Chapter

The Role of Minimally Invasive Surgery in the Treatment of Lung Cancer

Güntuğ Batihan and Kenan Can Ceylan

Abstract

Lobectomy plus regional lymph node dissection remains the gold standard treatment method in early-stage lung cancer. However, with the demonstration of the safety and efficacy of minimally invasive approaches, the expression of surgery in this statement, replaced by thoracoscopic anatomical lung resection. Clinical studies have demonstrated the superiority of VATS in terms of postoperative pain, drainage time, length of hospital stay, and complications, moreover, long-term oncologic results are similar or better than thoracotomy. Therefore, VATS lobectomy is the preferred surgical method in early-stage lung cancer. Different surgical techniques are available in VATS and can be modified according to the surgeon's personal experience. Uniport can be applied as well as two or three port incisions. In this book section, I plan to focus on VATS lobectomy, technique-related tricks, complication management, and long-term oncologic results in early and locally advanced lung cancer.

Keywords: Lobectomy, minimally invasive surgery, robotic surgery, video-assisted thoracic surgery

1. Introduction

Lung cancer is the most common cancer and the leading cause of cancer death in both genders [1]. Its high frequency and high mortality increase the importance of early diagnosis and treatment in this disease. Despite promising recent advances in diagnosis and treatment methods, only a minority of patients have a cure chance. Resection of the primary tumor and mediastinal lymph node dissection/sampling is the gold standard treatment method in this group of patients. However, in these patients, lung resection was performed by open thoracotomy until the end of the '90s, regardless of the size of the tumor and the extent of cancer. Severe postoperative pain and long hospitalization and drainage periods could prolong the recovery period of the patients [2].

Following the technological developments include high-definition video monitors, robot-assisted technology, specialized thoracoscopic surgical instruments, and endomechanical stapling devices, the emergence of modern imaging systems and the use of appropriate surgical equipment has created the concept of "minimally invasive surgery". In the early 2000s, patient series including Video-assisted thoracic surgery (VATS) applications began to be published. This and many subsequent studies have demonstrated the superiority of VATS over a thoracotomy in terms of less postoperative pain and minimize complications hasten recovery and improve postoperative quality [3–6]. With the positive results of VATS, it has found a wide application area for the diagnosis and treatment of benign and malignant lung diseases.

In this section, the role and application areas of VATS in the diagnosis and treatment of lung cancer will be discussed rather than technical details.

2. Surgical technique

Although "tubeless" or "awake" VATS has been described and performed successfully by several authors, single-lung ventilation, which may be accomplished with either double-lumen endobronchial tubes or with single-lumen tubes and bronchial blockers, is often required for thoracoscopic lobectomy [7, 8].

The patient is positioned in full lateral decubitus position with slight flexion of the table at the level of the mid-chest, which allows slight splaying of the ribs to improve exposure in the absence of rib spreading.

The instruments and surgical technique used vary according to the number, location, and width of the port incisions. Although the number of port incisions and locations are the surgeon's preference, different applications and techniques have emerged over time.

2.1 Posterior approach

The posterior approach was first described by Walker WS in 1992. The main components of this approach include [6, 9]:

- The surgeon stands posterior to the patient.
- The utility incision is made at the 6th or 7th intercostal space anterior to latissimus dorsi muscle.
- The camera port is made through the auscultatory triangle, instead of the lower anterior axillary line;
- The aim is to dissect the hilar structures from the posterior to the anterior. For this purpose, the interlobar fissure must be opened first to identify and isolate pulmonary arterial branches.

The main advantages of the posterior approach include:

- Easy access to the posterior hilum.
- Easy access to subcarinal lymph nodes.
- A clear view of the posterior hilum allows safe dissection of the segmental artery and bronchial branches.

However, the interlobar fissure is incomplete in a considerable number of patients, and fissure dissection may cause parenchymal damage and prolonged air leak in the postoperative period. If the posterior approach is preferred, the interlobar fissure should be carefully dissected. Tissue glues, absorbable patches, or fibrin sealants can be used in the repair of injuries and air leaks that may occur in the parenchyma.

2.2 Anterior approach

The anterior approach, also known as the fissureless technique, was applied firstly in open thoracotomy in 1999. The application of this technique to VATS has been described recently [10–12]. In this technique, the surgeon stands anterior to the patient, and the camera port is placed at the anterior axillary line. The hilar structures are dissected from the anterior to the posterior. After the dissection of the bronchovascular structures is completed, the interlobar fissure is divided with endoscopic staplers and the lobe is removed from the thorax.

This approach aims to prevent postoperative air leaks due to fissure dissection.

2.3 3-port VATS

In this technique, the camera port-anterior port is located in the 7th or 8th intercostal space in the anterior axillary line, and the posterior port is located in the posterior axillary line in the same intercostal space. The utility port was usually placed in the anterior axillary line 4th intercostal space for an upper lobectomy or 5th intercostal space for a lower lobectomy (**Figure 1**). While the posterior port was

Figure 1.
Port incisions in the 3-port VATS technique.

previously placed from the upper and rear levels, it was modified over time, and the localization we described became more frequently applied [13].

2.4 2-port VATS

Since the additional contribution of the posterior port is not essential, VATS has become applied with two ports in some centers. The need for surgical retraction and manipulation can be provided by using another instrument via the utility port (**Figure 2**). However, apart from providing retraction, another feature of the posterior port that makes it useful is the introduction of the endoscopic stapling devices. Therefore, the absence of the posterior port should be compensated by appropriate maneuver and retraction of the lung.

2.5 Uniportal VATS

Uniportal VATS is firstly described by Dr. Gaetano Rocco for minor thoracic procedures include lung biopsies and pneumothorax operations [14]. Dr. Diego

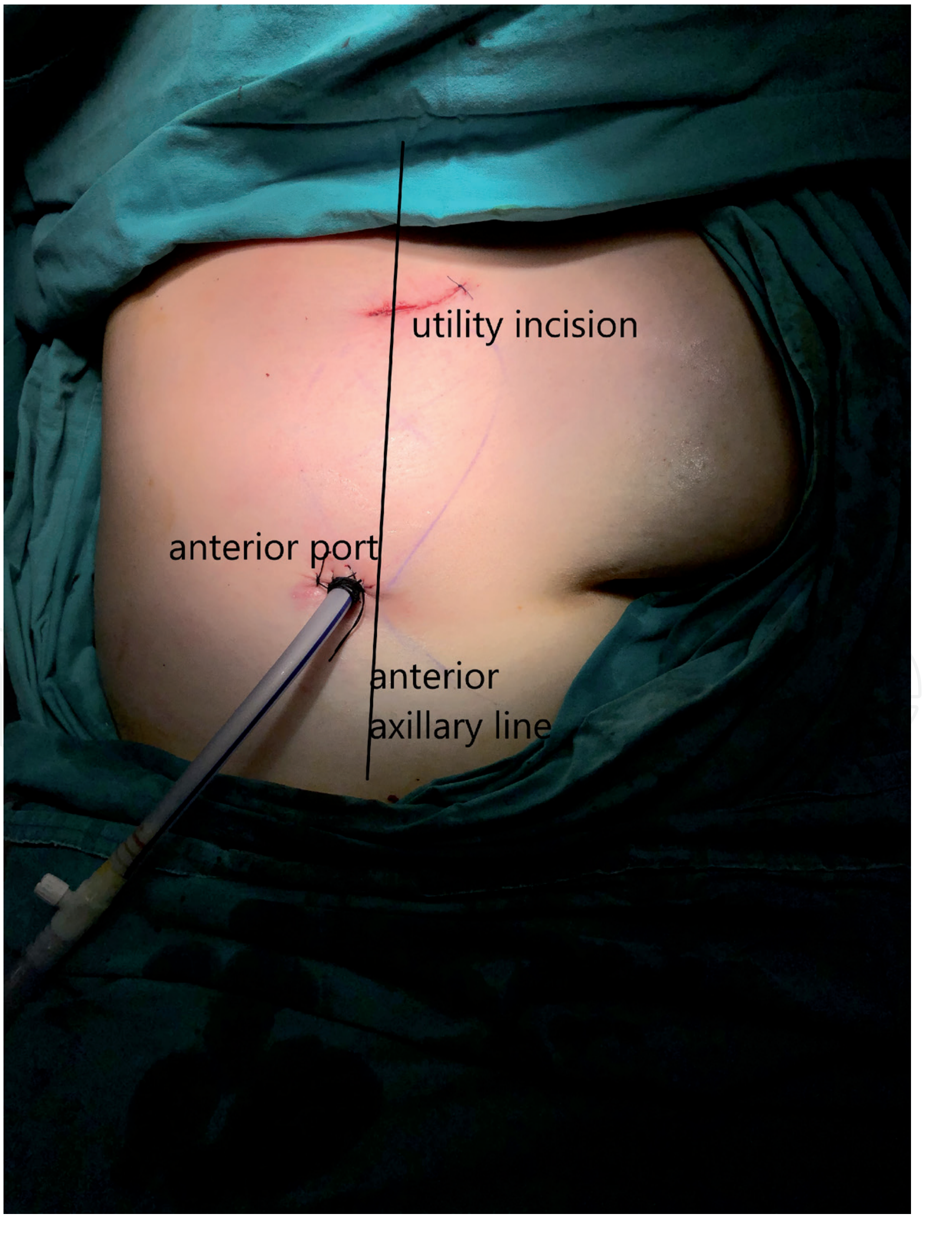

Figure 2.
Port incisions in the 2-port VATS technique.

Gonzalez Rivas shared his single port VATS lobectomy experience and became a pioneer in this regard [15, 16]. It has become preferred by many surgeons due to its advantages, such as causing less tissue damage and providing direct vision.

3–5 cm uniport incision is placed in the 5th intercostal in the anterior axillary line. A 5 mm diameter 30° video-thoracoscope is inserted through the same incision. Thus, the assistant and the surgeon share the same vision of direction. Although this is beneficial in terms of team cooperation, the working environment of the surgeon is somewhat limited.

Moreover, Gonzales Rivas successfully performed extended lung resections include bronchial, arterial, and double sleeve resections and raised the bar in uniportal VATS lobectomy [17]. Despite favorable surgical results, whether uniportal VATS has an additional benefit over traditional VATS is still controversial.

2.6 Needlescopic VATS

The main goal of this technique is to reduce the size of the incisions rather than the number of ports. It was aimed to minimize intercostal nerve damage and achieve better cosmetic results with the use of instruments and ports with a diameter of 3–5 mm instead of 10 mm ones used in conventional VATS [18].

The placement of the ports and the direction of the vision are the same as the 3-port VATS technique, and the utility port has to remain at 3–5 cm to extract the resection material. Surgeons who have appropriate instruments include 3 mm trocar, 3 mm 30° video-thoracoscope, and needlescopic grasper and do not prefer the uniportal VATS may prefer this technique.

2.7 Robot-assisted thoracic surgery

Advances in technology have enabled robots to be used in surgical procedures, and some authors started to share their first experiences in robotic thoracic surgery in the early 2000s [19].

It is thought that robotic surgery, which provides 3-dimensional vision and has articulated modern instruments, may allow the surgeon a safer dissection. With increasing experience, many thoracic surgery procedures are successfully performed with robotic surgery [20].

However, its use has not become widespread worldwide due to the system's higher cost, the time-consuming installation, and the lack of tactile feedback during surgery. It is possible to achieve similar surgical results with much less expense without sacrificing minimal invasiveness.

3. Diagnostic performance of VATS in patients with lung cancer

Despite advances in imaging technology techniques, including positron emission tomography (PET), integrated PET/computed tomography (CT) scans, PET/magnetic resonance imaging (MRI), multi-slice computed tomography, invasive diagnostic procedures continue to play an essential role in the management of the patient with lung cancer.

VATS provides the opportunity to evaluate for solitary pulmonary nodules, mediastinal or chest wall invasion by the primary tumor, pleural effusions/nodules, and mediastinal lymph nodes. Especially in the recent period, the use of targeted treatment methods has increased the need for tissue for mutation analysis. This situation has increased the diagnostic value of VATS and has widened its usage area.

3.1 Mediastinal staging

Evaluate the mediastinal and hilar lymph node status is essential for accurate staging of the lung cancer and to choose the appropriate treatment modality.

Noninvasive mediastinal staging methods include CT and PET/CT provide valuable clinical information however sensitivity, specificity, and negative predictive values insufficient to guide treatment decisions [21–23].

Abnormal lymph node (LN) is described as an LN with a short-axis diameter ≥ 1 cm). The median sensitivity and specificity of CT for identifying mediastinal lymph node metastasis are 55% and 81% [21].

PET can provide more accurate information about the differentiation of malignant and benign lymph nodes than CT. The median sensitivity and specificity of PET/CT for detecting lymph node metastases is ranges 80%- 88%, PET is successfully used in clinical staging and monitoring response to treatment in patients with lung cancer. However, the risk of false negativity is relatively high in lesions smaller than 1 cm and tumors with low metabolic activity (e.g. well-differentiated adenocarcinoma) [22, 23].

Cervical mediastinoscopy is the gold standard method for preoperative mediastinal lymph node staging in patients with lung cancer. The 2nd, 4th, and 7th station lymph nodes can be sampled by mediastinoscopy [24, 25]. Nowadays, cervical mediastinoscopy is performed with the help of a videomediastinoscope and it is named "video-assisted mediastinoscopy (VAM)" or "video-assisted mediastinal lymphadenectomy (VAMLA)" depending on the application technique [26].

Endobronchial ultrasound (EBUS) and endoscopic ultrasound (EUS), which are parts of minimally invasive procedures, are successfully applied with high sensitivity and specificity for mediastinal staging. Combined application of EBUS and EUS allows sampling of lymph node stations numbered 2R, 2 L, 4R, 4 L, 7, 8, and 9 with the sensitivity of 86% (95% CI, 82–90%) [21, 24, 27].

VATS is very useful in the evaluation of lymph nodes as well as the evaluation of the T factor of the tumor. It allows for access to almost every mediastinal lymph node station and total mediastinal lymphadenectomy can be applied [28]. With the right-sided VATS, lymph node stations numbered 2,4,7,8 and 9 can be sampled (**Figures 3** and **4**). Left-sided VATS is an ideal approach for sampling the 5th and 6th lymph node stations that cannot be reached by EBUS and mediastinoscopy.

Although the awake/tubeless VATS procedure has been described, general anesthesia and intubation with a double-lumen tube are usually required and it can only evaluate one side of the mediastinum. In conclusion, it is an approach that offers

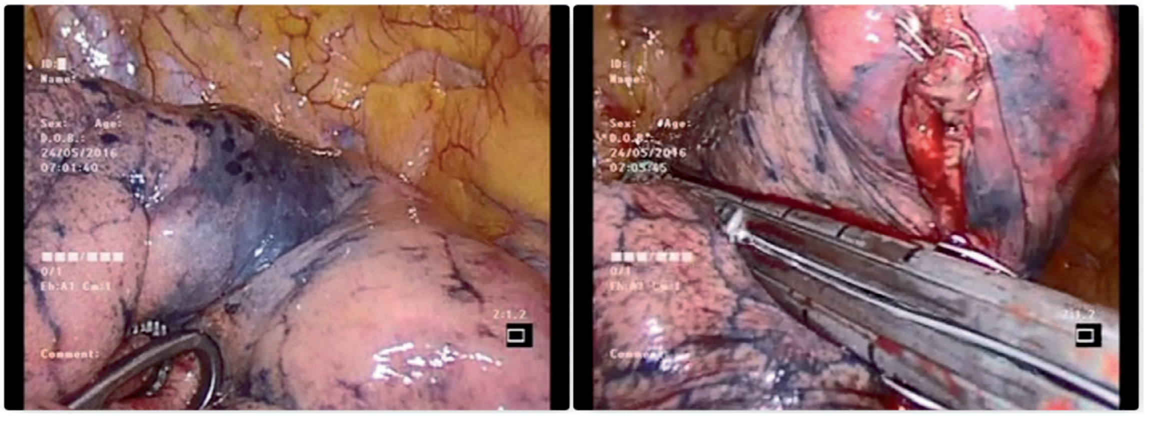

Figure 3.
Intraoperative image of the lung parenchyma after the CT-guided methylene blue labeling.

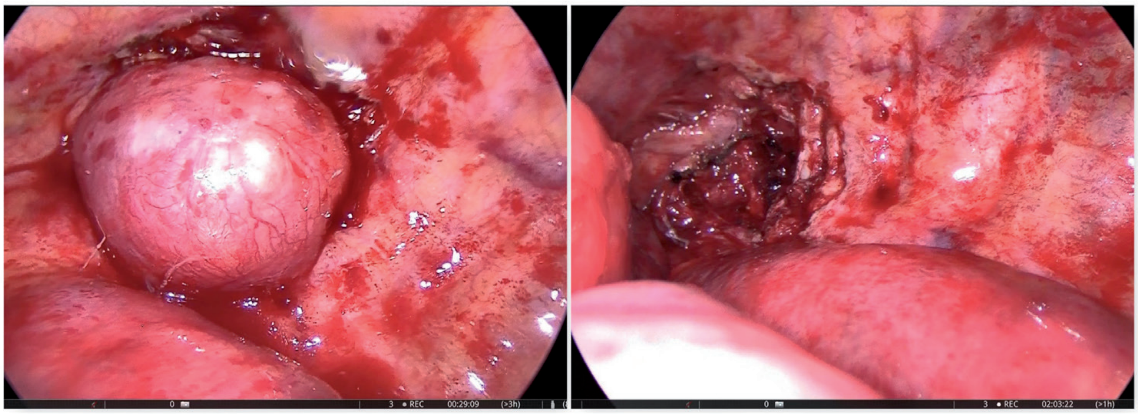

Figure 4.
VATS is also an effective method in the diagnosis and treatment of undiagnosed lesions located in the mediastinum. Para-aortic large mass resected and diagnosed as ectopic mediastinal thyroid.

high specificity and sensitivity values, especially in patients who require sampling of 5th and 6th lymph node stations or in whom complete lymph node dissection is planned.

3.2 Investigation of the pulmonary nodules

With the widespread use of radiological imaging methods, patients with newly detected pulmonary nodules constitute an important part of daily practice.

According to the recommendations of the Fleischner Society, solitary pulmonary nodules larger than 8 mm are recommended for further examination include tissue sampling regardless of cancer risk status [29]. CT-guided percutaneous transthoracic needle aspiration or transbronchial biopsy can be applied to pulmonary nodules with appropriate location and size. However, regardless of the location or size of the pulmonary nodule, sufficient material cannot always be obtained for cytopathological examination by transthoracic and transbronchial biopsy.

VATS is a useful approach for pulmonary nodules that cannot be sampled with minor diagnostic procedures. However, probe or digital palpation is very difficult for ground-glass opacity (GGO) lesions and nodules smaller than 1 cm. To solve this problem several pre-operative and perioperative marking techniques were described in the literature:

- Preoperative CT-guided injection of methylene blue [30].
- CT-guided positioning of a metal wire [31].
- CT-guided placement of a micro coil [32].
- Pleural dye marking using electromagnetic navigation bronchoscopy with or without radial endobronchial ultrasound [33].
- Gamma probe assessment after marking with Technetium-99 [34].
- The intrathoracic stamping method [35].

Each of the methods listed above has advantages and disadvantages and it is controversial which is the best method for marking the pulmonary nodules. We use the “CT-guided injection of methylene blue” method for marking the pulmonary nodules in our clinic (**Figure 5**). It is a simple, safe and effective procedure.

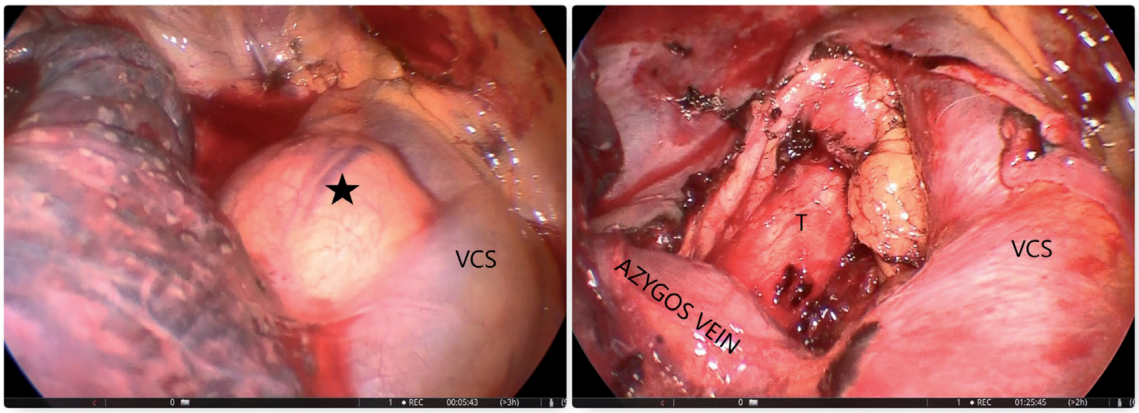

Figure 5.
The paratracheal lymph node, which could not be diagnosed by EBUS, was totally excised with VATS (VCS: Superior vena cava, T: Trachea, asterisk indicates paratracheal lymph node).

However, in order to ensure optimal labeling, the radiologist and the surgeon must be in good collaboration and the time between labeling and operation must be kept as short as possible.

4. The role of VATS in the surgical treatment of the lung cancer

Surgical resection in lung cancer has a relatively long history. First successful en bloc pneumonectomy reported by Graham and Singer in 1933 for the treatment of lung cancer. Lobectomies and segmentectomies were reported in the 1940s and 1950s and the first successful sleeve resection with right upper lobectomy for carcinoma in 1952 by Allison [36–38].

Today, anatomic pulmonary resection remains the best curative option in patients with early-stage lung cancer. The first VATS lobectomy series was reported in 1992 by Lewis [39].

In the following years, different surgeons defined unique techniques and pioneered the development of VATS however, the variability in the technique and the skeptical approach to published results prevented VATS from being widely accepted until the 2000s [40–42].

In addition to being technically feasible, superior postoperative results compared to thoracotomy have been effective in the general acceptance of VATS (**Figure 5**).

Long et al. conducted a prospective randomized trial comparing the quality of life after VATS vs. open lobectomy for clinically early-stage NSCLC [42]. It was stated that a month after operation both dyspnea and pain score were significantly lower in the VATS group.

In another study, Andretti et al. documented the results of 145 patients and compared the postoperative pain of patients who underwent VATS and mini thoracotomy. It was stated that significantly less pain was observed in the VATS group at the 1st, 12th, 24th and 48th postoperative hours [43].

The advantages of VATS over thoracotomy have also been revealed in other studies conducted with large patient groups:

McKenna Jr. et al. published experiences of 1,100 cases and reported 0.8% mortality and 15.3% morbidity [4].

In another study, Boffa et al. analyzed data of 9033 pulmonary resections for primary lung cancer by using the database of the Society of Thoracic Surgeons. In this study, VATS resection was performed in 2429 of 9033 patients. In the VATS group, the mortality rate was 2% and the overall morbidity was 32% [44].

Laursen et al. analyzed the results of 1379 patients who underwent lobectomy. In this study minor and major complications were found significantly lower in the VATS group [45].

Compared to the mortality (%1–2) and morbidity (%32–37) of open lobectomies from large series in the literature, the results are highly satisfactory [46].

The risk of compromising the oncological principles in VATS has been a matter of debate for a long time. However, in the retrospective large-scale studies, no significant difference was found between VATS and thoracotomy in terms of oncological results. Watanabe et al. reported no differences in the total number of lymph nodes, nodal stations, mediastinal nodes, and stations sampled during systematic lymph node dissection between VATS and thoracotomy groups [47].

Moreover, Yang et al. reported the long-term results of VATS and open lobectomy based on the National Cancer Data Base of the U.S. About three thousand patients with stage I NSCLC was matched with propensity score from >7,000 patients; the 5-year OS rates of the two groups were similar [48].

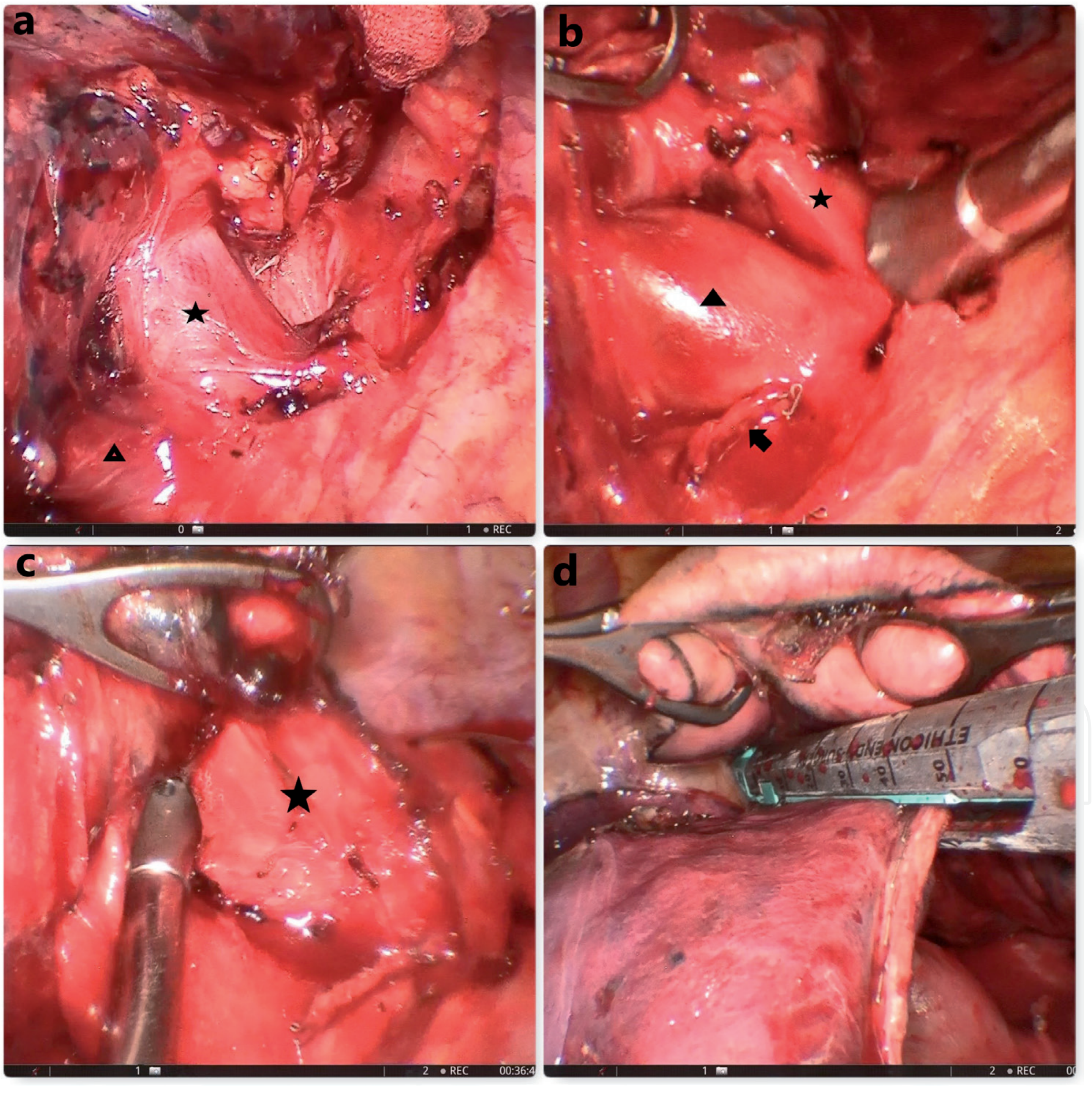

Figure 6.
A case of right upper lobectomy performed using the anterior approach. In the hilum, the upper lobe vein, artery and bronchus were dissected and divided sequentially from anterior to posterior. a. the asterisk indicates the vein of the right upper lobe and triangle indicates the middle lobe vein. b. the arrow indicates pulmonary vein stump. The asterisk and triangle indicate pulmonary arterial branches. c. after the dissection of the arterial branch of the right upper lobe, upper lobe bronchus was seen (asterisk). d. after dividing the vascular and bronchial structures belonging to the upper lobe, the interlobar fissure is finally divided with the help of endoscopic stapler.

Nowadays, the indications of VATS have expanded with the increasing experience. It can be successfully applied in cases with neoadjuvant therapy, tumor larger than 5 cm, chest wall invasion, need of sleeve resection, which was previously considered as a relative or absolute contraindication.

Park BJ et al. analyzed 428 patients who underwent induction chemotherapy for lung cancer and compared thoracotomy and minimally invasive surgical approaches in this patient group. There were not seen any differences in disease-free and overall survival between minimally invasive surgery and thoracotomy groups [49].

Huang et al. presented the results of 118 patients who underwent VATS bronchial sleeve lobectomy and postoperative complications were reported in only 2 patients.

In a study, we conducted in our clinic, which included 60 patients with tumors larger than 5 cm, mean drainage time and postoperative length of hospital stay were significantly shorter [50] (**Figure 6**).

5. Contraindications for VATS anatomic lung resection

With the widespread use of the VATS technique, many contraindications related to the procedure have been described [51]. However, these contraindications have changed over time, thanks to the increasing experience in VATS and the need-oriented developments and diversity of thoracoscopic instruments.

Many conditions such as the presence of endobronchial lesions, history of neoadjuvant treatment, pleural adhesions, and tumor larger than 3 cm, which were previously contraindicated for VATS, are not considered as contraindications by many surgeons today.

Sleeve resections with VATS can be successfully applied in patients with endobronchial lesions.

Moreover, many studies have demonstrated that VATS can be applied with low complication rates after neoadjuvant therapy or in cases with large tumors [49–52].

Large mediastinal vessel, pericardium, carina, and chest wall invasions can be considered relatively contraindicated for VATS. These kinds of major resections must be performed in high-volume institutions and by experienced surgeons.

6. Learning curve for VATS

Mc Kenna has been suggested that the length of the VATS lobectomy learning curve should consist of 50 lobectomies however, there are several personal and environmental factors that affect the learning curve associated with VATS lobectomy [53]. If we put aside personal factors such as instrument use, anatomy mastery and 3-dimensional thinking ability, there are 2 main factors affecting the learning curve: The size of the center and the presence of experienced surgeons who can supervise [51, 53, 54].

The prolongation of the time between the two cases will adversely affect the learning process. In centers where there are not many cases, this deficiency can be partially eliminated with VATS videos or simulators.

7. Conclusions

Minimally invasive thoracic surgery has made great progress in the past 20 years and today it has an important role in both diagnosis and treatment of lung cancer. However, VATS lobectomy is a relatively young technique and is still evolving.

The search for a less invasive technique is not specific to thoracic surgery and is a process that occurs in all surgical specialties. Fortunately, advancing technology supports this search in the best possible way.

Conflict of interest

The author declares no conflict of interest.

Acronyms and abbreviations

CT	Computed tomography
EBUS	Endobronchial ultrasound
EUS	Endoscopic ultrasound
MRI	Magnetic resonance imaging
NSCLC	Non-small cell lung cancer
PET	Positron emission tomography
VATS	Video-assisted thoracic surgery
VCS	Superior vena cav

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