth month of the pandemic, PCR-positive patients were diverted to COVID-19 hospitals, and treatments of other pulmonary diseases, thoracic oncologic patients, and emergent disorders were carried out more safely. In the second five months of the pandemic, our hospital started giving healthcare services for COVID-19 patients with 20% capacity in the isolated Unit. New protocols were launched to reduce the risk of operating on patients with possible COVID-19, including symptom screening, a polymerase chain reaction test for COVID-19, and computed tomography scans of the chest (Figure 1). The surgery decisions and suitable time were considered according to these findings and protocol.

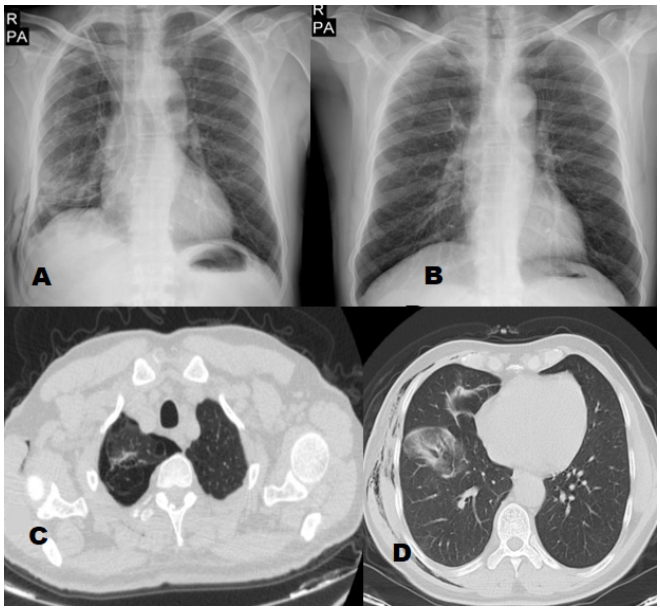

Figure 1. 51-years-old male patient admitted to our hospital with chest pain was diagnosed with pneumothorax. Chest X-ray showing chest tube inserted for pneumothorax (A), after tube removal (B), computed tomography showing the parenchymal lesions of PCR test positive patient (C,D).

Patients referred to surgery and living in Ankara are recommended for home isolation preoperatively. Whether they come from another city, they are placed in hospi-

tal isolation, and PCR for COVID-19, blood tests, pulmonary function tests, and other deficient laboratory tests are completed during the hospital stay, preoperatively.

Initially, surgeries of patients with severe and urgent conditions such as malignancy were planned priority, and follow-up with radiological or medical treatment was recommended for other conditions. Since we did not predict the progress of the pandemic at first, we prioritized patients whose mortality would increase if they were not treated within two months and other conditions were postponed. Chemotherapy-radiotherapy (neoadjuvant or definitive) was primarily preferred for patients at the limit of operability due to low pulmonary function test results or low-performance status, and then the patients were then re-evaluated after medical treatments.

On the day of admission, we confirmed that the patient was asymptomatic. Preoperative routine blood testing (lymphocyte count, C-reactive protein, ferritin, lactate dehydrogenase (LDH) levels especially confirmed) was requested to check SARS-CoV-2, and PCR tests were applied twice in preoperative 48 hours were also added. Preoperative thorax computed tomography (CT) was evaluated seven days before surgery. After the surgical procedure, patients were treated in a COVID-19-free thoracic surgery intensive care unit (Trauma patients were hospitalized in negative pressure isolated rooms of ICU until their PCR test results came out.). Then they discharge to our thoracic surgery department room that disinfection and droplet precautions were performed. Patients were also placed in an individual room, and only one asymptomatic companion was allowed to accompany and isolated during hospitalization. Visits from family members were not allowed.

The following variables of the patients were determined: Age, sex, comorbidities, physical status, oncological diagnosis, procedure, postoperative complications, length of hospital stay, postoperative respiratory symptoms, time from operation to symptoms, PCR test for SARS-CoV-2, chest CT, chest X-ray, need for hospital re-admission and early postoperative mortality (death within 30 days after the surgical procedure).

Results

Between March 11, 2020, and November 11, 2020, 1177 patients were treated in thoracic surgery clinics, and a 34.8% decrease occurred compared to last year in the same period (1806 patients, last year for the same eight-month period). 299 patients underwent surgery under general anesthesia during the pandemic. 948 patients were excluded due to the study protocol that includes patients with tube thoracostomy for pleural effusion or pneumothorax, closed pleural biopsies, local biopsies, and bronchoscopies that do not require general anesthesia or operating room usage.

A total of 299 patients (97 female/202 male) underwent surgery, and the median age of the patients was 50.4 (6-84 years), and hospital stay was 6.2 (0-40) days. 117 (39.1%) of patients had comorbidities. The demographics of the patients are summarized in table 1.

Table 1. Demographics of patients who had elective surgical procedures.

	n=299 (%)
Age, average (years)	50.4 (6-84 years)
Sex, n (%)	
Female	97 (32.4)
Male	202 (67.6)
Comorbidity, n (%)	117 (39.1%)
Diabetes	34 (11.3)
Hypertension	31 (10.3)
Cardiovascular disease	14 (4.6)
Other Malignancy	13 (4.3)
COPD	10 (3.3)
Central nervous disease	8 (2.6)
Thyroid disease	4 (1.3)
Tuberculosis	3 (1)
Physical status, ASA classification, n (%)	
I	2
II	124
III	161
IV	12
Oncological status, n (%)	139 (46.4)
Lung cancer	103 (55)
Pleural tumors	17 (5.6)
Mediastinal lymph nodes	8 (2.6)
Pulmonary metastases	6 (2)
Mediastinal tumors	5 (1.6)

Abbrev.: ASA; American Society of Anesthesiology, COPD; chronic obstructive pulmonary disease.

We performed 134 lung resections (120 lobectomies, 11 pneumonectomies, and three sublobar resections). Resections were performed in 32 patients via VATS and 102 with thoracotomy, and 8 of the patients underwent surgery after neoadjuvant chemotherapy. Mediastinal tumor excision was performed in 14 patients, VATS and pleura biopsy in 39, decortication in 39, diagnostic wedge resection via VATS in 44, metastasectomy in 6, bullae excision in 33, exploration for hemothorax in 10, trachea resection in 3, and cyst hydatic surgery in 11 cases. Nine of the patients underwent redo-surgery due to hematoma, hemothorax, and prolonged air leakage complications. Common complications were prolonged air leakage and pleural effusion, and complications occurred in 16.4% of patients (Table 2). Three deaths were recorded in the early stage (the first 30 days after surgery). A prolonged air leakage patient with COPD who was diagnosed with COVID-19 postoperative fifth day, a right pneumonectomy patient whose radiological findings are compatible with COVID-19 on the fourth postoperative day, but negative PCR results four times, and a patient with thymoma who underwent extended thymectomy without any COVID-19 findings were decreased (1%).

Table 2. Postoperative complications.

Complications	n=49 (16.4%)
Prolonged air leakage	19
Hemothorax	11
Pleural and pericardial effusion	3
Cardiovascular complications	7
Pneumonia	4
Brocho-pleural fistula	2
Chylothorax	2
Contralateral pneumothorax	1

In the first days of the pandemic, PCR test results were delayed for 2 or 3 days. Preoperative PCR samples were taken twice for each patient for 42 days, but none were positive, and over time, a single sample was taken and continued to be evaluated. By the second peak, we started to apply the PCR test twice again due to the widespread of COVID-19. The surgery decision was reviewed with the updated thorax tomographies within 3-10 days preoperatively. Although there were deficiencies in the first period, PCR was taken from almost all patients, whether they underwent surgery or not. The patients with COVID symptoms or a high risk of contact were not allowed to enter the clinic. If the PCR test result was positive, the patient was isolated in the COVID-19 service. In our study, 5 patients (1.6%) were positive perioperatively. The surgical procedure was postponed due to positive PCR results in 5 of 299 patients scheduled for surgery. Postoperative infiltration compatible with COVID-19 was detected in thorax tomography in 2 patients.

Since March 11, 2020, four nurses, two cleaning staff, and a secretary in the Thoracic Surgery Department, four nurses in Thoracic Surgery ICU, one operating theater staff, two doctors of anesthesia and thoracic surgery departments had COVID-19, and all healed without any complication.

The American College of Surgery (ACS) prepared a guide on March 24, 2020, to classify the hospitals and determine the necessity and urgency of surgery [4]. According to this guideline, Phase 1 hospitals with a small number of COVID-19 infected patients are not yet experiencing a severe increase and are in a period of sufficient intensive care capacity. It defines partially emergencies and surgical indications that can be performed under appropriate conditions. In Phase 2, only emergency surgeries are required in cases where many infected patients are envisaged, limited intensive care facilities or a rapidly increasing number of patients are foreseen. In hospitals of this density, surgery can be performed on patients whose survival will be adversely affected within a few days if surgery is not performed. Phase 3 is situations where all the hospital facilities are directed to COVID-19 patients, and intensive care service or appropriate material supply cannot be provided. In this process, the urgency for surgery should be limited to situations where the patient's survival will deteriorate within hours if not treated. According to this classification, our hospital services are in phase 1 for the first five months and phase 2 for two months.

Discussion

In the first half of 2020, a historical global crisis started with the COVID-19 outbreak caused by the SARS-CoV-2 Coronavirus. While many people were affected by severe illness, many lost their lives. Along with severe uncertainty in the health system, diagnosis, treatment, and prevention methods that cause concerns

about the healthcare workers' workforce and protective equipment have emerged. While elective surgeries were postponed in addition to changes in standard treatments, emergency surgical margins were frequently scrutinized. However, as urgent care for patients with confirmed or suspected COVID-19 is provided, there is also a concern regarding how to care for patients needing treatment for other diseases can be maintained [5]. There was a 34.8% decrease over the same period last year. This decrease is probably due to the selection of patients according to their urgency, the avoidance of patients to the hospital due to the risk of infection, and the lockdowns. We predict that the number of patients who underwent surgery will increase again with vaccinations, social immunizations, and the ease of the measures taken.

With the pandemic, it was necessary to make regulations to minimize infection and use resources efficiently. Due to the urgency of the patients' medical conditions and the density of pandemic patients, criteria were determined for the optimal use of the remaining facilities. This severe crisis will inevitably affect the diagnosis and treatment process for patients with lung space-occupying lesions. While surgery of some benign lesions may be delayed due to their slow progress, postponing surgery in lung malignancies may change the patient's prognosis and even result in tumor progression at a level that can threaten life.

In a multidisciplinary retrospective study of 34 patients, Lei et al reported the results of COVID-19 patients who were operated on during the incubation period without knowing they were infected [6].

According to this study, while the need for intensive care was 26.1% in COVID-19 patients who did not undergo surgery, 44.1% of the patients who operated for any reason required postoperative intensive care follow-up due to the development of organ dysfunction or the need for a mechanical ventilator. Advanced age, comorbidity, and prolonged operative time are associated with poor prognosis.

This increased mortality and morbidity caused us to increase the number of precautions before surgery, routine preoperative PCR tests, and treatment planning with appropriate isolation. Preoperative two negative PCR conditions were applied in our clinic for a while. Still, the application was continued by retaking a single PCR sample due to the lack of significant results and loss of economic and time.

Although there are no standard clinical, laboratory, or radiological findings that can be used in preoperative evaluation during the COVID-19 pandemic, we evaluated the possibility of infection in our clinic by setting our standards through detailed preoperative anamnesis, contact history questioning, close fever follow-up, CBC, biochemistry, CRP, coagulation parameters, and naso-oropharyngeal PCR samples, thorax CT taken in the near operative period.

One of the essential steps in diagnosing COVID-19 is the demonstration of nucleic acid amplification by Reverse-Transcriptase Polymerase Chain Reaction (PCR) of SARS-CoV-2 RNA. Thorax computed tomography (CT) sensitivity is 97.2% when evaluated for diagnosis, while PCR sensitivity is only 83.3%. Therefore, evaluating patients with clinical suspicion with thoracic CT is essential. [7]. Serological tests for immunity developed after infection and antibodies produced against SARS-CoV-2 are evaluated with ELISA. After the disease develops, IgM can be detected in the blood on the 12th day and IgG on the 14th day [8].

In the study of Cai et al [9], seven patients who underwent thoracic surgery procedures and were infected with COVID-19 were evaluated. Preoperative tomography images taken two weeks ago were re-examined, and one of the three patients had bilateral ground-glass opacities and died of COVID-19 postoperatively. Also, radiographic changes such as infiltrates, atelectasis, and pleural effusion were found in the early postoperative period in all seven patients.

Procedures that cause intense aerosol formation, such as respiratory function tests and bronchoscopy, are kept to a minimum or not performed in many clinics. In addition to COVID-19 screening, standard preoperative evaluation methods of patients scheduled for surgery are also delayed in the pandemic process.

It is of vital importance to determine the preoperative respiratory capacity in thoracic surgery operations. Likewise, the presence of an endobronchial lesion to be detected preoperatively, observation of a bleeding focus, or bronchoscopic procedures in which the surgical margin is evaluated are evaluation methods that may be decisive for our surgeries.

If the respiratory function tests cannot be performed, evaluating respiratory capacity is feasible with other

methods such as a 6-minute walking test, and the stair-climbing test can be done alternatively. Performing detailed preoperative respiratory function procedures (PFT, DLCO, VO2 max) is essential. Be aware of the risks of possible coagulation disorders, thrombosis, and embolism, and if necessary, prophylaxis and early treatment options should be evaluated.

It is essential to share all risks with the patient, provide detailed information, including the risk of infection during the perioperative hospitalization, and make a decision with the patient, if necessary, to refer to alternative treatment methods in cases where surgery cannot be performed.

In conclusion, the COVID-19 pandemic poses a significant challenge in deciding and managing surgical operations in patients with lung cancer and other lung conditions. SARS-CoV-2 is a highly contagious and life-threatening infection. The recent study results from limited cases suggest lung resection surgery may be a risk factor for death in COVID-19 patients during the perioperative period. Therefore, surgical treatment should be done with extreme caution during an epidemic. Implementing comprehensive protective measures such as preoperative PCR test, thorax CT before surgery, quarantine, and disinfection are essential to control nosocomial infection.

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Ethics approval

This retrospective analysis was approved by the Health Sciences University, Atatürk Chest Disease and Thoracic Surgery Research and Training Hospital Medical Specialty and Education Committee (No:2020/678).

Authors' contribution

SH,NS,LNÜA,Fİ,KA,PB,GF,SŞEG; contributed substantially to study design, data analysis and interpretation, and writing of the manuscript, the conception or design of the study, the acquisition, analysis, or interpretation of the study, drafting the work or revising it critically for important intellectual content, final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to accuracy or integrity of any part of the study are appropriately investigated and resolved.

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Original Article

Specific indication for tracheobronchial stenting in patients with postpneumonectomy bronchopleural fistula: massive air leakage and respiratory distress

Güntuğ Batıhan[1]*, Kenan Can Ceylan[2], Şeyda Örs Kaya[2]

[1]Department of Thoracic Surgery, Kars Harakani State Hospital, Turkey

[2]Department of Thoracic Surgery, University of Health Sciences, Dr. Suat Seren Chest Diseases and Surgery Medical Practice and Research Center, Turkey

ABSTRACT

Background: Postpneumonectomy bronchopleural fistula is still one of the complications that are difficult and time-consuming to treat despite advances in surgical technique and technology. Although many surgical and non-surgical methods have been described in its treatment, there is no consensus on the optimal approaches. In this study, we aimed to share our experience in tracheobronchial stenting and to evaluate the efficacy and safety of the modified silicone stents and J-shaped endobronchial self-expandable nitinol stent in patients with postpneumonectomy bronchopleural fistula presenting with severe dyspnea and massive air leak.

Materials and Methods: We retrospectively analyzed data of the patients who underwent tracheobronchial stenting for postpneumonectomy bronchopleural fistula between January 2010 and December 2020 in our center. Two different endobronchial stent types were used. Modified silicone and covered self-expandable nitinol stent. The clinical features of the patients and the results of the intervention were evaluated.

Results: A total of 10 patients with bronchopleural fistulas were treated with tracheobronchial stenting. Modified silicone stent was used in 4, full covered J-shape nitinol stent was used in 6 patients. No complications were observed during the procedure. After the placement of the tracheobronchial stent, air leakage ceased in all patients and their dyspnea regressed significantly.

Conclusions: Tracheobronchial stents are an appropriate treatment option in patients with postpneumonectomy bronchopleural fistula presenting with severe dyspnea and massive air leak.

Keywords: bronchopleural fistula, pneumonectomy, tracheobronchial stent.

Corresponding Author*: Guntug Batihan, MD. Department of Thoracic Surgery, Kars Harakani State Hospital, 36200, Yenişehir, Ismail Aytemiz Street 325, Kars, Turkey.
E-mail: gbatihan@hotmail.com Phone: +90 474 2125668
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Introduction

Bronchopleural fistula (BPF) which is one of the most serious complications that can be seen after lung resections is a communication between the tracheobronchial tree and the pleural space. The incidence of BPF is 4.5% to 20% after pneumonectomy and 0.5% to 1% after lobectomy. Clinical presentation can range from a nonspecific chronic cough to serious clinical conditions such as empyema, pneumonia, and respiratory failure [1-3].

Treatment includes pleural drainage and irrigation, surgically fistula repairment (with or without vascularized tissue transposition) and endoscopic approaches like stent implantation and tissue glue applications. Among the living tissue flaps, especially the omentum has been reported to be used in the prevention of BPF development, as well as in the treatment of fistula and infected pleural cavity. However, there is no consensus on the best treatment option and the treatment algorithm in patients with postoperative BPF. Undoubtedly, the clinical condition of the patient has a great influence on the choice of treatment method [4-7].

The use of bronchoscopic methods in BPF repair has always been an attractive alternative for the patient especially whose general condition is poor and cannot tolerate a major surgical intervention. However, patients with BPF are a very heterogeneous group in terms of their clinical status, fistula localization, and underlying etiologies therefore, subgroup studies are needed to create correct treatment algorithms.

Along with the heterogeneity in patient groups, endoscopic treatment methods also show a wide variety. Some of the endoscopic methods defined in the literature for closure of BPF are as follows: bronchial stents, tissue glue, coils, N-butyl cyanoacrylate glue, and bronchial occluders [8-15].

In this study, we aimed to present the results of endobronchial stenting in patients with postpneumonectomy bronchopleural fistula who have severe respiratory distress due to massive air leak.

Materials and Methods

The protocol of this study has been approved by the local ethics committee of our center. We retrospectively analyzed data of the lung cancer patients with postpneumonectomy bronchopleural fistula who underwent nonsurgical fistula repairment between January 2010 and December 2020 in our center. Among these patients, those who underwent endobronchial stent placement with rigid bronchoscopy were included the study. Endobronchial stents were preferred in patients with severe dyspnea due to massive air leakage and who could not tolerate a major surgical intervention due to their comorbid conditions.

BPF was diagnosed with flexible fiberoptic bronchoscopy, which performed on clinical suspicion in all patients. Chest computed tomography (CT) was carried out in all patients to evaluate the post-pneumonectomy cavity and contralateral lung. The chest tube was inserted in all patients and appropriate antibiotic therapy was administered.

Two different endobronchial stent types were used in patients: Modified silicon and covered self-expandable nitinol stent. The choice of stent to be used was determined by the localization of the fistula, the urgency of the patient's clinical condition, and the availability of material. The preoperative and postoperative dyspnea of the patients were evaluated with the visual analog dyspnea scale (VADS).

Endobronchial treatment

All the procedures were carried out at the operation theatre under general anesthesia. Endobronchial stents were implanted via the rigid bronchoscopy.

We used 2 types of stents in our study; modified silicone stent and J-shaped self-expanding fully covered nitinol stents.

Silicone stents were modified with two different techniques. In the first technique, the straight silicone stent was made conical by dividing it with an automatic stapler device in accordance with the bronchial stump length (Figure 1). This technique was applied in only one patient who had a long bronchial stump and a small fistula size. In the other technique, Y-shaped endobronchial Dumon® stent (Novatech SA, La Ciotat, France) customized by closing the one side with an automatic stapler device (Figure 2). The length of the closed limb was determined by the measurement of the bronchial stump with chest CT and bronchoscopy. After the customization, the stent was placed with the NOVATECH® stent applicator through the rigid bronchoscope.

J-shaped endobronchial self-expandable nitinol stent (Aerstent® Trachea Bronchus Nitinol Stent; Leufen Medical GmbH, Berlin, Germany) was placed through its own ready-to-use applicator (Figure 3). The distal and proximal diameters and lengths of the stent lumen were adjusted specifically for the patients.

Postoperative follow-up

After the operation patients were monitored for two hours in postoperative intensive care unit. In the postoperative day 1 chest X-ray, complete blood count, and C-reactive protein results were obtained. The antitussive medication (Oxolamine phosphate 150 mg t.i.d.) administered for seven days to prevent the displacement of the stent. Even if the air leak ended after endobronchial stent application, tube thoracostomy was not terminated in the early period. Two pleural culture negativity, observation of the stent in place in the bronchoscopic examination performed at the end of the first month, and the radiological observation that the postpneumonectomy space began to shrink were our indications for tube thoracostomy termination.

Patients who tolerated endobronchial stent well and did not require intravenous antibiotic treatment were discharged after 24 hours. At the end of the first week, the antibiotic treatment of the patients who were called for control was revised according to the secretion and pleural culture results. Routine bronchoscopic control was performed in the postoperative 1st month in all patients.

The primary outcome of this study the success of the stent in improving respiratory parameters in the early period. The visual analogue dyspnea scale (VADS) was used for measuring dyspnea before and after the stent implantation. The secondary outcome was the rate of BPF closure after the stent removal in long term follow-up.

Statistical Analyses

Statistical analysis was performed using the SPSS 25.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as counts and percentages. Continuous variables were expressed as mean value ± standard deviation (SD). The change in variables over time was analyzed by paired t-test. Statistical significance was set at p-value < 0.05 (All p values presented were 2-sided).

Results

Between January 2010 and December 2020, a total of 243 patients with a diagnosis of lung cancer underwent pneumonectomy. Among these patients, postpneumonectomy BPF developed in 19 (7.8%) patients. 10 patients who underwent tracheobronchial stent in the management of BPF were included in the study. The mean age of the patients was 56.8 ± 8.0. The median time from lung resection to the diagnosis of bronchopleural fistula was 5.4 months (range 1-12). There were 7 (70%) patients with right pneumonectomy, 3 (30%) with left pneumonectomy. The mean BPF size was 9.6 ± 10.8 mm. The characteristics of the patients are summarized in the table 1.

Table 1. Patient characteristics

No	Sex	Age	Operation	Time interval (month)	BPF size (mm)	Stent	Empyema	Complication	VADS-1	VADS-2
1	M	52	Right pneumonectomy	1	7	Modified silicone	No	Obstruction	7	4
2	M	53	Right pneumonectomy	1	4	Nitinol J-shape	No	No	6	4
3	M	68	Left pneumonectomy	2	3	Nitinol J-shape	Yes	No	8	5
4	M	65	Right pneumonectomy	11	3	Nitinol J-shape	Yes	Migration**	7	4
5	M	50	Right pneumonectomy	7	3	Nitinol J-shape	Yes	Obstruction	6	3
6	M	56	Left pneumonectomy	9	6	Modified silicone	Yes	No	8	5
7	M	66	Left pneumonectomy	12	5	Modified silicone*	Yes	No	6	5
8	M	50	Right pneumonectomy	4	5	Nitinol J-shape	Yes	No	7	4
9	M	63	Right pneumonectomy	3	30	Nitinol J-shape	Yes	No	8	4
10	F	45	Right pneumonectomy	4	30	Modified silicone	Yes	No	8	5

*Abbrev.: VADS; Visual analog dyspnea scale, *The stapled straight silicone stent was used in this case, ** The malposed stents were removed via rigid bronchoscopy.*

Full covered J-shape nitinol stent was used in 6 (Figure 1), a modified silicon stent was used in 4 patients (a modified Y-shaped silicone stent was used in 3 (Figure 2), stapled straight silicone stent was used in 1 patient (Figure 3). There wasn't seen any intraoperative complication. In the postoperative period stent migration was observed in one patient at the postoperative first month. The malposed stents were removed via rigid bronchoscopy. Stent occlusion due to granulation tissue and mucus plug was seen in 2 patients.

The mean dyspnea score measured by VADS was 7.10 ± 0.87 before the procedure and 4.30 ± 0.67 at the postoperative 1st week, and this difference was statistically significant ($p < 0.001$).

According to the long-term results, complete closure of the BPF was observed in 2 patients, and stents were terminated. Mortality due to disease progression was observed in 4 patients. In one patient tracheobronchial stent was terminated due to respiratory distress associated with stent malposition. Three patients with tracheobronchial stents are still being followed up.

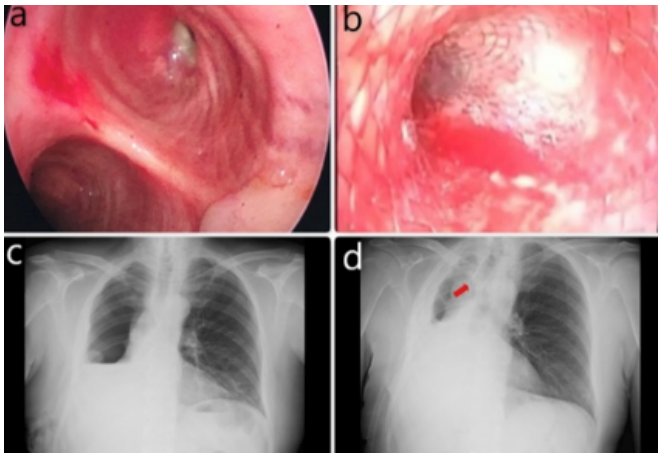

Figure 1. The advantages of covered nitinol stents are that they can be produced specifically for the patient and integrate with the tissue over time. Right sided BPF was detected **(a)**, J-shaped fully covered nitinol stent was placed **(b)**, preoperative and postoperative chest radiogram shows the dramatic resolution of the space in the right hemithorax **(c,d)**.

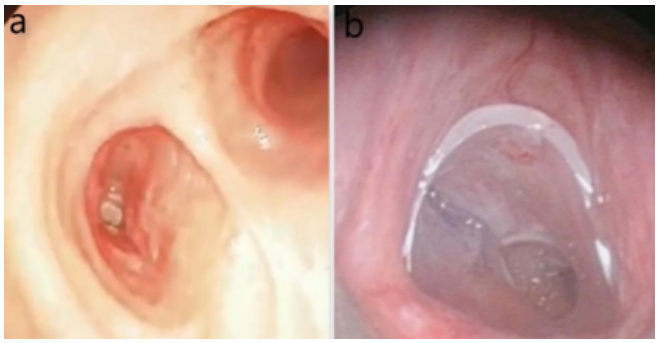

Figure 2. Y-shaped silicone stents can be modified by manual suturing or by automatic stapler. We prefer automatic stapler devices in our clinic. Left sided BPF was seen **(a)**, modified Y-shaped silicone stent was placed **(b)**.

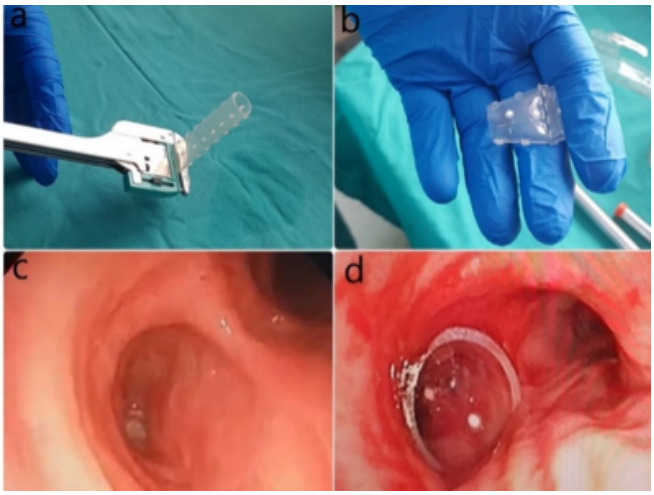

Figure 3. Modified straight silicone stent may be an alternative approach in patients with long bronchial stump and small fistula. One end of the straight silicone stent was stapled and cut according to the bronchial stump length **(a)**, the modified silicone stent was placed through the rigid bronchoscope with the appropriate applicator **(b)**, left sided BPF is seen **(c)**, the appropriate length of silicone stent completely obliterated the fistula opening **(d)**.

Discussion

Because it is associated with high morbidity and mortality, BPF is one of the most undesirable complications after lung resections. Although it can accompany many other clinical conditions, it is often seen after pneumonectomy. Its incidence following pneumonectomy ranging from 0.8% up to 8.5% and mortality ranging from 16% to 72% [1-3]. In our study, the BPF rate in patients who underwent pneumonectomy was found to be 7.8%. The slightly higher rate compared to the literature was attributed to the sociocultural status of the patient popu-

lation and low self-care, higher prevalence of comorbid conditions such as smoking, COPD, and tuberculosis.

Many surgical and non-surgical methods have been described in the treatment of bronchopleural fistulae. The first option in the treatment of early BPF after pneumonectomy is surgical repair of the bronchial stump with reoperation. Since there is almost always an infection in the pleural cavity in late BPF, the priority in treatment is to control this pleural infection. Drainage of air and infected pleural fluid from the pleural space should be performed via the chest tube thoracostomy and broad-spectrum antibiotic therapy must be initiated. There is no consensus on the optimal curative treatment method that should be applied after the control of the pleural infection. In suitable patients, transsternal transpericardial bronchial stump repair, thoracomyoplasty, omentopexy, open drainage methods (eg. thoracostoma) can be applied separately or as combined treatments [4-8].

However, these patients are generally not in a position to handle a major surgical intervention due to their poor performance status and the presence of comorbid conditions. Tracheobronchial stents can improve the general condition and performance status of patients and eliminate the risk of aspiration of the pleural content to the contralateral lung.

The use of various stent types to closure of the BPF has been previously described in the literature [8-13]. Amaral et al [15] reported the use of a silicone Y-shaped endobronchial stent with a mechanically stapled distal limb to support the closure of a BPF. Similarly, de Lima et al [16] suggested manually modified endobronchial stents to closure of the BPFs. Han et al [17] describes the use of customized Y-shaped, L-shaped and hinged self-expandable covered metallic stent to closure post pulmonary resection BPFs.

In this study we used J-shaped fully covered nitinol metallic stent in 6 patients and mechanically stapled Y-shaped or straight silicon Dumon stent in 4 patients. The biggest advantages of covered nitinol stents are that they can be modified individually and adhere to the bronchial wall by expanding at body temperature. However, their costs are much higher than the silicon stents, and procure covered nitinol stents may take several days as they are produced on-demand. In addition, fractures may occur in nitinol metallic stents due to coughing and respiratory movements or in case of migration, therefore, unlike silicone stents, it is not possible to place them again.

The biggest disadvantage that draws our attention in silicone stents is that the lumen opening is severely narrowed by folding in the presence of deviation in the tracheobronchial system. Therefore, we recommend the use of fully covered self-expendable nitinol stents in patients with severe deviation of the tracheobronchial system towards the postpneumonectomy space.

Placement of a stapled straight silicone stent is a new technique that was reported for the first time in the literature by Amaral et al [15]. We think that this technique would be more appropriate in patients with long bronchial stumps and small fistulas due to the lower risk of stent migration. For this reason, we applied it to only one patient who met these criteria and we achieved a successful result.

Several stent-related complications were described in the literature. The most common of these complications are stent migration, excessive granulation tissue, secretion retention, stent fracture and poor patient tolerance [8-10, 16-20].

In long term follow-up stent migration was seen in one patient with covered nitinol stent. The malposed stent was removed via rigid bronchoscope. Because fistula size decreased it was decided to follow the patient without a stent. The most seen long-term complication in our study was granulation tissue. Granulation tissue was observed in all patients who underwent stenting, but it was enough to narrow the airway in only 2 patients. In these patients, one with a silicone and the other with a covered nitinol stent, electrocauterization was performed via rigid bronchoscopy.

Unfortunately, we have not been able to terminate the thorax drainage tubes permanently among these patients. Short survival time and recurrent empyema are among the reasons for this condition. Bacterial colonization of

the stents and chronic contamination of the pleural space may facilitate the empyema occurrence. However, in our study, we do not have any data to prove this pathogenesis.

Because of the many potential stent-related complications mentioned above, we do not recommend endobronchial stenting as a routine treatment for postpneumonectomy BPFs. The general condition of the patient, survival expectancy and BPF occurrence time should be considered in the selection of the appropriate treatment method.

In conclusion tracheobronchial stents are useful in eliminating the risk of aspiration of infected pleural contents and reducing respiratory distress in patients with massive air leak. We suggest tracheobronchial stents in patients with late BPF that cause massive air leak, as they reduce respiratory distress and prevent aspiration of infected pleural contents. Depending on the general condition of the patient and the structure of the tracheobronchial system, nitinol or silicone stents may be preferred.

Declaration of conflicting interests

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

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Ethics approval

This study was approved by the local ethics committee of Health Sciences University Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital (approval number: 49109414-604.02).

Authors' contributions

KCC,SOK; conceptualized and designed the study, collected analyzed and interpreted the patient data regarding the pulmonary metastasis, co-wrote the paper, GB; collected and analyzed data, revised the final version of the manuscript and wrote the paper. All authors read and approved the final manuscript.

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Original Article

Investigation of the effect of surgical technique on survival and recurrence in thymoma

Merve Sengul Inan[1]*, Kubilay Inan[2], Selim Sakir Erkmen Gulhan[3], Koray Aydogdu[3], Pınar Bıcakcıoglu[3], Göktürk Fındık[3]

[1]Department of Thoracic Surgery, Gulhane Education and Training Hospital, Ankara, Turkey
[2]Department of Thoracic Surgery, Ankara City Hospital, Ankara, Turkey
[3]Department of Thoracic Surgery Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey

ABSTRACT

Background: Although rare, thymomas are common primary tumors of the anterior mediastinum. Herein we aimed to investigate the outcomes of thymoma surgeries, with a focus on survival rates and in reference to the demographic and histological characteristics of patients. The secondary aim is to identify the factors that affect recurrence.

Materials and Methods: Fifty-five patients were operated on for thymoma have been retrospectively evaluated according to their demographics, clinical characteristics, pathologies, complications, recurrences and survival.

Results: The mean SUVmax value was found to be 5.5 ± 2.05 and showed no correlation with mass diameter or stage ($p = 0.284$ and $p = 0.176$, respectively). The mean survival was 55.9 ± 35.31 months in the R0 resection group. Overall survival was not correlated with age and mass diameter at a statistically significant level ($p = 0.056$, $p = 0.108$ respectively). There was no difference in the frequency of recurrence between the WHO stages ($p = 0.775$). Conversely, when classified as per the Masaoka–Koga classification, recurrence was detected in all stage-4 patients ($p < 0.001$).

Conclusions: To date, there is no practical structure that classifies and integrates prognostic factors and creates a usable system out of them but, in thymomas, the best results are achieved by complete surgical resection.

Keywords: thymoma, thymectomy, tumor staging, VATS thymectomy

Corresponding Author*: Merve Sengul Inan, MD. Gulhane Training and Research Hospital, General Tevfik Saglam Street No: 1, Kecioren, Ankara, Turkey.
E-mail: drmervesengul@hotmail.com Phone: +090 5062889188
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Introduction

Thymomas originating from the epithelial cells of the thymus are the most common neoplasms of the anterior mediastinum. There have been some confusion regarding the staging of thymomas and their treatment management since they are encountered rarely. Over the last 50 years, various classifications of thymomas have been reported based on the content of non-neoplastic lymphocytes accompanying malignant epithelial cells of the thymus, the invasiveness of the tumor, and its localization in the thymus [1].

Invasiveness is the most important prognostic factor, and surgery remains to be the first choice in the treatment of thymomas at any stage where complete resection (R0) is attainable. The basic principle of thymus surgery is a full exploration of the mediastinum, en-bloc resection of the tumor and adjacent mediastinal adipose tissue, preservation of the phrenic nerves, and prevention of intrapleural spread. The surgical options in thymectomy include partial or median sternotomy, thoracotomy, video-assisted thoracic surgery (VATS), and robot-assisted surgery [2]. Including the thymoma surgeries performed in a single center during 12 years, the present study primarily intended to investigate the outcomes of these surgeries, with a focus on survival rates and about the demographic and histological characteristics of patients. The secondary aim is to identify the factors that affect recurrence.

Materials and Methods

Patient population and objectives

After approval from the local ethics committee of Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital (551/2017) we conducted a retrospective investigation of 55 patients with thymoma who underwent surgery for anterior mediastinal mass at the Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital Thoracic Surgery Clinic between January 2005 and December 2016 and whose postoperative pathology result indicated thymoma. Patients with thymic hyperplasia and carcinomas were excluded from the study.

Patients' age, gender, symptoms, smoking history, and comorbidities; the type of operation; the presence of myasthenia gravis (MG); thymic pathology; the length of hospital stay; drain duration; mass diameter; histological and clinical stage; maximum standard uptake value (SUVmax); the administration of radiotherapy and/or chemotherapy; complications; recurrence; and survival were recorded. Only VATS biopsy and no further resection were performed in 3 of the 55 cases. In 3 patients who underwent VATS with the goal of complete resection, perioperatively, it was understood that complete surgical resection could not be performed so only biopsy was performed. Survival according to surgical type and resection status was calculated on a total of 52 patients, excluding these three.

Pathological staging was performed in accordance with the staging criteria of both Masaoka–Koga and the World Health Organization (WHO). When staging was performed as per the WHO classification, the advanced component in mixed-type thymomas was taken as the basis.

Postoperative complications observed within the first 30 days were defined as early complications. Charlson comorbidity index was used to define and grade comorbidities [3]. As per this index, comorbid diseases are scored according to their severity. Comorbidities were given a score of 1–4 for mild–severe disease, and comorbidity was graded according to the weighted score obtained by summing the scores of comorbid diseases.

Preoperative evaluation and intraoperative indications

Posteroanterior and lateral X-ray imaging of the chest and computed tomography (CT) were performed preoperatively in all the patients. Routine blood and pulmonary function test results of the patients were also examined. Additionally, 27 (49%) patients were also examined using positron emission tomography (PET)-CT. All patients with a history of MG were first examined by neurologists before the administration of anesthesia, and then the treatment that was deemed appropriate for them was administered accordingly.

Surgical technique and follow-up

In all cases wherein total resection was attainable, in addition to the resection of the mass, with the surgical techniques performed (median-sternotomy, thoracotomy, VATS), the thymic vessels were also ligated. Additionally, all tissues that may belong to the thymus, which

were traced up to the diaphragm along the course of the phrenic nerve, were removed along with the mediastinal adipose tissues. If the mass had invaded the surrounding lung tissues, wedge resection was performed to resect it. Furthermore, observable pleural metastases were excised completely.

The postoperative pathology results of all the patients were evaluated by medical and radiation oncology specialists. A therapy regimen was planned for the patients in whom chemotherapy and/or radiotherapy was deemed necessary. After routine follow-ups on the 15th postoperative day and 3rd postoperative month, the patients were followed up with chest radiography every 3 months for up to 1 year and once every year thereafter. Patients in whom clinical and radiological suspicion of recurrence arose were examined using chest CT.

Statistical Analysis

Data were analyzed using the IBM SPSS Statistics statistical package program. The descriptive variables are presented as number of units (n), percentage (%), mean ± standard deviation ($\bar{x} \pm ss$), and median (Q1–Q3) values. To analyze the categorical variables, Pearson's chi-square and Fisher's exact tests were used. Shapiro–Wilk test and Q–Q plots were used for checking whether the numerical variables had a normal distribution. To compare the two groups, independent samples t-test and Mann–Whitney U analysis were performed for normally and non-normally distributed variables, respectively. The Kaplan–Meier method was used for survival analysis. Intergroup comparison of survival was performed using the log-rank test. To determine the correlation between two numerical values, Pearson's and Spearman's correlation analyses were performed for normally and non-normally distributed variables, respectively. The statistical significance level was set at $p \leq 0.05$.

Results

The age range of the patients was 10-73 years, and the median age was 48.7 years. In our study, 27.2% of the patients (n =15) were in their 50s and 20% (n =11) were in their 60s; these patients accounted for the majority of the study population. Furthermore, 24 (43.6%) patients were female and 31 (56.4%) were male.

Preoperative fine needle aspiration biopsy was performed for 15 (27.2%) patients. While 12 patients were diagnosed with thymoma, the remaining 3 patients were reported to have neurogenic tumor, thymic carcinoma, and lymphoid hyperplasia; this did not match with the postoperative pathological diagnosis.

The demographic and clinical characteristics of the patients as well as their stages classified as per the Masaoka–Koga and WHO classifications are shown in table 1.

Table 1. Demographic, clinical and histological characteristics of the patient.

Median age, year (range)	48.7 (10-73)
Gender, Male n (%)	31 (56.4)
Symptom, n (%)	
Shortness of breath	14 (25.4)
Chest pain	10 (18.1)
Weakness	9 (16.3)
Cough	4 (7.2)
Hemoptysis	1 (1.8)
Shoulder pain	1 (1.8)
None	16 (29)
MG, n (%)	6 (10.9)
Charlson Comorbidity Index, n (%)	
0	24 (43.6)
1	9 (16.3)
2	12 (21.8)
3	6 (10.9)
4	3 (5.4)
6	1 (1.8)
Who Classification, n (%)	
A	4 (7.2)
AB	13 (23.6)
B1	13 (23.6)
B2	15 (27.2)
B3	10 (18.1)
Masaoka Stage, n (%)	
Stage 1	24 (43.6)
Stage 2A	8 (14.5)
Stage 2B	11 (20)
Stage 3	9 (16.3)
Stage 4	3 (5.4)

Median sternotomy was performed in 32 cases, posterolateral thoracotomy was performed in 15 cases and VATS was performed in 5 cases. The median length of hospital stay and the median drain duration were shown in table 2.

Table 2. The median length of hospital stays and the median time of drain duration.

Surgery, n	VATS n=5	Posterolateral thoracotomy n=15	Median sternotomy n=32	P
Drain duration median day (IQR)	3 (2-4,5)[a]	4 (3-5)[ab]	4 (4-6)[b]	0.030
Length of hospital stay median day (IQR)	5.5 (4.25-7.75)[a]	9 (7-10)[ab]	11,5 (8-15)[b]	0.001

[a,b] The superscripts a, b indicate the differences between groups. There is no difference in groups with the same letters.

For 27 patients who underwent PET/CT, the mean SUVmax value was found to be 5.5 ± 2.05 and showed no correlation with mass diameter or stage (p = 0.284 and p = 0.176, respectively).

During the postoperative period, 10 (18.1%) patients received chemotherapy, 22 (40%) received radiotherapy, and 9 (16.3%) patients received both chemo and radiotherapy. While there were 13 patients (23.6%) who received radiotherapy alone. The mean follow-up period of the patients was 52.5 months.

There were three early complications in our study, and all of them were encountered in patients who underwent median sternotomy. Of these patients, sternal dehiscence developed in one patient and wound infection in another patient. Clinical improvement was achieved via wound debridement and meticulous wound care. Furthermore, postoperative pneumonia developed in one patient. Rapid clinical response was also achieved in this patient with antibiotic treatment. In our study, no early or late complications were observed in the VATS and thoracotomy group patients. In terms of the incidence of complications, there was no significant difference between the patients who received and those who did not receive radiotherapy and between the patients who received and those who did not receive chemotherapy (p = 0.163, p < 1.000). Additionally, the number of female and male patients did not differ in terms of their rates of incidence of complications (p = 0.314).

In our study, a total of ten patients died during the follow-up period. As per the Masaoka–Koga classification, one patient was in stage 1, two were in stage 2a, one was in stage 2b, four were in stage 3, and two were in stage 4a. One patient died in the early period due to postoperative myocardial infection, whereas another patient died due to respiratory failure secondary to massive pulmonary embolism in the 2nd postoperative month.

It was concluded that overall survival was not correlated with age and mass diameter at a statistically significant level (p = 0.056, p = 0.108 respectively).

Survival according to resection status

The mean survival was 55.9± 33.38 months in the R0 resection group (n = 43), 32.4 ± 22.44 months in the R1 resection group (n = 7), and 57 ± 23.45 months in the R2 resection group (n = 2). Considering the resection status, the R0 and R2 resection groups were found to differ from the R1 resection group at a statistically significant level in terms of survival (p = 0.005) (Figure 1).

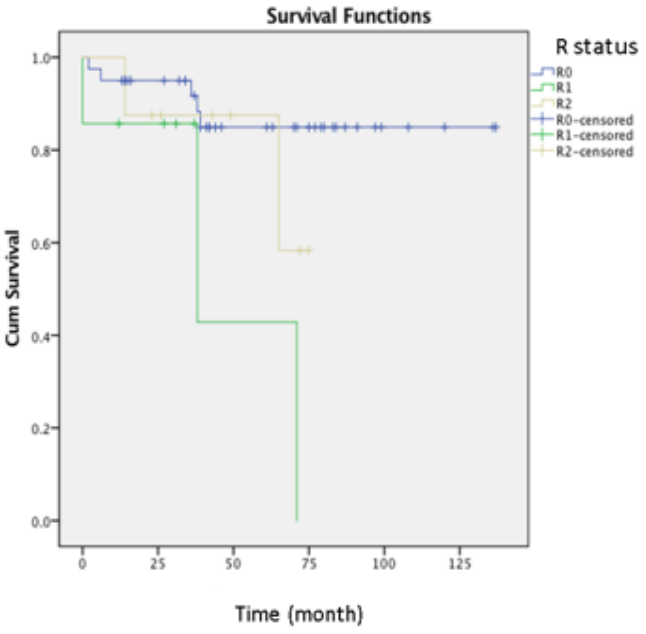

Figure 1. Survival according to resection status.

Survival according to WHO and Masaoka–Koga classifications

The overall survival of all the cases was found to be 52.49 months. When evaluated as per WHO classification, there was no significant difference between the groups in terms of overall and mean life expectancies. In contrast, when evaluated as per the Masaoka–Koga classification, there was a significant difference between the groups in terms of overall and mean survivals. The stage 1 patient group was found to significantly differ from the stage 3 and stage 4 patient groups (p < 0.001, both). The stage 2B patient group was also found to significantly differ from the stage 3 and stage 4 patient groups (p = 0.015, p = 0.004) (Figure 2).

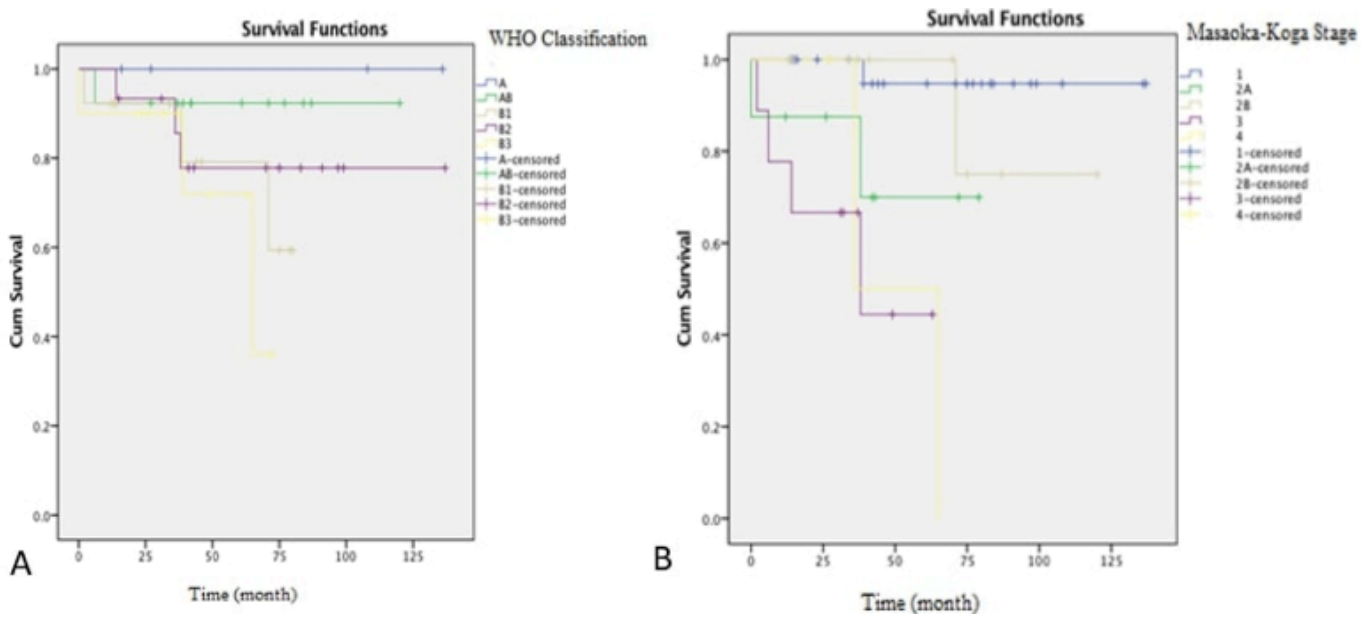

Figure 2. Survival according to WHO classification **(A)**, survival according to Masaoka–Koga classifications **(B).**

Survival according to chemotherapy and radiotherapy statuses

The mean survival was 31.5 ± 19.87 months in the group of patients who received chemotherapy (n = 10), whereas it was 57.16 ± 34.12 months in those who did not receive chemotherapy (n = 45). While the mean survival was 38.45 ± 22.91 months in the group of patients who received radiotherapy (n = 22), it was 61.85 ± 36.19 months in those who did not receive radiotherapy (n = 33). There was a significant difference in overall and mean survivals between the patients who received and those who did not receive postoperative chemotherapy (p = 0.002). Additionally, there was a significant difference in overall and mean survivals between the patients who received and those who did not receive postoperative radiotherapy (p < 0.001).

Recurrence rates according to the resection status

Recurrence was detected in 20% of the cases (n = 11). Recurrence rates according to the resection status are given in figure 2. When classified as per the WHO classification, there was no difference in the frequency of recurrence between the stages (p = 0.775). Conversely, when classified as per the Masaoka–Koga classification, recurrence was detected in all stage-4 patients (n = 3) (p < 0.001).

Discussion

Thymomas are relatively poorly understood malignancies due to their relative rarity and lack of cumulative data. Approximately 30% of patients with thymoma have MG [4]. The patients with MG accounted for 10.9% of the study population. The relationship between smoking history and thymoma has not been proven; however, 38.1% of the patients in our study had a history of smoking.

Preoperative diagnosis is not necessary for small, resectable tumors located in the anterior mediastinum that present with radiological features of typical thymoma. However, an interventional diagnostic procedure is required primarily in cases where nonoperative techniques or preoperative chemoradiotherapy is considered to be a better treatment modality or in patients with a high probability of having lymphoma. Fine needle aspiration biopsy has been reported to have a diagnostic success rate of 60% [5]. The diagnostic success rate in our study group was calculated to be 80%.

Although there are few reports on the utility of PET/CT in the diagnosis of thymic epithelial tumors, the number of patients in all these reports does not exceed 50. In our study, when patients were classified according to the WHO classification, the highest SUVmax value was found in patients with type B3 thymoma (mean SUVmax value; 7.52 ± 2.84); however, no significant difference was found between the groups. In contrast, when patients were classified according to the Masaoka–Koga classification, the highest SUVmax value was found in patients with stage 3 disease (mean SUVmax

value; 7.84 ± 3.57). In a 11-disease study by Nakajo et al, the researchers grouped patients with thymomas of type A, AB, and B1 in the low-risk group and those with thymomas of type B2, B3, and thymic carcinoma in the high-risk group and found that the SUVmax value was significantly higher in the high-risk group [6,7]. In our study, the mean SUVmax value was found to be 5.5 regardless of the mass diameter and disease stage.

In a study comparing VATS and open thymectomy, the group of patients who underwent VATS had short operative time, length of hospital stay, and drain duration and a lower rate of complications [8]. In our study, we did not encounter any complications in the VATS group patients. Consistent with the literature, the length of hospital stay and drain duration were shorter in the VATS group than in the open thoracotomy and median sternotomy groups ($p = 0.030$). In recent years, robot-assisted thoracoscopic surgery (RATS) has been increasingly performed for thymectomy. In a study comparing RATS, VATS, and sternotomy, it was underlined that intraoperative blood loss was significantly lower and drain duration and length of hospital stay were significantly shorter in the RATS group, whereas the sternotomy group was found to have the highest rate of complications [9].

It is extremely difficult to obtain reliable results from the small biopsies performed to establish the histological subtype of thymoma due to the wide variation in the characteristic morphological presentations of thymomas [10]. The WHO classification provides further insight in understanding thymomas at an advanced level and recommends specific subtypes for varying clinical characteristics encountered in patients. However, they are still not fully reliable in deciding the optimal treatment. It is now more clearly understood that type C (thymic carcinoma) is a distinct group and its prognosis is quite different from the others. Moreover, prognosis varies also among the other subtypes (A, AB, and B1–3) [11]. Histological classification is primarily used to distinguish thymic carcinoma from others.

The presence of multiple classification schemes and the variability among observers in determining the histological stage constitute another set of problems. Additionally it has yet to be clarified which subtype caused the difference. The outcomes obtained for patients in the A, AB, and B1 stages were found to be better than those obtained for patients in the B2 and B3 stages [12]. Nonetheless, based on the existing knowledge that we have, it would still be wise to accept the stage as a valid prognostic factor in thymoma.

Five-year survival rates are quite good even for stage 3 and 4 patients. 10-year survival rates for stage 1, 2, 3, and 4a are reported to be approximately 90%, 70%, 55%, and 35%, respectively [13]. In our study, the lowest rate of overall survival was observed in type B3 tumors (70%) classified according to the WHO classification and in stage 4 tumors (33.3%) classified according to the Masaoka–Koga classification; however, no significant difference was observed. This result can be attributed to the small number of the cases included in our study. Furthermore, the group of patients with stages classified according to the Masaoka–Koga classification was found to have significant differences in terms of recurrence.

Adjuvant therapies are not recommended for stage 1 thymomas that have been fully resected. Postoperative radiotherapy is recommended for patients with unresectable masses, incomplete resections, and those with capsular invasion following R0 resection [14]. In our study, 13 patients were administered radiotherapy because of microscopic capsule invasion that occurred following R0 resection. The risk of postoperative recurrence is high in stage 3 thymomas; therefore, radiotherapy is recommended in such cases [15]. In our study, there were nine patients in the stage 3 group, and seven of them (77.7%) received postoperative radiotherapy. One patient could not receive radiotherapy due to sternal dehiscence, whereas the remaining one patient died due to postoperative myocardial infarction and, therefore, could not receive radiotherapy. There are publications stating that postoperative radiotherapy does not offer benefits in stage 2 thymomas [14,16]. In our study, 10 (45.4%) of the 22 patients who received radiotherapy had stage 2 thymoma, and recurrence was observed in only one of these patients.

Preoperative induction chemotherapy is recommended to achieve R0 resection in patients who are thought to suitable for surgery [17]. In patients with sol-

itary or ipsilateral pleural metastases, induction chemotherapy or surgery is among the available options. In cases where tumors are unresectable, administering both chemotherapy and radiotherapy is recommended [16]. In our study, worse outcomes were observed in the groups receiving chemotherapy or radiotherapy, and this could be attributed to the stage and not the treatment. Therefore, this result cannot be interpreted to conclude that chemotherapy or radiotherapy has negative effects on survival.

Age is thought to affect survival to a lesser extent [18]. Our study concluded that age-related survival did not differ significantly between the studied groups. Additionally, it has been reported in the literature that age has no effect on recurrence [19]. In our study as well, no significant difference was found among the patients when their recurrence rates were compared according age ($p = 0.424$). If age does not have an effect on recurrence, it is not surprising that older patients have worse survival due to other comorbidities. In conclusion, it would be more accurate to consider that age is not a valuable prognostic factor.

Complete resection is actually the main factor whose prognostic importance has been proven in terms of survival and recurrence; however this parameter can only be assessed in patients who have undergone surgery. Many multivariate analyses have established that R0 resection is an independent prognostic factor [9]. In our study, since the patients in the R1 group died due to causes unrelated to thymoma, the R1 resection group was found to have a shorter survival rate than the R2 resection group.

In current study, recurrence was detected in all patients who underwent R2 resection, but no significant correlation was found between resection status and survival. The biggest shortcoming of Masaoka–Koga classification is the lack of a significant difference between patients who undergo complete resection and those who undergo incomplete resection of advanced tumors. However, there are studies in which high 5-year survival rates have been attained with extensive resection and reconstruction in operated patients, even in those in the advanced stages [9].

After primary surgical treatment, the patients with resectable thymoma should be followed up using chest CT scans performed once every 6 months for the first 2 years and then once a year for the next 10 years [20]. There are limited publications regarding the duration and frequency of follow-up and the radiological method that should be utilized in patients with thymoma. It is known that these patients have a high risk of developing secondary malignancies; however, there is no study that recommends performing screenings [12].

Since overall survival can be practically measured, it has been used in most cases to evaluate the surgical outcomes of thymic malignancies. However, it is not an ideal measurement because most patients with thymoma die due to causes unrelated to the disease and live for many years without recurrence. Recurrence is considered to be more useful as a parameter for assessing outcomes; however, it does not always cause death [18]. It seems more logical not to equate death with recurrence since death might occur due to any cause. Few studies have focused on recurrence and this is a field that definitely needs further research. [18-23]. In this study, recurrence was detected in a total of 11 patients (20%). The highest rate of recurrence was observed in type B2 tumors (26.7%) classified according to the WHO classification and in stage 4 patients (100%) classified according to the Masaoka–Koga classification.

This study has several limitations. First, it is a retrospective single-center study that is prone to selection bias and the sample size of the study is small. We also have limited postoperative follow-up information. Comparing the patients who received only chemotherapy and only radiotherapy with those who received chemoradiotherapy will provide valuable information by creating a more homogeneous patient group. The patients will be observed to see if recurrence will develop in the following years. Since robot-assisted surgery was not performed in any of the patients, we could not get the opportunity to compare this surgical method with the others.

In conclusion, there is an increasing need to predict the outcomes of patients with thymoma. When making clinical decisions regarding thymoma, completeness of the resection is primarily more valuable than the histo-

logical stage. The available data show that disease stage and complete resection are valuable prognostic factors. Furthermore, gender and presence of MG have been reported to have no prognostic value. The effect of tumor size and histology on prognosis should be investigated in future studies.

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Ethics approval

Approval was obtained from the local ethics committee of Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey (protocol number: (551/2017)).

Authors' contribution

MSI; conceptualization, designed the study, collected the data, contributed data analysis and wrote the paper. KI; collected the data and performed the analysis. SSEG; edited visualization, revised the final version of the manuscript. KA; edited visualization and data presentation. PB; revised the final version of the manuscript. GF; formulated and evaluated research goals. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work

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Original Article

No-touch isolation technique in early-stage non-small-cell lung cancer surgery: a retrospective study

Mehmet Çetin*[1], İlteriş Türk[2], Ebru Sayılır Güven[2], Göktürk Fındık[2], Koray Aydoğdu[2], Selim Şakir Erkmen Gülhan[2], Pınar Bıçakçıoğlu[2]

[1]Department of Thoracic Surgery, Omer Halisdemir University Training and Research Hospital, Niğde, Turkey
[2]Department of Thoracic Surgery, Ataturk Chest Disease and Thoracic Surgery Training and Research Hospital, Ankara, Turkey

ABSTRACT

Background: In parallel with the change in circulating tumor cells, the no-touch isolation technique is offered as an option to reduce recurrences of non-small-cell lung cancer. We aimed to examine the relationship of this technique with recurrence and survival in our clinic.

Materials and Methods: Among 675 patients who were operated on with the diagnosis of lung cancer between 2009 and 2015, 98 patients with tumor size of less than 3 cm in the postoperative pathology report, no visceral pleural invasion or lymph node involvement, and a negative surgical margin were included in the study. The patients were divided into two groups as patients treated with and without the no-touch isolation technique (i.e., a wedge resection group prior to lobectomy and a direct lobectomy group), and the results of recurrence and survival were evaluated statistically.

Results: While adenocarcinoma was observed more frequently in the wedge resection group, squamous cell carcinoma was observed statistically more frequently among patients treated with direct lobectomy ($p < 0.001$). There was no statistically significant difference in recurrence or survival rates between patients treated with and without the no-touch isolation technique ($p = 0.746$ and $p = 0.689$, respectively).

Conclusions: Although wedge resection before surgery is theoretically well grounded, we found that it was not clinically significant as a result of our study. The technique may prove beneficial in re-evaluating chemotherapy indications based on circulating tumor cells, especially in early-stage cases where patients have not received chemotherapy, and prospective studies are needed in this regard.

Keywords: lung cancer, wedge resection, circulated tumor cell, thoracic surgery

Corresponding Author*: Mehmet Çetin, MD, Department of Thoracic Surgery, Omer Halisdemir University Training and Research Hospital, Niğde, Turkey.
E-mail: mehmetcetn@gmail.com Phone: +90 5066139993
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Introduction

For patients with early-stage non-small-cell lung cancer (NSCLC), the primary treatment option remains lymph node dissection combined with anatomic lung resection despite alternative treatment approaches recently proposed [1]. Nevertheless, local recurrence or distant metastasis is observed in 30% of these cases and the 5-year survival rate is only 66-82% [2]. Evidence suggests that circulating tumor cells (CTCs) may be the leading cause of recurrence and distant metastasis, and studies have associated the presence of CTCs with significantly low survival rates [3-5].

The main surgical principle to prevent recurrence and distant metastasis is ligating the pulmonary vein before the artery during malignancy surgery [6]. However, the lobe is still manipulated during dissection of the pulmonary vein from the hilar structures and its rotation, potentially causing higher numbers of CTCs. Some authors argue that the CTC burden can be reduced by the no-touch isolation technique (NTIT), which involves the wedge resection of tumor-bearing tissue before the planned anatomical resection [2]. The technique has also yielded significant results in colorectal carcinoma and other non-pulmonary malignancy surgeries [7,8].

Thanks to protective mechanisms such as oxidative stress and immune response, the presence of CTCs in peripheral blood is not directly linked to their migration to distant tissues causing metastases [9]. However, a limited number of recent studies have reported significantly reduced recurrence after surgical resections with NTIT [6,7].

Here, we retrospectively compare the results of recurrence and survival among early-stage NSCLC patients who underwent lobectomy after NTIT or direct lobectomy.

Materials and Methods

Patient data

The initial population consisted of 675 patients operated on for NSCLC in our clinic between 2009 and 2015. We excluded patients with tumor size of >3 cm, non-anatomical resection, perioperative chemotherapy and radiotherapy, visceral pleural and lymph node invasion, or a positive surgical margin. As a result, the study included 98 NSCLC patients without indication for chemotherapy, who were followed with no postoperative treatment and had tumor size of <3 cm with no lymph node or visceral pleural invasion and a negative surgical margin.

The lobe was removed with the help of an endobag for all patients who were operated on with video-assisted thoracoscopic surgery (VATS). In addition, while performing lung resection, vein ligation was performed before the artery, adhering to standard surgical principles.

The patients were divided into two groups as the NTIT group treated with wedge resection before lobectomy and the non-NTIT group treated with direct lobectomy. In our clinical approach, intraoperative wedge resection is performed for patients who cannot be diagnosed with preoperative biopsy and a frozen sample is studied, while patients with a preoperative diagnosis directly undergo anatomic lung resection. The non-NTIT group included patients diagnosed with preoperative methods (transthoracic biopsy, bronchoscopy). We evaluated patient parameters such as age, gender, tumor size, tumor subtype (adenocarcinoma or squamous cell carcinoma), type of surgery, recurrence, time to recurrence, and survival, as well as factors affecting recurrence and survival. Local ethics committee approval was obtained (2012-KAEK-12/2399).

Statistical Analysis

The SPSS 22.0 statistical package program was used for the statistical analysis of data. Categorical variables were presented as number and percentage, while continuous variables were shown as mean ± standard deviation if normally distributed and as median (min-max) if not normally distributed. Pearson's chi-square test, Fisher's exact test, and the chi-square test with Yates continuity correction were used to compare categorical variables between independent groups. The normality of continuous variables was evaluated using visual methods (histogram and probability plot) as well as analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Our analysis revealed that the continuous variables were not normally distributed. We used the Mann-Whitney U test to compare the two groups for the other variables. The Kaplan-Meier method was used to calculate estimated survival and the patients who died from other causes were censored. Differences in survival rates were assessed using the log-rank test with regard to gender, presence of wedge resection, pathological subtype, and recurrence.

Results

Of the 98 patients in our study, 42 underwent wedge resection before anatomic resection (NTIT group) and 56 underwent direct anatomic resection (non-NTIT group). All wedge resections were performed with VATS, while anatomical lung resections were performed with VATS for 17 patients and thoracotomy for 81 patients. The

anatomical resections included lobectomy (n = 84), bilobectomy (n = 6), pneumonectomy (n = 5), segmentectomy (n = 2), and sleeve lobectomy (n = 1). Table 1 shows the patients' ages, gender distribution, tumor sizes, pathological tumor subtypes, recurrence rates, and time to recurrence by groups. We observed a significant difference between the groups in terms of tumor subtype. Adenocarcinoma cases were significantly more frequent in the NTIT group (27/15) than the non-NTIT group (17/56), whereas squamous cell carcinoma was significantly more frequent in the non-NTIT group (39/56) than the NTIT group (15/42) ($p < 0.001$).

Similarly, there was no significant difference between the groups regarding factors affecting survival. We detected no significant differences in recurrence, tumor subtype, gender, or survival (Table 2). The 5-year overall survival rate was 78.6% and the 10-year survival rate was 76.1%.

Figures 1, 2, and 3 show the survival graphs by recurrence, tumor subtype, and application of NTIT.

Table 1. Patients' characteristics and results of the analysis.

	Wedge group (n=42)	Control group (n=56)	p
Age (mean)	63.3±8.10	60.2±8.11	0.064
Gender (male), n (%)	37 (88.1)	52 (92.9)	0.419
Size (cm)	2.00±0.657	2.18±0.766	0.156
Pathology			
Adeno	27 (64.3)	17 (30.4)	<0.001
SCC	15 (35.7)	39(69.6)	
Recurrence	35 (83.3)	48 (85.7)	0.746
Recurrence time (mo)	80.5±34.6	84.6±40.6	0.248

Abbrev.: M/F; male/female, Adeno; adenocarcinoma, SCC; squamous cell carcinoma, mo: months

Table 2. Survival analysis of the patients according to covariates.

	Estimate (mean±SD)	95% CI	Log-rank (Mantel-Cox)
Gender			
Male	118.5±6.0	107.0-130.1	0.352
Female	124.3±7.3	110.2-138.5	
Wedge			
Absent	111.7±6.9	98.1-125.2	0.689
Present	123.4±8.0	107.8-139.1	
Recurrence			
Absent	116.5±5.4	105.9-127.1	0.128
Present	103.1±15.0	73.7-132.6	
Pathology			
Adeno	128.3±7.1	114.5-142.2	0.234
SCC	107.6±7.6	93.0-122.2	

Abbrev.: CI: Confidence interval, SD: standard deviation, Adeno; adenocarcinoma, SCC; squamous cell carcinoma

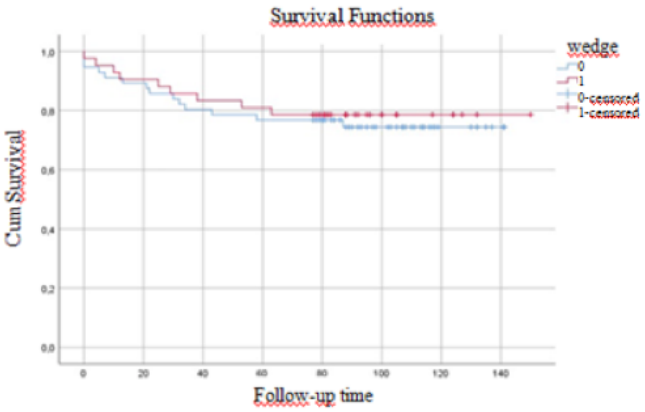

Figure 1. Survival analysis graph for application of no-touch surgery technique.

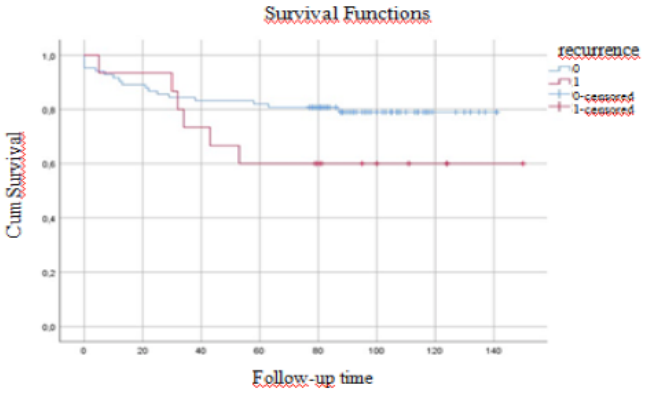

Figure 2. Survival analysis graph for recurrence.

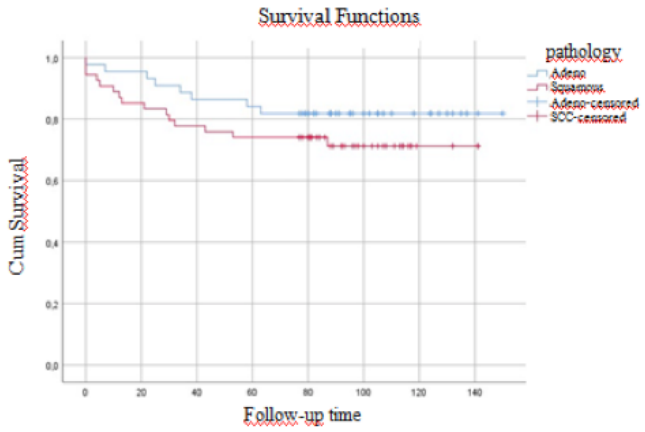

Figure 3. Survival analysis graph for subtype.

Discussion

Our investigation revealed no relation between application of NTIT, which involves the removal of the tumor together with the surrounding parenchymal tissue, i.e., wedge resection, before anatomical resection, and recurrence ($p = 0.746$). Similarly, we observed no significant link between pathological tumor subtype, age, gender, or the application of NTIT and survival ($p = 0.689$). The use of NTIT is based on the fact that the manipulation of the lung lobe containing the tumor leads

to an elevated level of CTCs. Numerous retrospective and prospective studies on CTCs in the literature have reported increased numbers of CTCs resulting from tumor manipulation, and especially in advanced lung cancer patients, which is, in turn, associated with higher recurrence and lower disease-free survival rates [10-13]. Evidence has also shown the role of CTCs in other cancer types besides lung cancer [14,15].

Yasukawa et al [6,7] evaluated the NTIT approach and reported its efficacy, but the breadth of inclusion criteria in their research rendered their results controversial. As is widely known, specific guidelines are available for chemotherapy indications in NSCLC. One parameter in these guidelines is pleural invasion, and the others are tumor size and lymph node involvement. Since cancer is considered systemic, the presence of these parameters strengthens this feature of the disease, making a case for the administration of adjuvant chemotherapy [16-19]. In one study, Yasukawa et al included tumors of all sizes [7]; in another study of them, they included tumors of <3 cm, but their findings are questionable because they did not exclude factors affecting the tumor stage, such as visceral pleural invasion. In contrast, the present study involved T1N0M0 (stage 1) patients without indications for chemotherapy, and all parameters influencing tumor stage, such as pleural invasion, were considered as exclusion criteria. The 5-year overall survival rate was 78.6% and the 10-year survival rate was 76.1%. It is thought that the reason for these high survival rates is the application of the exclusion criteria. However, due to the number of cases, further evaluations could not be made.

A previous study indicated the sensitivity of CTC detection in NSCLC to be 100% for stages 2-4 and about 50% for stage 1 patients. In addition, the specificity of CTC detection was almost 100%, whereas its sensitivity varied considerably depending on the method used [20,21]. Other studies on other tumor types have reported reduced circulating tumor DNA (ctDNA) levels for lower disease stages [14,22]. Diehl et al [23] and other authors investigating non-pulmonary malignancies [24] also showed decreased CTC levels after surgical resection, associating continued high levels with increased recurrence rates.

On the other hand, there is an ongoing debate as to whether a direct correlation exists between the presence of CTCs and clinical outcomes [25]. Recent improvements have allowed tumor diagnosis with liquid biopsy; still, not all tumors result in recurrence or distant metastasis, thanks to the body's various defense responses. In this regard, macrophage activity has been emphasized for CTCs. Other primary markers for tumor localization include tumor infiltration and compliance of host cells [26-30]. Therefore, prospective studies of large series limited to early-stage lung cancer cases without indications for chemotherapy are necessary to determine the clinical efficacy of NTIT decisively.

NTIT was significantly more frequently performed among adenocarcinoma cases than cases of squamous cell carcinoma in our cohort ($p < 0.001$). We consider the relatively central location of squamous cell carcinoma and the high diagnostic accuracy of preoperative bronchoscopy as the principal reasons for this finding. Yasukawa et al. also indicated a significantly higher rate of peripheral tumor localization in their wedge resection group [6]. In the practice of our clinic, bronchoscopy is routinely applied in preoperative evaluations before malignancy surgery. Therefore, the rate of preoperative diagnosis is high in cases of central tumors, and especially for the squamous cell carcinoma subtype. However, if there is a high suspicion of malignancy in peripherally located tumors in preoperative PET results, surgical resection will be planned for patients who are suitable for surgery whether or not the transthoracic biopsy result is diagnostic, and our clinical approach is to perform a diagnostic procedure with an intraoperative frozen section. For this reason, we frequently use surgical diagnostic methods for patients who are candidates for surgical resection and we think that this approach played a role in achieving the present results.

In light of our findings, we suggest postoperatively assessing CTC levels in early-stage NSCLC cases without chemotherapy indications. The effect of chemotherapy on recurrence, which is quite common even in early stages, should also be investigated over a possible threshold value.

The main limitation of our study is its retrospective design. The fact that it was a retrospective study brings with it the problem of obtaining follow-up data for the patients. Also, despite our diligent observance of oncological principles during wedge resection, additional manipulations may have occurred during processes such as pressing the parenchyma with a stapler. Finally, our inclusion criteria inevitably narrowed the study population to 98 cases.

In conclusion, although NTIT with wedge resection is theoretically well grounded, it is not clinically sig-

nificant based on our findings, and its necessity should be tested in studies with larger case series that include the presence of CTCs prospectively. The technique may prove beneficial in re-evaluating chemotherapy indications through CTC detection, especially for patients in early stages who have not received chemotherapy.

Declaration of conflicting interests

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Ethics approval

Local ethical committee approval of Ankara Keçiören Training and Research Hospital Ethical Committee (2012-KAEK-15/2399) was obtained for the study.

Authors' contributions

MÇ,IT: Conceptualized and designed the study, cowrote the paper; ESG: collected and analyzed data; GF: contributed to the organization and planning of the study; KA,SŞEG,PB: revised the final version of the manuscript.

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Original Article

Short- and long- term results of surgery in non-cystic fibrosis bronchiectasis: analysis of 7 years of follow-up

Oya Baydar Toprak[1]*, Alper Avci[2], Efraim Guzel[1], Burak Mete[3]

[1]Department of Chest Diseases, Cukurova University Faculty of Medicine, Adana, Turkey
[2]Department of Thoracic Surgery, Cukurova University Faculty of Medicine, Adana, Turkey
[3]Department of Public Health, Cukurova University Faculty of Medicine, Adana, Turkey

ABSTRACT

Background: There are limited data in the literature regarding the early and long-term results of surgery in non-cystic fibrosis bronchiectasis. The aim of this study is to contribute to literature with clear analysis of early postoperative complications and to determine the rate of postoperative complications in non-cystic fibrosis bronchiectasis.

Materials and Methods: One hundred two patients with non-cystic fibrosis bronchiectasis who underwent surgical resection participated in the study between April 2012 and November 2019 at Çukurova University. Patients were contacted by phone and scheduled for a face-to-face interview. For five patients who died during the postoperative period, mandatory information was collected through family members or from retrospective assessment of their medical records.

Results: Of the 102 patients, 47 (46.1%) were male and 55 (53.9%) were female, with an average age of 38.8 ± 14.0 years. The indication for surgery was hemoptysis in 16 (15.7%), recurrent pulmonary infections in 74 (72.5%), and suspicion of malignant transformation in 12 (11.8%) patients. The mean follow-up period was 71.4 ± 28 months. The early postoperative complication rate was 21.5% with no intraoperative fatality and a 4.9% mortality rate with long-term follow-up. The most common postoperative complications were surgical site infection and hemorrhage. The type of bronchiectasis (varicose bronchiectasis), lower forced vital capacity (FVC) and the diffusing capacity of the lung for carbon monoxide (DLCO) in the perioperative period were identified as risk factors for the development of postoperative complications. Long-term mortality was also higher in individuals who had early postoperative complications.

Conclusion: With low mortality and morbidity rates, surgical interventions in non-cystic fibrosis bronchiectasis remains a feasible choice in selected cases.

Keywords: non-cystic fibrosis bronchiectasis, bronchiectasis, surgery, postoperative complications, risk factors

Corresponding Author*: Oya Baydar Toprak, MD. Cukurova University Faculty of Medicine, Department of Chest Diseases, Mithat Ozhan Avenue Balcalı Hospital, 01330 Balcali, Adana, Turkey
E-mail: oyabaydarr@yahoo.com.tr Phone: +90 5053970076
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Introduction

Bronchiectasis is a chronic lung illness marked by a vicious cycle of airway infection and inflammation that results in irreversible structural damage to the small airways and occasionally the surrounding lung tissue [1]. Although pulmonary rehabilitation, proper immunization, and microbial eradication therapy are the most significant treatments for bronchiectasis, alternative experimental treatment options and surgery are also useful in certain circumstances. The goal of surgical bronchiectasis therapy is to interrupt the vicious loop of bronchiectasis by removing non-functional lung segments and preventing contamination of surrounding lung zones. The most prevalent grounds for surgery are recurrent infections with persistent symptoms such as productive cough, purulent sputum, and hemoptysis [2,3].

The prevalence of bronchiectasis has been estimated at 53-566/100,000 population as the prevalence increases with age and the female gender [4-8]. The age-adjusted mortality rate for bronchiectasis has been reported at 1437.7/100,000 population [7]. Several longitudinal studies have described up to a 30% mortality at 1-year follow-up after suffering an exacerbation, particularly in the presence of chronic obstructive pulmonary disease [9-11]. Surgical therapies for adult patients with bronchiectasis are not recommended, with the exception of individuals with localized illness and a high exacerbation frequency, even if all other elements of their bronchiectasis therapy have been optimized [12]. Operative mortality with curative surgery, on the other hand, is nearly 0%-1.4%, and the risk of postoperative complications is roughly 15%-16.2% [2,13]. Moreover, 71.5% of the adult population who underwent surgery reported complete symptom relief, whereas 20.2% reported a reduction in preoperative symptoms [2].

There is limited data in the literature regarding the early and long-term results of surgery in non-cystic bronchiectasis. The aim of this study is to contribute to the literature with clear analysis of early postoperative complications and to determine the rate of postoperative complications associated with surgery of non-cystic fibrosis bronchiectasis. The secondary outcomes include the indications for the surgical decision, the long-term symptoms after surgery, and long-term mortality after non-cystic fibrosis bronchiectasis surgery.

Materials and Methods

Study design and data collection

This research is a cross-sectional study and includes a retrospective review of medical records with the approval of the ethical committee of Çukurova University. Between April 2012 and November 2019, 102 patients with non-cystic fibrosis bronchiectasis who underwent surgical resection participated in the study. All of the patients who had regular follow-up and who had been recorded in the medical records of Çukurova University, Faculty of Medicine, Balcali Hospital were contacted by phone and scheduled for a face-to-face interview. For five patients who died during the postoperative period, mandatory information was collected through family members or from retrospective assessment of their medical records. Each participant had pathologically verified bronchiectasis.

This study consisted of two-phases: face-to-face interview and retrospective analysis of medical records. Sociodemographic characteristics (age, gender, occupation, and comorbidities) and changes in respiratory symptoms compared to the preoperative period were evaluated for each participant who was interviewed face to face after receiving informed consent. Retrospective data were gathered by using questions posed during face-to-face interviews as well as records from hospitals and health systems.

Preoperative evaluation

Each participant's preoperative examination included complete sociodemographic data and symptom analysis, as well as imaging modalities (high resolution computed tomography) to determine the number of affected lobes and a full pulmonary function test.

Pulmonary function tests (PFTs) were performed by using a calibrated Sensor Medics V-Max 20 Spirometer (Jaeger MS-PFT Analyser Unit, Wiasys Healthcare GmbH, Höchberg, Germany). The patients had not received any oral or inhaled short-acting beta-2 agonists within 8 hours of testing. Baseline forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) were measured three times, and the best of the three measurements was recorded. Total lung capacity was measured using the helium dilution technique (Jaeger MS-PFT Analyser Unit, Wiasys Healthcare GmbH). The diffusing capacity of the lung for carbon

monoxide (DLCO) was measured by using the single breath method. The results are presented as the percentages of predicted values.

Surgical procedures

Each surgery was performed after single-lung ventilation was established through a double-lumen endotracheal tube. A thoracotomy was performed on 87 patients, and 15 patients were treated by video-assisted thoracoscopic surgery.

Postoperative treatment and follow-up

Following the procedure, each participant in the trial was visited daily, and appropriate diagnostic tests and management of early postoperative complications were applied.

Definitions of postoperative complications

The European perioperative clinical outcome definitions were used in the diagnosis of postoperative complications [14]. Early postoperative complications are defined as those observed until discharge and late postoperative complications are defined as those detected during follow-up visits.

Statistical Analysis

SPSS 22 program (IBM Corp., Armonk, NY, USA) was used in the analysis of the data. Data are presented as number, percentage, arithmetic mean, standard deviation, median, interquartile range. Kolmogorov Smirnov test was used as the normal distribution test. Parametric tests were preferred in the analysis of normally distributed data, and non-parametric tests were preferred in the analysis of non-normally distributed and categorical data. Mann Whitney U test, t test, Chi-square test, Binary logistic regression test, Cox regression test were used in the analysis. Binary logistic regression analysis was used to estimate the risk of developing complications and Cox regression analysis was used to estimate the mortality risk. A value of $p < 0.05$ was considered statistically significant.

Results

The 102 patients included 47 (46.1%) males and 55 (53.9%) females, with an average age of 38.8 ± 14.0 years. Prior to surgery, all patients had had a productive cough for 12.3 ± 3.2 months.

The indication for surgery was hemoptysis in 16 (15.7%), recurrent pulmonary infections in 74 (72.5%), and suspicion of malignant transformation in 12 (11.8%) of the patients. The mean follow-up period was 71.4 ± 28 months (median: 66 months; min: 0, max: 119 months). The average sputum quantity expectorated per day was 85.6 ± 57 mL. Of note, 76 (74.2%) patients had had at least one hemoptysis episode in their life.

A total of 116 surgical procedures were applied to the 102 patients. Bilateral surgery was performed in two patients. The surgery was thoracotomy in 87 (85.3%) patients and video-assisted thoracoscopic surgery in 15 (14.7%) patients. Specifically, 10 (9.8%) of the surgeries were pneumonectomy, 67 (65.7%) were lobectomy, 12 (11.8%) were bilobectomy, 23 (22.5%) were segmentectomy, and 4 (3.9%) had wedge resection. The most common surgery was left lower lobectomy (n = 30, 29.4%). The most common type of segmentectomy was lingulectomy (n = 14, 13.7%).

There was no intraoperative mortality. Perioperative complications were seen in 22 (21.5%) patients. One patient died due to respiratory failure during the early postoperative period (postoperative day 3). Five (4.9%) patients died during long-term follow-up. Sociodemographic characteristics and perioperative results of the patients are given in table 1.

When examining the frequencies of complications, long-term ex status, and improvement in symptoms were examined according to the surgical procedure utilized (laparoscopic/thoracotomy), there were no significant differences (Table 2).

The logistic regression model established to predict the development of complications was significant (Omnibus test $p = 0.016$). The dependent variable of the model is the presence of complications and the independent variables are the technique used in the treatment (reference category: thoracotomy) and the type of bronchiectasis (reference category: cylindrical type). Among the variables included in the model, the risk of developing complications in the presence of varicose bronchiectasis, in which the type of bronchiectasis is important, was 8.44 times higher than in cylindrical bronchiectasis (Table 3).

Table 1. Sociodemographic and disease-related characteristics.		
Gender	n	%
Female	55	53.9
Male	47	46.1
Surgery technique		
Thoracotomy	87	85.3
VATS	15	14.7
Surgical indication		
Hemoptysis	16	15.7
Recurrent infection	74	72.5
Suspicion of malignancy	12	11.8
Bronchiectasis type		
Cystic	61	59.8
Varicose	21	20.6
Cylindrical	20	19.6
Complications		
None	80	78.4
Any complications	22	21.6
Early postoperative complications		
Hemorrhage	5	4.9
Pneumonia	3	2.9
Surgical site infection	6	5.9
Atelectasis	3	2.9
Respiratory failure	2	2.0
Prolonged air leak	2	2.0
Exitus due to respiratory failure	1	1.0
Number of bronchiectacic lobes		
1	40	39.2
2	41	40.2
3	14	13.7
4	6	5.9
5	1	1.0
Improvement in symptoms		
(+)	81	79.4
(-)	21	20.6
Exitus in follow-up period		
(-)	97	95.1
(+)	5	4.9
Total	102	100.0

Table 2. Postoperative complications according to surgery technique.			
	Surgical Technique (column %)		
Postoperative complication	Thoracotomy n=87	Thoracoscopy n=15	p
(-)	76(77.0)	13(86.7)	0.514
(+)	20(23.0)	2(13.3)	
Postoperative complication			
Hemorrhage	5(25.0)	0(0)	
Pneumonia	3(15.0)	0(0)	
Surgical site infection	6(30.0)	0(0)	
Atelectasis	2(10.0)	1(50.0)	0.247
Respiratory failure	2(10.0)	0(0)	
Prolonged air leak	1(5.0)	1(50.0))	
Exitus due to respiratory failure	1(5.0)	0(0)	
Exitus in follow-up period			
(-)	82(94.3)	15(100.0)	0.444
(+)	5(5.7)	0(0.0)	
Improvement in symptoms			
(+)	69(79.3)	12(80.0)	0.629
(-)	18(20.7)	3(20.0)	

Table 3. Estimation of postoperative complications in Logistic Regression Analysis.

	b	SE	OR	95% CI for OR Lower	Upper	p
Surgery technique thoracotomy vs thoracoscopy	0.696		2.006	0.397	10.141	0.400
Bronchiectasis type						0.031
varicose vs cylindirical	2.133		8.441	1.048	67.957	0.045
cystic vs cylindirical	0.636		1.889	0.157	22.748	0.616

The preoperative PFTs were obstructive in 33 (32.4%), restrictive in 21 (20.6%), and normal in 48 (47.1%) patients. When comparing the PFT values according to the postoperative complication, the FVC and DLCO values were significantly lower in the patients who had developed complications (Table 4).

In the Cox regression analysis performed to evaluate the factors affecting long-term survival, the technique used was not important for survival, but the development of complications was important. Specifically, the risk of mortality in the later period was 13.92 times higher in patients who had developed complications compared with patients who had not developed complications (Table 5, Figure 1).

Table 4. Comparison of PFTs according to postoperative complications.

	Postoperative complications				
	(-)		(+)		
	X±S.S.	Median (IQR)	X±S.S.	Median (IQR)	**p**
FEV1 L	2.28±0.75	2.23(0.86)	2.13±1.06	2.08(1.77)	0.434
FEV1	74.70±18.88	76.25(28.9)	64.42±25.68	62.50(45,0)	0.105
FVC L	3.04±0.93	2.92(1.19)	2.90±1.23	2.72(1.89)	0.427
FVC	83.18±17.79	81.35(24.20)	73.82±23.82	70.35(35.20)	0.046
FEV1/FVC	75.96±11.95	77.57(16.67)	71.37±12.42	71.68(17.63)	0.118
DLCO	77.05±15.26	78.00(24)	66.86±19.24	67.00(28)	**0.017**

Table 5. Cox Regression Analysis for estimation of mortality.

	B	Sig.	O.R.	95,0% CI for Exp(B) Upper
Surgical technique	-13.00	0.988	0.00	0.000 .
Postoperative complications	2.63	0.019	13.92	1.556 124.63

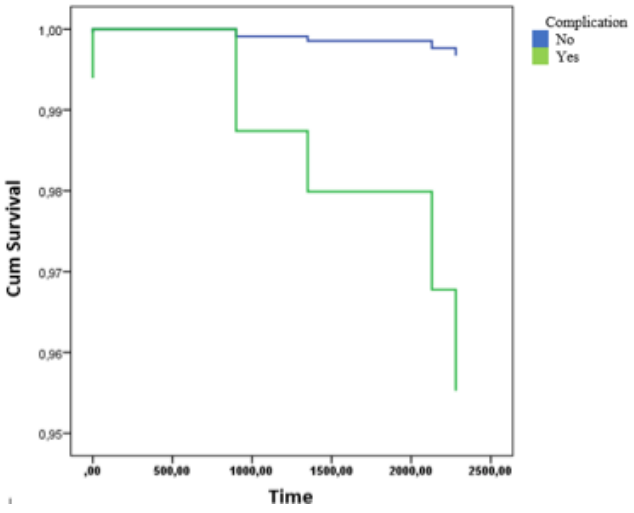

Figure 1. Survival function by presence of complications.

Discussion

Early postoperative complications after non-cystic fibrosis bronchiectasis surgery were found in 21.5% of our patients, with no intraoperative fatality and 4.9% mortality in the long-term follow-up. The most common postoperative complications were surgical site infection and hemorrhage. The type of bronchiectasis (varicose bronchiectasis) and lower FVC and DLCO values in the perioperative period were identified as risk factors for the development of postoperative complications. Long-term mortality was also higher in individuals who had had early postoperative complications.

Surgical site infection and hemorrhage were the most prevalent early postoperative complications. A previous study comparing surgical and conservative treatment strategies in bronchiectasis revealed an early postoperative complication rate as 33.5%; the complications were mild in 64% of the cases [15]. An older study with a high mortality rate showed 27.4% of the patients had postoperative complications [16]. In another study dealing with unilateral bronchiectasis cases, there were

postoperative complications in 15% of patients; the most common was bleeding [13]. Operative morbidity was seen in 11% of patients, with 3.5% experiencing serious and 7.5% experiencing mild complications [17]. A Portuguese study concluded that the postoperative complication rate including temporary broncho-pleural fistulae, hemorrhage, and atrial arrhythmias was 15% [18]. In a study with an average hospitalization period of 8.5 days, the morbidity rate was 16%, including prolonged air leaks, expansion defects, and wound infections [19]. A more recent study determined that the incidence of postoperative complications was 14.6% [20]. A comprehensive study revealed postoperative complications in 19.6% of the participants; these complications included sputum retention, postoperative air leak for more than 2 weeks, empyema, pneumonia, bronchopleural, atelectasis, postoperative bleeding, and respiratory insufficiency that required mechanical ventilation [21]. A recent study in Europe detected complications including atelectasis (15%), pleural effusion (21%), or prolonged air leak (21%) in 53% of the patients with bronchiectasis [22]. In a study dealing with surgery of a destroyed lung lobe, the postoperative mortality rate was 10.6% [23]. In a recent study with a large number of patients, postoperative complications (most commonly wound infections, atelectasis, and prolonged air leak) were observed in 9.7% of patients [24]. A large study from China reported a postoperative complication rate of 16.2% [25]. The data from the present study are compatible with the literature.

This study revealed no intraoperative fatality and a 4.9% mortality rate in the long-term follow-up. A very old study showed an early postoperative mortality rate of 3.1% and an overall postoperative mortality rate of 3.5%, possibly due to underdeveloped surgical techniques [16]. As time has passed, new studies have revealed better results of surgery in bronchiectasis. In a small study, patients with unilateral bronchiectasis had no intraoperative death and no late deaths [13]. In 1982, Annest et al [26] reported late deaths in 8% of patients, attributable to pulmonary causes. Three studies from Turkey showed a 1%-1.7% operative mortality rate in surgical treatment of bronchiectasis [17,19,20]. In a study conducted in a series of 790 patients, there was no intraoperative mortality, while the postoperative mortality rate was 1.1%. The reasons of death were mainly pneumonia, pulmonary embolism, and acute respiratory distress syndrome [25]. A study of 90 patients from Germany showed no operative mortality in the first 30 days after surgery [21]. A recent study revealed that 3.3% of the participants had died due to postoperative complications, namely due to acute myocardial infarction [22]. Another recent study showed a 90-day mortality rate of 0% [24]. Both intraoperative and postoperative mortality in the present study are within tolerable limits and are consistent with the literature. Based on these findings, it can be concluded that surgery can be a preferred therapeutic option for non-cystic fibrosis bronchiectasis under certain circumstances.

In the present study, varicose bronchiectasis and lower FVC and DLCO values in the perioperative period were identified as risk factors for the development of postoperative complications, and long-term mortality was higher in individuals who had developed early postoperative complications. A study evaluating risk factors of postoperative results showed that complete resection independently predicted a symptom-free outcome, an FEV1 of less than 60% of the predicted value predicted an incomplete resection, and preoperative antibiotic therapy independently predicted postoperative complications [20]. Another study showed that complete recovery was rarely achieved in patients with Pseudomonas aeruginosa infection and obstructive airway disease, but the number of patients was very small. Moreover, neither FEV 1 nor FVC alone was of use for predicting the outcome of surgery while the FEV1/FVC ratio was significant in prediction of cure [13]. In a previous study, logistic regression extracted the type of bronchiectasis (cylindrical), the existence of sinusitis, and the type of resection (complete/incomplete) for prognostic discrimination with statistical significance [21]. A large study from China showed that only a preoperative FEV1 of < 50% was associated with postoperative complications in univariate analyses. Multivariate analysis found no factors that were significantly associated with postoperative complications. The same study revealed that preoperative renal failure was associated with an elevated risk of postoperative death. The logistic regression analysis of a large study showed that tuberculous bronchiectasis, the type of bronchiectasis (saccular versus others), and the type of resection (incomplete or complete) were three independent factors associated with a poor surgical outcome [25]. There

have only been a few studies about surgery in non-cystic fibrosis bronchiectasis. Of course, it is challenging to identify risk factors with such limited data. Nevertheless, researchers have identified various risk factors, and our findings have added to the literature in this regard.

In the present study, nearly three quarters of the patients with non-cystic fibrosis bronchiectasis who underwent surgical resection had improved symptoms. An older study showed 71% improved symptoms after surgical intervention of bronchiectasis [16]. In a Turkish study, after surgical treatment, 82.5% of patients were free of symptoms and the remaining 17.5% had a reduction in preoperative symptoms [20]. In a study conducted with a limited number of patients and in which patients with unilateral bronchiectasis were evaluated, 72.5% reported complete recovery, while 27.2% showed improvement in symptoms [13]. In another study from Turkey, the pulmonary symptoms disappeared in 66.9% of the patients after surgery, and only 3.6% of patients had persistent or worsened symptoms [17]. A recent study showed 67% of patients considered their own health as "excellent" after surgery, 30% as "good," and 3% reported "no change" [22]. A detailed study showed that 60.5% of the patients were asymptomatic, 14.1% had improved symptoms, and 14.8% showed no improvement or worsened conditions [25]. The data from the present study is consistent with the literature and reinforces the effectiveness of surgery on symptom relief.

Although the study was done in Turkey, one of the nations where tuberculosis is rampant and bronchiectasis is relatively common, the study's main limitation is the small number of patients from a single center. Because the research was carried out at a tertiary health care institution, the individuals admitted are frequently advanced cases who have had trouble receiving treatment at other health centers. This might explain why the postoperative morbidity was somewhat greater than predicted.

Despite breakthroughs in preventative measures, medical therapy, and follow-up, surgery, with its low mortality and morbidity rates, remains a viable option for the treatment of non-cystic fibrosis bronchiectasis in selected individuals. This option meets the patients' clinical and social expectations.

Declaration of conflicting interests

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Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval was granted by the Ethics Committee of Cukurova University (Protocol No: 122/2022).

Authors' contribution

OBT,AA,EG; material preparation, data collection and analysis, OBT,BM, EG; the first draft of the manuscript was written by, All authors read and approved the final manuscript. All authors contributed to the study conception and design.

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Case Report

Is surgical treatment necessary in trans-sternal nail gun injury?

Omer Faruk Demir*, Omer Onal, Oguzhan Turan

Department of Thoracic Surgery, Faculty of Medicine, University of Erciyes, Kayseri, Turkey

ABSTRACT

Nail gun injuries have been reported in the medical literature since the introduction of these tools in 1959. The number of injury cases is increasing over time due to the increasing use of nail guns in the construction industry. While the most common site of nail gun injuries is non-dominant hand and fingers, rarely head, thoracic, abdominal, and cardiac injuries have been reported. Depending on the injured organ, the primary method of treatment for such injuries, which have catastrophic consequences, is appropriate surgical interventions.

Keywords: conservative treatment, nail gun, trauma

Corresponding Author*: Omer Faruk Demir, MD. Erciyes University Medical Faculty, Department of Thoracic Surgery, 38039, Kayseri, Turkey.
E-mail: ofdemir@erciyes.edu.tr Phone: +90 3522076666
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Introduction

Since their introduction in 1959, nail guns are increasingly used in the modern construction industry due to being inexpensive, easy-to-access, and time-saving tools [1]. In general, it is estimated that the mortality rate of nail gun injuries is similar to stabbing injuries. Injuries mostly occur in limbs such as hands and feet. Abdominal, cranial, thoracic, and cardiac injuries are much less common. The primary method of treatment is surgery [2,3].

Here, we present a patient with a rare transsternal injury and suspicion of tracheal perforation who was preferred to be treated conservatively, and his treatment strategy for discussion.

Case Report

A 37-year-old male patient, a furniture worker, was admitted to a local hospital in July 2020 for injury to the chest area by a nail bounced after the firing of a nail gun. The patient who had stable vital signs and no active bleeding on initial examination was referred to our hospital for further treatment and intervention after the administration of tetanus prophylaxis. The examination of the patient with no active bleeding revealed a nail in the sternum above the manubrium sterni about 2 cm below the incisura jugularis (Figure 1a).

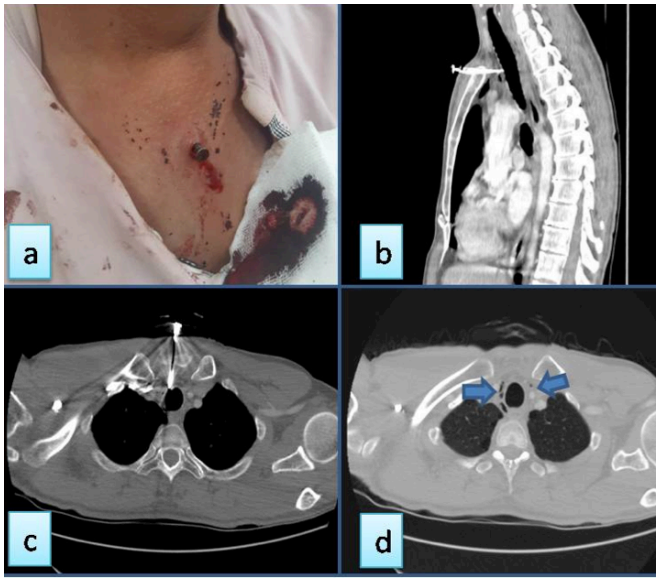

Figure 1. Photography of nail in the sternum of the patient **(a)**, sagittal **(b)** and axial **(c)** CT images showing the transsternal localization of the nail and minimal pneumomediastinum **(d)** (arrows).

The respiratory sounds of the patient with a blood pressure of 110/70mmHg, a heart rate of 72/min, and a respiratory rate of 15/min, who did not describe hemoptysis, were auscultated normal. The laboratory tests showed that Hb was 15mg/dL, and WBC was 12,000/mm3. The patient with a stable condition underwent contrast-enhanced computed tomography of the chest (CT) and neck to determine the relationship of the injury with the great vessels and the trachea. His CT showed a foreign body extending from the sternum to the anterior wall of the trachea, and pneumomediastinum (Figures 1b-d).

The foreign body was found to have a distance from the major vessels, but the possibility of tracheal injury could not be excluded. After the patient was transferred to the operating room and all equipment, including sternotomy, was prepared, bronchoscopy was first performed under general anesthesia and the trachea was checked. In the operating room, the patient's trachea was observed to be intact, and the nail was removed by pulling backward manually in accordance with the tract line. The patient with no active bleeding and no air leak was kept under general anesthesia in the operating room for 20 minutes. The patient, who had no change in vital signs and no bleeding, was transferred to the intensive care unit and closely monitored. For prophylaxis, he was given 2 grams of ampicillin 3 times a day. Daily acute phase reactants and close hemoglobin monitoring were performed. No increase was detected in CRP, procalcitonin values and WBC count. Also no decrease was identified in Hgb value. The oral intake of the patient, who was followed up without oral intake for two days, was initiated gradually since he had no swallowing difficulty or respiratory complaints. He did not have fever during the follow-ups. On day 5 of the follow-up, the patient was discharged with recommendations. Written informed consent was obtained from the parents for publication of his data.

Discussion

Nail gun injuries have been reported in the medical literature since their introduction in 1959 [1]. Basically, nail guns are produced in 2 different forms as slow-speed nail guns triggered by a pneumatic system and high-speed nail guns triggered by an explosive cartridge. While the velocity of the fired nails ranges from 97.7 to 121.1 ft/s in such tools, this velocity can reach up to 300-2200 m/s in conventional weapons [4].

These tools are used in the construction industry on wood, plastic, light metal, and even concrete surfaces. Although special permits are required for high-speed

tools, slow-speed ones can easily be supplied in daily life without training. The incidence of such injuries increases with the increasing use of nail guns in the construction industry. Nail gun injuries mostly occur in adults in the form of occupational accidents. There are also rare reported cases of suicide and children [2,3].

The most common site of injury is hand and fingers, followed by wrist, forearm, foot and toes, knee, and eye. Abdominal, thoracic, cranial, and cardiac injuries are much less common. The mortality rate varies depending on the velocity, size of the nail, and the injured organ. Although overall mortality rates are similar to stabbing injuries (25%), unlike firearm and stabbing injuries, sudden abundant bleeding is rare, including cardiac injuries [5].

This is due to the fact that the object (nail) causing the injury still remains in the tissue. Therefore, it should be kept in mind that abundant bleeding may occur when the foreign body is removed [6].

General recommendations for keeping such patients alive are rapid interventions. Unstable patients should be immediately transferred to the operating room without any examination. Thoracic injuries are mostly seen on the anterior thoracic wall. Therefore, anterior thoracotomies are primarily preferred depending on the location of the injury. Median sternotomy is preferred for precordial injuries. In stable patients, hemothorax, pneumothorax, pneumomediastinum, and other complications can be preoperatively evaluated using imaging techniques such as chest radiographs, and thoracic CT. In the literature, conservative treatment is a treatment modality mostly preferred for limb injuries [2,3].

Our patient underwent thoracic CT to evaluate the trachea more clearly, because of being hemodynamically stable and the location of the injury. The CT showed pneumomediastinum and the close relationship of the sharp tip of the foreign body with the trachea. However, tracheal injury could not be excluded. Although the patient did not complain of hemoptysis, it was thought that any bleeding that may result from the removal of the foreign body may jeopardize the patient by filling the trachea from an injury to the trachea. After all preparations were made for a possible sternotomy in order to reduce potential risky situations, it was decided to determine the condition of the trachea clearly by performing bronchoscopy under general anesthesia in the operating room setting. In the case of an injury, it was planned to protect the patient's airway from possible bleeding by pushing the endotracheal tube cuff distally to the injury to secure the airway. Therefore, fiberoptic bronchoscopy was primarily performed under general anesthesia, although it has never been used for such patients. After ensuring that the trachea was intact, the nail in the sternum of the patient was removed manually while the patient was intubated. After waiting for 20 minutes in the operating room for any active bleeding following the removal of the nail, the patient was transferred to the intensive care unit.

Nail guns are tools with the potential to cause catastrophic bleeding and fatal injuries. Basically, prevention and education are the most appropriate ways to reduce mortality caused by these injuries. In thoracic injuries, it should be kept in mind that conservative treatment can be used for patients with a stable condition, no active bleeding, and confirmed to have no organ injury, even in cases of transsternal injuries, provided that all measures are taken for emergency intervention in, while unstable patients should be rapidly intervened.

It is seen in the literature that the frequency of injuries related to nail guns has increased due to the rapid developments in the construction sector. We are in favor of modifying such devices in order to prevent this situation and to reduce the possibility of injury. Nail guns can be fired very easily. There are types that can be fired even without coming into contact with a rigid structure. From our point of view, these guns should not be able to be fired without touching a hard surface. At the same time, we believe that it will seriously reduce possible accidents that may occur a few seconds between ignitions after being triggered. Another important point is that the firing speed of pneumatic nail guns is higher than many guns. Therefore, these types of nail gun uses must be subject to special permissions.

Declaration of conflicting interests

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Authors' contributions

OFD,OO,OT: conceived and designed the current case report, co-wrote the paper, collected the clinical data. The authors discussed the case under the literature data together and constituted the final manuscript.

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Case Report

A case report of lung cancer: is it spread through air spaces or endoluminal metastasis?

Huseyin Yildiran[1]*, Guven Sadi Sunam[2], Fikret Kanat[3], Atilla Can[1], Halil Sen[1]

[1]Department of Thoracic Surgery, Selcuk University Medical Faculty, Konya, Turkey
[2]Thoracic Surgeon, Istanbul, Turkey
[3]Department of Pulmonology, Selcuk University Medical Faculty, Konya, Turkey

ABSTRACT

Lung cancer is the most common cause of death due to malignancy and early diagnosis is important for surgical treatment. Endotracheal and endobronchial metastasis after left upper lobectomy is a very rare condition in the patient who was followed up for one year postoperatively. By the presented case, it was aimed to determine the approach and etiology of this clinical condition.

Keywords: Lung cancer, metastasis, spread through air space

Correspondence Author*: Huseyin Yildiran, MD. Department of Thoracic Surgery, Selcuk Universitesi Tip Fakultesi, Alaeddin Keykubat Kampus, 42130 Selcuklu, Konya, Turkey.
E-mail: h-yildiran@hotmail.com Phone: +90 3322243918
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Introduction

Non-small cell lung cancer (NSCLC) accounts for approximately 80% of all lung cancers. Early diagnosis is crucial in the effectiveness of surgical treatment [1]. The disease recurrence of primary lung cancer is most common in the first two years after lobectomy [2]. Therefore, frequent postoperative monitoring is required.

This case is rare and interesting due to the presence of multiple endobronchial and endotracheal metastases in the first year after lobectomy performed for stage I lung primary squamous cell carcinoma (SCC).

Case Report

A malignant nodular lesion was detected in the left upper lobe hilum during the examination of a 68-year-old male patient with a presenting complaint of irritant cough. Flexible bronchoscopy revealed a vegetative mass in the left upper lobe bronchus that did not extend to the lingular bronchus (Figure 1).

After a bronchial biopsy and bronchoalveolar lavage revealed SCC, a left upper lobectomy with thoracotomy was performed after screening for systemic metastasis. The primary lesion was diagnosed as SCC in histopathology and was one cm in diameter, with 34 lymph nodes and bronchial margin biopsies removed during dissection being negative. Definitive diagnosis was stage IA1 lung SCC.

The patient's follow-up was uneventful until suspicious nodular lesions were detected on the tracheal wall and right main bronchus entrance in the thorax computed tomography taken a year after the surgery, and bronchoscopy was performed again (Figure 2).

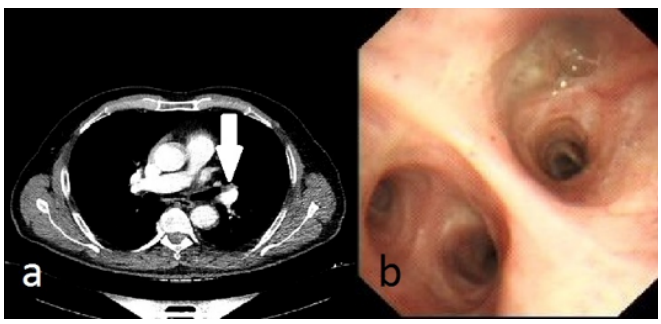

Figure 1. Preoperative thorax CT showing the primary endobronchial tumor (arrow) **(a)**, bronchoscopic image showing the endobronchial tumor totally obstructing the left upper lobe bronchus but not extending to the lingular bronchus **(b)**.

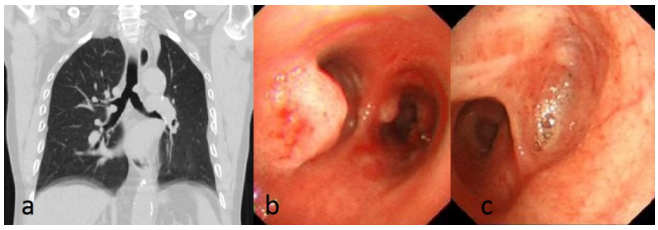

Figure 2. Thorax CT (coronal view) showing the endotracheal and endobronchial lesions **(a)**, bronchoscopic image showing the endotracheal and endobronchial metastasis in main carina and distal of trachea **(b)**. The bronchial stump of left upper lobe was normal **(c)**.

In bronchoscopy, multiple nodular lesions were detected in the posterior and distal trachea, left main bronchus entrance, right main bronchus, and secondary carina. The histopathological results of bronchoalveolar lavage and bronchial biopsy were SCC. PET CT was performed for restaging, and no lesion was detected except for the lesions in the airway. Carboplatin and paclitaxel chemotherapy protocol was applied to the patient and radiotherapy was administered. The lesions completely disappeared after treatment (Figure 3). He received radiotherapy again for the endotracheal lesion that developed in the proximal trachea six months after chemoradiotherapy (Figure 4), and his follow-up continues in the second postoperative year. Written informed consent was obtained from the parents for publication of his data.

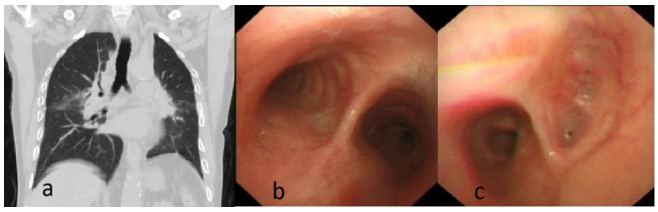

Figure 3. Thorax CT (coronal view) after chemoradiotherapy; endotracheal and endobronchial lesions completely disappeared **(a)**, and bronchoscopic images; carina **(b)**, left main bronchus and, bronchial stump of left upper lobe **(c)**.

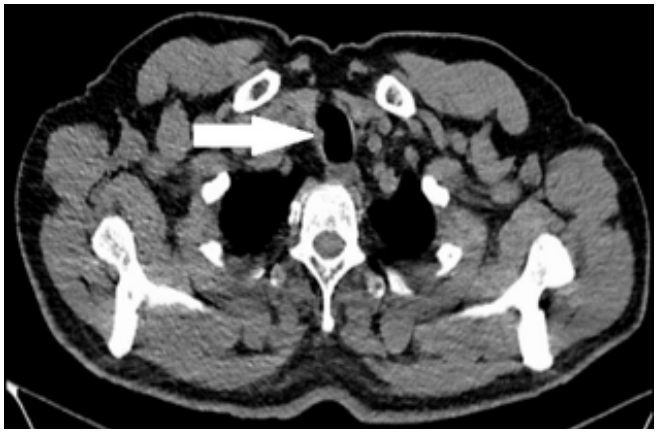

Figure 4. Thorax CT showing the endotracheal nodule located at proximal of the trachea (arrow).

Discussion

Surgery is the most effective treatment for early-stage lung cancer. Particularly, stage I and stage II cases greatly benefit from surgery. Follow-up is continued for intrathoracic or distant organ metastases after surgery. The most common areas of metastasis are the central nervous system, bone, liver, respiratory system, and adrenal glands. Endobronchial and endotracheal metastases of lung cancer are very rare. In the literature, metastasis in the bilateral main bronchus and trachea has rarely been published [3]. During follow-up, the cases may be asymptomatic or may present with respiratory findings such as wheezing and stridor.

Recently, the idea of spread through air space (STAS) has come to the fore for lung cancer. Although it is frequently encountered in SCC and adenocarcinoma cases, it has been reported that airway spread is also common in small cell lung carcinoma [4]. It was shown in a study that STAS was encountered in one third of resected lung SCC cases [5]. STAS formation is thought to be related to the spread of loose tumor fragments into the alveolar spaces [6]. Although STAS is encountered in all stages of lung cancer, its frequency increases in metastatic disease and is associated with poor prognosis [6]. Although reasons such as advanced age, sublobar, and limited resection have been suggested, it is known that STAS can be encountered even in complete anatomical resections [5]. In this case, malignant cells were detected in the bronchoalveolar lavage in both bronchoscopies performed before the preoperative diagnosis and after the detection of postoperative metastasis. This result suggests that there may be loose tumor fragments in the primary tumor. Although STAS and endobronchial and endotracheal metastases are conceptually presented as different clinical conditions for lung cancer, there may be a similar cause such as loose tumor fragments in the etiology of both.

In the present case, the detection of endotracheal and endobronchial metastases in the first postoperative year supports these findings in the literature, although left upper lobectomy was performed, and the bronchial margin was negative.

Endobronchial and endotracheal metastases have been associated with poor prognosis. The average surveillance in these cases has been reported as approximately 7.5 months [3]. After the chemoradiotherapy treatment of the presented case was completed, he was followed up for another 6 months without disease and received radiotherapy again due to a new lesion in the proximal trachea.

As in this case, differential diagnosis of STAS or endobronchial metastasis cannot be made on a single case, but we think it would be beneficial to be alert about STAS.

In conclusion, it is necessary to continue frequent follow-ups in operated lung cancer cases, even if they are stage I. Apart from the follow-up of parenchyma and distant organ metastases, it is of great importance that a careful evaluation is made in terms of endobronchial and endotracheal lesions. Endobronchial metastases should be kept in mind by clinicians and radiologists, and they should not avoid bronchoscopy in suspected cases, as small lesions are overlooked on CT. Thus, more studies with large series are needed to demonstrate whether endobronchial or endotracheal metastases are with airway spread. However, patients with malignant preoperative bronchoalveolar lavage should be followed carefully in terms of endobronchial or endotracheal metastases or STAS.

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Authors' contributions

HY, GSS, FK, AC, HS: conceived and designed the current case report, co-wrote the paper, collected the clinical data. The authors discussed the case under the literature data together and constituted the final manuscript.

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Case Report

Videothoracoscopic tracheal resection and reconstruction in postintubation tracheal stenosis: case report

Semih Erduhan, Celal Bugra Sezen*, Gamze Tanrıkulu, Yasar Sönmezoglu, Volkan Erdogu, Muzaffer Metin

Department of Thoracic Surgery, Health Sciences University, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Bronchoscopy of a 58-year-old female patient who complained of dyspnea after prolonged intubation revealed stenosis of approximately 2 cm in length at a distance of 2 cm from the carina. Upon that, the patient underwent tracheal resection and reconstruction with VATS using 3 ports. Operations can be performed safely through minimally invasive surgical approaches for tracheal stenoses at the thoracic level.

Keywords: video-assisted thoracoscopic surgery, post-intubation tracheal stenosis, tracheal resection, minimally invasive surgery, tracheal surgery

Corresponding Author*: Celal Bugra Sezen, MD. Department of Thoracic Surgery, Health Sciences University, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Kazlıçezme Mahallesi, Zeytinburnu İstanbul, Turkey
Email: bugrasezen@hotmail.com Phone: +90 5531605531
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Introduction

Tracheal stenosis most commonly occurs due to prolonged intubation. The main treatment modality for postintubation tracheal stenosis (PITS) is surgery. While open surgical approaches are frequently used in treatment, the publications in the literature on endoscopic surgical treatments are limited [1,2].

In this article, we evaluated our case who underwent tracheal resection and reconstruction with video-assisted thoracoscopic surgery (VATS), which is a rare approach in distal tracheal stenosis, based on the literature.

Case Report

A 58-year-old female patient has known diagnoses of diabetes, congestive heart failure, hypothyroidism, and peripheral neuropathy. The patient has a history of prolonged intubation due to myocardial infarction. The patient complains of severe shortness of breath after extubation. Thorax tomography revealed an area of stenosis starting approximately 2 cm above the carina (Figure 1). Bronchoscopy revealed a mixed-type stenotic tracheal stenosis area accompanied by malacia, narrowing the lumen by 70% in a 2 cm segment, ending 2 cm proximal to the carina (Figure 2). Tracheal resection with VATS was decided for the treatment of stenosis at the level of the thoracic trachea. A one cm camera port incision was made in the posterior axillary line from the 7th intercostal space and an incision was made from the 4th intercostal space for intubation, in the left lateral decubitus position. A 4 cm utility incision was made in the third intercostal space. Since the patient's tracheal stenosis area was 2 cm proximal to the carina, the stenotic trachea was resected, and then cross-field ventilation was started (Figure 3). The tracheal anastomosis was performed continuously with 3-0 polypropylene (PROLENE®, Ethicon, Inc.) sutures. Expansion of the right lung was prevented by using a right endobronchial blocker during the operation. The patient was discharged on the 7th postoperative day without complications. The patient is observed to be healthy in the first postoperative year, and the follow-up continues. Written informed consent was obtained from the parents for publication of her data.

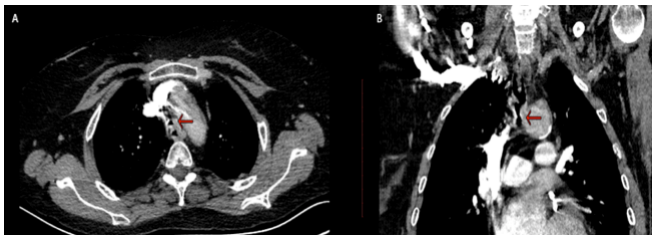

Figure 1. Axial **(A)**, and coronal **(B)** CT images showing tracheal stenosis (arrows).

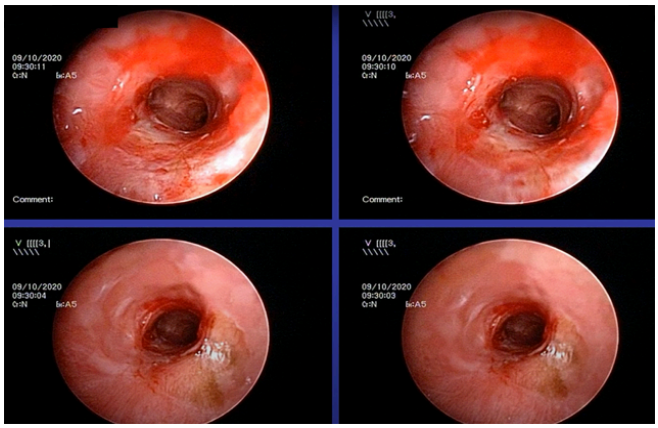

Figure 2. Fiberoptic bronchoscopy images showing; 70% stenosis at the distal end of the trachea, approximately 2 cm from the carina.

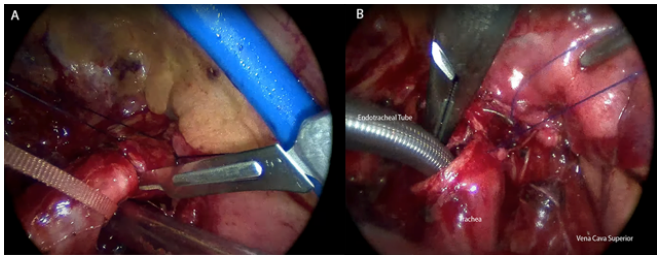

Figure 3. Intraoperative pictures showing; resection of the trachea **(A)**, and reconstruction with continued sutures **(B)**.

Discussion

Currently, major surgical operations can be performed through minuscule incisions by the advanced technology. There are quite a few publications in the literature on the endoscopic surgical treatment of benign tracheal stenosis. The most remarkable reason for this is the technical challenges of VATS. Many surgeons are reluctant to use this technique, particularly due to difficulties such as allowing intraoperative ventilation and performing the anastomosis in a narrow space. The concern about an intraoperative thoracoscopic major bleeding or the technical complication of performing radical resections by VATS in advanced cases are the main reasons for the low adoption. Major surgical operations (Tracheal resection and reconstruction, vascular and/or bronchial sleeve

resection and reconstruction) can be performed through minuscule incisions by the advanced technology.

The largest series in the literature is the series performed by Jiang et al [3] through VATS on a patient with 12 tracheal distal end stenosis with spontaneous breathing. The authors suggested that mobilization of the trachea is easier when the endotracheal tube is not used, and therefore spontaneous ventilation is effective. In our case, we preferred ventilation with an endotracheal tube, the most important reasons for this are to avoid potential intraoperative hypoxia and to minimize intraoperative complications.

During the operation anastomosis is much more challenging compared to open surgery because the intubation tube advances to the surgical site during intraoperative ventilation. Specifically, jet ventilation or extracorporeal support (ECMO-Extracorporeal Membrane Oxygenation) can be preferred to prevent this situation. Ko et al and Hoetzenecker et al have also stated that ECMO is much safer in airway surgery [4,5]. We preferred cross-field intubation at the onset of anastomosis in our case. Towards the end of the anastomosis, we performed selective lung ventilation using a right endobronchial blocker through the endotracheal tube. We think that through selective intubation, the tension of the anastomosis was adjusted more easily, and we have protected the patient from hypoxia. We did not prefer to use invasive surgical methods such as ECMO, since ventilation can be performed easily from the intraoperative surgical site and anastomosis can be performed rapidly by using endobronchial blockers when suturing is about to be completed.

Besides, one of the most important problems in sleeve resections and tracheal resections is the adjustment of anastomotic tension. Some authors use "interrupted sutures" for easier adjustment of the tension in the anastomosis and to avoid mixing of sutures [6]. On the other hand, Diego et al prefer "continue sutures" in sleeve resections [7]. We often prefer to continue sutures in our tracheal resection surgeries [8]. Thus, the anastomosis is completed not only in a shorter time but also the tension can be adjusted comfortably in the anterior part.

In conclusion, with the improving technological opportunities, major surgical procedures can be easily performed through minimally invasive techniques. We think that tracheal resection with VATS can be safely performed in distal stenosis of the trachea, instead of major incisions such as posterolateral thoracotomy.

Declaration of conflicting interests

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Authors' contributions

SE, CBS, GT, YS,VE, MM: conceived and designed the current case report, co-wrote the paper, collected the clinical data. The authors discussed the case under the literature data together and constituted the final manuscript.

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

Statistical Knowledge

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

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

Submission Process

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

Preparation of Manuscript

Cover Letter

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

Style and Format

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

Symbols, Units and Abbreviations

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

Manuscript Content

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

Title and Contact Information

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

Abstract

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

Keywords

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

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

Introduction

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

Materials and Methods

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

Results

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

Discussion

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

References

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

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

Articles in Journals

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

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

Tables and Figures

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

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

All tables and figures must be numbered consecutively as they are referred to in the text. Please refer to tables and figures with capitalization and unabbreviated (e.g., "As shown in Figure 2…", and not "Fig. 2" or "figure 2"). The tables and figures themselves should be given at the end of the text only, after the references, not in the running text.

The resolution of images should not be less than 118 pixels/cm when width is set to 16 cm. Images must be scanned at 1200 dpi resolution and submitted in jpeg or tiff format. Graphs and diagrams must be drawn with a line weight between 0.5 and 1 point.

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

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

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

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

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

Instruction to Reviewers

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

The language of the journal is English.

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

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

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

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

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All articles submitted for publication are strictly reviewed for their

originality,

methodology,

importance,

quality,

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

The overall rejection rate of the Current Thoracic Surgery is 29%.

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The average time during which the reviews of manuscripts are conducted is 41 days.

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The entire submission process for a manuscript is completed online through the self-explanatory online submission system.. The reviewers can reach their personal pages from the same address with their own passwords.

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

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Plagiarism is a serious problem and the most common ethical issue afflicting medical writing. Current Thoracic Surgery does not allow any form of plagiarism. In accordance with our journal policy, submitted manuscripts are screened with plagiarism software to detect instances of overlapping and similar text (iThenticate and others) at least two times (during the evaluation process and after acceptance). If the reviewers have any suspect, the editors can provide them information obtained by plagiarism screening tools.

An **approval of research protocols by an ethics committee** in accordance with international agreements ("WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (last updated: October 2013, Fortaleza, Brazil)", "Guide for the care and use of laboratory ani-

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

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Besides the rutine questions given at the reviewers' comment page, the reviewers can also use the questions below, when reviewing the manuscripts:

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2. Do you suspect any research or publication misconduct?

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4. Is the title of the article appropriate?

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8. Is the results section clear and satisfactory?

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Current Thoracic Surgery,
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Phone: +90 (538) 302 59 49
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