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REVIEW ARTICLE

Non-small cell lung cancer: pulmonary parenchyma resection in lung-compromised patients

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Summary

Surgery remains the primary curative treatment for patients who have early-stage non-small cell lung cancer (NSCLC). The proper use of surgical resection depends on a careful assessment of the extent of disease and the cardiopulmonary function. Because lung cancer is more common in patients who have chronic obstructive pulmonary disease (COPD), it is important to select carefully those patients who can safely undergo potentially curative therapy, thereby minimizing postoperative morbidity and mortality.

This article discusses the preoperative pulmonary assessment for patient selection, the preparation of high-risk patients, special surgical considerations, and patient management in the immediate postoperative period.

Key words: high risk patients, lung cancer, postoperative management, preoperative evaluation, surgical treatment

Preoperative evaluation

Assessment of risks

Patients with NSCLC who undergo evaluation for lung resection are usually smokers or former smokers, having an increased risk of vascular, cardiac, and pulmonary medical comorbidities. Major complications occur in approximately 9% and minor complications in 19% of elective operations for lung cancer. The overall mortality rate is approximately 3% for lobectomies and 6% for pneumonectomies. Most complications are cardiopulmonary and are related to several factors, including older age, diminished cardiopulmonary reserve, and the extent of resection, particularly a right pneumonectomy. Proper case selection and careful postoperative management help minimize the risk of complications [1-3].

COPD and lung cancer are linked by the patient's smoking history. Studies have also shown that lung cancer is far more common in patients who have COPD than in those who have normal physiologic airflow function, even when controlling for factors such as smoking and family and occupational diseases. The presence of COPD is also the predominant predictor and risk factor for postoperative respiratory-related complications [4-6].

Pulmonary assessment

The identification of high- and low-risk populations is important in the preoperative evaluation. It provides an appropriate perspective from which to discuss treatment options with the patient and identifies patients who may benefit from more extensive preoperative evaluation and interventions.

The initial pulmonary assessment is based on a complete patient history and physical examination and review of radiographic imaging studies. In addition to detecting symptoms of comorbid diseases, the history should elicit the patient's functional capacity for exercise. Cigarette smoking history, daily cough, sputum production, and history of asthma also help determine the pulmonary status.

All patients considered for thoracotomy should undergo pulmonary function testing (lung volumes, flow rates, and diffusing capacity) as part of their initial

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evaluation [7]. The testing is inexpensive, simple, and reproducible. Particular attention is paid to the forced expiratory volume in 1 second (FEV_1), the forced vital capacity (FVC), and the diffusing capacity for carbon monoxide (DLCO). Values obtained during testing are compared with predicted values to generate a predicted result percentage of these parameters. The predicted pulmonary values are determined by the patient's age, gender, and height.

Predicted values of FEV_1 and FVC between 80 and 120% are considered normal. A reduction in FEV_1 predicted percentage (FEV_1%) and in the ratio of FEV to FVC is consistent with an obstructive disease (classified as mild, moderate, or severe). Patients with low FEV_1%, low FVC, and preserved FEV_1/FVC have a restrictive deficit. Obstructive deficits are most commonly detected in patients who have lung cancer because cigarette smoking is a cause of obstructive lung disease and airflow obstruction is an independent risk factor for development of lung cancer [7].

Normal test results generally do not require further evaluation. A pneumonectomy can be tolerated in the absence of cardiac disease or other severe comorbid conditions. For patients with abnormal results, however, further testing is required to stratify more accurately the population at higher risk and decide on the extent of resection that can be safely performed [8].

Predicting postoperative pulmonary functions

Patients with borderline pulmonary function could be falsely considered medically inoperable if the function of each lung is assumed to be equal. This situation is particularly true with hilar lesions as opposed to peripheral lesions because of the greater interference of pulmonary function by the former caused by its more central location. To determine the best method of predicting postoperative pulmonary function, radionuclide perfusion scans have been used in combination with the preoperative pulmonary function tests. Predictions, such as the predicted postoperative FEV_1 ($ppoFEV_1$) and the ppoDLCO, have been calculated. These predicted values are established by applying the results of the split-function studies from radionuclide perfusing lung scan using the following formula for a lobectomy or a pneumonectomy: $ppoFEV_1$ = preoperative FEV_1 X (1 - fractional contribution of the lung or lobe to be removed). The same formula is used to predict the other parameters. A loss of pulmonary function after pneumonectomy or lobectomy has been shown to be accurately predicted this way, and the predicted postoperative values are related to postoperative morbidity and mortality [8-12].

Exercise testing is a useful complement to the preoperative evaluation [13]. It also has been combined with lung scanning to obtain a ppoVCKmax (maximal oxygen uptake) for the prediction of postoperative complications [14].

There are greatly varying recommendations as to the lowest acceptable value of $ppoFEV_1$. Traditionally, a patient with a $ppoFEV_1$ of less than 800 ml has been considered inoperable. Some centers, especially with experience from lung volume reduction surgery, have shown that resectional surgery is sometimes feasible, even in these patients, but they are at higher risk of complications and death [15-17]. Contemporary experience suggests that the percentage of predicted values for both FEV_1 and DLCO, rather than the absolute values, may be more important in predicting operative risk. Generally, a ppo-FEV_1% of less than 40% warrants further testing (exercise testing), and most authors would agree that a $ppoVO_2$max of less than 10 ml/kg/min (or 35% of the predicted value) indicates inoperability [18-20].

Arterial blood gas tensions and oxygen saturation

Preoperative hypoxemia or arterial oxygen saturation of less than 90% or a desaturation of greater than 4% during exercise has been associated with increased risk of postoperative complications. Further physiologic testing is advised in those patients before performing a lung resection [21-23].

Historically, hypercapnea ($PaCO_2$ of > 45 mm Hg) has been quoted as an exclusion criterion for resection. Few studies address this issue; however, they suggest that preoperative hypercapnea is not an independent risk factor for increased complications. More complete physiologic testing is also advised in patients being considered for lung cancer surgery if their $PaCO_2$ is greater than 45 mm Hg [24].

Risk indices to predict complications after pulmonary resection

More recently, different groups have been working on preoperative risk indices that would be used to predict mortality and complications after thoracic surgery. For example, the cardiopulmonary risk index, developed by Epstein et al. from retrospective data [25], combines a cardiac risk index (adapted from Goldman's criteria) and a pulmonary risk index. Initially, it seemed to correlate with complications and death rates, but when prospectively applied to a large population, this index failed to reliably predict outcome [26]. Pierce et al. [27] proposed the predicted postoperative product

(PPP) as the best predictor of surgical mortality. PPP is the algebraic product of the ppoFEV_1% and the ppoDLCO%. This concept is attractive because it incorporates elements of ventilatory function, gas exchange, lung perfusion, and proportion of lung to be resected. Their results, however, were poor when trying to predict complication rates. Based on Pierce et al's methodology, Melendez et al. [28] constructed the predictive respiratory quotient (PRQ) as follows: PRQ = ppoFEV_1% × ppoDLCO%^{2}/A - apO_2. By adding the alveolar-arterial oxygen gradient in the equation, PRQ seemed to predict the outcome better than other previously devised indices. The proposed index, however, has not yet been prospectively validated. Currently, very limited available data support the clinical use of preoperative risk indices [11,12].

Preparation for high-risk patients

It would seem rational that adequate preparation for thoracic surgery requires that the pulmonary function of each patient be maximized to reduce the risk of postoperative complications. Very few data, however, addressing this issue are available. One randomized study from 1970 showed that for a group of poor-risk patients, preoperative cessation of smoking, the use of bronchodilator drugs, the use of antibiotics when indicated, and pulmonary toilet by postural drainage and chest physiotherapy reduced the incidence of complications when added to postoperative pulmonary therapy [29].

Logically, all patients should be encouraged to quit smoking at least 2 to 4 weeks before surgery to decrease airway inflammation and pulmonary secretion production. In patients with reactive airways, bronchodilator treatment should be optimized and corticosteroid therapy (inhaled and occasionally short-course systemic therapy) is often helpful. Antibiotic therapy is sometimes needed to treat chronic bronchitis or postobstructive pneumonitis caused by the primary tumor.

The type of pulmonary rehabilitation usually offered to patients who have COPD and to patients being considered for lung transplantation or lung volume reduction surgery could also benefit patients who have lung cancer. Programs of supervised exercises for muscle training and pulmonary toilet, techniques for medication compliance, and nutritional support may improve surgical outcome. The potential benefit of preoperative rehabilitation, however, although a logical extension of the experience in patients with benign diseases, is not proven in patients who have lung cancer [30].

Surgical considerations

The option of a limited resection

Lobectomy or pneumonectomy is generally considered the procedure of choice for resectable bronchogenic carcinoma. Lesser resections by wedge excision or segmentectomy have been advocated by some investigators in retrospective studies for early-stage tumors [31-33]. The North American Lung Cancer Study Group performed a randomized clinical trial comparing lobectomy to lesser resection by large wedge or segmentectomy in peripheral stage IA carcinoma [34]. Patients undergoing limited resection experienced a higher rate of locoregional recurrence, but the risk of distant metastases was unaffected by the type of pulmonary resection. The death rate from cancer was lower in the lobectomy group, but the observed difference did not reach statistical significance. Patients who underwent lobectomy had a greater decrease in pulmonary function during the initial postoperative period. Limited pulmonary resection could thus be confined to patients with very limited pulmonary reserve, who might not otherwise tolerate the early decrease in lung function accompanying a lobectomy, and give them a chance for a curative treatment. Such patients should be carefully evaluated, however, to determine whether a lobectomy might benefit them by also allowing lung volume reduction.

Useful guidelines for determining the type of carcinoma that might be amenable to a limited resection include the following: a peripherally located lesion, a tumor less than 3 cm in diameter, margins easily encompassed by resection, no gross lymph node involvement, and a lesion ideally adjacent to a fissure [35].

The option of a sleeve lobectomy

Sleeve lobectomy is a lung-saving operation in which a portion of the main bronchus is removed in continuity with the involved lobe to preserve distal parenchyma. In carefully selected patients who have a centrally located tumor, sleeve lobectomy is an alternative to pneumonectomy. In patients whose pulmonary function is too compromised to tolerate an extensive resection, this option should be considered for anatomically suitable lesions [36-38].

Studies have shown that survival results with sleeve lobectomies are comparable to those achieved by conventional operations. Moreover, it has been demonstrated that the perfusion scan-derived ppo-FEV_1 was a good estimator of the real postoperative function (with a correlation coefficient of 0.87) [39]. The reanasto-

mosed lobes showed normal ventilation and perfusion. Furthermore, in many patients, the operation resulted in no measurable functional loss, a finding that reflects resection of poorly functioning lung caused by a central tumor [40].

Combined surgery for lung volume reduction and lung cancer

Some centers, having gained experience and success with lung volume reduction surgery, tried to extend the benefits of the volume reduction concept to a select group of patients with severe emphysema and early-stage lung cancer. Patients who would have been considered to have physiologically inoperable cancer can undergo resection of their cancer with overall improvement of their respiratory status. Combined surgery clearly should only be offered to a very select group of patients. The ideal candidate would have target areas of destroyed lung tissue, with the cancer located in the target lobe. In patients who have cancer located in an area of better-preserved lung, an experienced surgeon could probably consider a limited resection of the cancer in combination with a lung volume reduction. Thus, patients who have lung cancer and poor pulmonary function tests should not automatically be considered unfit for resection. Further experience with lung volume reduction operations alone and in combination with cancer surgery will help refine the indications and limitations of this approach [35-40].

Thoracoscopy

Videothoracoscopic (VATS) resections are gaining popularity. Theoretically, this approach should not allow more poor-risk patients to undergo resection because the amount of the lung removed is the same whatever the surgical approach. It seems, however, that a VATS resection could have a beneficial impact on the risk of postoperative pulmonary complications, with earlier recovery of expiratory muscle strength and walking capacity, probably from the decrease in chest pain in the first week after surgery [41].

VATS lobectomy seems to achieve the same long-term prognosis in patients who have clinical stage IA disease when compared with conventional thoracotomy [42]. Lung cancer patients who have completely resected disease have a good quality of life and high levels of functioning on intermediate- to long-term follow-up evaluations, with no significant difference between the VATS and thoracotomy groups [43].

No relative merit of VATS resection vs. lobectomy or sublobar resection performed by means of a muscle-sparing thoracotomy incision has been definitively shown. Well-designed prospective studies are needed to evaluate the potential superiority of VATS [42,43].

Postoperative management

The consensus is that early mobilization and pulmonary toilet in the immediate postoperative period are needed to minimize complications and that these contribute to prompt recovery. Good pain control is mandatory for patients' ability to exercise. Chest physiotherapy, incentive spirometry, and ambulation are important to avoid atelectasis, pneumonia, or respiratory failure after thoracotomy. Bedside bronchoscopy benefits selected patients for removal of retained secretions. In addition, the use of a mini tracheotomy for secretion aspiration can be helpful for some patients with impaired pulmonary reserve.

Conclusion

Every patient evaluated for lung resection should have preoperative pulmonary function testing. Patients with a significant decrease in FEV_1% (~60%~70% or less) should have a quantitative radionuclide perfusion scanning. Patients with a low ppoFEV_1% (~ 40%) should be considered for exercise testing because their risk for developing postoperative complications is higher. A VO_2max between 10 to 15 ml/kg/min or a ppoVO_2max of less than 10 ml/ kg/min would usually be considered prohibitive for surgery. Nevertheless, no single criterion should be used to exclude a patient from surgery. Rather, the use of multiple preoperative studies is needed to select patients who will tolerate and benefit from pulmonary resection. Surgical interventions other than standard lobectomies or pneumonectomies can be offered to selected high-risk patients. Experience from lung volume reduction surgery has shown that some patients who would have been considered inoperable can safely undergo resection of their lung cancer.

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