Journal of BUON **14:** 381-389, 2009

REVIEW ARTICLE

Non small cell lung cancer: surgical treatment in the elderly

A. Stamatelopoulos[1], F. Kadjianis[2], L. Zoganas[1]

[1]*Department of Thoracic Surgery and* [2]1st Department of General Surgery, "Red Cross" Hospital of Athens, Athens, Greece

Summary

Lung cancer resection in elderly patients is justified and has decreasing morbidity and mortality rates. Careful patient selection and operative planning are necessary, however. It is wise to have a diagnosis and staging done before the patient arrives in the operating theater. The surgeon should avoid extended resections when possible. In addition, elderly patients should be ambulated as soon as possible and adequate pain control should be ensured. Finally, the stage of the disease and occurrence of cardiopulmonary complications are the main determinants of outcome.

Key words: elderly, lung cancer, postoperative management, preoperative evaluation, surgical treatment

Introduction

There is no set definition of an elderly patient. The US Department of Health and Human Services Administration on Aging uses 65 years as a figure for aging statistics. As health care and technological improvements are made, the population of older people worldwide is increasing. The World Health Organization estimates that there will be 800 million people older than 65 years by 2025. It is estimated that the number of people living with cancer in the 2050 will be 2.6 million, whereas in 2000, 1.3 million people were living with cancer. The number of people older than 65 years living with cancer is also estimated to double over that time period. The authors of this study believe that patients who are 70 years or older have decreased cardiopulmonary reserve and that these individuals comprise the "elderly" population with respect to lung cancer resection. There are patients whose physiology doesn't go together with their chronological age, however, and all patients need to be assessed on an individual basis [1-5].

Cancer is the leading cause of death for men aged 60-79 years and for women aged 40-79 years. It is the second leading cause of death, after heart disease, for both men and women aged 80 years and older. Lung cancer has caused the most cancer deaths annually in men and women since the late 1980s when it surpassed breast cancer deaths in women. Physicians and health professionals caring for patients who have lung cancer need to assess the optimal treatment for small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) in the growing population of elderly individuals. This article focuses only on NSCLC [6-9].

The life expectancy of persons aged 70, 80 and 90 years in the United States is 14.4, 8.6, and 4.7 years, respectively. A 75-year-old person will spend 75% of the rest of his or her life living independently, and an 80-year-old individual will spend 50% of that time living independently. The argument that elderly patients will not benefit from lung cancer treatment because of short life expectancy or decreased quality of life because of their advanced age is not valid [10-13].

Characteristics

Earlier studies concluded that there was a different behavior of NSCLC in elderly patients. Elderly patients who were diagnosed with lung cancer seemed to have tumors that were less aggressive, more localized, and

Correspondence to: Athanassios G. Stamatelopoulos, MD, MSc, PhD. 79, Alexandras Avenue, 11474 Athens, Greece. Tel: +30 6944 324503, Fax: +30 210 6454474, E-mail: stamatel1970@yahoo.gr

Received 30-07-2008; Accepted 22-12-2008

slower to metastasize. Later studies demonstrated no age-related difference in behavior, stage at time of diagnosis (Table 1), or response to therapy. The issue of whether the subset of elderly patients who develop lung cancer more than 40 years after the cessation of smoking have a more indolent cancer than those who are still smoking and develop cancer has not been specifically studied. There are some data that younger patients diagnosed with NSCLC have more aggressive tumors. Four studies found a higher incidence of squamous cell cancer in older patients than in younger ones. In the studies by Mizushima et al. and Bemet et al. this finding was only true for men [9,11]. In the study by Sherman and Guidot, who compared distribution of cell type by age group, no statistical difference was found (Table 2) [12].

Symptoms and signs

Most elderly patients with lung cancer have symptoms or signs at the time of diagnosis. Nugent et al. found that 85% of patients older than 80 years had symptoms, the most common of which was cough. Many symptoms are nonspecific and can be attributed to other medical problems, such as ischemic cardiac disease, congestive heart failure, and chronic obstructive pulmonary disease. Cough, weight loss, and dyspnea occur in 40-50% of elderly patients who have lung cancer. Pain and hemoptysis are found in 20-40% of these patients. Hoarseness and dysphagia are lower in incidence (l-5%). Large-scale trials examining the utility of lung cancer screening showed no benefit for the general population, but there may be a role for lung cancer screening in elderly individuals, who have a two- to three-fold greater incidence of lung cancer compared with younger patients [9, 11,14,15].

Diagnosis and staging

Elderly patients have a higher incidence of other malignancies as well. In elderly patients with known prior malignancy, it is advantageous to know the diagnosis of lung masses or nodules before a surgical resec-

Table 1. Non-small cell lung cancer in elderly patients: distibution of stage

First author [Reference]	*Age (years)*	*Patients n*	*Stage (%)* *I*	*II*	*IIIA*	*IIIB*	*IV*
DeMaria [8]	>70	209	50	34	16	–	–
Bernet [11]	>70	120	60	21	19	–	–
Ishida [22]	>70	185	52	4	25	12	3
Mizushima [9]	>70	89	13	10	17	15	45
Osaki [41]	>70	272	40	9	33	7	9
Sioris [31]	>75	75	57	20	13	5	4
Sherman [12]	>70	64	64	3	33		–
Shirakusa [49]	>80	33	55	21	21	0	3
Nugent [10]	>80	108	33		18	49	
Koizumi [44]	>65	87	70	16	3	1	–
Massard [46]	>70	223	48	17	30		4
Morandi [42]	>70	85	57	14	22	7	

Table 2. Lung cancer in elderly patients: distribution of cell type

First author [Reference]	*Age (years)*	*Patients n*	*Histology (%)* *Squamous*	*Adenocarcinoma*	*Large cell*	*Small cell*
DeMaria [8]	>70	209	71	7	11	11
Bernet [11]	>70	120	64	22	10	4
Mizushima [9]	>70	89	47	29	3	4
Osaki [41]	>70	272	39	39	9	7
Sioris [31]	>75	75	48	40	12	0
Sherman [12]	>70	64	30	55	6	–
Shirakusa [49]	>80	33	36	48	–	–
Nugent [10]	>80	108	33	38	30	–
Koizumi [44]	>65	87	28	63	1	3
Massard [46]	>70	223	70	24	4	1
Morandi [42]	>70	85	60	34	2	4

tion is performed. A biopsy during bronchoscopy or percutaneous needle biopsy should be performed, if feasible. This allows better treatment planning and may eliminate unnecessary general anesthesia or thoracotomy in patients found to have metastatic disease or SCLC. Because most elderly patients have less cardiopulmonary reserve, avoidance of exploratory thoracotomy is advisable. In addition, to avoid risks of unnecessary or futile treatment, careful staging is vital. Mediastinoscopy or positron emission tomography should be performed in most, if not all, of elderly patients who are under consideration for lung resection. Multiple studies have shown poor outcome and prognosis for elderly patients undergoing surgery for N2 and N3 disease and, in general, these patients should not be treated surgicaly [10-12,14-17]. Thomas et al. found a survival benefit for those patients with locally advanced (T3 N0 M0, stage IIIA) NSCLC treated by resection, whereas Pagni et al. found poor survival in octogenarians with either T3 N0 or nodal stage IIIA disease. Thomas et al. also found increased complication rates after large chest wall resection. Elderly patients with T3 N0 disease should be considered for surgery only after careful consideration of an alternative treatment [14].

If metastatic disease is suspected, tissue confirmation is necessary before lung resection. Radiologists have become proficient at percutaneous liver and adrenal biopsies. Bone scans and brain MRI are required if patients have symptoms consistent with bone or brain metastases. Endoscopic ultrasound with biopsy is another useful diagnostic tool if suspicion exists for involvement of subcarinal lymph nodes or a paraesophageal mass that is not amenable to biopsy by mediastinoscopy, bronchoscopy, or percutaneous means [15,16].

Preoperative management

After primary lung cancer is determined in an elderly patient (and every patient), some fundamental tenets must be met before considering the patient for surgery. The length of expected survival after cancer resection must be long enough to justify recuperation time. These criteria are outlined by Pagni et al. [17] and are as follows: 1) The patient's expected lifespan with other concomitant disease must exceed the patient's survival with the unresected lung cancer (6-7 months); 2) The expected long-term survival benefit from the cancer resection must be long enough to justify the operation and recuperation from the operation; 3) The operative mortality risk must be low enough to warrant the operation; and 4) The operative morbidity must not cause excessive or chronic loss of quality of life. In a study of octogenarians, the same authors added another consideration of logical resource use [17,18]. In elderly patients, an assessment of the following factors will help the careful selection of appropriate candidates for surgery: 1) Pulmonary function; 2) Cardiac function; 3) Overall general condition; 4) Nutritional status; 5) Neurologic function; 6) Other medical problems; and 7) Social issues [19,20].

Naunheim et al. recommended that pulmonary function test criteria for lobectomy in octogenarian patients should include a partial pressure of arterial oxygen (PaO_2) of 65 mm Hg or greater, a partial pressure of arterial carbon dioxide ($PaCO_2$) less than 45 mm Hg, a diffusing capacity for carbon monoxide greater than 40% of predicted value, and a predicted postoperative forced expiratory volume in 1 second ($ppoFEV_1$) of 0.8 L. These are the same criteria used for most lung cancer resection candidates, regardless of age [21]. Ciriaco et al. found that patients aged 70 years and older with a preoperative FEV_1 of 55% or less of the predicted or a PaO_2 of 60 mm Hg or less had more postoperative complications compared with patients with a preoperative FEV_1 of 79% or greater or a PaO_2 of 82 mm Hg or greater [16]. Ishida et al. showed a correlation between the Brinkman index (number of cigarettes smoked per day x number of years smoked) and postoperative complications in patients aged 70 years and older, with a value of 801 being the critical number (roughly equivalent to 40 pack/years smoking history) [22]. Recommendations for estimation of the preoperative pulmonary status in octogenarians undergoing lung resection are more rigorous: a maximum ventilating volume (MVV) greater than 50% of the predicted and a preoperative FEV_1 of 50% or greater of the predicted values. For patients with borderline spirometry or PaO_2 findings, quantitative ventilation-perfusion scan or cardiopulmonary exercise testing to determine maximal oxygen uptake (VO_2max) can be used to select appropriate candidates for resection. The quantitative perfusion scan allows better estimation of the ppoFEV by quantifying the amount of function that each lung and each zone of each lung contributes. A VO_2max greater than 20 cc/kg/min or 75% of the predicted value predicts adequate pulmonary function after any lung resection [23]. This criterion is the same as the one generally used in patients undergoing lung resection, but elderly patients may need preoperative evaluation to confirm adequate function more often than younger patients [21-23].

Many elderly patients have cardiac disease, and preoperative assessment starts with a careful history for cardiac symptoms for ischemia or congestive failure, arrhythmia, or valvular heart disease. A 12-lead electrocardiogram (ECG) should be obtained and compared

with previous ECGs. The American College of Cardiology and the American Heart Association have published guidelines for cardiac workup for noncardiac surgery [24]. If there are relevant symptoms, medical history, or changes on the ECG, a stress test should be performed. The authors of this review favor a dobutamine stress echocardiogram if ischemia, valvular disease, decreased ventricular function, or congestive failure are suspected or known. If the stress test is negative for all of these conditions, the patient can proceed to surgery from a cardiac standpoint. If there is doubt, a cardiac catheterization or other testing is performed. The successful management of lesions or dysrhythmias by interventional cardiology or electrophysiology measures allows the patient to proceed to surgery in a more timely fashion. If cardiac surgery is necessary, nonsurgical treatment of the lung cancer for patients aged 70 years and older should be considered. Lung resection should be avoided in octogenarians who have cardiac disease that would require operative repair. If a patient is candidate for cardiac surgery, regardless of the planned lung surgery, appropriate therapy for the lung cancer can be reassessed, depending on the patient's recovery after cardiac surgery [21].

Another useful global assessment of the eligibility of elderly patients to have lung resection is a performance status scale, such as the Karnofsky or the Eastern Cooperative Oncology Group (ECOG) performance status scale. Naunheim et al. recommended a Karnofsky scale value of 80 or greater for an octogenarian to be eligible for lung resection. The patient should be questioned about his or her functional status, including ability to climb stairs, walk on level ground or inclines, and daily activities. Patients with poor functional status before surgery will likely worsen in the immediate postoperative period and have difficulty with rehabilitation, physical, and chest therapy. The overall outcome may be increased complications, lengthy rehabilitation, marked decrease in quality of life, and need for a different living arrangement after discharge [22-24].

Studies have demonstrated increased complication rates and poor outcome in patients with impaired nutrition [25,26]. The Mini Nutritional Assessment can easily evaluate nutritional status. It involves simple measurements and a brief questionnaire, which requires only 10 min to complete. It stratifies patients into one of three categories: 1) Adequately nourished; 2) At risk of malnutrition; or 3) Protein/caloric undernourished. Albumin level also helps determine nutritional status and may predict risk of postoperative complications [27,28].

A neurologic examination, as part of the physical examination, will identify potential problems, such as unsteadiness, weakness, mental status changes, visual problems, and memory deficits, which affect recovery from major surgery. Other medical problems requiring medical optimization include diabetes mellitus, hypertension and cerebrovascular disease. When more of these other comorbid diseases exist, the postoperative care and management of the elderly patient becomes more challenging [20].

Patients with previous malignancy who have been treated and are disease-free should not be considered inoperable for their lung cancer. Workup to ensure control of the previous cancer is recommended before proceeding with lung resection. Performing curative lung resection with other known malignancy that is not controlled is illogical and not beneficial [19,20].

Preoperative preparation

Atrial fibrillation, or flutter, is one of the most common postoperative complications. It can result in increases in length of stay, testing, laboratory studies, medications, including anticoagulation drugs, and may require cardioversion. It increases the risk of stroke from embolism. Because older age is the only risk factor for the development of postoperative atrial arrhythmia that has been observed in multiple studies, the authors of this review recommend prophylaxis with β-blockers, calcium channel blockers, d-sotalol, or amiodarone. The goal for β-blocker or calcium channel blocker dose before surgery is to lower the heart rate to 70 beats/min, if the patient's blood pressure permits. Amiodarone and sotalol are more costly, but do not have the same degree of risk of hypotension. Due to the long half-life of amiodarone it is vital to start its administration approximately 2 weeks before surgery. Patients taking anticoagulants should stop them with adequate time for the effect to dissipate. Tight glucose control has been proved to decrease the incidence of infection in patients with diabetes. In addition, the regulation of thyroid replacement in patients with hypothyroidism is necessary [24].

Smoking cessation should be emphasized. Previous literature suggests that once a patient quits, a minimum of 6 weeks before lung resection helps avoid the bronchorrhea that occurs while the bronchial mucosal is regenerating. The risk of pulmonary complications after lung resection is decreased with smoking cessation. Nicotine replacement, buproprion, and smoking cessation support groups aid in successful smoking abstinence [29].

The optimization of pulmonary status also includes compliance with pulmonary medications, treatment for pneumonia or bronchitis, and adequate time for recovery before general anesthesia and removal of a functioning lung. Preoperative breathing exercises and postoperative pulmonary rehabilitation have been shown to decrease

the incidence of pulmonary complications postoperatively [30]. Participation in postoperative pulmonary rehabilitation can be on an inpatient or outpatient basis and is supervised by pulmonary medicine physicians and physical therapists [23,24].

Social issues may need to be addressed preoperatively. A discharge disposition and the likelihood of the need for short-stay rehabilitation should be formulated. Studies have shown that 85-90% of elderly patients were discharged to home after lung resection [21].

Intraoperative management

Monitoring with ECG, pulse oximetry, end tidal CO_2, arterial line, and temperature are necessary. If available, Bispectral index (BIS), (Aspect Medical Systems, Newton, Massachusetts, www.aspectms.com) monitoring is helpful to determine and maintain the desired anesthetic depth. Adequate padding of the preoperative tests and the recognition of limitations of the range of motion of joints in elderly patients are of paramount importance while positioning these patients. The use of forced-air heating units will aid in maintaining patient temperature while the chest is open. Bladder catheterization allows gross assessment of end organ perfusion and volume status. If an epidural catheter is in place and being used during the operation, careful dosing is needed if local anesthetic is given to prevent hypotension from decreased sympathetic tone [24].

Intraoperative bronchoscopy is performed to assess endobronchial lesions and to check the planned bronchial tumor resection plane, if this has not been performed previously by the surgeon. Thomas et al. recommended lymph node sampling instead of total mediastinal lymphadenectomy to avoid possible complications of more radical dissection, such as recurrent laryngeal nerve palsy, chyle leak, or damage to the vagus nerve, phrenic nerve, esophagus, or tracheobronchial tree [14]. The risk of these complications is very low, however. We believe that the main advantage of lymph node sampling is shorter operative time for an elderly patient, with resulting decreased time of single-lung ventilation, atelectasis, and general anesthetic. Pneumonectomy, especially on the right side, should be avoided if possible, and sleeve resections are preferred if feasible with a clear margin [20,24].

Postoperative management

Patients can be transferred from the recovery room to a step-down unit or postsurgical telemetry unit. ECG monitoring should be performed for 4-5 days postoperatively or for the duration of the patient's hospital stay because of the 20-30% risk of supraventricular arrhythmia [28-31].

Pain control can be a challenging issue in elderly patients. Although many health care providers believe that elderly patients experience less pain than younger patients, pain perception studies do not uniformly support this idea. Confused elderly patients may not complain of pain or be believed when they complain of pain. Elderly patients are more sensitive to narcotic pain medications, the side effects of which include respiratory depression, pruritus, ileus, and urinary retention. Nausea seems to occur less frequently in elderly patients who may require lower doses of antiemetic medication than younger patients. Apart from narcotics pain control after thoracotomy can also be achieved by epidural infusion, pleural infusion, or intravenous patient-controlled analgesia. Intramuscular injections should be avoided in elderly patients because of the steep dose-response curve. Nonsteroidal anti-inflammatory drugs (NSAIDs) can be used as adjunct medication, but they usually will not provide enough pain relief on their own. The incidence of renal failure or gastrointestinal bleeding is rare when using low doses of NSAIDs [32].

Patients should be mobilized by the evening of surgery or the next day. Pulmonary toilet, cough, deep breathing, and incentive spirometry are helpful adjuncts to physical therapy. If the patient has emphysema, nebulizer or inhaler treatments are given. If secretions are problematic, a mini tracheostomy can be placed to aid suctioning [30].

Delirium may occur in as many as 60% of operated patients aged 65 years and older. Risk factors include older age, cardiopulmonary disorders, central nervous system disease, electrolyte abnormalities, gastrointestinal or genitourinary disorders, hypoalbuminemia, infection, polypharmacy, sensory deprivation, overstimulation, environmental changes, and trauma. Management starts with the recognition of delirium and an evaluation for medical causes. If a medical reason is found, it should be treated. Other interventions for treating delirium include reorienting the patient, decreasing sensory overload or deprivation, and reassuring the patient. If the patient is agitated and there is a risk of harm, small doses of haloperidol or resperidol can be used. Usage of benzodiazepines and diphenhydramine should be avoided, as these agents tend to increase confusion in elderly individuals. Ensuring that patients have personal possessions, such as eyeglasses and hearing aids, is also necessary. Consultation with geriatricians, neurologists, and psychiatrists will aid diagnosis and management [31].

Results of surgery

All studies confirm that there is a survival benefit with resection of NSCLC in elderly patients. For patients not undergoing surgical treatment, survival ranges from 6 months to 1 year, with or without other therapy [32-37]. Table 3 shows the operative outcomes after thoracotomy and lung resection by author. The operative mortality ranges from 1-21%. There was a correlation between the frequency of pneumonectomy rate and the perioperative mortality rate in some studies, but not in others. Bernet et al. performed pneumonectomy in 22% of their elderly patients and reported a 30-day mortality rate of only 2.5% [11]. They gave no data on in-hospital mortality, however. Yamamoto et al. found no increased mortality after pneumonectomy in elderly patients compared with younger patients [38]. The authors attributed the lack of increased mortality in elderly patients to very careful patient selection as evidenced by the significantly lower frequency of pneumonectomy (10 vs. 19%) performed in elderly patients compared with patients younger than 70 years. Mizushima et al. compared postoperative mortality and morbidity rates between patients younger than 70 years and patients aged 70 years and older who underwent pneumonectomy [15]. Both rates were higher in the elderly group, although there was no difference in prognosis between the two groups. Naunheim et al. recommended that pneumonectomy should no longer be performed in octogenarians because of the higher morbidity and mortality they encountered [21]. Whittle et al. used a random sample of Medicare claims data and found that the perioperative mortality rate of patients aged 70 years and older who had pneumonectomy was 17% during 1983-1985, whereas the perioperative mortality rate for lobectomy was 7.4% for patients aged 70 years and older [39]. Kiser and Detterbeck reviewed data from multiple studies for patients older than 70 years and found that mortality after pneumonectomy was 16-25% [40]. Despite these mixed findings, there is general consensus for performing lung conservation without sacrificing adequate cancer resection and avoidance of pneumonectomy when possible.

Cardiopulmonary complications are common in elderly patients. The most frequent complications early after the operation are atrial arrhythmias, pneumonia, prolonged air leak, and respiratory failure. Other common perioperative complications in elderly patients include delirium, congestive heart failure, bronchopleural fistula, stroke, and urinary retention. Osaki et al. found that the survival rate in octogenarians who underwent lung resection was lower in patients who had postoperative cardiopulmonary complications, whereas stage of disease, histologic cell type, or resectability had no influence on survival [41]. The number of patients was small (n=33), so these data must be interpreted with caution. Morandi et al. saw no significant difference in the rate of all complications between young and elderly patients (>70 years), but did find a higher rate of cardiovascular complications (14 vs. 29%; $p<0.01$) in elderly patients [42]. There was a trend toward a higher complication rate in elderly patients who underwent pneumonectomy compared with younger patients who also had pneumonectomy. The rates of respiratory and extrathoracic complications were statistically equivalent between the young and elderly groups. Ciriaco et al. found that patient survival at 12 months after resection was highly dependent on cardiorespiratory status [16]. Between 30 days and 12 months after resection, 10 of 75 patients died of cardiovascular complications

Table 3. Lung cancer resection in elderly patients: operative results

First author [Reference]	*Years*	*Age range years (mean)*	*Patients n*	*Perioperative mortality (%)*	*5-y survival (%)*	*Compl* [a] *(%)*	*Pneum (%)*
Yamamoto [38]	1969-98	71-82 (74)	132	2.9[b]	58	NA	10
Pagni [18]	1971-96	70-96 (75.2)	385	4.2[b]	NA	34	6
Bemet [11]	1972-94	70-85 (74)	120	2.5[c]	53	63	22
Ishida [22]	1974-89	>70	185	3[b]	48	37	6
Osaki [41]	1974-91	80-92 (82.4)	33	21[b]	32	67	9
Thomas [41]	1975-96	70-90 (74)	500	7.4[b]	34	19	27
Sioris [31]	1976-96	>75	75	9[b]	26	29	13
Sherman [12]	1977-84	70-84 (74.6)	64	9.4[c]	36	16	6
Naunheim [21]	1981-91	80-88 (82.7)	40	15[b]	25	45	12.5
Massard [46]	1983-92	70-84(72)	223	7.2[b]	33	27	29
Morandi [42]	1989-93	70-88 (73.4)	85	1.2[d]	28	55	13
Ciriaco [16]	1992-96	70-83 (76.3)	76	1.3[c]	53[e]	20	0

Compl: complications, NA: not available, Pneum: pneumonectomy. [a]all complications experienced during first 30 postoperative days or during same hospital stay, [b]30-day and in-hospital mortality, [c]in-hospital mortality only, [d]30-day mortality only, [e]4.5-year survival

(3 of heart failure, 2 of myocardial infarction, 1 of stroke) or respiratory failure (4 patients). Of these 10 patients, 8 had cardiorespiratory complications perioperatively. After 1 year, death was more likely caused by recurrent cancer. We believe that elderly patients are ideal candidates for minimally invasive lung resection. The avoidance of rib spreading and retraction should decrease the amount of postoperative complications caused by the inability to clear secretions, cough, breathe deeply, and ambulate secondary to pain.

A study by Mikami et al. showed decreased right ventricular (RV) function in the acute postoperative phase after thoracoscopic lobectomy compared with thoracotomy [43]. Koizumi et al. demonstrated improved pulmonary function results at 2.3 months in patients after thoracoscopic lobectomy compared with patients who had thoracotomy [44]. There may also be an immunologic benefit from less chest wall disruption and decreased inflammation. As thoracic surgeons become more proficient with thoracoscopic lobectomy, pneumonectomy, and mediastinal lymph node dissection, the pain and longer recovery time after thoracotomy may be alleviated. Thoracoscopy still exposes elderly patients to a general anesthetic and single-lung ventilation. There will also be situations in which thoracoscopy is not feasible or safe because of anatomic or technical factors, such as nodule location, pleural fusion, or physiologic inability to tolerate single-lung ventilation.

Koizumi et al. cautioned that surgeons must weigh the benefits of decreased chest wall damage from thoracoscopy vs. the increased length of the operation [44]. Operative times for video-assisted thoracoscopic (VAT) anatomic resection should decrease as surgeons become more familiar with VAT lobectomy and pneumonectomy. More studies comparing the hospital course and long-term outcomes of VAT resection in elderly patients will be published in the near future [45].

Surgeons need to assess and select which elderly patients are proper candidates for lung cancer resection [17,22,38,41,46]. The more involved workup and preoperative patient preparation are becoming routine as the patient population ages. The extent of surgical resection for each patient also needs consideration before arriving in the operating theater. There is a correlation with decreased morbidity and lesser extent of operation in many studies [16,31,39,47,48]. Sioris et al. reported complication rates of 13, 21, 50 and 60% after limited resection, lobectomy, bilobectomy, and pneumonectomy, respectively [31]. Lung conservation with adequate cancer resection is the goal. Segmentectomy and sleeve lobectomy rates may increase as the population ages. In Thomas et al. series, elderly patients had higher mortality rates after extended resections for chest wall, great vessel, carinal, main bronchus, or esophagus invasion [14]. Although Sioris et al. found a correlation of the extent of surgery with morbidity, they found no correlation with the extent of operation and mortality [31]. The same conclusion was reached by Bernet et al. Thomas et al. used "extended" resection when discussing resection of tissues other than lung, however, whereas Sioris et al. and Bernet et al. applied the term to increasing amount of lung tissue removed [11,14,31].

Survival for all comers is shown in Table 3. Most of these studies do not include patients with stage IV NSCLC, because those patients' disease is considered inoperable. Long-term survival rates from several studies by stage are shown in Table 4. The most important determinant of long-term survival is not chronologic age, but the extent of cancer. Ishida et al. compared perioperative morbidity and mortality and overall survival between a group of patients aged 29-69 with a group of patients aged 70 or older [22]. There was no significant difference in postoperative complication or perioperative mortality rate between the two groups. In addition, there was no difference in 5-year overall survival rates or survival by stage between the young and elderly groups. Morandi et al. also found no differences in survival between young and elderly groups [42].

Table 4. Lung cancer in elderly patients: survival rates

First author [Reference]	*Age (years)*	*Patients n*	*5-year survival by stage (%)*				
			I	*II*	*IIIA*	*IIIB*	*IV*
Yamamoto [38]	>70	132	58	–	–	–	–
Ishida [22]	>70	185	67	40	32	39	18
Mizushima [9]	>70	89	27[a]		1.5[a]		
Sioris [31]	>75	75	32	41[b]	22	12	0
Sherman [12]	>70	64	45	–	15		–
Shirakusa [49]	>80	33	79	–	31		–
Massard [46]	>70	223	51	37	15		

[a]3-year survival, [b]includes only stage IIB patients; stage IIA survival not calculated

Pagni et al. reported results of resection after neoadjuvant therapy; no difference in morbidity or mortality was found in their elderly patients [18]. Details about the regimen of neoadjuvant therapy administered were not given, however. Mizushima et al. and Sherman and Guidot found no difference in survival between younger and elderly patients who underwent neoadjuvant or adjuvant therapy [12,15]. Again, details of the regimens were not provided. Fowler et al. found a 43% mortality rate in patients with a median age of 55 years who had pneumonectomy after neoadjuvant therapy [47]. In elderly patients with decreased reserve, resection after chemoradiation will likely result in unacceptably high mortality and morbidity rates [48].

Conclusions

Age is sometimes used as an excuse not to resect NSCLC. Nugent et al. [10] noted that, although only 6% of patients younger than 45 years had stage I or II disease, 33% underwent surgical resection. In contrast, of the 33% of elderly patients who had stage I or II disease, only 6% underwent surgical resection. Elderly patients who are carefully selected for lung resection are undoubtedly stronger physiologically than others of the same age. Patients with adequate predicted postoperative lung function, no contraindications from other medical problems, good performance status, and social support should be offered standard resection for early-stage NSCLC.

References

1. Prentice T (Ed): World Health Report. Fifty facts from the World Health Report 1998. Available at: www.who.int/2001/archives/1998/pdf/factse.pdf. (Accessed August 24, 2003).
2. Simmonds MA. Cancer Statistics, 2003: further decrease in mortality rate, increase in persons living with cancer. CA Cancer J Clin 2003; 53: 54.
3. Jemal A, Murray T, Samuels A, Ghafoor A, Ward E, Thun MJ. Cancer Statistics 2003. CA Cancer J Clin 2003; 53: 5-26.
4. National Center for Health Statistics. In: Sonaik E (Ed): US Department of Health and Human Services. Hyattsville (MD): Census; 2000.
5. Katz S, Branch LG, Branson MH, Papsidero JA, Beck JC, Greer DS. Active life expectancy. N Engl J Med 1983; 309: 1218-1224.
6. Holmes EF, Heame E. Cancer stage-to-age relationship: implications for cancer screening in the elderly. J Am Geriatr Soc 1981; 29: 55-57.
7. Ershler WB, Socinski MA, Greene CJ. Bronchogenic cancer, metastases and aging. J Am Geriatr Soc 1983; 31: 673-676.
8. DeMaria LC, Cohen HJ. Characteristics of lung cancer in elderly patients. J Gerontol 1987; 42: 540-545.
9. Mizushima Y, Kashii T, Yoshida Y, Sugiyama S, Kobayashi M. Characteristics of lung cancer in the elderly. Anticancer Res 1996; 16: 3181-3184.
10. Nugent WC, Edney MT, Hammerness PG, Dain BJ, Maurer LH, Rigas JR. Non-small cell lung cancer at the extremes of age: impact on diagnosis and treatment. Ann Thorac Surg 1997; 63: 193-197.
11. Bemet F, Brodbeck R, Guenin M et al. Age does not influence early and late tumor-related outcome for bronchogenic carcinoma. Ann Thorac Surg 2000; 69: 913-918.
12. Sherman S, Guidot CE. The feasibility of thoracotomy for lung cancer in the elderly. JAMA 1987; 258: 927-930.
13. Baranovsky A, Myers MH. Cancer incidence and survival in patients 65 years of age and older. CA Cancer J Clin 1986; 36: 27-41.
14. Thomas P, Piraux M, Jacques LF, Gregoire J, Bedard P, Deslauriers J. Clinical patterns and trends of outcome of elderly patients with bronchogenic carcinoma. Eur J Cardiothorac Surg 1998; 13: 266-274.
15. Mizushima Y, Hirofumi N, Sugiyama S et al. Survival and prognosis after pneumonectomy for lung cancer in the elderly. Ann Thorac Surg 1997; 64: 193-198.
16. Ciriaco P, Zannini P, Carretta A et al. Surgical treatment of non-small cell lung cancer in patients 70 years of age or older. Int Surg 1998; 83: 4-7.
17. Pagni S, Federicon JA, Ponn RB. Pulmonary resection for lung cancer in octogenarians. Ann Thorac Surg 1997; 63: 785-789.
18. Pagni S, McKelvey A, Riordan C, Federico JA, Ponn RB. Pulmonary resection for malignancy in the elderly: is age still a risk factor? Eur J Cardiothorac Surg 1998; 14: 40-45.
19. Mohr DN. Estimation of surgical risk in the elderly: a correlative review. J Am Geriatr Soc 1983; 31: 99 -102.
20. Ebner H, Sudkamp N, Wex P, Dragojevic D. Selection and preoperative treatment of over-seventy-year-old patients undergoing thoracotomy. Thorac Cardiovasc Surg 1985: 33: 268-271.
21. Naunheim KS, Kesler KA, D'Orazio SA, Fiore AC, Judd DR. Lung cancer surgery in the octogenarian. Eur J Cardiothorac Surg 1994; 8: 453-456.
22. Ishida T, Yokoyama H, Kaneko S, Sugio K, Sugiraachi K. Long-term results of operation for non-small cell lung cancer in the elderly. Ann Thorac Surg 1990; 50: 919-922.
23. Smith TP, Kinasewitz GT, Tucker WY, Spillers WP, George RB. Exercise capacity as a predictor of post-thoracotomy morbidity. Am Rev Respir Dis 1984; 129: 730-734.
24. Eagle K, Berger PB, Calkins H et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery-executive summary. Anesth Analg 2002; 94: 1052-1064.
25. Dempsey DT, Mullen JL, Buzby GP. The link between nutritional status and clinical outcome: can nutritional intervention modify it? Am J Clin Nutr 1988; 47: 352-356.
26. Jagoe RT, Goodship THJ, Gibson GJ. The influence of nutritional status on complications after operations for lung cancer. Ann Thorac Surg 2001; 71: 936-943.
27. Nourhashemi F, Andrieu S, Rauzy O et al. Nutritional support and aging in preoperative nutrition. Curr Opin Clin Nutr Metab Care 1999; 2: 87-92.
28. Busch E, Verazin G, Antkowiak JG, Driscoll D, Takita H. Pulmonary complications in patients undergoing thoracotomy for lung carcinoma. Chest 1994; 105: 760-766.

29. Camu F, Beckers S. The anesthetic risk of tobacco smoking. Acta Anaesthesiol Belg 1991; 42: 45-56.
30. Castillo R, Haas A. Chest physical therapy: comparative efficacy of preoperative and postoperative in the elderly. Arch Phys Med Rehab 1985; 66: 376-379.
31. Sioris T, Salo J, Perhoniemi V, Mattila S. Surgery for lung cancer in the elderly. Scand Cardiovasc J 1999; 33: 222-227.
32. Egbert AM. Postoperative pain management in the frail elderly. Clin Geriatr Med 1996; 12: 583-599.
33. Mizushima Y, Hirofumi N, Sugiyama S et al. Survival and prognosis after pneumonectomy for lung cancer in the elderly. Ann Thorac Surg 1997; 64: 193-198.
34. Yellin A, Benfield JR. Surgery for bronchogenic carcinoma in the elderly. Am Rev Respir Dis 1985; 131: 197 (Letter).
35. Lee-Chiong TL Jr, Matthay RA. Lung cancer in the elderly patient. Clin Chest Med 1993; 14: 453-478.
36. Kirsh MM, Rotman H, Bove E et al. Major pulmonary resection for bronchogenic carcinoma in the elderly. Ann Thorac Surg 1976; 22: 369-373.
37. Harviel JD, McNamara JJ, Straehley CJ. Surgical treatment of lung cancer in patients over the age of 70 years. J Thorac Cardiovasc Surg 1978; 75: 802-805.
38. Yamamoto K, Padilla Alarcon J, Calvo Medina V et al. Surgical results of stage I non-small cell lung cancer: comparison between elderly and younger patients. Eur J Cardiothorac Surg 2003; 23: 21-25.
39. Whittle J, Steinberg EP, Anderson GF, Herbert R. Use of Medicare claims data to evaluate outcomes in elderly patients undergoing lung resection for lung cancer. Chest 1991; 100: 729-734.
40. Kiser AC, Detterbeck FC. General aspect of surgical treatment. In: Detterbeck FC, Rivera MP, Socinski M, Rosenman JE (Eds): Diagnosis and treatment of lung cancer. Philadelphia: WB Saunders, 2001, pp 141-143.
41. Osaki T, Shirakusa T, Kodate M, Nakanishi R, Mitsudomi T, Ueda H. Surgical treatment of lung cancer in the octogenarian. Ann Thorac Surg 1994; 57: 188-192.
42. Morandi U, Stefani A, Golinelli M et al. Results of surgical resection in patients over the age of 70 years with non small cell lung cancer. Eur J Cardiothorac Surg 1997; 11: 432-439.
43. Mikami I, Koizumi K, Tanaka S. Changes in right ventricular performance in elderly patients who underwent lobectomy using video-assisted thoracic surgery for primary lung cancer. Japan J Thor Cardiovasc Surg 2001; 49: 153-159.
44. Koizumi K, Haraguchi S, Hirata T, et al. Video-assisted lobectomy in elderly lung cancer patients. Japan J Thor Cardiovasc Surg 2002; 50: 15-22.
45. Yim AP, Wan S, Lee TW, Arifi AA. VATS lobectomy reduces cytokine responses compared with conventional surgery. Ann Thorac Surg 2000; 70: 243-247.
46. Massard G, Moog R, Wihlm JM et al. Bronchogenic cancer in the elderly: operative risk and long-term prognosis. Thorac Cardiovasc Surg 1996: 44: 40-45.
47. Fowler WC, Langer CJ, Curran WJ, Keller SM. Postoperative complications after combined neoadjuvant treatment of lung cancer. Ann Thorac Surg 1993; 55: 986-989.
48. Damhuis RAM, Schutte PR. Resection rates and postoperative mortality in 7,899 patients with lung cancer. Eur Respir J 1996: 9: 7-10.
49. Shirakusa T, Tsutsui M, Iriki N et al. Results of resection of bronchogenic carcinoma in patients over the age of 80. Thorax 1989; 44: 189-191.