The Physiologic Evaluation of Patients With Lung Cancer Being Considered for Resectional Surgery*

Michael A. Beckles, MB, BS; Stephen G. Spiro, MD; Gene L. Colice, MD, FCCP; Robin M. Rudd, MD

The preoperative physiologic assessment of a patient being considered for surgical resection of lung cancer must consider the immediate perioperative risks from comorbid cardiopulmonary disease, the long-term risks of pulmonary disability, and the threat to survival due to inadequately treated lung cancer. As with any planned major operation, especially in a population predisposed to atherosclerotic cardiovascular disease by cigarette smoking, a cardiovascular evaluation is an important component in assessing perioperative risks. Measuring the FEV_1 and the diffusing capacity of the lung for carbon monoxide (DLCO) measurements should be viewed as complementary physiologic tests for assessing risk related to pulmonary function. If there is evidence of interstitial lung disease on radiographic studies or undue dyspnea on exertion, even though the FEV_1 may be adequate, a DLCO should be obtained. In patients with abnormalities in FEV_1 or DLCO identified preoperatively, it is essential to estimate the likely postresection pulmonary reserve. The amount of lung function lost in lung cancer resection can be estimated by using either a perfusion scan or the number of segments removed. A predicted postoperative FEV_1 or DLCO < 40% indicates an increased risk for perioperative complications, including death, from lung cancer resection. Exercise testing should be performed in these patients to further define the perioperative risks prior to surgery. Formal cardiopulmonary exercise testing is a sophisticated physiologic testing technique that includes recording the exercise ECG, heart rate response to exercise, minute ventilation, and oxygen uptake per minute, and allows calculation of maximal oxygen consumption ($\dot{V}O_2max$). Risk for perioperative complications can generally be stratified by $\dot{V}O_2max$. Patients with preoperative $\dot{V}O_2max$ > 20 mL/kg/min are not at increased risk of complications or death; $\dot{V}O_2max$ < 15 mL/kg/min indicates an increased risk of perioperative complications; and patients with $\dot{V}O_2max$ < 10 mL/kg/min have a very high risk for postoperative complications. Alternative types of exercise testing include stair climbing, the shuttle walk, and the 6-min walk. Although often not performed in a standardized manner, stair climbing can predict $\dot{V}O_2max$. In general terms, patients who can climb five flights of stairs have $\dot{V}O_2max$ > 20 mL/kg/min. Conversely, patients who cannot climb one flight of stairs have $\dot{V}O_2max$ < 10 mL/kg/min. Data on the shuttle walk and 6-min walk are limited, but patients who cannot complete 25 shuttles on two occasions will have $\dot{V}O_2max$ < 10 mL/kg/min. Desaturation during an exercise test has been associated with an increased risk for perioperative complications. Lung volume reduction surgery (LVRS) for patients with severe emphysema is a controversial procedure. Some reports document substantial improvements in lung function, exercise capability, and quality of life in highly selected patients with emphysema following LVRS. Case series of patients referred for LVRS indicate that perhaps 3 to 6% of these patients may have coexisting lung cancer. Anecdotal experience from these case series suggest that patients with extremely poor lung function can tolerate combined LVRS and resection of the lung cancer with an acceptable mortality rate and good postoperative outcomes. Combining LVRS and lung cancer resection should probably be limited to those patients with heterogeneous emphysema, particularly emphysema limited to the lobe containing the tumor. ***(CHEST 2003; 123:105S–114S)***

Key words: cardiopulmonary exercise testing; diffusing capacity; predicted postoperative lung function; preoperative assessment; spirometry

Abbreviations: BTS = British Thoracic Society; CPET = cardiopulmonary exercise test; DLCO = diffusing capacity of the lung for carbon monoxide; LVRS = lung volume reduction surgery; ppo = predicted postoperative; %ppo = percentage of predicted postoperative; SaO_2 = arterial oxygen saturation; $\dot{V}O_2max$ = maximal oxygen consumption

While surgery remains the best option for cure for lung cancer, many potentially resectable tumors occur in individuals with abnormal pulmonary function usually due to cigarette smoking. These patients may be at increased risk for immediate perioperative complications and long-term disability following resection of functioning lung tissue. Cigarette smoking will also predispose these patients to other comorbid conditions, specifically atherosclerotic cardiovascular disease, which will further increase the perioperative risks. Consequently, the preoperative physiologic assessment of a patient being considered for surgical resection of lung cancer must consider the immediate perioperative risks from comorbid cardiopulmonary disease, the long-term risks of pulmonary disability, and the threat to survival due to inadequately treated lung cancer.

Little information is available on long-term survival of patients deemed inoperable because of physiologic limitations, especially compared to a group with similar physiologic limitations who underwent surgical resection. One study reported that the long-term survival curve for five high-risk patients undergoing operation was no different than for 39 similar patients deemed inoperable, despite a higher initial mortality in the group undergoing resection.[1] The balance between perioperative risks and inadequate cancer treatment may be shifting, because surgical techniques and anesthetic and postoperative care have improved. Morbidity and mortality rates following lung resection are lower now than in the past.[2] Postoperative cardiopulmonary complications historically noted to be of greatest concern after lung resection, *eg*, acute hypercapnea, mechanical ventilation lasting > 48 h, arrhythmias, pneumonia, pulmonary emboli, myocardial infarction, and lobar atelectasis requiring bronchoscopy,[3] now may be more effectively managed.

Following lung resection, it is generally accepted that postoperative lung function will decrease. Serial studies have shown that lung function and exercise capability decrease within the first several months following lung cancer resection, but may recover to a small extent by 6 months.[4,5] It had been assumed that there would be lower limits on the acceptability of postoperative lung function, below which quality of life would be unacceptable due to pulmonary disability.[6] However, data relating changes in actual quality of life to removal of functioning lung tissue in patients with compromised lung function are limited. This issue has become particularly difficult to interpret with the recent resurgence of interest in lung volume reduction surgery (LVRS), and the possibility of simultaneously resecting a lung cancer and improving lung function with LVRS.

Ideally, the task of the preoperative physiologic assessment is to identify patients at high risk for perioperative complications and long-term disability from lung cancer resection surgery using the least invasive tests possible. The purpose of this preoperative physiologic assessment is twofold: to enable adequate counseling of the patient on treatment options and risks so that they can make a truly informed decision, and to identify possible steps to reduce the risks of perioperative complications and long-term pulmonary disability.

General Issues for Lung Cancer Surgery

All patients with lung cancer should be seen by a physician interested in the management of this disease. Patients seen by specialists will have higher rates of diagnosis, referral to surgeons and oncologists, and treatment with better outcomes.[7,8] A multidisciplinary team approach is essential in the assessment of these patients. The proposed procedure should be discussed with the patient and relatives.

Age should not be a reason to deny patients with lung cancer access to lung cancer services.[9] As the population ages, the number of patients ≥ 70 years old will rise; it is estimated that ≥ 40% of patients with lung cancer in 2005 will be ≥ 75 years old.[8] For elderly patients (> 70 years old), the mortality from reported series for lobectomy is between 4% and 7%, and for pneumonectomy averages 14%.[2,10,11] These rates are higher than for patients < 70 years old and the differential between the mortality of pneumonectomy and lobectomy is larger in elderly patients when compared to younger patients, but these differences may be more a function of comorbidity than age alone. Information is limited on the mortality rates for lung cancer resection in the very elderly (> 80 years old) but suggest that the very elderly can tolerate lobectomy.[10]

As with any planned major operation, especially in a population predisposed to atherosclerotic cardiovascular disease by cigarette smoking, a preoperative cardiovascular risk assessment should be performed. The approach to this risk assessment (Table 1) has been described in the American College of Cardiology and American Heart Association guidelines for perioperative cardiovascular evaluation for noncar-

*From the Department of Respiratory Medicine (Dr. Beckles), Royal Free Hospital, London, UK; Department of Respiratory Medicine (Dr. Spiro), Middlesex Hospital, London, UK; Pulmonary, Critical Care and Respiratory Services (Dr. Colice), Washington Hospital Center, Washington, DC; and Department of Medical Oncology (Dr. Rudd), St. Bartholomew's Hospital, Smithfield, London, UK.
Correspondence to: Stephen G, Spiro, MD, Department of Respiratory Medicine, The Middlesex Hospital, Mortimer St, London W1T 3AA, United Kingdom; e-mail: stephen.spiro@uclh.org

Table 1—*Clinical Predictors of Increased Preoperative Cardiovascular Risk**

Major	
	Unstable coronary syndromes
	Recent myocardial infarction with evidence of important ischemic risk by clinical symptoms or noninvasive study
	Unstable or severe angina
	Decompensated congestive heart failure
	Significant arrhythmia
	Severe valvular disease
Intermediate	
	Mild angina pectoris
	Prior myocardial infarction by history or pathologic Q waves
	Compensated or prior congestive heart failure
	Diabetes mellitus
Minor	
	Advanced age
	Abnormal ECG (left ventricular hypertrophy, left bundle-branch block, ST-T abnormalities
	Rhythm other than sinus rhythm
	Low functional capacity (*eg*, inability to climb stairs)
	History of stroke
	Uncontrolled systemic hypertension

*Adapted from Eagle et al.[12]

diac surgery.[12] The presence of coronary artery disease increases the risk of nonfatal myocardial infarction or death within 30 days of noncardiac surgery.

Reommendations

1. Patients with lung cancer should be seen by physicians interested in the management of this disease. Level of evidence, fair; benefit, substantial; grade of recommendation, B
2. Patients with lung cancer should be assessed by a multidisciplinary team for their suitability for surgery; there should be liaison between the chest physician, thoracic surgical team, and oncologist in all cases prior to surgery. Level of evidence, poor; benefit, substantial; grade of recommendation, C
3. Patients with lung cancer should not be denied lung resection surgery on the grounds of age alone. Level of evidence, fair; benefit, substantial; grade of recommendation, B
4. Patients with lung cancer undergoing surgery should have a preoperative cardiologic evaluation carried out according to established guidelines. Level of evidence, fair; benefit, substantial; grade of recommendation, B

Spirometry and Diffusing Capacity

The FEV_1 obtained by spirometry is the most commonly used test to assess suitability of patients with lung cancer for surgery. Spirometry should be performed when the patient is in clinically stable condition and receiving maximal bronchodilator therapy. The FEV_1 can be expressed in either absolute values or as a percentage of predicted.

There have been several studies looking at the minimum absolute values of FEV_1 that, as a single measurement, will predict whether a patient will survive a pneumonectomy and still have a good level of habitual activity. Many studies are retrospective and have small numbers of patients. A review of the literature suggests an $FEV_1 > 2$ L as a safe lower limit for pneumonectomy and > 1.5 L for a lobectomy.[13,14,15] In the British Thoracic Society (BTS) guidelines, data from $> 2,000$ patients in three large series in the 1970s have shown that a mortality rate of $< 5\%$ can be achieved if the preoperative FEV_1 is > 1.5 L for a lobectomy and > 2 L for a pneumonectomy.[10] A major pragmatic difficulty in assembling our recommendations is that the literature is heavily based on making predictions for resection using absolute values of FEV_1. This approach might bias against older patients, people of small stature, and female patients who might tolerate lower levels of lung function. Although it is not possible to recalculate percentage of predicted values from the BTS data, an $FEV_1 > 80\%$ predicted also indicates that the patient should be considered suitable for pneumonectomy without further evaluation.[16]

Interest in the diffusing capacity of the lung for carbon monoxide (DLCO) as a useful marker of operative risk was stimulated by a study of Ferguson et al,[17] who related preoperative DLCO to postresection morbidity and mortality in 237 patients. Patients were selected for surgery on the basis of clinical evaluation and spirometry, but not the DLCO, which was also measured. They found the preoperative DLCO expressed as a percentage of predicted to have a higher correlation with postoperative deaths than the FEV_1 expressed as percentage of predicted, or any other factor tested. They noted a DLCO of $< 60\%$ predicted was associated with increased mortality. Also, the risk of pulmonary complications increased twofold to threefold with a DLCO $< 80\%$ normal.

Spirometry and DLCO measurements should be viewed as complementary physiologic tests. If there is evidence of interstitial lung disease on radiographic studies or undue dyspnea on exertion, even though the FEV_1 may be adequate, a DLCO should be obtained. In a prospective study of 137 patients with operable tumor, those with an $FEV_1 > 80\%$ predicted, a DLCO $> 80\%$ predicted, and no significant cardiac history were all suitable for pneumonectomy.[16] There were no deaths in this group. In this study, patients with either an FEV_1 or a DLCO < 80% predicted had additional physiologic testing performed.

Recommendations

5. In patients being considered for lung cancer resection, spirometry should be performed. If the FEV_1 is > 80% predicted normal or > 2 L, the patient is suitable for resection including pneumonectomy without further evaluation. If the FEV_1 is > 1.5 L, the patient is suitable for a lobectomy without further evaluation. Level of evidence, fair; benefit, substantial; grade of recommendation, B
6. In patients being considered for lung cancer resection, if there is evidence of interstitial lung disease on radiographic studies or undue dyspnea on exertion, even though the FEV_1 might be adequate, DLCO should be measured. Level of evidence, fair; benefit, substantial; grade of recommendation, B
7. In patients being considered for lung cancer resection, if either the FEV_1 or DLCO are < 80% predicted, postoperative lung function should be predicted through additional testing. Level of evidence, fair; benefit, substantial; grade of recommendation, B

Predicted Postoperative Values of Lung Function

The extent of further evaluation in patients with diminished pulmonary reserve depends on the extent of planned pulmonary resection: pneumonectomy, lobectomy, wedge resection, or segmentectomy. In patients with compromised lung function preoperatively, it is therefore essential to estimate the likely pulmonary reserve postresection. Approaches to obtaining the predicted postoperative (ppo) lung function have relied on several different methods to estimate the amount of functioning lung tissue that would be lost along with the surgical resection. The methods used, including ventilation scans,[14,18–21] perfusion scans,[6,14,18–24] quantitative CT,[25,26] and simply counting the number of segments to be removed,[23,27] seem to provide similar quantitative estimates of ppo lung function. Recommended approaches use a radionuclide perfusion scan with Tc-labeled macroaggregates of albumin to estimate the ppo FEV_1 and DLCO after pneumonectomy and the number of segments remaining for postlobectomy values.[10] The percentage of ppo (%ppo) values for FEV_1 and DLCO are routinely used instead of absolute values.

%ppo FEV_1 After Pneumonectomy

%ppo FEV_1 is calculated using the following formula, which can also be used to calculate ppo and %ppo DLCO:

$$\text{ppoFEV1} = \text{preoperative } FEV_1 \times (1 - \text{fraction of total perfusion for the resected lung})$$

where ppo FEV_1 is expressed as percentage of predicted to calculate the %ppo FEV_1. The preoperative FEV_1 is taken as the best measure postbronchodilator. A quantitative radionuclide perfusion scan is performed to measure the relative function of each lung. Although several studies have demonstrated good correlation between the actual postoperative FEV_1 and the ppo FEV_1,[14,19,28] the %ppo values estimated by the perfusion method may be up to 10% less than actual measured values 3 months postresection. This therefore errs on the side of safety.[23,24,29]

%ppo FEV_1 After Lobectomy

The value of %ppo FEV_1 is strongly correlated with the actual postoperative FEV_1 when considering the number of segments to be removed at operation.[14,27] Calculating the %ppo FEV_1 by the number of segments removed is similar to the method used for perfusion scan:

$$\text{ppo}FEV_1 = \text{preoperative } FEV_1 \times (\text{No. of segments remaining/total No. of segments})$$

where ppo FEV_1 is expressed as a percentage of predicted to give %ppo. The lungs have the following 19 segments: right upper lobe (3 segments), right middle lobe (2 segments), right lower lobe (5 segments), left upper lobe (3 segments), lingual (2 segments), and left lower lobe (4 segments). This method can also be applied to segmentectomies because lobectomy does not cause a significantly greater loss of function when compared to segmentectomy.[30] This same formula may be used to calculate ppo and %ppo DLCO.

Olsen et al[6] suggested a threshold ppo FEV_1 of 0.8 L as the lower limit for surgical resection. However, Pate and colleagues[31] found that patients with a mean ppo FEV_1 of 0.7 L tolerated thoracotomy for lung cancer resection. This experience might have reflected resection of less lung tissue than anticipated. The main objection to using an absolute value of ppo FEV_1 as a threshold for operability is that it might prevent older patients, small stature people, and females patients, all of whom might tolerate a lower absolute FEV_1, from having a potentially curative lung cancer resection. Consequently, establishing a threshold for lung function expressed as %ppo rather than absolute ppo would be desirable.

Case series with small numbers of patients have shown that perioperative risks increase substantially when the %ppo FEV_1 is < 40% of predicted normal.[18,23,24,32–34] Markos et al[18] reported that three of six patients with a %ppo FEV_1 < 40% died in the perioperative period. Wahi et al[34] found a perioperative mortality rate of 16% in patients with a %ppo FEV_1 of < 41%, vs 3% with those with better predicted lung function. Pierce and colleagues[23] found that 5 of 13 patients with a %ppo FEV_1 < 40% died soon after operation, and Bolliger et al[24] reported that 2 of 4 patients with similar lung function died of respiratory failure perioperatively. Nakahara et al[35,36] found an especially high postoperative mortality rate (6 of 10 patients, 60%) when the %ppo FEV_1 was < 30%.

As a result of the observation by Ferguson et al[17] that the DLCO, expressed as the %ppo, was a strong predictor of mortality, others have also found that perioperative risks increase substantially when the %ppo DLCO < 40%.[17,18,23] Pierce et al[23] suggested that a product of %ppo FEV_1 and %ppo DLCO < 1,650 might serve as a more discriminating threshold for perioperative risk assessment. Others have made a similar observation.[37]

Although a %ppo FEV_1 or DLCO < 40% indicates increased risk for perioperative complications, including death, from lung cancer resection, these patients can be successfully operated on. Ribas et al[37] described a selected group of 65 patients who met these physiologic criteria but still underwent curative intent lobectomy/wedge resection (n = 44) or pneumonectomy (n = 21). There were only four postoperative deaths (6.2% mortality rate), and cardiopulmonary complications occurred in 31 patients (47.7%). Although this study indicates that lung cancer resection can be performed with an acceptable perioperative risk even in patients with poor lung function reserve, it is prudent to more thoroughly evaluate these patients prior to pulmonary resection.

Recommendation

8. In patients with lung cancer being considered for surgical resection, either a %ppo FEV_1 < 40% or a %ppo DLCO < 40% indicate a high risk for perioperative death and cardiopulmonary complications. These patients should undergo exercise testing preoperatively. Level of evidence, fair; benefit, substantial; grade of recommendation, B
9. In patients with lung cancer being considered for surgical resection, either a product of %ppo FEV_1 and %ppo DLCO < 1,650 or a %ppo FEV_1 < 30% indicate a very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options for their lung cancer. Level of evidence, poor; benefit, substantial; grade of recommendation, C

Exercise Testing

Cardiopulmonary Exercise Testing

Formal cardiopulmonary exercise testing (CPET) is a sophisticated physiologic testing technique that includes recording the exercise ECG, heart rate response to exercise, minute ventilation, and oxygen uptake per minute. Maximal oxygen consumption ($\dot{V}O_2max$) is calculated from this type of exercise test. Algorithms for the preoperative physiologic assessment of patients being considered for lung cancer resection have incorporated use of CPET as an adjunct to estimating the %ppo FEV_1 and DLCO.[10,16] However, there remains the practical difficulty as to when to recommend CPET, as it is readily acknowledged not to be widely available. We have taken the view of the BTS recommendations that exercise testing should be performed if perfusion lung scanning and calculation of %ppo FEV_1 and DLCO confirms borderline function (< 40%). It is suggested that if an institution is not equipped to perform CPET, patients in high-risk groups should be sent to a specialist center for this evaluation.

Numerous studies have examined the relationship between $\dot{V}O_2max$ and perioperative complications. Risk for perioperative complications can generally be stratified by $\dot{V}O_2max$. Patients with a preoperative $\dot{V}O_2max$ of > 20 mL/kg/min are not at increased risk of complications or death.[1,18,31,38–41] Those patients with $\dot{V}O_2max$ < 10 mL/kg/min have a very high risk for postoperative complications.[3,10,16,24,32,42,43] Bechard and Wetstein[42] reported that 2 of 7 patients with $\dot{V}O_2max$ < 10 mL/kg/min died in the postoperative period; Olsen et al[43] described deaths in 5 of 11 patients; and Holden and colleagues[32] noted deaths in 2 of 4 patients. $\dot{V}O_2max$ < 15 mL/kg/min indicates an increased risk of perioperative complications.[1,3,44,45] However, it should be noted that not all authors agree that perioperative complication rates can that clearly be stratified by $\dot{V}O_2max$.[37]

In patients with borderline lung function, $\dot{V}O_2max$ may be helpful in further evaluating the risk for perioperative complications. Morice et al[40] showed that in subjects with a ppo FEV_1 < 33%, eight patients underwent lobectomy because $\dot{V}O_2max$ > 15 mL/kg/min was achieved, and no fatal complications occurred. Other studies have made similar observations.[4,31] In patients with both a low %ppo FEV_1 and a low %ppo DLCO (both < 40% predicted), $\dot{V}O_2$max < 15 mL/kg/min indicates a group with a very high surgical risk.[44]

Pulmonary Artery Pressures and DLCO

Measurements of pulmonary arterial pressure during exercise have not proven to be helpful in predicting which patients will acquire perioperative complications.[37,43] A study by Wang et al[46] found that measuring DLCO during exercise was a better predictor of perioperative risk than $\dot{V}O_2$max, but is a technically demanding technique and not readily available.

Stair Climbing and Walking Tests

If CPET is unavailable, another type of exercise test should be considered. Stair climbing has historically been used as a surrogate CPET. If patients were able to climb three flights of stairs, they were considered suitable candidates for lobectomy. Pneumonectomy candidates were expected to be able to climb five flights of stairs. This approach was found to correlate with lung function: climbing three flights reflected an FEV_1 > 1.7 L and five flights indicated an FEV_1 > 2 L.[47] However, stair climbing is not performed in a standardized manner. The duration of the test, speed of ascent, number of steps per flight, height of each step, and criteria for stopping the test have not been well defined. However, in general terms, patients who can climb five flights of stairs will have a $\dot{V}O_2$max > 20 mL/kg/min. Conversely, patients who cannot climb one flight of stairs will have a $\dot{V}O_2$max < 10 mL/kg/min.[48]

Other surrogate CPETs are the shuttle walk and the 6-min walk, but data on the value of these tests in predicting $\dot{V}O_2$max are limited.[49] The shuttle walk requires that patients walk back and forth between two markers set 10 m apart. The walking speed is paced by an audio signal and the walking speed is increased each minute in a graded fashion. The end of the test occurs when the patient is too breathless to maintain the required speed. In one study, inability to complete 25 shuttles on two occasions suggested a $\dot{V}O_2$max of < 10 mL/kg/min.[50] For the 6-min walk, patients are instructed to walk as far as possible in the time allotted. Rest during the test is permissible. Interpretation of the distance walked in 6 min is currently not well standardized.[51]

Desaturation

Desaturation during an exercise test has been associated with increased risk for perioperative complications.[18,23,37,52] Greater than 4% desaturation indicates an increased risk for perioperative complications.[10]

Recommendations

10. In patients with lung cancer being considered for lung resection, $\dot{V}O_2$max < 10 mL/kg/min indicates a very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options for their lung cancer. Level of evidence, poor; benefit, substantial; grade of recommendation, C
11. Patients being considered for lung cancer resection who have $\dot{V}O_2$max < 15 mL/kg/min and both a %ppo FEV_1 and DLCO < 40% should be considered at very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options for their lung cancer. Level of evidence, poor; benefit, substantial; grade of recommendation, C
12. Patients being considered for lung cancer resection who walk < 25 shuttles on two shuttle walks or < one flight of stairs should be considered at very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options for their lung cancer. Level of evidence, poor; benefit, substantial; grade of recommendation, C

Arterial Blood Gas Tensions

Historically, hypercapnea ($PaCO_2$ > 45 mm Hg) has been quoted as an exclusion criterion for lung resection.[16,53,54] This recommendation was made on the basis of the association of hypercapnea with poor ventilatory function.[55] The few studies that address this issue, however, suggest that preoperative hypercapnea is not an independent risk factor for increased perioperative complications. Stein et al[56] showed hypercapnea was associated with serious postoperative respiratory difficulties in five patients; there were no deaths, despite a $PaCO_2$ > 45 mm Hg. In two series of lung cancer patients undergoing surgery,[57,58] perioperative complications were not higher in patients with preoperative hypercapnea. Preoperative hypoxemia, an arterial oxygen saturation (SaO_2) < 90%, has been associated with an increased risk of postoperative complications.[52]

Recommendations

13. In patients being considered for lung cancer surgery, $Pa_{CO_2} > 45$ mm Hg is not an independent risk factor for increased perioperative complications. However, further physiologic testing is advised. Level of evidence, poor; benefit, substantial; grade of recommendation, C
14. In patients being considered for lung cancer surgery, $Sa_{O_2} < 90\%$ indicates an increased risk for perioperative complications, and further physiologic testing is advised. Level of evidence, poor; benefit, substantial; grade of recommendation, C

Methods To Reduce Perioperative Risks

LVRS

LVRS for patients with severe emphysema is a controversial procedure. Some reports document substantial improvements in lung function, exercise capability, and quality of life in highly selected patients with emphysema following LVRS.[59] However, recently published results from a larger prospective, randomized, controlled trial indicate an increased mortality rate after LVRS in patients with either homogenous emphysema or a low DLCO.[60] Case series of patients referred for LVRS indicate that perhaps 3 to 6% of these patients may have coexisting lung cancer.[61,62] Anecdotal experience from these case series suggest that patients with extremely poor lung function can tolerate combined LVRS and resection of the lung cancer with an acceptable mortality rate and surprisingly good postoperative outcomes.[61–67]

McKenna et al[61] reported 11 cases of lung cancer (3%) in their group of 325 patients referred for LVRS. These 11 patients had an average preoperative FEV_1 of 0.65 L (range of FEV_1 percent predicted of 12 to 29%). None of these patients would have been acceptable for lung cancer resection based on traditional criteria but all underwent combined LVRS and resection of stage 1 lung cancers, either with lobectomy or wedge resection. There were no deaths or major complications; lung function and exercise capability were improved postoperatively. There have been other promising reports on the combination of LVRS and lung cancer resection in patients with very poor lung function.[62–67] Combining LVRS and lung cancer resection should probably be limited to those patients with heterogeneous emphysema, particularly emphysema limited to the lobe containing the tumor.[67,68]

Smoking Cessation

While smoking is strongly associated with lung cancer, it is also associated with an increased risk of postoperative complications. However there is little clinical evidence to suggest that smoking cessation before surgery is beneficial. One study in cardiac patients found that cessation of smoking 8 weeks prior to surgery decreased the perioperative complication rate; this is an impractical length of time in the context of surgery for lung cancer.[69]

Pulmonary Rehabilitation

As yet, there are no robust data to recommend the routine use of preoperative pulmonary rehabilitation for patients with lung cancer.

Recommendation

15. In patients with very poor lung function, combined LVRS and lung cancer resection may be considered if emphysema is heterogeneous and involves primarily the lobe to be resected. Level of evidence, poor; benefit, substantial; grade of recommendation, C

Summary

Patients with lung cancer often have concomitant obstructive lung disease and/or atherosclerotic cardiovascular disease as a consequence of their smoking habit. These diseases may place these patients at increased risk for perioperative complications, including death, after lung cancer resection. A careful preoperative physiologic assessment will be useful to identify those patients at increased risk and to enable an informed decision by the patient about the appropriate therapeutic approach to treating their lung cancer. This preoperative risk assessment must be placed in the context that lung cancer surgery is the most effective currently available treatment for this disease.

Summary of Recommendations

1. Patients with lung cancer should be seen by physicians interested in the management of this disease. Level of evidence, fair; benefit, substantial; grade of recommendation, B
2. Patients with lung cancer should be assessed by a multidisciplinary team for their suitability for surgery; there should be liaison between the chest physician, thoracic surgical team, and oncologist in all cases prior to surgery.

Level of evidence, poor; benefit, substantial; grade of recommendation, C

3. Patients with lung cancer should not be denied lung resection surgery on the grounds of age alone. Level of evidence, fair; benefit, substantial; grade of recommendation, B
4. Patients with lung cancer undergoing surgery should have a preoperative cardiologic evaluation carried out according to established guidelines. Level of evidence, fair; benefit, substantial; grade of recommendation, B
5. In patients being considered for lung cancer resection, spirometry should be performed. If the FEV_1 is > 80% predicted normal or > 2 L, the patient is suitable for resection including pneumonectomy without further evaluation. If the FEV_1 is > 1.5 L, the patient is suitable for a lobectomy without further evaluation. Level of evidence, fair; benefit, substantial; grade of recommendation, B
6. In patients being considered for lung cancer resection, if there is evidence of interstitial lung disease on radiographic studies or undue dyspnea on exertion, even though the FEV_1 might be adequate, DLCO should be measured. Level of evidence, fair; benefit, substantial; grade of recommendation, B
7. In patients being considered for lung cancer resection, if either the FEV_1 or DLCO are < 80% predicted, postoperative lung function should be predicted through additional testing. Level of evidence, fair; benefit, substantial; grade of recommendation, B
8. In patients with lung cancer being considered for surgical resection, either %ppo FEV_1 < 40% or %ppo DLCO < 40% indicate a high risk for perioperative death and cardiopulmonary complications. These patients should undergo exercise testing preoperatively. Level of evidence, fair; benefit, substantial; grade of recommendation, B
9. In patients with lung cancer being considered for surgical resection, either a product of %ppo FEV_1 and %ppo DLCO < 1,650 or %ppo FEV_1 < 30% indicate a very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options. Level of evidence, poor; benefit, substantial; grade of recommendation, C
10. In patients with lung cancer being considered for lung resection, $\dot{V}O_2max$ < 10 mL/kg/min indicates a very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options. Level of evidence, poor; benefit, substantial; grade of recommendation, C
11. Patients being considered for lung cancer resection who have $\dot{V}O_2max$ < 15 mL/kg/min and both %ppo FEV_1 and DLCO < 40% should be considered at very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options. Level of evidence, poor; benefit, substantial; grade of recommendation, C
12. Patients being considered for lung cancer resection who walk < 25 shuttles on two shuttle walks or less than one flight of stairs should be considered at very high risk for perioperative death and cardiopulmonary complications. These patients should be counseled about nonoperative treatment options. Level of evidence, poor; benefit, substantial; grade of recommendation, C
13. In patients being considered for lung cancer surgery, $PaCO_2$ > 45 mm Hg is not an independent risk factor for increased perioperative complications; however, further physiologic testing is advised. Level of evidence, poor; benefit, substantial; grade of recommendation, C
14. In patients being considered for lung cancer surgery, SaO_2 < 90% indicates an increased risk for perioperative complications, and further physiologic testing is advised. Level of evidence, poor; benefit, substantial; grade of recommendation, C
15. In patients with very poor lung function, combined LVRS and lung cancer resection may be considered if emphysema is heterogeneous and involves primarily the lobe to be resected. Level of evidence, poor; benefit, substantial; grade of recommendation, C

References

1 Walsh GL, Morice RC, Putnam JB Jr, et al. Resection of lung cancer is justified in high-risk patients selected by exercise oxygen consumption. Ann Thorac Surg 1994; 58:704–710

2 Damhuis RA, Schutte PR. Resection rates and postoperative mortality in 7,899 patients with lung cancer. Eur Respir J 1996; 9:7–10

3 Brutsche MH, Spiliopoulos A, Bolliger CT, et al. Exercise capacity and extent of resection as predictors of surgical risk in lung cancer. Eur Respir J 2000; 15:828–832

4 Nezu K, Kushibe K, Tojo T, et al. Recovery and limitation of exercise capacity after lung resection for lung cancer. Chest 1998; 113:1511–1516

5 Ali MK, Ewer MS, Atallah MR, et al. Regional and overall pulmonary function changes in lung cancer. Thorac Cardiovasc Surg 1983; 86:1–8

6 Olsen GN, Block AJ, Tobias JA. Prediction of postpneumonectomy pulmonary function using quantitative macroaggregate lung scanning. Chest 1974; 66:13–16
7 Muers MF, Haward RA. Management of lung cancer. Thorax 1996; 51:557–560
8 Brown JS, Eraut D, Trask C, et al. Age and the treatment of lung cancer. Thorax 1996; 51:564–568
9 Expert Advisory Group. A policy framework for commissioning cancer services. London, UK: Department of Health, 1995
10 BTS guidelines: guidelines on the selection of patients with lung cancer for surgery. Thorax 2001; 56:89–108
11 Yellin A, Hill LR, Lieberman Y. Pulmonary resections in patients over 70 years of age. Isr J Med Sci 1985; 21:833–840
12 Eagle KA, Brundage BH, Chaitman BR, et al. Guidelines for perioperative cardiovascular evaluation for noncardiac surgery: report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 1996; 27:910–948
13 Boushy SF, Billig DM, North LB, et al. Clinical course related to preoperative and postoperative pulmonary function in patients with bronchogenic carcinoma. Chest 1971; 59: 383–391
14 Wernly JA, DeMeester TR, Kirchner PT, et al. Clinical value of quantitative ventilation-perfusion lung scans in the surgical management of bronchogenic carcinoma. Thorac Cardiovasc Surg 1980; 80:535–543
15 Miller JI Jr. Physiologic evaluation of pulmonary function in the candidate for lung resection. Thorac Cardiovasc Surg 1993; 105:347–351
16 Wyser C, Stulz P, Soler M, et al. Prospective evaluation of an algorithm for the functional assessment of lung resection candidates. Am J Respir Crit Care Med 1999; 159:1450–1456
17 Ferguson MK, Little L, Rizzo L, et al. Diffusing capacity predicts morbidity and mortality after pulmonary resection. Thorac Cardiovasc Surg 1988; 96:894–900
18 Markos J, Mullan BP, Hillman DR, et al. Preoperative assessment as a predictor of mortality and morbidity after lung resection. Am Rev Respir Dis 1989; 139:902–910
19 Corris PA, Ellis DA, Hawkins T, et al. Use of radionuclide scanning in the preoperative estimation of pulmonary function after pneumonectomy. Thorax 1987; 42:285–291
20 Ali MK, Mountain CF, Ewer MS, et al. Predicting loss of pulmonary function after pulmonary resection for bronchogenic carcinoma. Chest 1980; 77:337–342
21 Bria WF, Kanarek DJ, Kazemi H. Prediction of postoperative pulmonary function following thoracic operations. Thorac Cardiovasc Surg 1983; 86:186–192
22 Giordano A, Calcagni ML, Meduri G, et al. Perfusion lung scintigraphy for the prediction of postlobectomy residual pulmonary function. Chest 1997; 111:1542–1547
23 Pierce RJ, Copland JM, Sharpe K, et al. Preoperative risk evaluation for lung cancer resection. Am J Respir Crit Care Med 1994; 150:947–955
24 Bolliger CT, Wyser C, Roser H, et al. Lung scanning and exercise testing for the prediction of postoperative performance in lung resection candidates at increased risk for complications. Chest 1995; 108:341–348
25 Wu MT, Chang JM, Chiang AA, et al. Use of quantitative CT to predict postoperative lung function in patients with lung cancer. Radiology 1994; 191:257–262
26 Wu MT, Pan HB, Chiang AA, et al. Prediction of postoperative lung function in patients with lung cancer. AJR Am J Roentgenol 2002; 178:667–672
27 Zeiher BG, Gross TJ, Kern JA, et al. Predicting postoperative pulmonary function in patients undergoing lung resection. Chest 1995; 108:68–72
28 Ladurie ML, Ranson-Bitker B. Uncertainties in the expected value for forced expiratory volume in one second after surgery. Chest 1986; 90:222–228
29 Bolliger C, Jordan P, Soler M, et al. Pulmonary function and exercise capacity after lung resection. Eur Respir J 1996; 9:415–421
30 Takizawa T, Haga M, Yagi N, et al. Pulmonary function after segmentectomy for small peripheral carcinoma of the lung. Thorac Cardiovasc Surg 1999; 118:536–541
31 Pate P, Tenholder MF, Griffin JP, et al. Preoperative assessment of the high-risk patient for lung resection. Ann Thorac Surg 1996; 61:1494–1500
32 Holden DA, Rice TW, Stelmach K, et al. Exercise testing, 6-min walk, and stair climb in the evaluation of patients at high risk for pulmonary resection. Chest 1992; 102:1774–1779
33 Gass GD, Olsen GN. Preoperative pulmonary function testing to predict postoperative morbidity and mortality. Chest 1986; 89:127–135
34 Wahi R, McMurtry MJ, DeCaro LF, et al. Determinants of perioperative morbidity and mortality after pneumonectomy. Ann Thorac Surg 1989; 48:33–37
35 Nakahara K, Monden Y, Ohno K, et al. A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer. Ann Thorac Surg 1985; 39:260–265
36 Nakahara K, Ohno K, Hashimoto J, et al. Prediction of postoperative respiratory failure in patients undergoing lung resection for lung cancer. Ann Thorac Surg 1988; 46:549–552
37 Ribas J, Diaz O, Barbera JA, et al. Invasive exercise testing in the evaluation of patients at high-risk for lung resection. Eur Respir J 1998; 12:1429–1435
38 Bechard D. Pulmonary function testing. In: LoCicero J III, ed. Diagnostic procedures in thoracic diseases: chest surgery clinics. Philadelphia, PA: W.B. Saunders, 1992; 565–586
39 Richter Larsen K, Svendsen UG, Milman N, et al. Exercise testing in the preoperative evaluation of patients with bronchogenic carcinoma. Eur Respir J 1997; 10:1559–1565
40 Morice RC, Peters EJ, Ryan MB, et al. Exercise testing in the evaluation of patients at high risk for complications from lung resection. Chest 1992; 101:356–361
41 Bolliger CT, Soler M, Stulz P, et al. Evaluation of high-risk lung resection candidates: pulmonary haemodynamics vs exercise testing. Respiration 1994; 61:181–186
42 Bechard D, Wetstein L. Assessment of exercise oxygen consumption as preoperative criterion for lung resection. Ann Thorac Surg 1987; 44:344–349
43 Olsen GN, Weiman DS, Bolton JWR, et al. Submaximal invasive exercise testing and quantitative lung scanning in the evaluation for tolerance of lung resection. Chest 1989; 95: 267–273
44 Bolliger CT, Jordan P, Soler M, et al. Exercise capacity as a predictor of postoperative complications in lung resection candidates. Am J Respir Crit Care Med 1995; 151:1472–1480
45 Smith TP, Kinasewitz GT, Tucker WY, et al. Exercise capacity as a predictor of post-thoracotomy morbidity. Am Rev Respir Dis 1984; 129:730–734
46 Wang JS, Abboud RT, Evans KG, et al. Role of CO diffusing capacity during exercise in the preoperative evaluation for lung resection. Am J Respir Crit Care Med 2000; 162:1435–1444
47 Bolton JWR, Weiman DS, Haynes JL, et al. Stair climbing as an indicator of pulmonary function. Chest 1987; 92:783–787
48 Pollock M, Roa J, Benditt J, et al. Estimation of ventilatory reserve by stair climbing. Chest 1993; 104:1378–1383
49 Solway S, Brooks D, Lacasse Y, et al. A qualitative systematic

overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. Chest 2001; 119:256–270
50 Singh SJ, Morgan MD, Scott S, et al. Development of a shuttle walking test of disability in patients with chronic airway obstruction. Thorax 1992; 47:1019–1024
51 ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166:111–117
52 Ninan M, Summers KE, Landreneau RJ, et al. Standardised exercise oximetry predicts postpneumonectomy outcome. Ann Thorac Surg 1997; 64:328–333
53 Celli BR. What is the value of preoperative pulmonary function testing? Med Clin North Am 1993; 77:309–325
54 Zibrak JD, O'Donnell CR, Marton K. Indications for pulmonary function testing. Ann Intern Med 1990; 112:763–771
55 Tisi GM. Preoperative evaluation of pulmonary function. Am Rev Respir Dis 1979; 119:293–310
56 Stein M, Koota G, Simon M. Pulmonary evaluation of surgical patients. JAMA 1962; 181:765–770
57 Kearney DJ, Lee TH, Reilly JJ, et al. Assessment of operative risk in patients undergoing lung resection: importance of predicted pulmonary function. Chest 1994; 105:753–759
58 Harpole DH, Liptay MJ, DeCamp MM Jr, et al. Prospective analysis of pneumonectomy: risk factors for major morbidity and cardiac dysrhythmias. Ann Thorac Surg 1996; 61:977–982
59 Geddes D, Davies M, Koyama H, et al. Effect of lung-volume-reduction surgery in patients with severe emphysema. N Engl J Med 2000; 343:239–245
60 National Emphysema Treatment Trial Research Group. Patients at high risk of death after lung-volume-reduction surgery. N Engl J Med 2001; 345:1075–1083
61 McKenna RJ, Fischel RJ, Brenner M, et al. Combined operations for lung volume reduction surgery and lung cancer. Chest 1996; 110:885–888
62 DeMeester SR, Patterson GA, Sundaresan RS, et al. Lobectomy combined with volume reduction for patients with lung cancer and advanced emphysema. Thorac Cardiovasc Surg 1998; 115:681–688
63 Clark T, Martinez F, Paine R, et al. Lung volume reduction surgery alters management of pulmonary nodules in patients with severe COPD. Chest 1997; 112:1494–1500
64 DeRose JJ, Argenziano M, El-Amir N, et al. Lung reduction operation and resection of pulmonary nodules in patients with severe emphysema. Ann Thorac Surg 1998; 65:314–318
65 Rozenshtein A, White CS, Austin JHM, et al. Incidental lung carcinoma detected at CT in patients selected for lung volume reduction surgery to treat severe pulmonary emphysema. Radiology 1998; 207:487–490
66 Allen GM, DeRose JJ. Pulmonary nodule resection during lung volume reduction surgery. AORN J 1997; 66:808–818
67 Edwards JG, Duthie DJR, Waller DA. Lobar volume reduction surgery: a method of increasing the lung cancer resection rate in patients with emphysema. Thorax 2001; 56:791–795
68 Mentzer SJ, Swanson SJ. Treatment of patients with lung cancer and severe emphysema. Chest 1999; 116:477S–479S
69 Warner MA, Divertie MB, Tinker JH. Preoperative cessation of smoking and pulmonary complications in coronary artery bypass patients. Anesthesiology 1984; 60:380–383