

Jun Wang
Mark K. Ferguson
Editors

Atlas of Minimally Invasive Surgery for Lung and Esophageal Cancer



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 Springer

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1.1 Background

Minimally invasive surgery (MIS) of the thorax was introduced about 100 years before the publication of this atlas. It began primarily as a diagnostic modality, and was taught to me during my training in the late 1970s. The applications of thoracoscopy 40 years ago were limited to pleura biopsies and drainage of pleural effusions. There were no dedicated instruments other than a suction cannula and biopsy forceps, and viewing was limited to the operator looking directly through a small diameter low resolution telescope. Thus the technique was not used commonly. Technological advances in the late 1980s and beyond offered improved telescope optics, compact high resolution video cameras, and instrumentation including tissue and vascular staplers. These advances permitted performance of complex procedures such as lobectomy, esophagectomy, and mediastinal operations. A small number of adventurous surgeons were pioneers in establishing the safety and utility of these operations, from which many other surgeons and their patients have benefitted.

The first MIS operations included lung biopsy and pleural procedures for pneumothorax and empyema. In the early 1990s the first major lung resections were reported, which initially in many centers were non-anatomic resections—SIS lobectomy, or stapled in-situ lobectomy—in which most hilar structures associated with a lobe were stapled collectively. Anatomic resections as they are now performed followed quickly, however, and reports from single institutions of large experiences with outstanding results were first published in 2006 [1]. Esophagectomies performed with hybrid procedures or exclusive minimally invasive approaches were first reported in the early 1990s, with the first large series of successful cases published in 2003 [2].

Despite these advances, general adoption of minimally invasive thoracic surgery was slow. The majority of surgeons in the West who had routine access to minimally invasive resources had not been trained to do MIS surgery and were reluctant to take time from their busy practices to develop MIS skills. Training in MIS general surgery was in its infancy, and the variety of procedures thought to be appropriate for MIS techniques was limited to cholecystectomy in carefully selected patients and biopsies. Thus, even younger thoracic surgeons didn't have a very extensive background in MIS resulting from their general surgery training. No certified training courses existed early on, and surgeons interested in learning the techniques had to search out an

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experienced mentor and arrange to spend the necessary time observing; such mentors were soon overwhelmed with requests by potential observers and found it difficult to meet the demand. A system of sponsored training courses for thoracic surgeons in practice wasn't introduced until 1992, when the Society of Thoracic Surgeons created an infrastructure and curriculum for MIS training in thoracic surgery that served the needs of the physicians until training during fellowship became routinely available.

Training in MIS thoracic surgery remains less regulated than training in MIS general surgery. The latter effort includes a skills course (Fundamentals of Laparoscopic Surgery), the successful completion of which is required prior to graduation from residency and obtaining board certification in the United States [3]. No such curriculum for MIS thoracic surgery has been developed in the US. Efforts in other regions of the world are similarly underdeveloped. Skills needed for MIS thoracic surgery are demonstrably different than those learned during abdominal surgical training. However, we expect our graduating thoracic trainees to be skilled in MIS techniques without having developed skills definitions, the infrastructure for simulation training, or methods of determining competency. Clearly there is considerable room for improvement in how we train and certify young thoracic surgeons in MIS abilities.

1.2 Frequency of MIS Thoracic Surgery in Developed Countries

It is difficult to determine exactly how many lung and esophageal resections are performed annually using minimally invasive techniques. Outside of the United States there are no large databases that mandate recording of such practices. Even within the US the collection of such data are often inaccurate and analyses of such data can be misleading. A few resources in the US that help provide some insights include the Nationwide Inpatient Sample (NIS), the SEER (the Surveillance, Epidemiology, and End Results) Program, NSQIP (the National Surgical Quality Improvement

Program of the American College of Surgeons), the State Inpatient Database (SID) and the Society of Thoracic Surgeons (STS). These data sets are not available for direct inspection, and so we must assess outcomes from reports published in scientific journals.

1.3 Video Assisted Thoracic Surgery (VATS) Lobectomy

The incidence of VATS is related in part to the percentage of patients with early stage lung cancer and reflects to some extent the expertise of the contributing surgeons, which is greater in the STS, NSQIP and SID datasets (Table 1.1) [4–9]. The NIS demonstrated an increase in VATS usage from 26 % early in the study to 39 % in the final year of the study [8]. Overall, the percentage of major lung resections performed by VATS in the US is moderate, is increasing over time, and likely will have exceeded 50 % at the time of this publication.

Assessment of the frequency of MIS resections performed in Europe is a little more difficult because of the fragmented nature of the data. A review of published results demonstrates surprising differences among countries in the use of VATS for lobectomy. The EPITHOR project in France demonstrated a fourfold increase in the use of VATS for lobectomy from 2005 to 2012, culminating in an incidence of nearly 11 % [10]. In Denmark from 2007 to 2011, clinical stage I lung cancer was treated by VATS lobectomy in 47 % of patients [11]. The European Society of Thoracic Surgeons (ESTS) Database, a large voluntary effort including nearly all European countries, demonstrates a very variable penetration of VATS techniques at present, with Denmark having the highest percentage and many countries lacking centers of excellence [12]. The overall rate is between 10 % and 15 % (Table 1.2) [10–14].

The rates of VATS use for lobectomy in other developed countries are difficult to determine. From an analysis of the literature, no nationwide databases reporting such results were available from Japan, Taiwan, South Korea, or Australia.

Table 1.1 Frequency of use of VATS for lung resection among large US databases

Author	Database	Time period	Total patients	VATS patients
Paul [4]	STS	2002–2007	6,323	20 %
Paul [5]	SEER	2007–2009	6,008	22 %
Farivar [6]	STS	2010–2011	10,525	44 %
Mungo [7]	NSQIP	2005–2012	6,567	37 %
Harrison [8]	NIS	2008–2011	19,353	32 %
Kent [9]	SID	2008–2010	33,095	38 %

STS Society of Thoracic Surgeons, *SEER* Surveillance Epidemiology and End Results Program, *NSQIP* National Surgical Quality Improvement Program, *NIS* Nationwide Inpatient Sample, *SID* State Inpatient Database

Table 1.2 Frequency of use of VATS for lobectomy in European databases

Author	Database	Time period	Total patients	VATS patients
Thorsteinsson [13]	Iceland	1994–2008	404	0 %
Licht [11]	DLCR	2007–2011	2,230	47 %
Morgant [10]	Epithor	2005–2012	34,006	3.2 %
Begum [12]	ESTS	2010–2012	Not stated	11.3 %
Falcoz [14]	ESTS	2007–2013	28,771	9.5 %

DLCR Danish Lung Cancer Registry, *ESTS* European Society of Thoracic Surgeons

1.4 Minimally Invasive Esophagectomy (MIE)

The very low relative frequency of esophageal cancer compared to lung cancer, especially in Western countries, makes identification of rates of MIE quite difficult. In a survey of esophageal surgeons reported in 2010, the frequency of minimally invasive approaches worldwide was about 30 %. This figure varied considerably according to surgeon specialty, being highest for general surgeons (57 %) and lowest for surgical oncologists and cardiothoracic surgeons (20 %) [15]. Data from the STS Database for 2001–2011 indicate that 14 % of patients underwent MIE [16]. In Japan in 2011, the frequency of hybrid or totally minimally invasive esophagectomy was 33 % [17]. From these limited data it appears that the acceptance of minimally invasive approaches in developed countries remains limited.

1.5 Growth of MIS Thoracic Surgery in Developing Countries

Penetration of minimally invasive techniques into developing countries is very uneven. Obstacles to growth include lack of resources (equipment for thoracoscopy or laparoscopy; trained support staff; non-specialist anesthesiologists) and lack of training for surgeons. Whereas in most developed countries trainee instruction in thoracic MIS is routine and usually required, such is not the case in many developing countries. In centers of excellence that have high volumes of practice, particularly in India and China, VATS lobectomy and MIE are routine. In such centers more than 80 % of lobectomies are performed using VATS, and more than 90 % of esophagectomies are done via MIE.

1.6 Status of MIS Thoracic Surgery

There can be little doubt that VATS lobectomy and MIE are accepted as standard approaches to surgery for lung and esophageal cancer. The chapters in this atlas clearly identify outcomes after MIS and demonstrate numerous advantages over open surgery. Short-term benefits have been conclusively demonstrated, oncologic equivalence in terms of nodal harvest is similar to open operations, and oncologic equivalence in terms of long-term survival is apparent. What remains to be fully elucidated is relative costs, or cost-effectiveness, particularly for robotic thoracic MIS.

1.7 Future Areas of Study

Complex minimally invasive thoracic surgery was introduced in the early 1990s, less than 25 years before the publication of this atlas. In that short span of time its growth and acceptance have been remarkable. We can anticipate continued growth of this application in the developing world, and will also see rapid advancement in a variety of elements of MIS, including education, technology, and outcomes (Table 1.3).

Table 1.3 Target areas for future study of thoracic minimally invasive surgery

Education and training
Learning curves for competency and proficiency
With mentoring
Without mentoring
Current approaches to education
Training program
Centers of excellence
Specialized fellowships
Simulation training
How much can this shorten the learning curve?
Models
Animal models
Tissue models (perfused, unperfused)
3-D printed models, other artificial materials
Virtual models
Improved performance
Ergonomics
Double or single port techniques
More advanced complex operations including double sleeve resections
Advanced technology
Powered staplers
Tissue site marking
Measurement of perfusion for tumor, lymph node, or vessel identification
Ultrasound applications
Hybrid procedures
Robotics
Standard resections
Advanced resections
Single port or hybrid approaches
Technological enhancements (tissue perfusion, ultrasound, automated processes)
Improved clinical care
Fast tracking to discharge
Cost-effectiveness

1.8 Education

Education is the primary means by which MIS thoracic surgery will expand and evolve. How we provide education to our trainees and to practicing surgeons who haven't yet learned the techniques is an ongoing challenge. In most developed countries there is sufficient expertise and volume in training programs to permit all trainees to emerge having achieved competence in MIS thoracic surgery. Whether this goal is sufficient is unclear. We would all like our trainees to achieve a higher level of performance than mere competence by the time of their graduation. Whether this could be achieved through increased use of simulation training needs to be investigated. A number of models are currently or soon will be available, and identification of appropriate targets for simulation training is underway.

For practicing surgeons who have not previously learned MIS techniques, training is available in short courses, but application of the lessons learned in such courses is likely to be slow and fraught with difficulty without proper ongoing mentoring. The learning curve under such circumstances can be steep, putting the surgeon and patients at risk (medical-legal/financial risk for the former, personal health risk for the latter). Society needs to identify improved methods of training practicing surgeons in new approaches and technologies that minimizes threats to surgeons' income and practice integrity, optimizes opportunities for ongoing mentoring, and minimizes patient risk.

1.9 Surgeon Performance

Improving performance should be every surgeon's lifelong goal. This may be accomplished through a variety of means, including using new instruments, new approaches, or by varying the steps of an operation. Surgeons are studying comparative surgeon ergonomics of different patient positions for minimally invasive operations. Advances in thoracoscopy for complex operations include growing use of double and single port techniques, and studies are needed to determine whether these provide benefit to our patients. As surgeon experience with minimally invasive surgery grows, increasingly complex operations are being done more routinely, including sleeve resection, double sleeve resection, and en bloc chest wall resection, to name a few.

1.10 Advances in Technology

A variety of technological enhancements are becoming available for minimally invasive surgery. Powered staplers may provide improved access of staplers to difficult areas, and may improve the consistency and quality of staple lines. Tissue perfusion for assessment of vessel anatomy, identification of

regional lymph nodes, and evaluation for reconstructive organ ischemia is increasingly being used. Ultrasound for identification of tumors, nodes, and regional vessels is currently used sporadically, but as technological enhancements and surgeon familiarity grow, ultrasound use is likely to increase dramatically. Finally, advances in chemical testing of plume from electrocautery has the possibility of determining whether tissue is malignant or benign without frozen section and can help assess adequacy of resection margins.

1.11 Robotics

Robotic operations are growing in frequency and popularity. This technology is cost-prohibitive at present for many institutions and certainly for most developing countries. As the technology improves and use grows, costs are likely to decrease substantially, providing access to most levels of the market. We have yet to determine appropriate applications of robotics in thoracic surgery. Certainly many experienced surgeons are capable of performing almost any operation using the robot, but whether this adds benefit to the patient in terms of costs or outcomes has not been determined for most operations. Potential benefits of the robot include decreased operating time (experienced surgeons only), improved accuracy of dissection (wide range of wristed movements; minimization of surgeon tremor and tissue movements related to heart beat, etc; three-dimensional imaging; image magnification), better ergonomics, and availability of advanced technologies (tissue/vessel perfusion, powered staplers), to name a few. There remain concerns about added costs, added OR time when inexperienced users or operating room teams are involved, and patient safety when there is an increased risk of technological malfunctions.

1.12 Improved Patient Care

Our ultimate goals as surgeons are to improve patient care and the outcomes of care. Minimally invasive techniques offer shorter operative times, faster recovery from anesthesia, reduced pain, reduced risk of postoperative complications, shortened duration of hospital stay, and faster return to activity. The predictability of these outcomes permits patients to be "fast-tracked" to discharge, which helps reduce unnecessary testing, further reduces duration of hospital stay, and is associated with a decreased risk of complications. Resources are conserved and overall costs are substantially reduced.

Identifying practices that are cost-effective benefits all patients by enabling better distribution of resources. This process can help reduce the overall costs of healthcare and

lessen the financial burden of healthcare on society. It is incumbent on surgeons who are endeavoring to advance the art and science of minimally invasive surgery to consider evaluation of cost-effectiveness as part of their efforts. It is often easier to make such evaluations during the growth of a new technology or application rather than after such as become a standard of care.

Conclusion

There have been remarkable advances in minimally invasive thoracic surgery in the past 25 years. Despite this, utilization of this approach remains limited. This atlas has the potential to help expand the growth of minimally invasive thoracic surgery by providing a background including indications, limitations, and benefits, and by offering detailed descriptions for virtually all aspects of minimally invasive surgical care of lung and esophageal cancer. For surgeons who are relatively unfamiliar with VATS or MIE, this atlas will encourage them to use these approaches more often. For surgeons who understand the basics of VATS and MIE, the atlas will enable them to take on more complex operations with confidence.

There is considerable opportunity for advancing techniques and technology in minimally invasive thoracic surgery. Hopefully this atlas will stimulate surgeons to identify ways of enhancing patient care. Imagine the future, and work towards that future for the benefit of our patients.

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Part I

Minimally Invasive Surgery for Lung Cancer

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2.1 Overview of Minimally Invasive Surgery in Lung Cancer

Yin-Kai Chao and Hui-Ping Liu

2.1.1 History of Development of Minimal Invasive Thoracic Surgery

The application of thoracoscopy can be traced back to 100 years ago, when Dr. Jacobaeus first reported his experiences in the diagnosis and treatment of pleural effusions by thoracoscope in 1909 [1]. Most patients who needed to undergo thoracoscopy at that time suffered from pulmonary tuberculosis [2]. The development of fibro-optic light transmission, the illumination and the image processing techniques, as well as the refinement of related instruments made video-assisted thoracoscopy more easily and broadly applied after the 1990s [3, 4]. And now video-assisted thoracic surgery (VATS) has become a basic and important technique for a thoracic surgeon.

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2.1.2 Definition of VATS Lobectomy

Frequently, minimal invasive thoracic surgery for lung cancer includes three approaches: (1) VATS, (2) Hybrid VATS and (3) Hand-assisted VATS. VATS usually refers to thoracic surgery that involves insertion of instruments through one (Uniport) or two to four small chest incisions under two-dimensional video images, and hand-assisted VATS mainly refers to thoracic surgery performed by inserting the surgeon's hand into the chest cavity through one of the chest incisions to control the target organs under a two-dimensional video images. A "Hybrid VATS" was defined as using a rib spreading retractor and operates directly through the thoracotomy (usually 8–10 cm in length). In these cases the camera is only used for illumination. Recently VATS can be performed through uniportal or subxiphoid approach for lung lesion.

In 2012, the VATS Lobectomy Consensus Meeting was held in Edinburgh, UK, which marked the 20th anniversary of this procedure. For the first time in history, consensus agreements on several important issues on VATS lobectomy,

including its definition, patient eligibility, surgical standard of care were reached [5]. Since then, the Cancer and Leukemia Group B (CALGB) definition has become the globally accepted state-of-the-art VATS lobectomy technique [6], which comprised (1) no use of rib-spreading, (2) a maximum length of 8 cm for the utility incision (3) individual dissection of pulmonary vessels and bronchus. While a small retractor is only acceptable in selected circumstances, such as conducting complex procedures (e.g. sleeve resection) or delivery of a large specimen.

2.1.3 Minimally Invasive Surgery in Lung Cancer: Current Evidence

In the current era, a prospective, randomized comparison of open versus VATS lobectomy for lung cancer will likely never occur, leaving us to rely on the best available current evidence to draw meaningful clinical conclusions. In the following sections, several important studies to address this issue.

2.1.3.1 Impact on Perioperative Outcome

Perioperative outcomes of VATS versus open lobectomy have been compared in one small prospective trial and five retrospective case control series, and one large systematic review including more than 6,000 patients [7–12]. All of these studies indicate less perioperative morbidity for VATS lobectomy (10–30%) than for open lobectomy (20–50%). The mortality rates are similar between the two procedures. Table 2.1 summarizes the published studies that directly compare VATS versus open lobectomy.

2.1.3.2 Oncological Perspective

Critics of VATS lobectomy suggest that inadequate nodal sampling and the potential for port site contamination by tumor will lead to inferior survival compared to open lobectomy. Important studies comparing nodal clearance and survival between VATS and open lobectomy were discussed in the following sections.

Nodal Clearance: VATS Versus Open

Three prospective trials have investigated the adequacy of nodal sampling during VATS lobectomy. The first is a small trial of 29 patients [13]. What is unique about this study is that following VATS dissection, a thoracotomy was carried out by another surgeon and any remaining mediastinal lymph nodes were removed. Based on weight and number of nodes, the authors concluded that only 2–3% of nodal tissue was “missed” with thoracoscopic techniques. Two other randomized studies have also documented an equal degree of lymph node clearance between VATS and open procedure. In the second trial, the mean number of hilar and mediastinal nodes removed during open lobectomy were 8 and 13 respectively, exactly the same as in the VATS group. Furthermore, an equal number of patients were upstaged to N1 or N2 disease in each group [14]. In the third trial, 39 patients were randomized to undergo either a complete VATS or an “Hybrid-VATS” (in which the thoracotomy was 10 cm in length and rib-spreading was used) [15]. In the complete VATS group 32 nodes were submitted for pathologic review, compared to 29 in the control group ($p=0.12$).

Table 2.1 Studies comparing perioperative outcome between VATS and open procedure

Author/year	Study design	Procedure	N	Morbidity rate (%)	Mortality rate	LOS (days)
Kirby, 1995	Prospective	VATS	25	24	0 %	7.1
		Open	30	53	0 %	8.3
Whitson, 2008	Systematic review	VATS	3114	16.4	NA	8.3
		Open	3256	31.2	NA	13.3
Handy, 2009	Retrospective	VATS	49	10	4.1 %	5.2
		Open	192	22.5	2.6 %	6.6
Villamizar, 2009	Retrospective	VATS	284	31	3 %	4
		Open	284	51	5 %	5
Flores, 2009	Retrospective	VATS	398	23	0.3 %	5
		Open	343	33	0.3 %	7
Stephens, 2014	Retrospective ^a	VATS	307	37	<1 %	4
		Open	307	19	2 %	6
Nwogu, 2015	Retrospective ^a	VATS	175	14.9	1.7 %	5.4
		Open	175	25.1	1.7 %	8

^aPropensity matched analysis; LOS Length of Stay, VATS Video-assisted thoracoscopic surgery

Long Term Survival

The first and only randomized trial to report survival data was published in 2000 from Japan [14]. In this trial 100 patients with clinical stage IA lung cancer were randomized to either a VATS or open lobectomy. With the median follow-up of 4.9 years, 6% of patients in both group developed a local recurrence. The 5-year survival was 85% in the open group and 90% in the VATS group ($p=0.91$).

Several retrospective reports support the aforementioned findings. In these separate reports, the 5-year survival for VATS lobectomy is near 80%, similar to that for open

lobectomy (75–82%). In a 2008 systematic review, Whitson and colleagues provided an analysis of 39 studies comparing VATS with open lobectomy [16]. In this study, patients with VATS lobectomy had similar survival when compared with those who underwent open resection. At 4 years, patients who underwent VATS lobectomy even had improved survival versus patients with open lobectomy (88.4% vs 71%; $p=0.003$), suggesting that VATS lobectomy is at least oncologically equivalent to open lobectomy. Table 2.2 summarized the major findings from the aforementioned studies.

Table 2.2 Studies comparing survival of VATS versus open lobectomy for early-stage non-small cell lung cancer

Author/year	Study design	Procedure	N	5 years-survival (%)	P value
Sugi, 2000	Prospective randomized	VATS	48	90	N.S
		Open	52	85	
Yang, 2009	Retrospective	VATS	43	79	N.S
		Open	98	82	
Flores, 2009	Retrospective	VATS	398	79	N.S
		Open	343	75	
Whitson, 2008	Systematic review	VATS	3114	80	N.S
		Open	3256	65.6	
Stephens, 2014	Retrospective	VATS	307	78	N.S
		Open	307	73	

VATS Video-assisted thoracoscopic surgery, N.S Not significant

2.1.4 Summary

To the best of my knowledge, there has been no publication thus far demonstrating inferior outcomes of VATS lobectomy compared to open thoracotomy. Without a doubt, VATS has completely revolutionized modern thoracic surgery and significantly improved patient outcomes over the last two decades.

2.2 Physiologic Evaluation of Candidates for Lung Cancer Resection

Sean C. Wightman and Mark K. Ferguson

2.2.1 Introduction

One goal of perioperative surgical care is to minimize postoperative complications. This process includes preoperative decision making, intraoperative judgment and technical considerations, and postoperative care. Knowing which clinical factors are associated with complications permits physicians to assess which candidates are appropriate for major surgery. Furthermore, it allows patients to both understand the risk of procedures and make an informed decision on agreeing to a planned operation versus pursuing an alternative treatment modality. The development and standardization of algorithms for evaluation of risk has made risk estimation more uniform. There is increasing understanding of how to mitigate risk through appropriate preoperative interventions or through altering standard surgical approaches to minimize risk while maintaining the original treatment objectives. Knowing potential risks for a given patient allows the treatment teams to allocate intraoperative and postoperative resources to identify and treat complications more efficiently, thus increasing resiliency.

2.2.2 Background

After pulmonary resection, there are substantial changes in the physiology of the cardiopulmonary system. Lung resection decreases postoperative pulmonary function as measured by forced expiratory volume in the first second (FEV1) and the shuttle walk test [17]. While FEV1 decreases maximally the first few days postoperatively, it improves to only 75 % of predicted values at 1 month and 85 % at 3 and 6 months [17]. Similarly, the shuttle walk test is 70 % of its preoperative value when assessed at 1 month and improves to 84 % of preoperative values when reassessed at 6 months [17]. The immediate postoperative decrease is related to reduced respiratory mobility of the ribs and diaphragm after a thoracic operation, predominantly due to pain. This subsequently leads to decreased pulmonary expansion, alveolar collapse, and subsequent atelectasis [18].

The changes in pulmonary spirometry are associated with the degree of pulmonary resection performed. For patients undergoing a segmentectomy, FEV1 and forced vital capacity (FVC) are relatively preserved [19]. After lobectomy, and once recovered from the initial postoperative period, spirometry values for FVC, FEV1 and total lung capacity (TLC) are reduced by 7–10 % [20]. For those patients undergoing pneumonectomy, FVC, FEV1, and TLC are typically decreased by 30–35 % [20]. In patients undergoing wedge or lobectomy, no postoperative changes in cardiac hemodynamics are observed [21]. Pneumonectomy is associated with elevated right ventricular volumes at end-systole and end-diastole, while right ventricular ejection fraction is decreased by 10 % [21]. The decreased ejection fraction after pneumonectomy is likely due to the increased afterload, while the increased right heart volume compensates to improve ejection based on the Frank-Starling Curve. These changes underline the importance of preoperative evaluation to determine which patients are likely to tolerate surgery without increased cardiopulmonary risk.

General anesthesia adversely affects pulmonary function by relaxing respiratory muscles leading to a reduction in functional residual lung volume. This in turn collapses bronchioles leading to atelectasis [22]. These changes contribute to postoperative hypoxemia and can last many days after surgery. A thoracotomy incision reduces chest wall compliance leading to decreased total lung volume due to limited expansion. Appropriate pain control and minimally invasive procedures are thought to limit this physiologic restriction.

Induction chemotherapy reduces diffusion capacity of the lung for carbon monoxide (DLCO) in 15 % of patients [23]. This reduction does not typically affect clinical symptoms and only 2 % of patients are ineligible to proceed with surgery based on the change in DLCO. For heavy smokers, the reduction after induction chemotherapy is greater. The relation of induction chemotherapy to increased post-operative complications is controversial [23, 24]. Due to pulmonary changes after induction chemotherapy, an updated assessment of the patient's lung function should be obtained [25].

Lung resection is associated with the development of postoperative complications including pulmonary, cardiovascular, infectious, surgical, and others (Table 2.3). Some postoperative complications are associated with specific preoperative patient characteristics, permitting risk stratification. The two most common categories of complications, pulmonary and cardiovascular, are listed in Table 2.4 with their preoperative predictive variables. Aside from demographics, significant predictive ability is found in cardiac and pulmonary function. For this reason, specific evaluation of these parameters should be performed in all patients undergoing major lung resection regardless of the surgical approach [26].

Table 2.3 Classification of postoperative complications after lung resection

Category	Components
Pulmonary	Prolong postoperative intubation
	Reintubation for respiratory insufficiency
	Prolonged postoperative air leak
	Atelectasis requiring bronchoscopy
	Pleural effusion requiring drainage
	Pneumonia
	Adult respiratory distress syndrome
	Pneumothorax required intervention
Cardiovascular	Arrhythmia requiring intervention
	Myocardial infarction
	Pulmonary embolism
	Use of inotropic agents
	Deep venous thrombosis requiring therapy
Cerebrovascular	Cerebrovascular accident
	Transient ischemic attack
	Delirium
Surgical	Bronchopleural fistula
	Chylothorax
	Recurrent nerve injury
	Bleeding requiring reoperation
	Other reoperation
Infectious	Empyema
	Wound infection
	Sepsis
Other	Acute renal insufficiency
	Urinary retention
	Postoperative transfusion

Table 2.4 Preoperative parameters associated with complication categories

Complication category	Preoperative parameters
Pulmonary	FEV1, FEV1%
	DLCO%
	Stair climb, shuttle walk, 6 min walk
	Peak VO ₂
	Age
	Smoking status
	Induction therapy
	Body mass index (BMI)
Cardiovascular	FEV1, FEV1%
	Age
	Diabetes mellitus
	Coronary artery disease
	Renal insufficiency
	Cerebrovascular disease

2.2.3 Pulmonary Assessment

Physiologic assessment of lung function includes measurement of both ventilatory capacity and gas exchange capacity. Each of these is an independent predictor of postoperative complications, especially cardiopulmonary complications [27–32]. The most useful spirometric parameters are the forced expiratory volume during the first second expressed as a percent of predicted (FEV1%) and the predicted postoperative value for this parameter estimated based on the amount of lung to be resected (ppoFEV1%). Gas exchange capacity is assessed by measurement of the diffusing capacity of the lung for carbon monoxide (DLCO), which is an estimate of pulmonary capillary surface area or pulmonary capillary blood volume. The value is often corrected for hemoglobin, which provides a more accurate assessment of gas exchange ability. In contrast, corrections for lung volume are not typically performed, as the basis for such corrections are not physiologically sound. DLCO is usually expressed as a percent of predicted (DLCO%) or as an estimate of expected postoperative function (ppoDLCO%).

Predicted postoperative values are more accurate than preoperative values in estimating the risk of postoperative complications as well as long-term survival [33, 34]. Preoperative alterations in FEV1% may be related to underlying lung disease, neuromuscular disorders, prior lung surgery, extreme obesity, and other conditions (Table 2.5). Alterations in DLCO% may be related to serum hemoglobin level, primary lung disease, disorders of the pulmonary vasculature, and cardiac insufficiency. Predicted postoperative values of FEV1% and DLCO% usually can be

accurately estimated using the functional segment counting technique [35].

$$\text{Postoperative value} = \text{Preoperative value} \times (\text{Postoperative segments} / \text{Functional preoperative segments})$$

The accuracy of such estimates can be affected by the location of the resected lobe (upper versus lower) and the presence of heterogeneous distribution of emphysematous changes [36]. In patients with heterogeneous lung disease, prior lung resection, or major airway obstruction, more accurate estimates are obtained using quantitative ventilation/perfusion scans or quantitative computed tomography [37–39].

Exercising testing is also a useful method for evaluating patients' postoperative risk after lung resection, as it assesses the interactive function of the respiratory and cardiovascular systems [40–45]. Although the routine use of exercising testing provides slightly more accurate risks of postoperative complications, its use is usually reserved for patients who are identified as being at increased risk based on pulmonary function testing. Selective use decreases the costs and duration of the preoperative evaluation. Exercise testing can be performed using low technology methods (stair climb, 6 min walk test, shuttle test) or using high technology testing, usually measurement of peak oxygen consumption during maximal exercise (peak VO_2), which is typically performed during cycle ergometry. Exercise testing may not be possible in some patients because of lower extremity weakness, cardiovascular disease, or other physical limitations, and is often precluded because of the lack of availability the required equipment and expertise to use it.

Table 2.5 Causes of abnormal lung function tests

Parameter tested	Cause of abnormal result	Etiology
FEV1%	Chronic obstructive pulmonary disease	Decreased air flow
	Asthma	Decreased air flow
	Interstitial lung disease	Loss of alveoli
	Major airway obstruction	Decrease air flow
	Chest wall disorders	Loss of lung volume
	Severe obesity	Impaired diaphragm excursion
	Prior lung resection	Loss of lung volume
	Phrenic nerve dysfunction	Impaired diaphragm excursion
	Dysfunction of respiratory muscles	Impaired air flow
DLCO%	Anemia	Low oxygen carrying capacity
	Polycythemia	Increased oxygen carrying capacity
	Emphysema	Loss of pulmonary capillary surface area
	Obstructive lung disease	Gas trapping
	Interstitial lung disease	Increased alveolar wall thickness
	Pulmonary edema	Increased alveolar wall thickness
	Congestive heart failure	Increased alveolar wall thickness
	Pulmonary hypertension	Increased vascular wall thickness
	Low cardiac output	Low blood flow limiting gas delivery
	Restrictive lung disease	Loss of pulmonary capillary surface area
	Pulmonary embolism	Decreased pulmonary blood flow

2.2.4 Cardiac Assessment

The American College of Cardiology and the American Heart Association (ACC/AHA) guidelines stratify procedures by their level of risk and in turn identify patients who have clinical risk factors placing the patient at increased cardiac risk during non-cardiac procedures [46]. According to the ACC/AHA, major lung resection qualifies as having intermediate risk (a cardiac risk of 1–5 %). If patients are undergoing an elective lung resection, they should be evaluated and screened for severe or increasing angina, recent myocardial infarction (MI), decompensated heart failure, severe arrhythmias, or severe valvular disease. If any of these symptoms or history is present, the patients should have an appropriate cardiac work-up and management prior to an elective lung resection. If no history is present, patients are then evaluated for typical physical activity levels based on metabolic equivalents (METs). One MET is expended during effectively taking care of one's self daily by dressing and feeding. Four METs are expended doing light work around the house or climbing a flight of stairs. If a patient meets the 4 MET threshold, the likelihood of important cardiovascular disease in the absence of symptoms is low and the operation can be planned. If less than 4 METs are typically expended or if METs are unknown, clinical risk factors of ischemic heart disease, heart failure, stroke, diabetes, and renal insufficiency are evaluated. If none is present, proceeding with the operation is appropriate. If one or more risk factors are present, a non-invasive stress test should be considered prior to scheduling an operation.

2.2.5 Perioperative Risk

2.2.5.1 Cardiac Risk Scoring Systems

The European Respiratory Society (ERS), the European Society of Thoracic Surgery (ESTS), and the American College of Chest Physicians (ACCP) recommend cardiac evaluation prior to lung assessment as recommended by the ACC/AHA. An index was developed to identify patients at high risk for complications in patients undergoing major noncardiac surgery [47]. The Revised Cardiac Risk Index (RCRI) identifies patients at increased risk for cardiac death, myocardial infarction, and cardiac arrest. The index is based on preoperative risk factors including a history of ischemic heart disease, congestive heart failure, cerebrovascular disease (stroke or TIA), the presence of diabetes mellitus requiring insulin therapy, the presence of chronic kidney disease with a creatinine >2 mg/dL, and planned high risk surgery including intrathoracic surgery [47]. Patients with 0, 1, 2, or more risk factors are divided into classes I, II, III, or IV respectively. This correlates with progressively increasing risks of major cardiac complications.

Recalibration of the RCRI to a system for risk estimation specific to lung resection was recently performed, resulting in the Thoracic RCRI (ThRCRI). The ThRCRI is a four-class risk score based on weighted values for serum creatinine, coronary artery disease, cerebrovascular disease, and extent of lung resection. Classes A, B, C, and D are assigned from the cumulative risk score, which correlates well with an increasing incidence of major cardiovascular complications [48–51]. This risk score also is predictive of the long-term risk of death in patients undergoing resection for lung cancer [52].

2.2.5.2 Cardiopulmonary Risk Algorithms

Algorithms for risk assessment and preoperative pulmonary evaluation were developed by both the ERS/ESTS and the ACCP [25, 45, 53]. Both recommend cardiac risk assessment for all patients; those found to be at increased risk should undergo a preoperative cardiology evaluation. The ACCP recommends pulmonary assessment of FEV1 and diffusion capacity for carbon monoxide (DLCO) with calculation of the predicted post-operative values (Fig. 2.1). If both the ppoFEV1% and ppoDLCO% are >60 %, no further testing is needed. If either the ppoFEV1% or ppoDLCO% is <60 %, but both are >30 %, a stair climb or shuttle walk test should be performed. If either of the predicted post-operative values is <30 %, a formal cardiopulmonary exercise test with maximal oxygen consumption assessment (peak VO_2) is recommended. Those patients with <25 shuttles or <22 m climbed in low-tech testing should proceed to high-tech cardiopulmonary exercise testing with measurement of peak VO_2 . Patients with a peak VO_2 >15 mL/kg/min do not have importantly increased risk. Those with a peak VO_2 10–15 mL/kg/min are at increased risk, and a detailed discussion of the relative risks and benefits associated with surgery as well as alternative treatments should take place. Those patients found to have a peak VO_2 of <10 mL/kg/min are at substantially increased risk and non-operative treatment should be seriously considered.

The ERS/ESTS guidelines also rely on FEV1, DLCO, and measurement of peak VO_2 [25, 45]. The ERS/ESTS guideline starts with assessment of a patient's of FEV1 and DLCO (Fig. 2.2). If the values are >80 % of predicted, surgery can proceed without further testing. If one of the values are <80 % of predicted, then a measurement of peak VO_2 is obtained. If this is >20 mL/kg/min, then the recommendation is for surgery. If it is <10 mL/kg/min, then non-operative management is recommended. If it is 10–20 mL/kg/min, then ppoFEV1 and ppoDLCO are reviewed. If both the ppoFEV1% and ppoDLCO% are >30 %, then it is reasonable to proceed with surgery. If one or both are <30 %, then surgery is only performed if the predicted post-operative peak VO_2 is >10 mL/kg/min.

Fig. 2.1 The American College of Chest Physicians algorithm for preoperative cardiopulmonary function assessment [37]

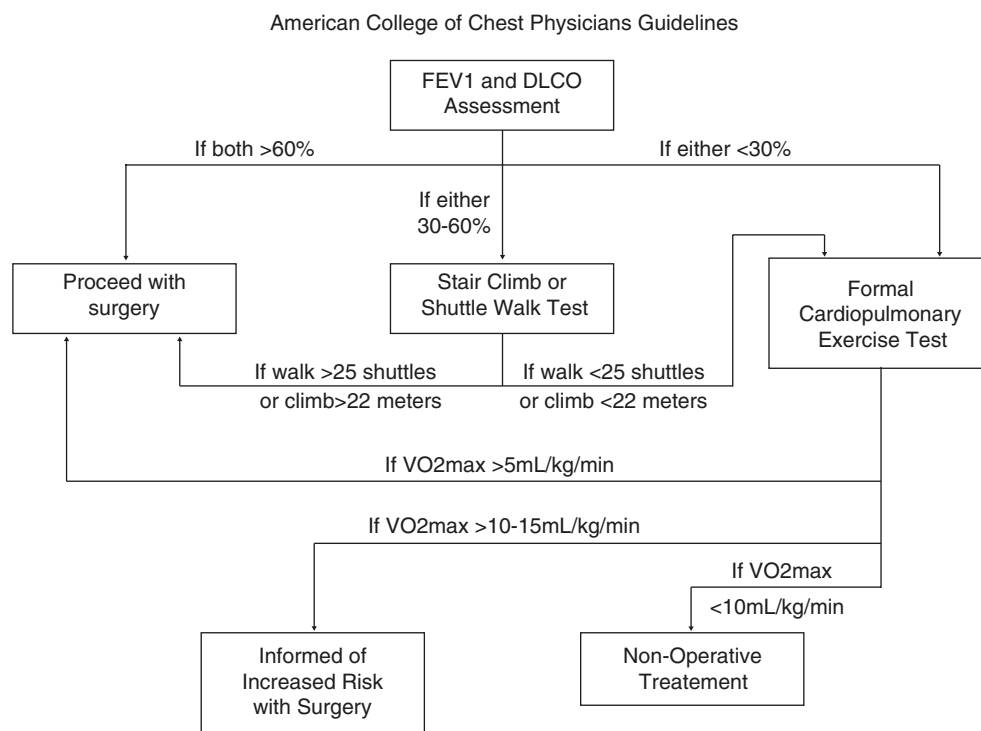
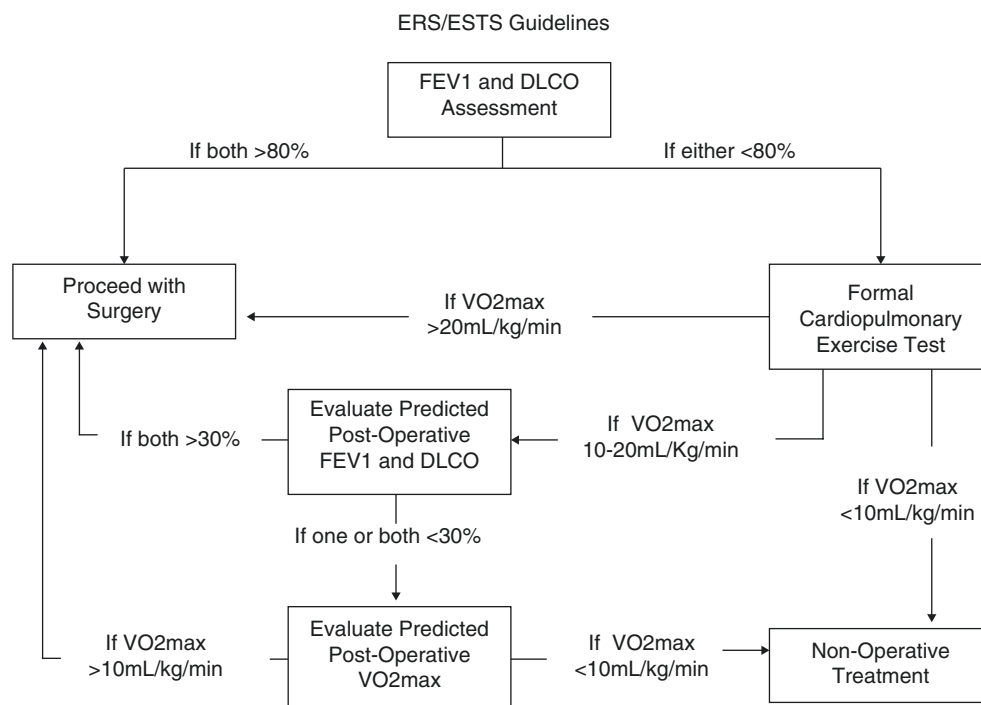


Fig. 2.2 The European Respiratory Society and the European Society of Thoracic Surgery algorithm for preoperative cardiopulmonary function assessment [29]



The main differences between the AACP and ERS/ESTS guidelines are that the ERS/ESTS is quicker to obtain the measurement of peak VO_2 and doesn't utilize a stair climb or shuttle walk test. The AACP also recommends initially using the ppoFEV1% and ppoDLCO% while the ESTS guidelines utilize this later in the algorithm.

Utilization of these guidelines has been variable and a review of the compliance to the ERS/ESTS guidelines demonstrated that nearly 20% of cases were non-compliant due to the omission of the exercise test [54].

2.2.6 Preoperative Risk Reduction

2.2.6.1 Smoking

A Society of Thoracic Surgeons database study evaluated the impact of patient's smoking on perioperative risk [55]. Many patients undergoing lung resection are either current or past smokers. Perioperative mortality decreased in relation to the interval of smoking cessation. Major pulmonary complications were more frequent in current or past smokers [55]. Over time, smoking cessation mitigates these risks but no optimal time interval was identified.

2.2.6.2 Preoperative Physical Rehabilitation

Preoperative exercise therapy in lung cancer patients undergoing resection demonstrates mixed results [56]. Some studies demonstrate decreased hospital length of stay and pulmonary complications while others demonstrate no difference between the groups. Using the patient's mean distance walked per day to calculate an estimated peak VO_2 , also including age and DLCO%, is more predictive of postoperative cardiorespiratory complications than the peak VO_2 measured during a standard exercise test [57]. Due to a narrow preoperative window after cancer diagnosis, it is difficult to determine if an intense program will strengthen or simply fatigue those with poor preoperative conditioning. Furthermore, it is difficult to know if frequent outpatient sessions are feasible due to patient commitment, and inpatient rehabilitation is often cost prohibitive. Because of

the limited and conflicting data surrounding preoperative rehabilitation, future research is needed in the area.

2.2.6.3 Frailty

Frailty is a clinical state with decreased physical function and low physiologic reserves [58]. It is the frail patient's low organ system reserves, due to diseases, decreases activity, inadequate nutrition, and physiologic changes that are attributed to poor clinical outcomes. These poor reserves make physical compensation difficult in times of acute stress; like undergoing pulmonary resection. Assessment of frailty ranges from in-person encounters, usually in the form of an office visit, to a developed frailty index involving functional, medical, and cognitive health. More than 50% of potential lung resection candidates are pre-frail or frail. Frailty is associated with adverse perioperative outcomes after lung resection; as an aging-frailty index increases, both morbidity and mortality increased incrementally [59].

There is increasing interest in identifying methods of mitigating frailty preoperatively, which theoretically may reduce perioperative risk. These include nutritional, pharmacologic, and physical interventions such as strength and/or endurance training. Early results demonstrate that physical interventions provide the most consistent positive results, and that results can be achieved in a time period suitable for planning lung cancer surgery [60].

Conclusions

Utilization of algorithms guide risk assessment and help quantify risk probability for an individual patient in the perioperative period. Research continues to change the assessment protocols of patients and their estimated risk. Algorithms not only aide surgeons in selecting appropriate patients for operations, but also allow patients to make informed decisions on risks and benefits prior to lung resection or alternate therapy. Future research is still needed in areas of patient optimization prior to surgery after cancer diagnosis as well as continued improvement in preoperative risk stratification for postoperative complications.

2.3 Staging and Selection of Patients for Minimally Invasive Lung Cancer Resection

Christopher W. Seder and Michael J. Liptay

2.3.1 Introduction

Lung cancer remains the leading cause of death from malignancy worldwide [61]. Accurate staging of non-small cell lung cancer (NSCLC) is essential for prognostication and determination of the optimal treatment strategy. Proper risk stratification and patient selection is equally important; every patient must be assessed for both operability and resectability. The terms operability and resectability are often used interchangeably, however they represent different concepts [62]. Operability refers to a patient's cardiopulmonary fitness and physiologic ability to undergo the required surgery. Alternatively, resectability describes the tumor characteristics and how that relates to the ability to achieve a curative operation. A given patient being considered for pulmonary resection can have any combination of operability and resectability.

All patients with lung cancer should be evaluated, staged, and treated in a multidisciplinary fashion, which includes input from thoracic surgeons, medical and radiation oncologists, pathologists, radiologists, and palliative care specialists [63]. The thoracic surgeon is an integral part of this process and is primarily responsible for the selection of patients for lung resection and technique in which it is performed. With rapid technologic advances instrumentation and increasing experience with advanced endoscopy and video-assisted thoracoscopic surgery (VATS), the range of operations able to be performed in a minimally invasive fashion is growing. There is emerging evidence that VATS may actually expand the patient population able to benefit from anatomic pulmonary resection [64–68].

2.3.2 Staging

Accurate staging is essential in the evaluation, prognostication, and treatment of patients with NSCLC. The Table 2.6 details the 7th edition of the TNM classification for non-small cell lung cancer [69]. In the absence of systemic metastases, the status of a patient's mediastinal lymph nodes directs the overall treatment strategy, since those with N2 metastasis are often treated with induction therapy prior to surgical consideration and those with N3 disease are not offered surgical intervention.

2.3.2.1 Radiographic Staging

While modern computed tomography (CT) scanners provide excellent anatomic detail relative to tumor location and surrounding structures, its ability to identify mediastinal nodal metastases in patients with NSCLC is marginal, with a sensitivity and specificity of 55 % and 81 %, respectively [70]. Accordingly, the American College of Chest Physicians (ACCP) clinical staging guidelines recommended that all patients with NSCLC and no suspicious extrathoracic abnormalities on chest CT undergo positron emission tomography (PET) imaging to evaluate for metastases, with the exception of peripheral clinical stage IA tumors and ground glass opacities [70]. 18F-flouro-2-deoxy-D-glucose (FDG) is injected intravenously and its metabolite accumulates in cells with relatively high metabolic activity, such as malignant or inflammatory cells. This provides a qualitative estimate of cellular activity and a standardized uptake value (SUV) can be calculated. Although there is a high degree of variability between scanners, centers, and interpreting radiologists, an SUV less than 2.5 is generally considered normal.

Multiple early studies, including the American College of Surgeons Oncology Group (ACOSOG) Z0050 and PET in Lung Cancer Staging (PLUS) trial, demonstrated the ability of PET and integrated PET-CT scan to reduce the number of “unnecessary thoracotomies” compared to conventional imaging [71–73]. These studies demonstrated a number needed to scan of only five patients to avoid 1 non-therapeutic thoracotomy, defined as thoracotomy for benign disease or pathologic N2 disease, exploratory thoracotomy, or that resulting in recurrence or death within 1 year. Although the use of PET-CT has been shown to accurately upstage patients with N2 disease not recognized by conventional imaging, the risk of identifying false positive mediastinal activity and potentially denying patients curative resection also exists. A subgroup analysis of the Early Lung Positron Emission Tomography (ELPET) trial [74] examining 149 patients who underwent both PET-CT and mediastinoscopy with or without thoracotomy with lymph node sampling demonstrated positive and negative predictive values of 64 % and 95 %, respectively for PET-CT scans [75]. Eight patients in this trial had a positive PET-CT, but no evidence of pathologic nodal involvement. The modest positive predictive value of current PET-CT imaging reinforces the importance of pathologic confirmation of mediastinal lymph node involvement. On the contrary, the high negative predictive value of PET-CT, demonstrated across multiple studies, suggests that in patients with clinically T1N0 NSCLC, preoperative pathologic assessment can reasonably be omitted [76]. This is supported by the National Comprehensive Cancer Network (NCCN) clinical practice guidelines, which recommend preoperative pathologic staging in all cases except clinical stage IA NSCLC [77].

Table 2.6 TNM classification for non-small cell lung cancer (7th Edition) [69]

Primary tumor (T)			
Tx		Primary tumor cannot be assessed, or the tumor is proven by the presence of malignant cells in sputum or bronchial washing but is 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, no bronchoscopic evidence of invasion more proximal than the lobar bronchus (not in the main bronchus); superficial spreading of tumor in the central airways (confined to the bronchial wall)	
T1a		Tumor ≤2 cm in the greatest dimension	
T1b		Tumor >2 cm but ≤3 cm in the greatest dimension	
T2		Tumor >3 cm but ≤7 cm or tumor with any of the following: Invades visceral pleura Involves the main bronchus ≥2 cm distal to the carina Associated with atelectasis/obstructive pneumonitis extending to hilar region but not involving the entire lung	
T2a		Tumor >3 cm but ≤5 cm in the greatest dimension	
T2b		Tumor >5 cm but ≤7 cm in the greatest dimension	
T3		Tumor >7 cm or one that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, or parietal pericardium; Or tumor in the main bronchus <2 cm distal to the carina but without involvement of the carina Or associated atelectasis/obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe	
T4		Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina Or separate tumor nodule(s) in a different ipsilateral lobe	
Regional lymph nodes (N)			
Nx		Regional lymph nodes cannot be assessed	
N0		No regional node metastasis	
N1		Metastasis in ipsilateralperibronchial and/or ipsilateralhilar lymph nodes and intrapulmonary nodes, including involvement by direct extension	
N2		Metastasis in the ipsilateralmediastinal and/or subcarinal lymph node(s)	
N3		Metastasis in the contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes	
Distant metastasis (M)			
Mx		Distant metastasis cannot be assessed	
M0		No distant metastasis	
M1		Distant metastasis	
M1a		Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion	
M1b		Distant metastasis	
Stage	T	N	M
IA	T1a	N0	M0
	T1b	N0	M0
IB	T2a	N0	M0
IIA	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
	T2b	N0	M0
IIB	T2b	N1	M0
	T3	N0	M0

(continued)