Evaluation of Risk for Thoracic Surgery

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KEYWORDS

• Functional staging • Operative risk • Shared decision making

KEY POINTS

- There should be an attempt, whatever the pathologic status, to discuss all thoracic surgical patients in a multidisciplinary setting.
- A meticulous preoperative physiologic assessment allows the surgeon and wider team to identify those at highest risk.
- The functional assessment can help the surgeon to identify areas for optimization to potentially reduce risk.
- This information should be shared clearly and openly with the patient in a "shared decision making" process.

INTRODUCTION

The surgical decision-making process has undoubtedly changed over the last couple of decades. Traditionally the surgeon, often practicing in relative isolation, would act on intuition, which would have reflected training and previous experience. In the current climate of surgeon outcome reporting, decision making in surgery often reflects not only the surgeon's thoughts but the wider multidisciplinary team and, perhaps more importantly, the patient's views. The decision-making process can therefore become much more complicated than the intended surgical procedure.

There is no doubt that surgery has always been associated with risk. The prediction and assessment of risk is more recent and continues to develop. Historically, when the patient was not considered "fit enough" for a surgical procedure, they may have been referred elsewhere for "conservative" management, which often represented a large and diverse group of nonsurgical treatment strategies. Each surgical procedure has its own recognized profile of risks and complications. It must also be remembered that risk, for both surgeon and patient, is relative. For instance, the thoracic surgeon may quote an operative mortality of 6% to a patient likely to need pneumonectomy

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for non–small cell lung cancer (NSCLC): this will mostly be deemed acceptable. However, what will both surgeon and patient think if a similar rate was suggested for intervention for a middle-aged patient with recurrent pneumothorax?

Although there is no doubt that surgeons have developed risk-prediction models to inform and develop their own practice, it may also be representative of the increasing role of clinical governance in health systems around the world. It is now reasonably common for surgeons to have to defend their own decision making including the major decision to offer a patient surgery. The traditional sense of using one's intuition is difficult to defend when asked if a thorough risk assessment was undertaken to allow for clear objectivity.

Some surgical specialties have little influence over what arrives in their care. However, it is important to remember that in many aspects of thoracic surgical practice, the patient will have been referred after extensive discussion in a multidisciplinary team (MDT) setting. In the United Kingdom it is mandatory that a patient with cancer is discussed in this setting. This well-described approach allows for specialists with different areas of expertise to input their views on a management plan and allow formation of the best treatment plan for a patient. In respect of solid cancers, surgical resection still generally remains the best chance of a relative cure and thus, whatever the potential risk, should be discussed extensively. The traditional view that the decision to not offer someone surgery remains more difficult than the one to proceed with surgery remains relevant.

ESTIMATION OF CARDIOVASCULAR RISK

A major portion of most thoracic surgeons' practice will involve surgical resections for early-stage lung cancer. This patient group will frequently have a significant cigarette smoking history that is itself associated with an increased risk of underlying cardiovascular comorbidity. There is evidence to show that the risk of major cardiac complications including ventricular arrhythmias, pulmonary edema, and cardiac arrest after major anatomic lung resection is approximately 3%.[1,2] There is published guidance that can be consulted by the thoracic surgeon regarding cardiac risk evaluation in patients being considered for lung cancer resection surgery. The 2 major guidelines from the American College of Chest Physicians and the European Respiratory Society/European Society Thoracic Surgeons (ERS/ESTS) joint task force are very similar.[3,4] They are closely based on the American College of Cardiology/American Heart Association (ACC/AHA) 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery.[5]

Both guidelines recommend the use of a scoring system to estimate the risk of major perioperative cardiac events. In 1999, Lee and colleagues[1] developed the Revised Cardiac Risk Index (RCRI) for patients undergoing major nonurgent surgery. The RCRI, which is a 6-factor cardiac risk index, includes history of coronary artery disease, cerebrovascular disease, insulin-dependent diabetes, congestive heart failure, serum creatinine level greater than 2 mg/dL, and high-risk surgery. All factors are equally weighted.

Brunelli and colleagues[4] refined this and recalibrated the RCRI in a large population of candidates being submitted to major anatomic lung resection, producing the thoracic (Th)RCRI. The aim was to make it more specific to thoracic surgeons and their patients. A simplified weighted score composed of 4 out of the original 6 factors has been shown to be reliably associated with major cardiac mortality. The factors have different weights: history of coronary artery disease, 1.5 points; cerebrovascular disease, 1.5 points; serum creatinine level greater than 2 mg/dL, 1 point; and

pneumonectomy, 1.5 points. The recent American College of Clinical Pharmacy (ACCP) guidelines state that a ThRCRI with a score of 1.5 or higher is one of the reasons to refer for a cardiology opinion. At this stage patients should be investigated as per ACC/AHA guidance, which recommends noninvasive investigation including an echocardiogram.[5] The ThRCRI has been clearly validated by numerous studies.[6,7]

PULMONARY FUNCTION

Full spirometry and diffusing capacity provide important information for the thoracic surgeon. The forced expiratory volume at first second (FEV_1) and predicted postoperative (ppo)FEV_1 have been extensively used to stratify risk but should no longer be considered in isolation. There is a significant number of studies demonstrating that a reduced FEV_1 or ppoFEV_1 is associated with increased morbidity and mortality in patients proceeding with lung resection. Licker and colleagues[8] showed that an FEV_1 of less than 60% is an independent risk factor for morality and respiratory morbidity. However, several studies have shown that consideration of an FEV_1 in isolation is not a good indicator of postoperative outcome.[9,10] This is particularly apparent in patients with chronic obstructive pulmonary disease (COPD), which obviously represents a significant portion of any thoracic surgeon's practice.

Ferguson and colleagues[11] first demonstrated the importance of the carbon monoxide lung diffusion capacity (DLCO) as an independent assessment of surgical risk. This study showed that an impaired DLCO was related to the development of postoperative respiratory complications and death. When the DLCO decreased to less than 60%, the complication rate was 50% with a mortality of 20%. Berry and colleagues[12] confirmed similar findings in 2010. Studies have shown that a substantial proportion of patients with normal FEV_1 have a reduced DLCO, and even for non-COPD patients a low DLCO or ppoDLCO is associated with increased risk of pulmonary complications and mortality.[13,14] This evidence supports the concept that DLCO should be measured in all candidates to lung resection regardless of their baseline FEV_1.

EXERCISE TESTS

Exercise testing remains a critical component of a thorough preoperative functional assessment. It has a role in assessing the entire oxygen transport system with a view to the detection of deficit that may manifest as perioperative morbidity or mortality. There is now a wide and informative body of literature analyzing exercise assessment in patients being considered for lung cancer resection surgery. Published guidelines include those from the ERS/ESTS, ACCP, and the British Thoracic Society/Society for Cardiothoracic Surgeons.[3,4,15]

The general consensus is that the cardiopulmonary exercise test (CPET) is the gold standard for functional assessment and risk stratification in patients proceeding to lung resection. However, there is literature showing that the CPET is not always readily accessible.[16] As such, other forms of exercise testing are regularly used including the 6-minute walk test, stair-climbing test, and the shuttle test.

Low-technology testing is used to describe exercise testing not including CPET. The 6-minute walk test has been used since the 1960s and has been extensively studied. Most recently, Marjanski and colleagues[17] demonstrated that patients walking less than 500 m had both increased postoperative morbidity and length of hospital stay. Current clinical guidance recommends that it should not be used in selecting patients for operation.

Conversely, current guidelines do support the use of the shuttle walk test. One of the more recent studies examining this from Fennelly and colleagues[18] showed that

patients walking further than 400 m experienced a very low rate of perioperative complications. As such, guidelines suggest that patients who can complete 400 m on the shuttle walk test are fit to undergo surgical resection.[3]

Stair climbing has often been seen practically as an exercise test that the surgeon can directly engage with during the patient's preoperative review. It is well validated as an exercise test. Brunelli and colleagues[19] measured oxygen consumption during stair climbing, whereby 98% of patients climbing more than 22 m had a positive predictive value of 86% to predict a V_{O_2} peak of 15 mL/kg/min. As such, current clinical guidance suggests that patients able to ascend greater than 22 m can proceed with lung resection.[3]

CPET provides a detailed and broad physiologic evaluation of the patient that allows for measurement of the maximal oxygen consumption ($V_{O_{2max}}$). The $V_{O_{2max}}$ was the first ergometric measurement found to be related to postoperative morbidity and mortality. In 1995, Bolliger and colleagues[20] showed that patients with a $V_{O_{2max}}$ of less than 60% of predicted had postoperative morbidity approaching 90%. Brunelli and colleagues[21] demonstrated that the $V_{O_{2max}}$ is the best predictor of respiratory morbidity. This study showed that a $V_{O_{2max}}$ of less than 12 mL/kg/min had a mortality rate of 13%, whereas patients with a $V_{O_{2max}}$ of greater than 20 mL/kg/min had no mortality. As such, patients with a $V_{O_{2max}}$ greater than 20 mL/kg/min can safely proceed with surgical resection including pneumonectomy and can be classed as low risk. Conversely a $V_{O_{2max}}$ less than 10 mL/kg/min is now generally regarded as a contraindication to lung resection: case series have shown that patients with $V_{O_{2max}}$ below this threshold have a very high risk of postoperative mortality.[3]

The pulmonary function and exercise test evaluations have been integrated in an algorithm to guide fitness evaluation (**Fig. 1**[3]).

A $V_{O_{2max}}$ between 10 and 15 mL/kg/min is associated with an increased risk of postoperative mortality. For patients who fall within this range, the minute ventilation to carbon dioxide output (V_E/V_{CO_2}) slope can be helpful because it has been shown to be an independent predictor of mortality. Brunelli and colleagues[22] demonstrated that patients with a $V_E/V_{CO_2} \geq 35$ were 3 times as likely to develop postoperative respiratory morbidity. Shafiek and colleagues[23] confirmed this value and verified V_E/V_{CO_2} as a predictor of increased morbidity and mortality.

V_E/V_{CO_2} slope has not yet been included in guidelines for estimation of fitness before surgery. However, Salati and Brunelli[24] have proposed an algorithm incorporating this parameter to refine the moderate risk group (**Fig. 2**).

Low-technology testing can be safely and efficiently used as a first-line screening exercise test in candidates for lung resection. If the patient is not able to meet the thresholds set out in current guidance, they should ideally be referred for formal CPET.

IMPLICATIONS OF RISK ASSESSMENT

One of the advantages of performing a thorough preoperative functional assessment is to potentially allow for optimization of those patients at higher risk. It does not mean that the option for surgery should be immediately removed. In the setting of lung cancer, there is obviously critical importance in reducing the time to definitive treatment. However, careful consideration must be paid to smoking cessation and completion of a program of pulmonary rehabilitation or "prehabilitation." The problems faced by patients continuing to smoke through lung surgery is well described and recognized in clinical practice. A longer length of preoperative time from smoking cessation has been shown to decrease operative mortality. It is therefore important to try and help the patient engage with smoking cessation services, especially when deemed at increased risk.

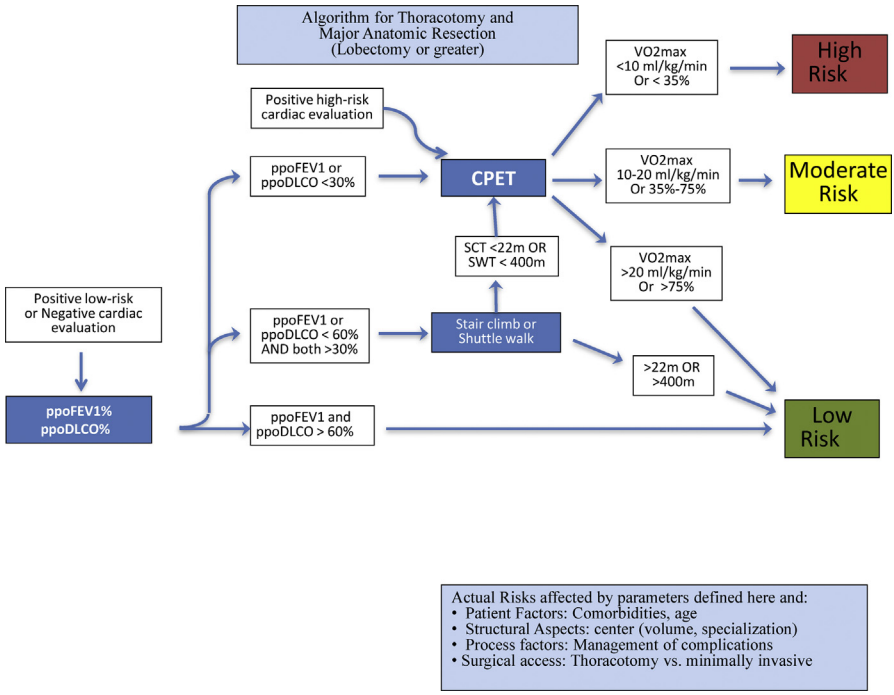

Fig. 1. American College of Chest Physicians functional evaluation algorithm for lung resection candidates. (*Adapted from* Brunelli A, Kim AW, Berger KI, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143: e166S-90S; with permission.)

The ACCP guidance recommends that high-risk patients should be referred for pulmonary rehabilitation.[3] In the setting of lung volume reduction (LVRS), this has been shown to improve breathlessness, quality of life, an exercise tolerance.[25] In respect of lung cancer resection surgery, one study has shown that a preoperative regimen reduced the patients' length of stay.[26] Pulmonary rehabilitation can present difficult challenges before lung cancer resection surgery, given that time to surgery is critical. However, in the future the format in which pulmonary rehabilitation can be offered is likely to continue to develop. Technology is enabling for app-based programs, meaning that it can be available almost immediately for the patients to use.[27]

Surgical risk-prediction algorithms are now available to help the thoracic surgeon to objectively estimate complications. A thorough preoperative functional assessment before surgery is important because even the apparently "healthy" patient may have undetected but significant cardiorespiratory impairment, which could put the patient at high risk of major perioperative complications.

SPECIAL CONSIDERATIONS

Risk Assessment of Candidates for Pneumonectomy

Pneumonectomy is still associated with a 6% risk of perioperative mortality.[28] This operation is a consistent risk factor for major cardiac events[2] and 30-day mortality.[29] The physiologic burden imposed by such a large lung resection to the cardiorespiratory system warrants a meticulous functional workup. In the authors' institution, all

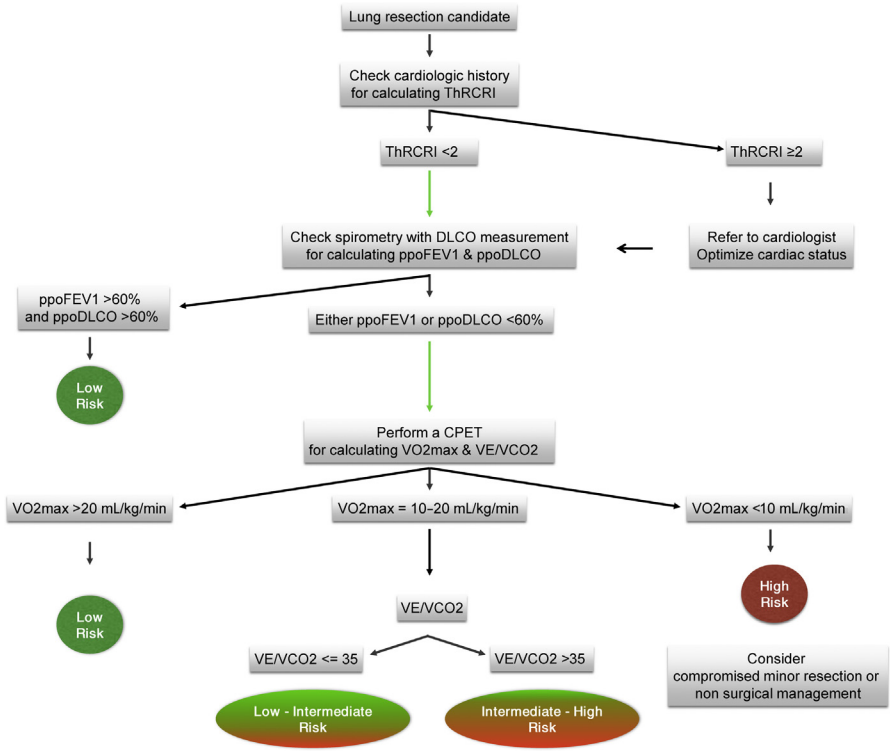

Fig. 2. Functional algorithm incorporating the V_E/V_{CO_2} slope as measure to refine the risk stratification. (*From* Salati, M., Brunelli, A. Risk Stratification in Lung Resection. Curr Surg Rep 2016; 4, 37; with permission.)

candidates for pneumonectomy undergo a quantitative perfusion scan to estimate the $ppoFEV_1$ and are systematically referred to a CPET.

Risk Stratification in Patients Receiving Neoadjuvant Chemotherapy

A recent study from the ESTS database has shown that neoadjuvant chemotherapy was associated with similar rates of 30-day mortality after lobectomy or pneumonectomy compared with matched patients not receiving chemotherapy. However, neoadjuvant chemotherapy was associated with higher cardiopulmonary morbidity and when combined with radiotherapy was associated with a 2-fold higher risk of mortality following pneumonectomy.[30] A similar recent analysis from the National Cancer Database of more than 130,000 patients undergoing lung resection for lung cancer found an increased incidence of 30-day and 90-day mortality after neoadjuvant treatment.[31]

Neoadjuvant chemotherapy has been found to be associated with structural changes in the lung leading to decreased diffusion capacity, which in turn may predispose to development of postoperative respiratory complications.[32–35] The evidence from the literature warrants a re-evaluation of the pulmonary function after completion of the chemotherapy treatment and before lung resection to evaluate possible changes, particularly in diffusion capacity.[3,4]

Does Ability to Undergo Minimally Invasive Surgery Change the Pulmonary Risk Profile?

Minimally invasive thoracic surgery is known to be associated with improved early postoperative outcomes in comparison with thoracotomy. Both robotic and thoracoscopic lung resections have been associated with lower rates of morbidity and mortality.[36–38] The benefits of a minimally invasive thoracic approach are particularly evident in patients with prohibitive pulmonary functions.[39] For this reason, the ACCP guidelines recommend that patients deemed at high risk for resection should be considered for minimally invasive surgery if feasible.[3] At this stage there is no sufficient evidence to suggest a different risk-assessment strategy in candidates for minimally invasive surgery. The advancement in technology, pain management, and enhanced recovery program may contribute in a future to offer lung cancer surgery to an increasing number of patients. Future guidelines should reflect these changes by elaborating the cumulative body of evidence in this field.

SHARED DECISION MAKING

One of the most important intimations of preoperative risk assessment is to provide scientific data to inform the shared decision making (SDM) process with the patient.

Little is known on how to measure patients' participation in SDM in patients with early-stage NSCLC. SDM is a concept defined by the National Institute of Health and Care Excellence (NICE) as a process whereby care or treatment options are fully explored along with their risks and benefits. The NICE document makes clear that persons both receiving and delivering care need to understand what is important to the other person. In the United States, the Institute of Medicine identified engaging patients and supporting patient decision making as an essential component of care, especially during a crisis.[40]

Regarding NSCLC, however, treatment effectiveness guidance is still mainly based on survival data[15,41]; there are no studies adequately comparing treatments' effectiveness in terms of impact on patients' quality of life (QOL).[42,43] Particularly in early-stage lung cancer, the lack of long-term QOL data after treatments has highlighted the importance of understanding whether a truly informed "shared decision" is made when discussing the situation with the patient. To develop SDM guidelines or integrate this concept into the existing decisional algorithms and guidelines, in the last 2 decades an increasing number of studies investigating the overall lack of concordance between physician and patient perceptions of the decisional context has been reported. Most of these studies have shown that concerns and treatment strategies were insufficiently discussed between the patients and physicians.[44,45]

Computerized interactive methods with outcome probabilities tailored to individual patients are new strategies to potentially increase communication, patient engagement, and documentation of consent. Online decision aids for treatment decision making resulted in a positive influence on clinicians' decisions and has been already developed for advanced-stage NSCLC.[46]

The main value of the SDM has been the improvement of patients' knowledge of their treatment trajectory to improve patients' adherence and satisfaction. In recent years, this strategy has been promoted also as a means to reduce health care overtreatment and costs.[47] Indeed, 20% of patients who participate in SDM choose less invasive surgical options and more conservative treatment than do patients who do not use decision aids.[48]

Patients with lung cancer have expressed their aversion to risk acceptance: however, facing the cancer progression and no alternatives for cure, patients are willing to

take extremely high risks of postoperative complications and surgery-related death.[49] On the other hand, they are always more demanding about the risks of a permanent and long-lasting disability: the interference of cancer treatment in their daily lifestyle is one of the main treatment outcomes for the patient. Information about residual QOL after surgical treatment become mandatory when medical alternatives have been implemented in a decision-making algorithm, such as stereotactic ablative radiotherapy (SABR) for early-stage lung cancers. The growing size of the older population and the increasing number of lung cancer screening scans are slightly changing the populations facing the surgical decision-making process. Increasing numbers of patients older than 75 years are being diagnosed with thoracic malignancies, and advancements in medical treatments now offer valid alternatives. Most importantly, holistic comprehension of cognitive abilities in older people has to be taken into account by the surgeons explaining the surgical risks. Hopmans and colleagues[44] interviewed in 2015 early-stage NSCLC patients submitted to either SABR or surgery. Guidance by the clinician and conduct of the clinician were found to be the most important factors for the patients during the decision-making process. Both SABR and surgery were only offered to 28.9% of patients. In another recent qualitative article, most patients preferred to not be aware of mortality risks. Surgery was the only treatment discussed for most patients, and they preferred clinicians to make treatment decisions because of the belief that clinicians know best.[45] However, Sullivan and colleagues[50] surveyed 114 patients with early-stage NSCLC 4 to 6 months after radical treatments (either SABR or surgery): more participants valued independence and QOL as “most important” compared with survival or cancer recurrence.

Furthermore, with the shift of health care in involving patients in medical decisions, the burden on patients to understand health-related information so as to make fully informed choices needs to be fully investigated. However, patients who are disadvantaged by poverty, lack of education, or linguistic barriers are also likely to make informed decisions without a real comprehension of risks and benefits. In an ideal health care system, all the people may be able to access the decision aids regardless their social and financial background. In real life, low numeracy also distorts perceptions of risks and benefits of screening, reduces medication compliance, impedes access to treatments, and impairs risk communication.[51]

Patient participation in the SDM may also play a role in increasing the QOL after the treatment. There are insufficient data to confirm this theory in our specialty, but results from the NELSON screening trial, for example, showed that subjects who did not make an informed decision to participate in lung cancer computed tomography screening trial did not experience worse QOL during screening than subjects who did make an informed decision.[52] In breast reconstruction surgery, patients who adopted a more active role, whether using an informed or shared approach, had higher general patient satisfaction and physical component QOL scores compared with patients whose decision making was paternalistic.[53]

SUMMARY

The concept of surgical risk continues to progress. There has been development of surgical risk-prediction models that have been adapted successfully for use in thoracic surgery. A meticulous preoperative physiologic assessment allows the surgeon and wider MDT to identify those at the highest risk. This then enables potential optimization of individuals deemed at high risk in an attempt to reduce this risk and also allows the surgeon and patient to engage in a full and frank discussion regarding treatment planning. However, caution is advised because no risk-prediction model in

isolation is the perfect tool, and the clinical acumen and surgical intuition of an expert physician remains of critical importance in this process.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

1. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999;100:1043–9.
2. Brunelli A, Varela G, Salati M, et al. Recalibration of the revised cardiac risk index in lung resection candidates. Ann Thorac Surg 2010;90:199–203.
3. Brunelli A, Kim AW, Berger KI, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:e166S–190.
4. Brunelli A, Charloux A, Bollinger CT, et al. ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy). Eur Respir J 2009;34:17–41.
5. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. Circulation 2007;116:e418–99.
6. Brunelli A, Cassivi SD, Fibla J, et al. External validation of the recalibrated thoracic revised cardiac risk index for predicting the risk of major cardiac complications after lung resection. Ann Thorac Surg 2011;92:445–8.
7. Ferguson MK, Celauro AD, Vigneswaran WT. Validation of a modified scoring system for cardiovascular risk associated with major lung resection. Eur J Cardiothorac Surg 2012;41(3):598–602.
8. Licker MJ, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. Ann Thorac Surg 2006;81:1830–7.
9. Brunelli A, Al Refai M, Monteverde M, et al. Predictors of early morbidity after major lung resection in patients with and without airflow limitation. Ann Thorac Surg 2002;74:999–1003.
10. Brunelli A, Xiumé F, Refai M, et al. Evaluation of expiratory volume, diffusion capacity, and exercise tolerance following major lung resection: a prospective follow-up analysis. Chest 2007;131:141–7.
11. Ferguson MK, Little L, Rizzo L, et al. Diffusing capacity predicts morbidity and mortality after pulmonary resection. J Thorac Cardiovasc Surg 1988;96:894–900.
12. Berry MF, Villamizar-Ortiz NR, Tong BC, et al. Pulmonary function tests do not predict pulmonary complications after thoracoscopic lobectomy. Ann Thorac Surg 2010;89:1044–51.

13. Brunelli A, Refai MA, Salati M, et al. Carbon monoxide lung diffusion capacity improves risk stratification in patients without airflow limitation: evidence for systematic measurement before lung resection. Eur J Cardiothorac Surg 2006;29(4): 567–70.
14. Ferguson MK, Vigneswaran WT. Diffusing capacity predicts morbidity after lung resection in patients without obstructive lung disease. Ann Thorac Surg 2008; 85(4):1158–64.
15. Lim E, Baldwin D, Beckles M, et al. Guidelines on the radical management of patients with lung cancer. Thorax 2010;65:iii1–27.
16. Charloux A, Brunelli A, Bollinger CT, et al. European Respiratory Society and European Society of Thoracic Surgeons Joint Task Force on Fitness for Radical Therapy. Lung function evaluation before surgery in lung cancer patients: how are recent advances put into practice? A survey among members of the European Society of Thoracic Surgeons (ESTS) and of the Thoracic Oncology Section of the European Respiratory Society (ERS). Interact Cardiovasc Thorac Surg 2009;9:925–31.
17. Marjanski T, Wnuk D, Bosakowski D, et al. Patients who do not reach a distance of 500 m during the 6-min walk test have an increased risk of postoperative complications and prolonged hospital stay after lobectomy. Eur J Cardiothorac Surg 2015;47:213–9.
18. Fennelly J, Potter L, Pompili C, et al. Performance in the shuttle walk test is associated with cardiopulmonary complications after lung resections. J Thorac Dis 2017;9(3):789–95.
19. Brunelli A, Xiume F, Refai M, et al. Peak oxygen consumption measured during the stair-climbing test in lung resection candidates. Respiration 2010;80(3): 207–11.
20. Bolliger CT, Jordan P, Solèr M, et al. Exercise capacity as a predictor of postoperative complications in lung resection candidates. Am J Respir Crit Care Med 1995;151:1472–80.
21. Brunelli A, Belardinelli R, Refai M, et al. Peak oxygen consumption during cardiopulmonary exercise test improves risk stratification in candidates to major lung resection. Chest 2009;135:1260–7.
22. Brunelli A, Belardinelli R, Pompili C, et al. Minute ventilation-to-carbon dioxide output (V_E/V_{CO2}) slope is the strongest predictor of respiratory complications and death after pulmonary resection. Ann Thorac Surg 2012;93:1802–6.
23. Shafiek H, Valera JL, Togores B, et al. Risk of postoperative complications in chronic obstructive lung disease patients considered fit for lung surgery: beyond oxygen consumption. Eur J Cardiothorac Surg 2016;50:772–9.
24. Salati M, Brunelli A. Risk stratification in lung resection. Curr Surg Rep 2016;4:37.
25. Ries AL, Make BJ, Lee SM, et al. The effects of pulmonary rehabilitation in the national emphysema treatment trial. Chest 2005;128:3799–809.
26. Weinstein H, Bates AT, Spaltro BE, et al. Influence of preoperative exercise capacity on length of stay after thoracic cancer surgery. Ann Thorac Surg 2007; 84:197–202.
27. Park S, Kim JY, Lee JC, et al. Mobile phone app-based pulmonary rehabilitation for chemotherapy-treated patients with advanced lung cancer: pilot study. JMIR Mhealth Uhealth 2019;7:e11094.
28. Salati M, Brunelli A, Decaluwe H, et al, ESTS DB Committee. Report from the European Society of Thoracic Surgeons Database 2017: patterns of care and perioperative outcomes of surgery for malignant lung neoplasm. Eur J Cardiothorac Surg 2017;52(6):1041–8.

29. Brunelli A, Cicconi S, Decaluwe H, et al. Parsimonious Eurolung risk models to predict cardiopulmonary morbidity and mortality following anatomic lung resections: an updated analysis from the European Society of Thoracic Surgeons database. Eur J Cardiothorac Surg 2020;57(3):455–61.
30. Brunelli A, Rocco G, Szanto Z, et al. Morbidity and mortality of lobectomy or pneumonectomy after neoadjuvant treatment: an analysis from the ESTS database. Eur J Cardiothorac Surg 2020;57(4):740–6.
31. Yendamuri S, Groman A, Miller A, et al. Risk and benefit of neoadjuvant therapy among patients undergoing resection for non-small-cell lung cancer. Eur J Cardiothorac Surg 2018;53(3):656–63.
32. Roberts JR, Eustis C, Devore R, et al. Induction chemotherapy increases perioperative complications in patients undergoing resection for non-small cell lung carcinoma. Ann Thorac Surg 2001;72:885–8.
33. Leo F, Pelosi G, Sonzogni A, et al. Structural lung damage after chemotherapy fact or fiction? Lung Cancer 2010;67(3):306–10.
34. Cerfolio RJ, Talati A, Bryant AS. Changes in pulmonary function tests after neoadjuvant therapy predict postoperative complications. Ann Thorac Surg 2009; 88(3):930–5.
35. Leo F, Solli P, Spaggiari L, et al. Respiratory function changes after chemotherapy: an additional risk for postoperative respiratory complications? Ann Thorac Surg 2004;77(1):260–5.
36. O'Sullivan KE, Kreaden US, Hebert AE, et al. A systematic review and meta-analysis of robotic versus open and video-assisted thoracoscopic surgery approaches for lobectomy. Interact Cardiovasc Thorac Surg 2019;28(4):526–34.
37. Paul S, Altorki NK, Sheng S, et al. Thoracoscopic lobectomy is associated with lower morbidity than open lobectomy: a propensity-matched analysis from the STS database. J Thorac Cardiovasc Surg 2010;139(2):366–78.
38. Falcoz PE, Puyraveau M, Thomas PA, et al, ESTS Database Committee and ESTS Minimally Invasive Interest Group. Video-assisted thoracoscopic surgery versus open lobectomy for primary non-small-cell lung cancer: a propensity-matched analysis of outcome from the European Society of Thoracic Surgeon database. Eur J Cardiothorac Surg 2016;49(2):602–9.
39. Burt BM, Kosinski AS, Shrager JB, et al. Thoracoscopic lobectomy is associated with acceptable morbidity and mortality in patients with predicted postoperative forced expiratory volume in 1 second or diffusing capacity for carbon monoxide less than 40% of normal. J Thorac Cardiovasc Surg 2014;148(1):19–28.
40. Hurria A, Naylor M, Cohen HJ. Improving the quality of cancer care in an aging population: recommendations from an IOM report. JAMA 2013;310(17):1795–6.
41. Scott WJ, Howington J, Feigenberg S, et al. Treatment of non-small cell lung cancer stage I and stage II: ACCP evidence-based clinical practice guidelines (2nd edition). Chest 2007;132(3 Suppl):234s–42s.
42. Louie AV, van Werkhoven E, Chen H, et al. Patient reported outcomes following stereotactic ablative radiotherapy or surgery for stage IA non-small-cell lung cancer: results from the ROSEL multicenter randomized trial. Radiother Oncol 2015; 117(1):44–8.
43. Pompili C, Franks KN, Brunelli A, et al. Patient reported outcomes following video assisted thoracoscopic (VATS) resection or stereotactic ablative body radiotherapy (SABR) for treatment of non-small cell lung cancer: protocol for an observational pilot study (LiLAC). J Thorac Dis 2017;9(8):2703–13.

44. Hopmans W, Damman OC, Senan S, et al. A patient perspective on shared decision making in stage I non-small cell lung cancer: a mixed methods study. BMC Cancer 2015;15(1):959.
45. Powell HA, Jones LL, Baldwin DR, et al. Patients' attitudes to risk in lung cancer surgery: a qualitative study. Lung Cancer 2015;90(2):358–63.
46. Chow H, Edelman MJ, Giaccone G, et al. Impact of an interactive on-line tool on therapeutic decision-making for patients with advanced non-small-cell lung cancer. J Thorac Oncol 2015;10(10):1421–9.
47. Oshima Lee E, Emanuel EJ. Shared decision making to improve care and reduce costs. N Engl J Med 2013;368(1):6–8.
48. Stacey D, Paquet L, Samant R. Exploring cancer treatment decision-making by patients: a descriptive study. Curr Oncol 2010;17(4):85–93.
49. Cykert S, Kissling G, Hansen CJ. Patient preferences regarding possible outcomes of lung resection: what outcomes should preoperative evaluations target? Chest 2000;117(6):1551–9.
50. Sullivan DR, Eden KB, Dieckmann NF, et al. Understanding patients' values and preferences regarding early stage lung cancer treatment decision making. Lung Cancer 2019;131:47–57.
51. Reyna VF, Nelson WL, Han PK, et al. How numeracy influences risk comprehension and medical decision making. Psychol Bull 2009;135(6):943–73.
52. van den Bergh KA, Essink-Bot ML, van Klaveren RJ, et al. Informed decision making does not affect health-related quality of life in lung cancer screening (NELSON trial). Eur J Cancer 2010;46(18):3300–6.
53. Ashraf AA, Colakoglu S, Nguyen JT, et al. Patient involvement in the decision-making process improves satisfaction and quality of life in postmastectomy breast reconstruction. J Surg Res 2013;184(1):665–70.