

Preoperative evaluation for lung cancer resection

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ABSTRACT

During the last decades lung cancer is the leading cause of death worldwide for both sexes. Even though cigarette smoking has been proved to be the main causative factor, many other agents (e.g., occupational exposure to asbestos or heavy metals, indoor exposure to radon gas radiation, particulate air pollution) have been associated with its development. Recently screening programs proved to reduce mortality among heavy-smokers although establishment of such strategies in everyday clinical practice is much more difficult and unknown if it is cost effective compared to other neoplasms (e.g., breast or prostate cancer). Adding severe comorbidities (coronary heart disease, COPD) to the above reasons as cigarette smoking is a common causative factor, we could explain the low surgical resection rates (approximately 20-30%) for lung cancer patients. Three clinical guidelines reports of different associations have been published (American College of Chest Physicians, British Thoracic Society and European Respiratory Society/European Society of Thoracic Surgery) providing detailed algorithms for preoperative assessment. In the current mini review, we will comment on the preoperative evaluation of lung cancer patients.

KEYWORDS

Lung cancer; surgery; preoperative

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Introduction

During the last decades lung cancer is the leading cause of death

worldwide for both sexes (1). Even though cigarette smoking has been proved to be the main causative factor, many other agents [e.g., occupational exposure to asbestos (2) or heavy metals (3), indoor exposure to radon gas radiation (4), particulate air pollution (5)] have been associated with its development.

Even though there are no randomized, controlled studies comparing surgical to non-surgical treatment options for early stage lung cancer, retrospective analyses showed that surgery is the most effective radical treatment approach (6,7). Lung cancer usually causes symptoms when the disease is locally advanced or metastatic. Recently screening programs proved to reduce

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Table 1. Parameters of thoracscore for predicting in-hospital mortality for patients requiring thoracic surgery.

Age (<55, 55-65, >65 years)
Sex
ASA classification (≤ 2 , ≥ 3)
Performance status according to Zubrod scale (≤ 2 , ≥ 3)
Severity of dyspnea according to Medical Research Council Scale (≤ 2 , ≥ 3)
Priority of surgery (elective, urgent/emergency)
Extent of resection (pneumonectomy, other)
Diagnosis (malignant, benign)
Comorbidity score

ASA, American Society of Anesthesiologists.

mortality among heavy-smokers (8) although establishment of such strategies in everyday clinical practice is much more difficult and unknown if it is cost effective compared to other neoplasms (e.g., breast or prostate cancer). Adding severe comorbidities (coronary heart disease, COPD) to the above reasons as cigarette smoking is a common causative factor, we could explain the low surgical resection rates (approximately 20-30%) for lung cancer patients (9-11).

Age alone is not a contraindication and nowadays about one third of patients undergoing surgical resection for lung cancer are >70 years old (12). Elderly should be treated according to the same therapeutic algorithms as younger patients based on holistic evaluation and calculated risk rates. After a detailed staging plan (PET-CT, EBUS/EUS guided TBNA) patients with limited disease should undergo evaluation for their cardiorespiratory reserves so an informed decision could be taken based on objective measurements and risk/benefits ratio. Three clinical guidelines reports of different associations have been published [American College of Chest Physicians (12), British Thoracic Society (13) and European Respiratory Society/European Society of Thoracic Surgery (14)] providing detailed algorithms for preoperative assessment.

Perioperative morbidity and mortality

The extent of lung resection is strongly associated with mortality, with pneumonectomy demonstrating 2-3 times higher mortality compared to lobectomy (15,16). Thirty-days mortality for lobectomy was 2.3% and 7% for pneumonectomy according to data of National Lung Cancer Audit in England from 2004 to 2010 (10,991 patients) (17). A database analysis among 18,800 lung cancer resections showed that significant prognostic factors

for mortality were: pneumonectomy, bilobectomy, American Society of Anesthesiologists (ASA) Physical Status Scale rating, Zubrod performance status score, renal dysfunction, induction chemoradiation therapy, steroid use, older age, urgent procedures, male gender, forced expiratory volume in 1 second (FEV₁), and body mass index (18).

Controversial results exist about mortality among the elderly (19,20) but all guidelines recommend that careful selection of patients >75-80 years old—based on objective measurements—is mandatory. Thoracic Surgery Scoring System (Thoracscore) is a well-validated, multidimensional tool (21) that includes nine variables (Table 1) and could predict the risk of death with acceptable accuracy for clinical practice. Such tools could be used as part of a medical interview to quantify the perioperative risk to the patient and enable him to take an informed decision.

We should emphasize that surgical experience is an important contributing factor as both surgeon's expertise (thoracic surgeons compared to general surgeons) as well as hospital-volume of procedures have been associated with perioperative mortality, resectability rates and long-term survival (22-24).

Postoperative morbidity reaches 40% while the main adverse are: atrial arrhythmias, prolonged chest tube drainage and air leak, respiratory complications (sputum retention, pneumonia, empyema), hemorrhage, wound infection, chylothorax and recurrent laryngeal nerve injury (25,26).

Assessment of cardiovascular risk

Guidelines (12-14) agrees that cardiovascular evaluation should be the first step across preoperative assessment for lung cancer resection. Taking into account that the majority of these patients are over 60 years old and current/former smokers, they usually have prior diagnosis of heart disease or represent a potentially high-risk population. Major cardiac-related adverse events are reported in 2-3% of patients postoperatively (27). Thoracic revised cardiac risk index (ThRCRI) is a validated tool (27) that includes four parameters (pneumonectomy, 1.5 points; previous ischemic heart disease, 1.5 points; previous stroke or transient ischemic attack, 1.5 points; creatinine >2 mg/dL, 1 point) and could be used to categorize patients. Those with >1.5 points, recent diagnosis of active heart disease (e.g., unstable angina, severe aortic stenosis, significant arrhythmias) or limited exercise capacity should be sent for cardiologic consultation. Medical history for risk factors, clinical examination, noninvasive evaluation for coronary artery disease—preferably using cardiopulmonary exercise testing—as well as echocardiography for quantification of ventricular and valves function are usually indicated. Myocardial infarction within the last 30 days is

considered as a contraindication for the resection (13).

We should continue prior medication (β -blockers, antiplatelet agents, statins) and initiate them if there is an indication independent of the surgery in very high-risk patients. Use of clopidogrel does not increase the possibility of bleeding in the perioperative period while patients with a coronary artery stent should not stop it (28).

Prophylactic use of extended-release β -blockers is not indicated as in a randomized study it increased both mortality and stroke rate (29). Similarly prophylactic coronary artery revascularization was not associated with short or long-term positive results even though current data are referred to patients who undergo major vascular surgery (30,31). Coronary artery revascularization is proposed when there is an absolute indication irrespective of the planned lung cancer resection (14).

Assessment of respiratory function and exercise capacity

It is strongly recommended that all patients who are candidates for surgical treatment of lung cancer should undergo both spirometry (FEV_1) and measurement of diffusing capacity for CO (DLco) (12-14). As these two parameters represent function of different lung compartments (FEV_1 is mainly associated with airflow limitation while DLco describes function of the alveolar-capillary membrane), it has been proved that they are not strongly correlated (32). Preoperative FEV_1 and DLco as well as calculated predicted postoperative (ppo) have been independently associated with morbidity and mortality rates in several studies (33-37). It is interesting to mention that patients with COPD demonstrate only a slight loss or even increase in respiratory function parameters after surgery and this is attributed to removal of emphysematous parenchyma around the tumor ("lobar volume reduction effect") (38,39). So the decision for surgery for COPD patients should be based mainly on exercise capacity tests rather than static lung function measurements.

Calculation of ppo values should be based on perfusion scan for patients undergoing pneumonectomy: $ppo\ FEV_1 = preoperative\ FEV_1 \times (1 - \text{fraction of the total perfusion for the resected lung})$. On the other hand the following equation is used for lobectomy or segmentectomy: $ppo\ FEV_1 = preoperative\ FEV_1 \times (19 - \text{removed segments} - \text{obstructed segments} / 19 - \text{obstructed segments})$. The same equations are used for ppo DLco. Even though ppo values are correlated with postoperative morbidity (40), they are usually achieved >1 month after surgery (41) and early postoperative FEV_1 is a better predictor of survival (42).

Patients with preoperative FEV_1 and DLco >80% predicted or ppo FEV_1 and ppo DLco >60% predicted are considered of low

risk even to undergo pneumonectomy (12,14). If both ppo FEV_1 and ppo DLco are <60% predicted then it is necessary to evaluate patient's exercise capacity. This could be done either with low-cost tests (shuttle walk test, stair-climbing) or with a cardiopulmonary exercise test (CPET). The latter is a maximal exercise test that assesses both respiratory and cardiac response to stress. Maximal oxygen consumption ($VO_2\ max$) as well as signs of ischemic heart disease (ECG abnormalities) or heart failure (low anaerobic threshold) is important for the preoperative evaluation. The main disadvantage of this technique is its high cost and is not available in many thoracic surgery departments.

Shuttle walk test and stair-climbing are strongly correlated with CPET (43,44). A cut-off point of 400 m for the former and 22 m for the latter correspond to $VO_2\ max >15\ mL/kg/min$ which is considered enough for performing lobectomy or segmentectomy. Patients with either ppo FEV_1 or ppo DLco 30-60% pred. should be evaluated with low-cost exercise tests and if these are above the critical cut-off points then the planned resection is considered of acceptable risk (45). We should mention that stair-climbing test has not been standardized (speed, number of steps per flight, specific criteria for ending the test).

CPET is indicated for patients with limited lung function reserves according to static measurements (ppo FEV_1 or ppo DLco <30% pred.) (12). In centers where the test is available we recommend to use it to the majority of the patients (FEV_1 or DLco <80%) as published studies about its role on preoperative evaluation are much more than low-cost exercise tests. Patients with $VO_2\ max >20\ mL/kg/min$ or >75% pred. could be undergone even pneumonectomy (46,47). On the contrary those with $VO_2\ max <10-12\ mL/kg/min$ or <35% pred. represent a high risk group and major anatomic resection is contraindicated (48,49). An intermediate risk group is consisted of patients with $VO_2\ max = 10-15\ mL/kg/min$ (50,51). In this case an informed decision should be taken from the patient in collaboration with the surgeon or alternative treatments could be discussed (wedge resection, 3D or stereotactic radiotherapy, radiofrequency ablation).

There are three published guidelines papers of different medical societies. ACCP guidelines have a step-by-step approach—mimicking everyday clinical practice for many thoracic surgery departments—starting with lung function measurements, and then propose low-cost exercise capacity tests and finally CPET. On the other hand ERS/ESTS guidelines recommend CPET for those with either FEV_1 or DLco <80% which is not available for many centers while ppo values are used later in the algorithm. BTS guidelines give a detailed approach for staging the disease but there are no proposed cut-off points for FEV_1 or DLco.

Additionally there are a number of strategies that could reduce perioperative morbidity and mortality in patients with marginal lung function reserves. Multidisciplinary approach is essential in order to implement such an individualized treatment. Smoking cessation (52), VATS lobectomy instead of lateral thoracotomy (53), lung volume reduction surgery simultaneously with tumor resection in COPD patients with emphysema of the upper lobes (54), programs of pulmonary rehabilitation pre and after surgery (55) is important supportive/alternative care for severely compromised patients with underline chronic pulmonary diseases.

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