Chapter

Minimally Invasive Surgery for the Management of Lung Cancer

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Abstract

Lung cancer is the leading cause of cancer-related death and the most diagnosed cancer. The treatment of Non-Small Cell Lung Cancer (NSCLC) depends on clinical staging. Surgical radical resection is recommended for patients with stage 1 or 2 of disease and represents the treatment of choice. In the last decades, the surgical approach for lung cancer changed moving from an open approach to a minimally invasive approach, represented by Video Assisted Thoracic Surgery (VATS) and Robot-Assisted Thoracic Surgery (RATS). In this chapter, we illustrate the characteristics of lung cancer, the diagnosis, the classification, the staging and the preoperative evaluation. Then we focus on the surgical treatment of lung cancer and on how it has changed during the years. We explain the open approach represented by the traditional posterolateral thoracotomy and by the muscle-sparing thoracotomy. We illustrate VATS approach and evolution: from the hybrid approach to the pure VATS that can be triportal, biportal or even uniportal. Then, we focus on RATS approach, characterized by the use of multiple ports in the same intercostal space and how it evolved toward the uniportal approach. The objective is to combine the advantage of uniportal VATS (lower postoperative pain, enhanced recovery) and RATS (better visualization, more degrees of movements).

Keywords: NSCLC, thoracic surgery, VATS, RATS, Uniportal, minimally invasive surgery

1. Introduction

1.1 Epidemiology

Lung cancer is one of the main causes of death in several countries. The incidence of lung cancer is 3% in men and 1% in women. 236.740 new cases of lung cancer and 130.180 deaths have been recorded in 2022 [1]. 5-years survival rate is 21.7%, in particular it is 15% for men and 19% for women [2]. It represents the first cause of death for tumor for men and the second for women.

Cigarette smoking is the main risk factor for lung cancer, because of its carcinogenic chemicals. Relative risk of lung cancer is related to number of cigarettes smoked per day, years of smoking and level of tar in cigarettes. Exposed non-smokers also have an increased relative risk of developing lung cancer.

Many agents, such as asbestos, beryllium, cadmium, chromium, diesel fumes nickel, are known as carcinogens. They increase the risk of lung cancer in exposed people, especially in smokers. About 80–90% of lung cancer is caused by smoking. The risk of lung cancer is increased in ex-smokers than in never smokers [3]. Some genetic factors, such as overexpression of Epidermal Growth Factor (EGFR), are related to the development of non-small cell lung cancer (NSCLC) [4].

1.2 Lung cancer screening

The National Lung Screening Trial (NLST) was the first trial to demonstrate that early diagnosis of lung cancer with annual low-dose CT scan in individuals with high-risk factors reduces the mortality rate related to this disease of 20% compared to chest radiographs. In this trial, individuals with high-risk factors were current or former smokers with a 30 or more pack-year smoking history, 55 to 74 years of age with no evidence of lung cancer [5]. Different organizations such as European Respiratory Society (ERS), European Society of Radiology (ESR), European Society of Thoracic Surgeons (ESTS), European Alliance for Personalized Medicine (EAPM), European Society of Medical Oncology (ESMO) e Swiss University Hospitals recommend lung cancer screening with low-dose CT scan. Anyway, low-dose CT screening and follow-up do not substitute smoking cessation.

1.3 Classification and prognostic factors

World Health Organization (WHO) divides lung cancer into two main categories non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The 80% of lung cancer is represented by NSCLC. It is divided into two groups: (1) non-squamous: adenocarcinoma, large-cell carcinoma and other subtypes; (2) squamous cell carcinoma [6]. **Table 1** summarizes WHO classification of lung cancer.

In the last decades, the histological definitions of NSCLS become critical for the development of new therapies based on the histotype. Diagnosis can be obtained with morphological criteria based on hematoxylin and eosin stain or specific stains, such as May-Grunwald-Giemsa, but immunohistochemistry is crucial for the definition of poorly differentiated NSCLC or Not Otherwise Specified (NOS).

Immunohistochemical investigation can be conducted both on histological or cytological samples.

The study of the molecular characteristics of lung cancer, the individuation of disease-associated mutations (EGFR mutations) or immune biomarkers (PD-L1) is crucial for target therapy, that is effective in patients with specific mutations [7].

1.4 Clinical manifestations

Lung cancer can manifest with symptoms like cough, dyspnea, pain, fatigue or hemoptysis. Symptoms related to advanced stages of disease are weight loss, pleural effusion, dysphagia, lymphadenopathy, paraneoplastic syndromes [8].

Epithelial tumors
Papillomas
Squamous cell papilloma, NOS Squamous cell papilloma, inverted Glandular papilloma Mixed squamous cell and glandular papilloma
Adenomas
Sclerosing pneumocytoma Alveolar adenoma Papillary adenoma Bronchiolar adenoma/ciliated muconodular papillary tumor Mucinous cystadenoma Mucous gland adenoma
Precursor glandular lesion
Atypical adenomatous hyperplasia Adenocarcinoma in situ Adenocarcinoma in situ, nonmucinous Adenocarcinoma in situ, mucinous
Adenocarcinomas
Minimally invasive adenocarcinoma Minimally invasive adenocarcinoma, nonmucinous Minimally invasive adenocarcinoma, mucinous Invasive non-mucinous adenocarcinoma Lepidic adenocarcinoma Acinar adenocarcinoma Papillary adenocarcinoma Micropapillary adenocarcinoma Solid adenocarcinoma Invasive mucinous adenocarcinoma Mixed invasive mucinous and nonmucinous adenocarcinoma
Colloid adenocarcinoma
Fetal adenocarcinoma
Adenocarcinoma, enteric type
Adenocarcinoma, NOS
Squamous precursor lesion Squamous cell carcinoma, NOS Squamous cell carcinoma, keratinizing Squamous cell carcinoma, nonkeratizing Basaloid squamous cell carcinoma Lymphoepithelial carcinoma
Large cell carcinoma
Adenosquamous carcinoma
Sarcomatoid carcinomas Pleomorphic carcinoma Giant cell carcinoma Spindle cell carcinoma Pulmonary blastoma Carcinosarcoma
Other epithelial tumors NUT carcinoma Thoracic SMARCA4-deficient undifferentiated tumor
Salivary gland-type tumors Pleomorphic adenoma Adenoid cystic carcinoma Mucoepidermoid carcinoma Hyalinizing clear cell carcinoma Myoepithelioma Myoepithelial carcinoma
Lung neuroendocrine neoplasms
Precursor lesion Diffuse idiopathic neuroendocrine cell hyperplasia
Neuroendocrine tumors Carcinoid tumor, NOS/neuroendocrine tumor, NOS Typical carcinoid/neuroendocrine tumor, grade 1 Atypical carcinoid/neuroendocrine tumor, grade 2
Neuroendocrine carcinomas Small cell carcinoma Combined small cell carcinoma Large cell neuroendocrine carcinoma Combined large cell neuroendocrine carcinoma
Tumors of ectopic tissues

Melanoma
Meningioma
Mesenchymal tumors specific to the lung
Pulmonary hamartoma
Chondroma
Diffuse lymphangiomatosis
Pleuropulmonary blastoma
Intimal sarcoma
Congenital peribronchial myofibroblastic tumor
Pulmonary myxoid sarcoma with EWSR1-CREB1 fusion
PEComatous tumors Lymphangioleiomyomatosi PEComa, benign PEComa, malignant
Hematolymphoid tumors
MALT lymphoma
Diffuse large B-cell lymphoma, NOS
Lymphomatoid granulomatosis, NOS Lymphomatoid granulomatosis, grade 1 Lymphomatoid granulomatosis, grade 2 Lymphomatoid granulomatosis, grade 3
Intravascular large B-cell lymphoma
Langerhans cell histiocytosis
Erdheim-Chester disease

Table 1.
WHO classification of lung cancer.

2. Diagnosis

Clinical suspicion of lung cancer is based on clinical evaluation and history (smoking history, symptoms, age, previous cancer history, family history, other lung disease). Chest X-ray is generally the first investigation performed. Incidental radiological finding of a suspected lung cancer is frequent and it often presents as a solitary or peripheral nodule. Suspicion findings have to be investigated by CT with contrast (**Figure 1**). Radiological features of the pulmonary nodule that suggest the diagnosis of lung cancer are: size, shape and density. The size of the neoformation and especially its growth over time is closely related to the risk of malignancy. However, the doubling of the volume of the nodule in less than 7 days indicates benign lesion (inflammation/infection). Spiculation, irregular margins and pleural retraction are associated with an increased risk of malignancy. Density of the neoformation can be homogeneous or inhomogeneous and varies from solid lesions to "ground glass" or partially solid lesions [9, 10].

Positron Emission Tomography/Computed Tomography (PET/CT) is playing a significant role as a potential diagnosis and staging test in patients with non-small cell lung cancer (NSCLC) [11] and allows, moreover, to direct the biopsy on suspect areas with elevated glucidic metabolism, increasing the likelihood of reaching a diagnostic result.

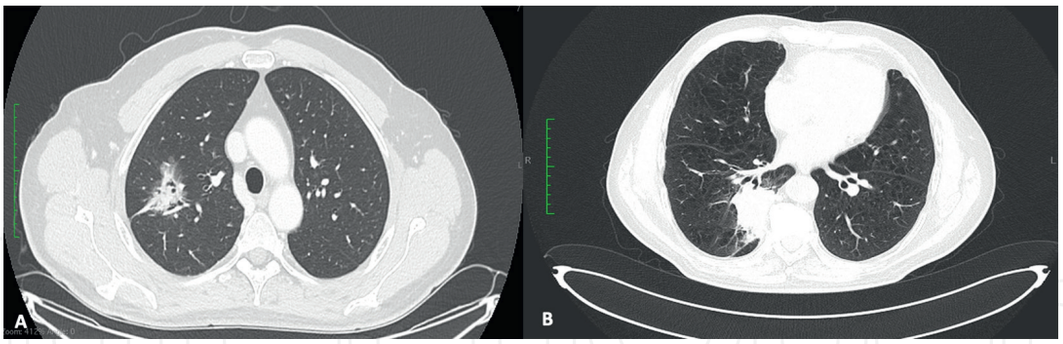

Figure 1.
Examples of lung cancer at CT scan: (A) tumor located at right upper lobe; (B) tumor located at right lower lobe.

Tissue diagnosis employs several techniques:

- Sputum cytology
- Bronchoalveolar Lavage (BAL)
- Image-guided transthoracic needle core biopsy or fine needle aspiration
- Bronchoscopy with biopsy or Transbronchial Needle Sspiration (TBNA)
- EBUS-guided biopsy
- EUS-guided biopsy

If a preoperative tissue diagnosis cannot be obtained, the alternative is intraoperative diagnosis (wedge resection or needle biopsy). The choice of diagnostic technique mainly depends on the location of the lesion (central or peripheral) but also on the size of the tumor and the clinical condition of the patient [12, 13].

In case of abnormal mediastinal and/or hilar lymph nodes at CT and/or PET, needle aspiration EBUS or EUS-guided is recommended. If malignant nodal involvement is not found by this techniques, surgical staging is recommended [12].

3. Staging and TNM classification

Lung cancer staging is necessary to establish the prognosis and the therapeutic program. Staging involves performing a contrast-enhanced CT scan of the chest and upper abdomen to determine local invasiveness, nodal involvement and distant metastasis, particularly in the liver and adrenal glands. The evaluation of these parameters defines the staging of the neoplastic disease according to the TNM system. TNM classification is universally accepted and routinely applied in clinical practice. The T category describes the size and the extension of the primary tumor; the N category defines regional lymph node involvement; the M category establishes presence of distance metastases. **Table 2** summarizes VIII edition of the TNM classification for lung cancer [13].

T	Primary tumor
TX	Primary tumor cannot be assessed or tumor proven by presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*
T1	Tumor ≤3 cm in greatest dimension surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[1]
T1mi	Minimally invasive adenocarcinoma[2]
T1a	Tumor ≤1 cm in greatest dimension[1]
T1b	Tumor >1 cm but ≤2 cm in greatest dimension[1]
T1c	Tumor >2 cm but ≤3 cm in greatest dimension[1]
T2	Tumor >3 cm but ≤5 cm with any of the following features[3]: • Involving main bronchus regardless of distance from the carina, but without involving the carina • Invading visceral pleura • Presence of atelectasis or obstructive pneumonitis that extends to hilar region (involving part or entire lung)
T2a	Tumor >3 cm but ≤4 cm in greatest dimension
T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3	Tumor >5 cm but ≤7 cm in greatest dimension or direct invasion of chest wall (including superior sulcus tumor), phrenic nerve, parietal pericardium or separate tumor nodule(s) in the same lobe as the primary tumor
T4	Tumor >7 cm in greatest dimension or invasion of diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina or separate nodule(s) in a different ipsilateral lobe to that of the primary tumor
N	Regional lymph nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph nodes metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and7or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal and hilar, ipsilateral or contralateral scalene or supraclavicular node(s)
M	Distant metastasis
M0	No distant metastasis
M1	Presence of distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe to that of the primary tumor or tumor with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion[4]
M1b	Single extrathoracic metastasis[5]
M1c	Multiple extrathoracic metastases to one or more organs

[1]*The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.*

[2]Solitary adenocarcinoma, ≤3 cm with a predominately lepidic pattern and ≤ 5 mm invasion in any 1 focus.
[3]T2 tumors with these features are classified as T2a if ≤4 cm in greatest dimension or if size cannot be determined, and T2b if >4 cm but ≤5 cm in greatest dimension.
[4]Most pleural/pericardial effusions with lung cancer are due to tumor. In a few patients, however, multiple microscopic examinations of pleural/pericardial fluid are negative for tumor. In these the effusion should be excluded as a staging descriptor.
[5]This includes involvement of a single distant (nonregional) lymph node.

Table 2.
TNM classification.

In cases where CT does not show evidence of distant metastases, imaging staging should be completed with 18-FDG PET-CT, which has higher sensitivity and specificity than contrast-enhanced CT and higher sensitivity than (18)F-FDG PET in staging NSCLC in detecting extrathoracic and bone metastases. PET/TC has, however, low sensitivity in detecting brain metastases [14]. Staging brain MRI with contrast is used to evaluate the presence of cerebral metastases in patients with neurological symptoms or in the investigation of a suspected CT lesion [15].

Staging is divided into clinical staging (presurgical) and pathologic staging (after surgical resection of the tumor, lymph nodes or metastases) (**Table 3**).

4. Treatment of early stage lung cancer

Radical surgery allows to obtain a full recovery or to significantly improve the prognosis in patients with early stage disease and is not recommended for patients with advanced disease. Surgery needs to be taken in consideration in NSCLC stage I, II and in selected stage IIIA/IIIB (T1-T2, N2 single station, non-bulky). It should be performed in high-volume centers, by expert surgeons. It has been demonstrated that the outcome of patients undergoing lung resection for lung cancer is better for those treated in high-volume centers [16]. Before surgery, lung cancer patients need to be studied in order to define their operability. A tumor that can be completely resected with surgery is considered resectable. Even if a tumor is anatomically resectable, it is necessary to evaluate if the patient can tolerate surgery and is functionally operable according to his functional preoperative situation and, most importantly, his predicted postoperative status, especially with regard to respiratory and cardiovascular function. Cardiorespiratory evaluation is mandatory for patients that are candidate to a lung resection surgery, in order to predict the operatory risk and postoperative lung function. Lung function is evaluated mainly with: spirometry, Diffusion Lung CO (DLCO), hemogasanalysis, ergometric tests, lung perfusion scintigraphy. In case of lower values (FEV1 and DLCO <80%), Cardio Pulmonary Exercise Testing (CPET) is indicated and if the maximal oxygen consumption (VO2max) is less than 10 mL/kg/min the risk of serious postoperative complications is high. For cardiovascular assessment, the use of recalibrated thoracic Revised Cardiac Risk Index (RCRI) is recommended (**Table 4**).

An RCRI <2 has been reported to be associated with a low-cardiac risk, and no additional tests are needed. However, an RCRI >2 has been associated with an increased cardiac risk and a cardiac consultation with non-invasive testing is recommended [17, 18].

STAGE	T	N	M
Occult carcinoma	TX	N0	M0
0	Tis	N0	M0
IA1	T1mi	N0	M0
	T1a	N0	M0
IA2	T1b	N0	M0
IA3	T1c	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
IIIA	T1a	N2	M0
	T1b	N2	M0
	T1c	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
IIIC	T3	N3	M0
	T4	N3	Mo
IVA	Any T Any T	Any N Any N	M1a M1b
IVB	Any T	Any N	M1c

Table 3.
Staging of NSCLC.

Brunelli et al. [19] proposed a physiologic evaluation resection algorithm for major anatomic resection (lobectomy or greater).

For positive and low-risk or negative cardiac evaluation, we calculate postoperative FEV1 (ppoFEV1) and postoperative DLCO (ppoDLCO):

Weighted factors	Points
Ischaemic heart disease	1.5
History of cerebrovascular disease	1.5
Serum creatinine >2 mg/dL	1
Pneumonectomy planned	1.5
Classes of risk	
A	0
B	1–1.5
C	2–2.5
D	>2.5

Table 4.
Recalibrated thoracic revised cardiac risk index.

- If ppoFEV1 or ppoDLCO <30%, cardiopulmonary exercise test (CPET) is recommended.
    - If VO2max is >20 ml/kg/min or > 75%, the patient is considered at low risk for major anatomic resection.
    - If VO2max is 10–20 ml/kg/min or 35–75%, the patient is at moderate risk for major anatomic resection.
    - If VO2max is <10 ml/kg/min or < 35%, the patient is at high risk for major anatomic resection.
- If ppoFEV1 or ppoDLCO <60% and both >30%, stair climb or shuttle walk is recommended.
    - If stair climb is >22 m or shuttle walk is >400 m, the patient is considered at low risk for major anatomic resection.
    - If stair climb is <22 m or shuttle walk is <400 m, cardiopulmonary exercise test (CPET) is recommended.
- If ppoFEV1 and ppoDLCO is >60%, the patient is considered at low risk for major anatomic resection.

For positive high-risk cardiac evaluation, cardiopulmonary exercise test (CPET) is mandatory:

- If VO2max is >20 ml/kg/min or > 75%, the patient is considered at low risk for major anatomic resection.
- If VO2max is 10–20 ml/kg/min or 35–75%, the patient is at moderate risk for major anatomic resection.

- If VO2max is <10 ml/kg/min or < 35%, the patient is at high risk for major anatomic resection.

A multidisciplinary evaluation is necessary to discuss the different therapeutic options and their potential results. The surgical procedure depends on the extent and the localization of the tumor and on the cardiopulmonary reserve of the patients. Preoperative or intraoperative cytohistologic diagnosis is recommended before anatomic lobectomy, bilobectomy or pneumonectomy. Anyway, when the diagnosis is technically difficult to obtain, or it is at high risk for the patient and the radiological and clinical probability of lung cancer is high, it is possible to perform an anatomic resection without tissue confirmation of lung cancer.

Anatomic lobectomy with mediastinal lymphadenectomy is the gold standard treatment for lung cancer.

When the lesion is not resectable through a lobectomy, for instance if it infiltrates the main bronchus or the main artery, or if it invades the fissure to the adjacent lobe, pneumonectomy is indicated.

If anatomically applicable and if negative margin can be achieved, sleeve lobectomy is preferred over pneumonectomy.

Anatomic segmentectomy is acceptable for Ground Glass Opacities (GGO) or for very early stage of disease (Tis or T1a) or in patients who are not eligible for lobectomy. It is possible because GGO more often are diagnosed as in situ adenocarcinoma or minimally invasive adenocarcinoma. When segmentectomy is performed, parenchymal resection margins should be 2 cm or more, or they should be the size of the nodule or larger. In these cases, segmentectomy is preferred over wedge resection [20].

5. Surgical techniques

5.1 Thoracotomy

The first pulmonary resection for lung cancer was performed in 1912. At the beginning, surgical resection for lung cancer was pneumonectomy. In 1960s, lobectomy was recognized as the gold standard treatment. Traditional surgical approach was a 15–20 cm posterolateral thoracotomy. This traditional approach implies the resection of multiple muscle layers (latissimus dorsi and serratus anterior) and ribs divarication with metal retractors. Ribs fractures are common during divarication and sometimes ribs segments are resected to avoid fractures and to improve surgical exposure. This kind of thoracotomy allows an optimal view of the hilum and the use of two hands by the surgeon. This incision can result in pain and shoulder and chest wall dysfunction. 44% of patients undergoing thoracotomy develop chronic pain for 1 year after the procedure and 29% of patients experience pain for more than 1 year after surgery [21].

Noirclerc et al. [22] were the first to describe the muscle-sparing thoracotomy. The objective of this approach is to preserve muscles, in particular the latissimus dorsi. This technique reduces postoperative complications and consents a better postoperative mobilization of the shoulder, compared to traditional posterolateral thoracotomy.

5.2 Video-assisted thoracic surgery (VATS)

During the last decades, Minimally Invasive Surgery (MIS) was applied for lung cancer surgery. The first Video-Assisted Thoracoscopic Surgery (VATS) for lung resection was performed in the early 1990s [23]. At the beginning, the term VATS indicated the use of a videothoracoscope during thoracic surgery procedures, performed through traditional thoracotomy. For example, Okada et al. [24] described a hybrid approach, with a mini-thoracotomy and a camera port, used to see areas not visible with direct vision. Substantially, hybrid approach integrated direct and thoracoscopic vision. Then, there was the development of "pure" VATS using only thoracoscopic vision.

Most centers use a 3–5 cm utility incision located anteriorly, one port for the optic and another port located posteriorly. Gossot et al. [25] described pure thoracoscopic lobectomy using three incisions with a mini-thoracotomy for the extraction of the lobe. McKenna Jr. et al. [26] use three or occasionally four ports.

Hansen et al. [27] perform a standardized anterior three-port approach, with the ports located always in the same place, independently of the lobe to resect: a utility incision of 4–5 cm is located anteriorly at the 4th intercostal space, the 1–1,5 cm camera port is located anteriorly at the level of the diaphragm (8th intercostal space) and a posterior 1,5 cm incision is done at the same intercostal space.

Burfein and D'Amico perform double-port VATS lobectomy [28]: a 2 cm camera port is located at the 7th or 8th intercostal space in the mid-axillary line and a utility incision of 4,5 cm is located anteriorly at the 5th or 6th intercostal space. The double-port technique is characterized by a different lung exposure and the camera has to be moved between the camera port and the utility incision during surgery.

In all cases, systematic lymph node dissection is performed.

Compared to open approach, VATS lung resection is associated with lower postoperative pain, lower incidence of postoperative complications (including atrial fibrillation, atelectasis, prolonged air leak), shorter length of hospitalization, lower postoperative mortality. The reduced hospitalization also consents a rapid access to adjuvant chemotherapy [29]. Different studies analyzed the oncological equivalence of VATS compared to open approach. Some studies aimed to analyze the effectiveness of nodal dissection in VATS compared to that obtained with thoracotomy. Medbery et al. [30] affirmed that there is no difference in staging if nodal dissection is performed in high-volume centers. According to Watanabe et al. [31] a complete lymphadenectomy is possible in VATS also in N2 stage intraoperatively diagnosed. A retrospective study of the National Cancer Data Base (NCDB) showed no difference in nodal staging and overall survival between patients operated in VATS or in open resections [26]. It is also demonstrated that there is no difference in long-term survival [32].

During the years, VATS surgery evolved to a uniportal approach, with only a single incision used for all instruments and for lobe extraction. Rocco et al. [33] were the first to describe the uniportal approach in 2004 for wedge resection, not performing lobectomies. Gonzales-Rivas et al. [34] did the first uniportal VATS lobectomy in 2010. The utility incision is done at the 5th intercostal space, its size is the same of the utility incision used for triple or double-port approach. The surgeon and the assistant are placed both in front of the patient in order to have the same vision and to coordinate movements. A 30 degrees camera is used and it follows the instruments, giving

a vision that closely resembles that of the open approach. Uniportal VATS lobectomy follows the same principles of all major pulmonary resection in VATS. Dissection of veins, arteries, bronchus and fissure is performed, with a complete mediastinal lymphadenectomy.

Different studies compared the outcome of uniportal and "multiportal" VATS, demonstrating a reduction of complications, length of hospitalization and duration of drain tube. Uniportal VATS also allows for a reduction in postoperative pain due to several factors. Firstly, it involves only one intercostal space, minimizing the overall surgical trauma. Secondly, the absence of trocars eliminates the potential compression on the intercostal nerve that may occur during the movements of the camera in traditional multiport VATS procedures [35]. An interesting evolution of the uniportal VATS was the development of the subxiphoid approach, in order to reduce the pain due to intercostal nerve damage [36]. It also can be used to treat bilateral disease, even if the visualization is limited, compared to transthoracic techniques [37]. More studies are necessary to compare subxiphoid to transthoracic approach.

General anesthesia with single lung ventilation is required for lung surgery and it is obtained through a double lumen endotracheal tube or through a bronchial blocker. The patient is positioned in lateral position. Both the surgeon and the assistant stay in front of the patient in order to have the same vision. In general, the port position is the same for every lobectomy. A 30° videothoracoscope and long and curved instruments are usually used. Hilum dissection is performed bluntly with instruments, suction device, peanuts or energy devices. Vascular and bronchial elements are isolated and resected through linear endo-staplers. Also the fissure is divided with endo-stapler device. The specimen is extracted using an endo-bag. The chest tube is inserted in the camera port at the end of surgery. Then, the lymphadenectomy is done mainly using energy device.

Lymphadenectomy is necessary for the correct staging of the disease. Systematic lymph node dissection is recommended. Anyway some authors recommend the lobe-specific mediastinal lymphadenectomy. According to them, nodal metastasis is related to the localization of the primary tumor: upper lobe tumors tend to metastasize upper lymph nodes and lower lobe tumors tend to spread to the inferior and subcarinal nodes [38]. Systematic mediastinal lymph node dissection allows the detection of more metastatic lymph nodes and a better oncologic outcome than lobe-specific nodal dissection [39]. Gooseman and Brunelli [40] recommend systematic lymphadenectomy and in particular, even for the selected cases in which lobe-specific nodal dissection could be accepted (peripheral T1 squamous cell carcinoma), they recommend always the dissection of subcarinal lymph nodes.

The surgeon has to be prepared to convert to thoracotomy in case of technical difficulties in dissection or in case of bleeding.

5.2.1 Right upper lobectomy

The first step involves performing a mediastinal release maneuver. The lung is retracted anteriorly and the posterior pleura is dissected at the level of the bronchial bifurcation. It helps the dissection of the bronchus from the anterior approach. Then, the lung is retracted posteriorly and the dissection of the veins is performed. Once identified and dissected the upper lobe vein, it is resected with vascular endo-stapler. The resection of the vein exposes the pulmonary artery. The arterial branches to the upper lobe (truncus anterior and ascending arteries) are dissected and divided through

vascular endo-stapler. Then, the bronchus is divided through bronchial stapler and the fissure is completed with endo-stapler device. The specimen is extracted in an endo-bag through the utility incision.

5.2.2 Left upper lobectomy

The lung is retracted anteriorly and the posterior pleura is dissected in order to identify the posterior artery and to facilitate the maneuvers with the anterior approach. The lung is retracted posteriorly and, after the identification of the veins, the upper lobe vein is dissected and divided through endo-stapler, exposing the pulmonary artery and the upper lobe bronchus. The arterial branches for the anterior, posterior and apical segments and the lingular branches are exposed and divided through vascular endo-staplers. Then, the upper bronchus and the major fissure are divided through endo-staplers. The specimen is extracted in an endo-bag through the utility incision.

5.2.3 Middle lobectomy

The middle lobe vein is dissected and divided. Then the fissure to the lower lobe and the bronchus to the middle lobe are divided through endo-staplers. Then the artery branches are dissected and divided and at the end the fissure to the upper lobe is completed through endo-stapler. The specimen is extracted in an endo-bag through the utility incision.

5.2.4 Lower lobectomies

The first step of lower lobectomies is represented by the division of the inferior pulmonary ligament. This confers mobility to the lobe and exposes the vein to the lower lobe. The lower lobe vein is dissected and divided with endo-stapler (**Figure 2**). Then the procedure can continue in two ways: the surgeon can dissect the arterial branches to the lower lobe (for the apical segment and for the basal pyramid) and the bronchus to the lower lobe within the fissure. The other option is represented by the fissureless technique: after the dissection and resection of the vein, the lower lobe is retracted cranially and the plane between the bronchus and the artery is dissected and

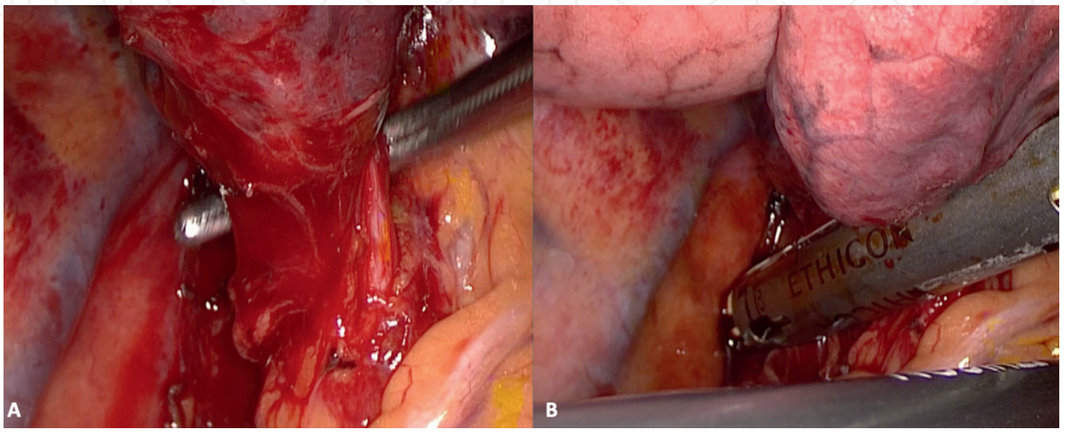

Figure 2.
Right lower lobectomy: (A) right lower lobe vein dissection; (B) right lower lobe division through endo-stapler.

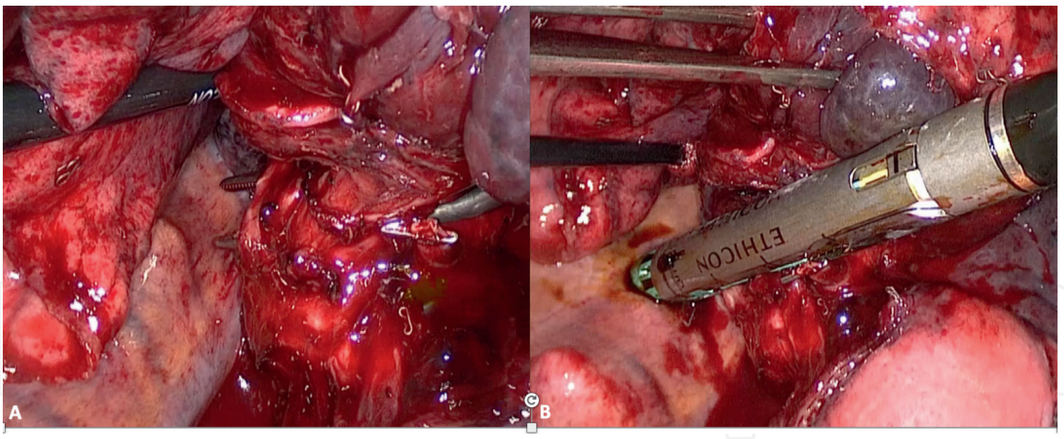

Figure 3.
Right lower lobectomy: (A) dissection right lower lobe bronchus; (B) division of right of right lower lobe bronchus through endo-stapler.

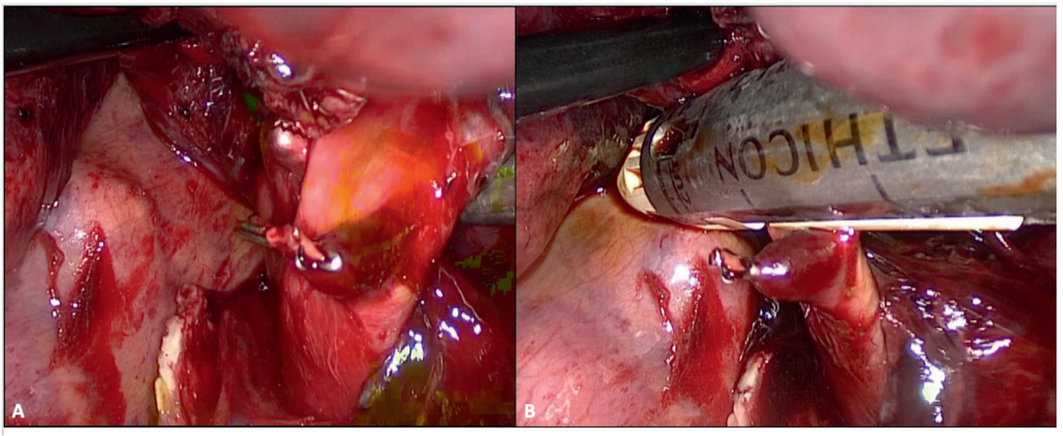

Figure 4.
Right lower lobe artery: (A) dissection and (B) division of right lower lobe artery through endo-stapler.

the bronchus is divided through endo-stapler (**Figure 3**). Then, the arterial branches are divided and the fissure is divided at last (**Figure 4**). The specimen is extracted in an endo-bag through the utility incision.

5.3 Robotic-assisted thoracic surgery (RATS)

The most recent minimally invasive technique applied to thoracic surgery is robotic approach. The progress in the field of robotic technology generated interest in thoracic surgeons, that started to perform Robot-Assisted Thoracic Surgery (RATS). The first robotic lobectomies were described by Morgan et al. [41] and by Ashton et al. [42] in 2003. Since then, robotic lobectomy started to be performed in different centers. Cerfolio et al. [43] described their initial results using a completely portal 4-arm robotic operation with insufflation of carbon dioxide. The four ports are located at the same intercostal space (7th intercostal space). They achieved a complete R0 resection, performing a median number of 5 mediastinal lymph node station dissections. They recorded a significant reduction in morbidity and hospital stay compared to thoracotomy. When compared to VATS, Kent et al. [44] reported less postoperative pain and a rapid return to normal activities.

In 2021, Yang et al. [45] were the first to describe a uniportal RATS lobectomy for a tumor located in the right upper lobe. A single 4 cm incision was made at the 4th intercostal space on the mid-axillary line. The 30° camera arm was placed on the upper end of the incision and the two instrument arms were placed intercrossed inside the chest. With this approach, they were able to perform a radical lobectomy and lymphadenectomy. The recovery was fast and the patient was discharged three days after surgery.

RATS consents a three-dimensional (3D) high-definition view, intuitive articulation of the robotic hands and more flexibility of instruments, with seven degrees of motion. Its superior instrumentations consent to perform accurate and safe dissection, in particular lymph node dissection that is crucial for the correct staging of lung cancer. It also can be used for difficult cases at high risk of conversion such as central tumors, sleeve lobectomy and pneumonectomy. To date, studies comparing VATS and RATS lobectomy do not show significant differences in terms of outcome. For this reason, a challenging question arises regarding the cost-benefit analysis [46, 47].

6. Conclusions and future perspectives

At the beginning of the era of minimally invasive thoracic surgery, a great limit of the technique was represented by the vision, because of the low definitions of cameras. Surgeons preferred the direct vision to have a better control of the procedure. The progress in the field of technologies consented to have high-definition cameras also with additional features, such as 3d vision or integration with augmented reality surgery navigation systems. Nowadays, cameras are largely used by surgeons even in thoracotomy approach to improve visualization and lightning. The progress made in the field of instrumentations has been appreciated by surgeons and instruments made for minimally invasive surgery such as endo-staplers are now used also for open approach, because of their thickness and flexibility.

Another challenge for VATS surgery is the use of rigid instruments that have to be moved through the rigid chest wall. Human hand consents to perform several traction and counter-traction movement and provides tactile feedback. With the development of minimally invasive surgery, that limits the tactile feedback, surgeons started to operate mainly relying on the vision. This happens, in particular, in RATS. Since the chance to palpate nodules or ground glass opacities is little in VATS and even null in RATS, surgeons has to rely only on visual signals. For this reason, they can use intraoperative ultrasound or they can mark nodules with coils in hybrid operating room [48]. Also artificial intelligence is developing in order to help surgeons during procedures.

The field of minimally invasive thoracic surgery is developing in two directions: reducing the number and the size of the surgical access (uniportal VATS) and increasing the use of RATS. The objective is to combine the advantage of uniportal VATS (lower postoperative pain, enhanced recovery) and RATS (better visualization, more degrees of movements).

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