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GERIATRIC GENERAL THORACIC SURGERY

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Continuing improvements in instrumentation, anesthetic and surgical techniques, and post-operative management allow the thoracic surgeon to operate on the oldest patients with the expectation of successful outcomes. However, when elderly patients require thoracic surgery and scarce resources in support of such specialized care must be allocated, the need to provide care to younger patients may become a factor in the decision whether to operate on the elderly patient. One may argue that age-based criteria for therapy merely reflect the balance that must be struck between the cost of treatment and its potential long-term benefit. The implication is that age, either alone or combined with other factors, may so profoundly decrease the clinical efficacy of certain treatments as to make them either useless or potentially harmful to older people. The potential benefit of treatment must then be weighed against the few remaining years of life to be gained. The countervailing point of view sees age as a very poor predictor of clinical outcome and highlights the possibility that elderly patients may be denied potentially effective care as a consequence of false assumptions that are based on their age alone. Faulty medical information or physician bias are the sources of these assumptions. Medical decision making concerning elderly patients, although anchored in risk-benefit estimates among individuals, is inseparable from broader social issues related to the perceived value of the elderly age group. Resource allocation in health care institutions, priority setting in medical education, and the direction of research initiatives all reflect the way our society views the older person, and they directly affect decision making by physicians. The general tendency of the literature from surgeons on benign and malignant diseases of the lungs and esophagus has been to report what one was able to get away with and not to shed light on mechanisms of injury and repair in the older patients that might affect outcomes and thus attitudes about recommending major operations on elderly patients. This review is intended to bring together the accumulated experience of the past 20 years with the older population and serious lung and esophageal disease, and thus to highlight the areas most in need of further research.

METHODS

The search was conducted on the National Library of Medicine's PubMed database. The time period covered was from January 1982 to October 2002. The search strategy combined various terms for general thoracic surgical procedures (general or specific commonly performed operations, including the esophagus, lung, and mediastinum), the terms *elective* and *emergency*, and various terms for perioperative care, complications, and outcomes. Additional requirements were either that the publication be a review, clinical trial, randomized controlled trial, or meta-analysis, or that terms for risk or age factors be present as title words or MeSH headings. Terms denoting advanced age were *age factors*,

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age, aging, elderly, geriatric, gerontologic, older, or octogenarian, nonagenarian, or centenarian. Finally, animal research was systematically excluded.

LUNG CANCER

Lung cancer accounts for 15% of all cancers. It is responsible for 30% of cancer deaths, more than cancers of the breast, colon, prostate, and ovary combined, and the incidence is growing throughout the world. Currently, it is the leading cause of cancer death among both men and women. The American Cancer Society estimated that there would be 169,500 new cases of lung cancer in the United States in 2001.¹ The number of Americans who would die from this disease was estimated at 157,400. The peak incidence of lung cancer in the life span of Americans occurs in their fifties. The effects of toxic exposures accumulate with age, and lung cancer is increasingly a disease of those aged 65 years and over. The treatment of lung cancer relies predominantly on surgery, chemotherapy, and radiation. All these modalities impose considerable demands on patient physiology. Age-related declines in cardiovascular or respiratory reserve may limit the utility of these treatments.

The majority of lung cancers fall into one of two histologic categories. Small-cell lung cancers are derived from neuroendocrine cells, and non-small-cell lung cancers are epithelial in origin. Surgery is generally limited to the early stages of small-cell lung cancer, where little lung is removed and the physiologic stresses are smaller. In contrast, surgical resection is potentially curative for non-small-cell lung cancer. Adenocarcinoma and squamous cell cancers are the predominant subtypes.

Sociodemographic differences appear in both the incidence and the outcome of lung cancer. The risk of lung cancer for men in the United States is approximately twice that for women. The peak incidence occurs between the ages of 75 and 79, at the rate of 357 per 100,000.² This compares with an incidence among persons aged 50 to 54 years of only 58.2 per 100,000. The overall probability of 5-year survival is currently 15.6%. The age at diagnosis affects the probability of survival to a much greater degree than that which can be explained by actuarial factors. A person diagnosed with lung cancer at age 45 has a 22.8% chance at 5-year survival, but those diagnosed past the age of 65 have a 13.7% rate.

Cigarette smoking is the prime risk factor for the development of lung cancer. The current epidemic of lung cancer reflects smoking patterns of the years 1950 to 1980. Recently, there has been a significant decline in the incidence of lung cancer among men. Among women, there has been an increase in both its incidence and mortality. This rise parallels changes in smoking patterns. The percentage of men who smoked fell 19% between 1965 and 1985, while the rate for women decreased by only 6%. Any optimism regarding the end of the current epidemic is dampened by the fact that there is a significant increase in the percentage of teenagers who smoke. Public education regarding the risks of smoking, combined with legislative limits on the sale or promotion of cigarettes, may help reverse this tide.³

The majority of lung cancers are diagnosed when the disease is already advanced. This accounts for the very high mortality rate. At presentation, only 15% of patients have disease that is localized within the lung and potentially amenable to surgical removal.⁴ Overall, 85% of all patients die within 5 years of their diagnosis. In cases of distant

spread, no available therapy is curative. Several clinical trials among elderly patients have demonstrated improvement in overall survival as well as quality of life with chemotherapy for advanced non-small-cell lung cancer.⁵ Despite numerous advances in surgery, chemotherapy, and radiation, median survival for most patients after treatment remains only 2 years. Long-term survival is most common among asymptomatic patients with stage I cancers that undergo resection. The proportion of patients who present for treatment at such an early stage is quite small, ranging from 5% to 10%. The diagnosis may be made as a result of chest radiographs done for other indications or screening procedures among high-risk individuals. The percentage of stage I non-small-cell cancers that prove to be resectable is approximately 90%.⁶ The few remaining patients are usually unresectable because they have inadequate pulmonary reserve or major contraindications for general anesthesia. In recent published series, operative mortality for stage I lung cancer approaches zero. The 5-year survival rate after operation for stage I cancer ranges from 53% to 100%, with those patients with stage IA having 73% to 100% survival.⁷⁻¹³ This compares with a 5-year survival rate of only 10% among patients with screen-detected stage I disease that was not operated upon.¹⁴ Cancer progression accounted for the mortality of these nonresected patients in 80% of cases. Patients who are free of disease at 5 years have a 90% chance of surviving 10 or more years after operation. The high rate of resectability and the low operative mortality associated with early lung cancers are compelling arguments for those who are working to introduce screening programs among populations at risk.

The study at Johns Hopkins, the Mayo Clinic, and Memorial Sloan Kettering sponsored by the National Cancer Institute found that mass screening for lung cancer with sputum cytology and standard chest radiography failed to reduce lung cancer mortality.^{15,16} This was interpreted as evidence against the utility of screening for lung cancer. There were concerns that screening resulted in the overdiagnosis of lung cancers. It was possible that screening had led to the detection of slowly growing lung cancers that would otherwise not threaten the life of the patient before death occurred from other causes. Screening was also quite expensive, given the small number of cancers detected. The public health issues of cost and accessibility are still pertinent to the implementation of any mass screening program. Governments have developed population health models that may be useful in the economic evaluation of cancer control interventions and in the guidance of policy decision making.¹⁷ Costs are not limited to those of screening itself. The cost of any screening program includes not only the price of the tests but also the burden of any additional testing borne by patients who were initially positive on the screening test but ultimately found not to have cancer. Any increase in the survival rate among patients with screening-detected lung cancer may be offset by the morbidity and mortality of unnecessary surgery on patients who are falsely identified as having cancer. Lead-time bias is an additional confounding factor that may further limit the survival benefit of early detection programs for lung cancer.

Screening programs for lung cancer have focused on improving the diagnostic test. The development of new tools for the early detection of lung cancer has paralleled progress in molecular biology and computerized imaging technology. Standard sputum cytology now uses molecular probing of atypical cells.¹⁸ Immunostaining for heterogeneous nuclear ribonucleoproteins has led to the detection of preclinical lung cancer.¹⁹ The finding that molecular changes in shed epithelial cells may predict bronchial metaplasia and the subse-

quent development of lung cancer brings up the issues of chemoprevention, limited removal of mucosal cells via photodynamic laser therapy, and the potential use of aerosolized drug delivery systems. The Early Lung Cancer Action Project recently reported on the use of an annual helical computed tomography (CT) scan for the screening of lung cancer among 1000 heavy smokers aged 60 and over.²⁰ Almost one fourth of all screened individuals had a noncalcified nodule (233 of 1000). The researchers discovered 27 cancers; 87% of them were stage I. The CT detection rate was six times higher than that obtained by chest radiography alone. It would be expected that an increase in the sensitivity of the screening procedure would translate into more patients' being found at an earlier stage of the disease, when there is the greatest potential for resection and cure. Lead-time bias may, however, make any survival benefit more apparent than real. There are currently no prospective data on what impact, if any, that helical CT may have on the long-term outcome of patients with asymptomatic screen-detected lung cancer. A recent economic analysis of lung cancer screening, combining data from the Surveillance, Epidemiology and End Results (SEER) registry public-use database and published results from the Early Lung Cancer Action Project, found annual screening over a period of 5 years to be cost-effective (at approximately \$19,000 per life-year saved) when limited to a high-risk cohort of patients between ages 60 and 74 years.²¹ The widespread implementation of mass screening programs for lung cancer will likely await the development of less expensive CT scanners and automated forms of sputum cytology analysis. Annual screening among selected groups of high-risk elderly patients already may be economically justifiable and warranted.

Outcome studies in the surgical management of lung cancer have generally not included large cohorts of elderly patients, and little information exists as to age-specific changes in quality of life. Recent clinical trials using radiation and chemotherapy for the treatment of lung cancer have used quality-of-life indices as primary measures of outcome.²²⁻²⁴ Auchter et al used the Functional Assessment of Cancer Therapy-Lung (FACT-L) patient questionnaire to score the quality of life in patients enrolled in a radiotherapy trial for advanced inoperable lung cancer. This tool, which includes 33 scores for physical, functional, emotional, and social well-being and a 10-item subscale of lung cancer symptoms, was used to generate a trial outcome index.²⁵ Specific analyses of how chemotherapy may affect the aged patient are now reaching publication stage. The Elderly Lung Cancer Vinorelbine Italian Study (ELVIS) involved a multicenter randomized trial of single-agent chemotherapy versus best supportive care in patients over the age of 70 and used both survival and quality of life as endpoints.^{26,27} One-year survival in the vinorelbine group was 32% as compared with 14% in the best supportive-care arm. This trial, the first to examine chemotherapy for advanced lung cancer in elderly patients, found that the survival benefit was not gained at the expense of a poorer quality of life. Dyspnea, pain, and social, cognitive, and physical functioning scores were found to improve with treatment. The clinical efficacy of treatment was therefore measured in terms of patient well-being rather than simply months survived.

The standard surgical treatment for a localized cancer of the lung is surgery via thoracotomy and either lobectomy or pneumonectomy. There is a historical bias toward offering surgery only to younger patients. Many physicians have had grave reservations about proposing surgery to elderly patients, given the risks posed by general anesthesia, thoracotomy, and the loss of pulmonary function. It was also unclear whether lung cancer

is inherently different in older patients, more specifically, whether the elderly patient has a significantly more aggressive progression to death. If lung cancer in elderly patients is proven to be slow growing and of low potential for fatal outcome, a more conservative treatment approach can be justified that weighs natural life expectancy against the chronic progression of disease. Conversely, if lung cancer in the elderly person is significantly more aggressive and less amenable to surgery, a rather more conservative approach can be justified, with palliative treatment aimed mainly at preserving the patient's quality of life. The core of this debate has been settled; lung cancer among older patients is not an indolent disease. In a retrospective study of 80 patients aged 70 years and over, Harviel et al reported a mean survival of 3.5 months for untreated patients, 9.8 months for those receiving chemotherapy or radiation, and 30.6 months after resection, with an operative mortality of 18.2%.²⁸ Berggren et al reported a 5-year survival rate of 32% in a series of 82 patients aged 70 years and older who were operated upon for bronchogenic carcinoma. This contrasted with a 0% survival rate without operation.²⁹ Shirakusa et al reviewed their experience with resections among patients aged 80 years and over. A cumulative 5-year survival of 79% was noted for patients with stage I carcinoma.³⁰ A survival advantage has therefore been established among elderly patients undergoing resection for lung cancer.

Long-term survival among elderly patients after surgery for lung cancer must be balanced against the mortality risk of the operation itself. Studies from almost two decades ago had clearly correlated age above 65 years with increased mortality after thoracotomy. In 1973, Evans reported a postoperative mortality of 20% after major pulmonary resection for bronchogenic carcinoma among 114 patients aged 65 years and older.³¹ These patients came from 1804 cases of lung cancer, of all age groups, diagnosed between 1950 and 1971. The percentage of patients ultimately found to have resectable disease was 15%. The rate of resectability was not influenced by age. The age at diagnosis did not appear to correlate with the potential for curative resection and, by inference, clinical stage. Postoperative mortality rates were age related. Patients younger than 65 years had a hospital mortality of 10%. Patients aged 65 to 69 years had a 16% rate. Hospital mortality for patients aged 75 to 83 years was 26.6%. A 4-year survival rate of 39% was reported. This was compared with data from 780 patients over the age of 65 who were not candidates for surgery. A 1-year survival rate of less than 7% was documented in this group and was comparable to that seen among inoperable patients younger than 65 years. Surgery was justifiable among older patients since the natural history of lung cancer was not more indolent or slow growing among those who were elderly. Despite a higher rate of peri-operative mortality, the prospect of long-term survival after pulmonary resection in elderly patients was sufficiently high to justify the risk of operation. Ten years later, the Lung Cancer Study Group of North America again demonstrated a clear association between age and operative mortality after thoracotomy. Their 1983 report showed a 30-day postoperative mortality of only 1.3% for patients younger than 50 years. The mortality rate was found to rise with increasing age. Patients aged 60 to 69 years, 70 to 79 years, and over 80 years had mortality rates of 4.1%, 7%, and 8.1%, respectively.³²

More recent studies have indicated that the operative mortality rate after standard lung resection for patients between the ages of 70 and 80 is starting to approach that obtained among younger patients. In a review of 1079 patients undergoing thoracotomy for lung cancer, de Perrot et al noted a mortality rate of 1.3% for lobectomy or lesser resection

among patients younger than 60 years as compared with a 5.5% rate for older patients.³³ Cancer-specific long-term survival was equivalent for all age groups. Pagni et al studied 385 patients aged 70 years and older operated upon for lung cancer with curative intent. The operations consisted of lobectomy (77%), pneumonectomy (6%), bilobectomies (4%), and wedge or segmental resections (13%). The 30-day mortality risk for the elderly patients (aged 70 years and older) was compared with a cohort of 180 patients aged 69 years and younger. The mortality for all resections in the elderly group was higher (4.2% versus 1.6%). Mortality in the octogenarian group was 2.8%. Major morbidity was similar in the two groups (13.2% versus 13%). Pneumonectomy carried a higher risk for death, with 3 of 24 deceased. Mortality rates over time were also evaluated. Mortality among elderly patients in the early period of the study (1971 to 1982) was 11.1%. This declined to a rate of 2.6% over time (1983 to 1994). The authors concluded that functional elderly patients should not be denied curative lung resection on the basis of age alone, but they also cautioned against the use of pneumonectomy.³⁴ Harvey et al found the risk of operative mortality not to increase until after the age of 80.³⁵ In their study of 81 patients with surgery for non-small-cell lung cancer, these authors observed a mortality rate of 1.4% for patients under 70, 1.6% for patients between 70 and 79, and 17.6% for patients 80 years or older. The use of heparin prophylaxis against deep-vein thrombosis and pulmonary embolism was emphasized. The authors cautioned against the use of extended pulmonary resection. They also preferred limited wedge resection to lobectomy in patients with preoperative impairment of pulmonary reserve. Hanagiri et al reported no mortality among 18 octogenarians after resection. Half were lobectomies, and the remainder constituted various forms of parenchyma-sparing procedures. A 5-year survival rate of 42.6% was found, comparable to that obtained in younger patients.³⁶ Other centers have noted overall operative mortality rates of less than 2% for selected patients aged 70 and over, with intermediate-term survival rates comparable to those for younger patients.^{37,38}

A correlation between operative mortality and the extent of pulmonary resection was demonstrated in elderly patients. Evans noted a mortality rate of 15% after lobectomy as compared with 27% after pneumonectomy among patients aged 65 years and older.³¹ Bates reported on 100 patients over the age of 70 who had 26% mortality after pneumonectomy as compared with 14% after lobectomy.³⁹ No deaths were noted after segmental resection. Oliaro et al had a 9.1% mortality rate after pneumonectomy as compared with an overall mortality rate of only 3.1% among patients over 70 years of age.⁴⁰ Jensik et al advocated limited pulmonary resection for elderly patients with lung cancer and marginal physiologic reserve.⁴¹ More recent reports indicate that mortality may be decreasing even for pneumonectomy and suggest that there are fewer differences in operative mortality between different types of resection in properly selected patients older than 75 years.⁴² Tanita et al recorded no operative deaths in a highly selected series of 24 octogenarians undergoing more than single lobectomy.⁴³

Age alone is not a contraindication for pulmonary resection. A 1990 review of 185 patients 70 years old or older with non-small-cell lung cancer noted a 5-year survival of 48% after resection and an operative mortality rate of 3%.⁴⁴ Mortality and prognosis were similar to those associated with younger patients. No differences based on age were found with regard to histologic type, TNM (tumor, node, and metastasis) classification, and curability. Pulmonary complications occurred in 21% of the elderly patients and were correlated with impaired preoperative pulmonary function and smoking. Nonoperative

therapy or limited resection was recommended when postoperative pulmonary function was predicted to be less than 0.8 L/m² for vital capacity and 0.6 L/m² for forced expiratory volume in 1 second (FEV₁).^{45,46} Mane et al similarly found that age was not a predictor of poor long-term survival after resection for lung cancer.⁴⁷ Aoki et al analyzed the risks associated with pulmonary resection in 35 patients over the age of 80.⁴⁸ The operative mortality rate was 0%, with morbidity in 60%. There were 10 major pulmonary complications, including respiratory insufficiency following bacterial pneumonia and sputum retention. Although they concluded that surgical treatment was not contraindicated for octogenarians with lung cancer, the authors cautioned that preoperative low arterial oxygen, high alveolar-arterial oxygen diffusion gradient, and long operative times may place older patients at risk for serious postoperative pulmonary complications. A gross survey of 7099 patients in Japan evaluated 30-day operative mortality and its relationship to patient age. The mortality was 0.4% for patients younger than 60 years, 1.3% for those 60 to 69, 2.0% for those 70 to 79, and 2.2% for patients aged 80 and over.⁴⁹ In 2000, Bernet et al compared 92 patients younger than 50 years of age undergoing surgery for lung cancer with a comparable group of 120 patients older than 70 years. No difference was found in operative mortality between the two groups (2.2% versus 2.5%). Survival was similar in younger and older patients after surgical resection. The survival rate at 5 years, when adjusted for tumor stage, was 56% in patients younger than 50 years as compared with 53% in patients older than 70 years.⁴⁶ Oliaro et al assessed postoperative complications, mortality, and long-term survival after surgical therapy for non-small-cell cancer in 258 patients aged 70 years and older.⁴⁰ Overall postoperative mortality was 3.1%, with a morbidity rate of 39.1%. The rate of complication was significantly increased among patients with multiple concomitant diseases. Multivariate analysis found that survival was dependent on tumor stage and not on age. Five-year survival for stage I cancers was 73.6% as compared with 23% for stage II. They additionally found that highly selected elderly patients had a significantly higher rate of survival than did those patients who were operated upon when the criteria for surgery were less strict. The proper selection of patients for surgery was found to have as much influence on survival as the stage of the tumor. This finding highlights the importance of functional status, rather than chronologic age, as a determinant for good outcome after resection. The low mortality and acceptable survival data confirmed to the authors that surgery is worthwhile for selected elderly patients.

Advancements in anesthesia and pain management have certainly helped to reduce the mortality of standard pulmonary resections. Mortality rates after lobectomy among elderly patients are therefore now similar to those found among younger patients. Data indicate that although age is not associated with postoperative mortality, advanced age is associated with increased morbidity. A report on 331 patients undergoing major resection for lung cancer prospectively found that age over 60 years, male sex, pneumonectomy, and predicted postoperative FEV₁ are univariate predictors of increased risk for major complications.⁵⁰ When the effect of these variables was controlled for in a multivariate analysis, a low predicted postoperative FEV₁ remained the only significant independent predictor of complications. The researchers concluded that pulmonary resection should not be denied on the basis of traditionally cited preoperative pulmonary variables, and that this very simple calculated prediction of postoperative pulmonary function may help identify patients at increased risk for complications. Wang et al found low diffusing capacity for

carbon dioxide (Dlco) to predict a high risk for pulmonary complications after surgery and an increased length of hospital stay.⁵¹ Exercise testing, 6-minute walk distances, and stair climbing are used as adjuncts to the standard spirometric testing of high-risk patients.⁵²

Relatively small patient numbers and the fact that the patients are already highly selected for good performance status limit most studies dealing with the results of pneumonectomy in elderly patients. Specific inferences with respect to age-associated mortality and morbidity are therefore difficult to draw from retrospective descriptions. Although advanced age alone generally has not been predictive of death after pneumonectomy, retrospective studies have demonstrated higher mortality among elderly patients. Mizushima et al found a significantly higher operative mortality after pneumonectomy among patients over the age of 70 (22.2%) than among younger patients (3.2%).⁵³ The cancer-related prognosis for the elderly group was, however, comparable to that for younger patients across all stages. Age was not found to predict a poor prognosis for long-term survival. Despite the higher operative mortality, pneumonectomy was thought to be justified for the treatment of lung cancer in carefully selected elderly patients.

Bernard et al reviewed the results of pneumonectomy among 639 patients at the Mayo Clinic.⁵⁴ Associated conditions were found in 47.7%. These concurrent illnesses included chronic obstructive pulmonary disease (COPD) (28.6%), coronary artery disease (13.1%), cardiac arrhythmia (9.1%), and diabetes mellitus (8.5%). Complications occurred in 43.2% of patients; the vast majority of these were cardiopulmonary. The mortality rate observed was 7.0%. Advanced age was associated with postoperative cardiopulmonary morbidity in univariate analysis ($P < .0001$). Age was as important in determining morbidity as decreased FEV₁ and the presence of pre-existing cardiovascular disease. In multivariate analysis, advanced age was again found to be strongly associated with cardiopulmonary morbidity. Age alone did not prove to adversely affect postoperative mortality in either univariate or multivariate analysis. Appropriate selection of patients and meticulous peri-operative care were deemed paramount in minimizing the risk of pneumonectomy. These researchers recommended aggressive screening for the presence of occult cardiovascular disease and optimizing the patient's pulmonary function. Reversible conditions, such as smoking, infection, or bronchospasm, also should be addressed prior to surgery. Intra-operative techniques, such as intra-pericardial control of hilar vessels and tissue reinforcement of the bronchial stump, were recommended to minimize technical complications. Similar findings were found for patients undergoing combined pulmonary and chest wall resection for locally invasive lung cancer. An analysis of 201 patients undergoing surgical resection of lung cancers invading the chest wall was performed by the use of both univariate and multivariate methods. Age, nodal involvement, and depth of invasion were found to be the only independent factors predicting survival in completely resected patients.⁵⁵

Efforts have been made to identify factors that may be responsible for the higher operative mortality among elderly patients. Kirsh et al, in a 1976 report from the University of Michigan, reviewed 55 patients who had undergone curative resection for lung cancer.⁵⁶ This cohort came from a group of 75 patients, older than 70 years of age, who had been diagnosed with lung cancer between 1959 and 1969. Seventeen patients were deemed inoperable because of comorbidity, and three were found at operation to have unresectable disease. The remaining 55 patients had an operative mortality of 14% after lobectomy and

17% after pneumonectomy. Five-year survival was 30% and was comparable to that seen among younger patients. Overall operative mortality rates, for all age groups, from the same institution were 7% for pneumonectomy, 5.7% for lobectomy, 0% for segmentectomy, and 1.6% for thoracotomy alone. The researchers concluded that age per se does not have an adverse influence on long-term survival after pulmonary resection for bronchogenic carcinoma and that a decision to proceed with surgery should be made on the basis of cardiovascular status and pulmonary reserve. The higher rate of peri-operative mortality among elderly patients was attributed to difficulties in properly identifying poor-risk elderly patients prior to surgery. Accurate and precise guidelines for excluding patients from operation were therefore proposed. The guidelines proposed to indicate inoperability included:

- resting hypercapnia ($P_{CO_2} > 45$ mm Hg) or hypercapnia with exercise;
- hypoxemia ($PO_2 < 50$ mm Hg);
- $FEV_1 < 2000$ mL, $FVC < 2000$, or $MVV < 50\%$ of predicted for pneumonectomy;
- $FEV_1 < 1500$ mL for lobectomy;
- calculated $FEV_1 < 800$ mL after surgery.

All these indices related the risk of surgery to physiologic function without any specific reference to age. The researchers concluded that surgery for lung cancer can be safely offered to properly selected elderly patients with acceptable mortality and good potential for long-term survival.

Harpole et al found that age greater than 65 years, right-sided procedures, and the presence of dysrhythmia are associated with increased risk for major complication after pneumonectomy.⁵⁷ No identifiable factors were noted to predict mortality. Supraventricular dysrhythmias were found to be the most common complications reported to occur after pneumonectomy (24%), typically presenting 1 to 5 days after surgery. The patients at highest risk for these dysrhythmias were those older than 65 years and patients undergoing right-sided procedures, extrapleural pneumonectomy, or intrapericardial dissection. Joo et al reviewed 105 patients after pneumonectomy and noted a 10% complication rate with atrial fibrillation and respiratory failure predominating.⁵⁸ Continuous electrocardiographic monitoring for the early diagnosis of cardiac dysfunction was therefore recommended.

Despite the higher operative mortality documented among older patients, most authors advocated an aggressive surgical approach to lung cancer in elderly patients. Meticulous patient selection and preservation of pulmonary tissue were the hallmarks of studies that showed improved surgical outcome after resection in elderly patients. Breyer et al reported on 150 pulmonary resections for primary lung carcinoma among a highly selected group of patients over the age of 70 years.⁵⁹ Parenchyma-sparing procedures were used whenever possible, with segmental resection performed in 52 cases. Multiple logistic regression analysis determined that the amount of lung tissue removed, a history of congestive heart failure, and a history of previous pulmonary resection are all significantly related to an increased risk of major complications or death. The risk of major complication or death was not found to be related to age. Overall 5-year survival was 27%, with a hospital mortality of only 4%. The aggressive use of chest physiotherapy and aspiration bron-

choscopy among these elderly patients was credited for the low rates of complication and death after surgery. It was recommended that age alone is not a criterion to reject a patient for pulmonary resection. In 1987, Sherman and Guidot compared two groups of patients, under and over the age of 70, in terms of operative outcome after thoracotomy.⁶⁰ Although operative mortality in the elderly group was greater (9.4% versus 4.0%), no statistically significant difference in the postoperative complications, postoperative hospital stay, or actuarial survival was found. The researchers concluded that advanced age does not adversely affect prognosis, and they also urged that elderly patients with reasonable cardiopulmonary function have a potentially curative pulmonary resection. This conclusion was echoed in the geriatric literature of the day, as continued refinements in surgical care gradually lowered the mortality risk for lung cancer surgery among elderly patients to levels that began to approach those obtained in younger patients.⁶¹

The number of elderly patients who will require treatment for lung cancer is certain to increase. Standard lobectomy is safe and effective for older patients. The mortality and morbidity after either segmental or lobar resection is generally comparable to that achieved in younger patients. Elderly patients do appear to have an increased rate of complication after more extended resections that include either removal of chest wall or pneumonectomy. The majority of complications are either cardiac or respiratory. Mortality after extended resection is not substantially increased among elderly patients in most surgical series, likely because of the rigorous selection process that occurs prior to considering patients for radical surgery. Any consideration of pulmonary resection in elderly patients therefore mandates a rigorous review of preoperative cardiopulmonary reserve.^{62,63} Data from standard spirometry may be supplemented by exercise testing, blood gas analysis, measurement of diffusing capacity, and nuclear ventilation-perfusion studies. In multivariate analysis, advanced age and increasing extent of pulmonary resection was found to predispose the patient to cardiac arrhythmias.⁶⁴ A comprehensive system of surgical care must be considered for elderly patients undergoing major resection. Preoperative physical conditioning with incentive spirometry, graded exercise, and smoking cessation represents one aspect of this program. Intra-operative technique must be meticulous in order to minimize bleeding and tissue trauma. Effective pain control, early mobilization, chest physiotherapy, prophylaxis for deep-vein thrombosis, and electrocardiographic monitoring are important components of postoperative care. The Society of Thoracic Surgeons has a large database of perioperative outcomes and long-term results for coronary artery bypass grafting.⁶⁵ Recently, the society initiated a similar database for patients undergoing major thoracic surgical procedures.

Minimally invasive techniques of pulmonary resection may offer unique advantages to the elderly patient. Because a significant part of the morbidity of lung resection can be attributed to the pain of the incision with its resultant deleterious effects on pulmonary function, any reduction in the extent of the incision used to access the lung may result in decreased postoperative morbidity and mortality. Muscle-sparing thoracotomy was shown to decrease pain, length of hospital stay, and narcotic requirements as compared with standard incisions.⁶⁶ Video-assisted thoracic surgery (VATS) has been used for wedge resection and lobectomy in elderly patients.⁶⁷⁻⁷¹ Specialized surgical centers have demonstrated that these techniques are feasible and safe.⁷² Early results with VATS lobectomy have shown that survival results are comparable to those of open surgery in stage I lung cancer.^{73,74} Reductions in surgical complications, mortality, pain, narcotic use, postopera-

tive delirium, hospital cost, and length of stay have been described.^{75,76} Long-term survival data comparing VATS lobectomy with standard resection in elderly patients are not currently available.

The optimal care of the elderly patient undergoing pulmonary resection includes meticulous attention to detail before, during, and after operation. A multimodality approach to the surgical management of lung cancer in the elderly patient is therefore needed. Although few centers have a dedicated clinical pathway specifically designed for elderly patients, standard practice guidelines incorporate many of the core elements necessary for optimal care of the aged thoracic surgery patient. Key components of this approach begin with increased educational efforts to overcome potential bias among physicians who may not fully consider elderly patients as candidates for surgery. Additional features are lung cancer screening among older people, optimal preoperative testing of elderly patients, and appropriate referral to centers of specialized care. Cost-effective methods of preoperative conditioning will need to be developed.

***ThoracicSurg 1 (Level A):* Randomized controlled trials are needed of the effect on mortality and morbidity of the use of computed tomography screening for elderly patients with high-risk factors for the development of cancer.**

***ThoracicSurg 2 (Level B):* An instrument to assess age-specific outcomes, functional status, and quality of life for elderly lung cancer patients that is applicable to both preoperative and postoperative situations needs to be developed and validated.**

***ThoracicSurg 3 (Level A):* Ongoing large therapeutic lung cancer trials need to incorporate the age-specific instrument described in ThoracSurg 2.**

***ThoracicSurg 4 (Level B):* A preoperative tool to assess the general function of the elderly patient having a major pulmonary procedure needs to be developed and validated.**

***ThoracicSurg 5 (Level B):* A multivariate analysis using the Society of Thoracic Surgeons Database or other collections of cases and aimed at defining the most important risk factors for adverse surgical outcomes should be performed. The instrument should include measures of the patient's functional capacity as well as pulmonary functions.**

***ThoracicSurg 6 (Level B):* A method of preoperative optimization that addresses the most important risk factors for morbidity and mortality from pneumonectomy should be developed and tested.**

***ThoracicSurg 7 (Level A):* Randomized controlled trials are needed to compare the efficacy of preoperative optimization methods with current best medical practices.**

***ThoracicSurg 8 (Level A):* Randomized controlled trials are needed to evaluate video-assisted thoracic surgery techniques for lobectomy; the trials should compare outcomes, including long-term survival in elderly patients, with those of standard open procedures.**

BENIGN DISEASES OF THE LUNGS

The two most common disease states that impact the lung health of elderly persons are pneumonia and chronic bronchitis. The Centers for Disease Control and Prevention published the discharge statistics for 2000 in advance form in 2002.⁷⁷ The data demonstrate that hospitalization for those aged 65 and over continues to rise while all other groups have shown a continued decline. Pneumonia was found to be the third most common reason behind heart disease and fractures for hospitalization in this age group. Pneumonia and chronic bronchitis combined were second only to heart disease as the first diagnosis at the time of discharge from the hospital. In the elderly age group, pneumonia is the fifth most common cause of death.

Chronic bronchitis and emphysema are the subject of intense investigation by the government. The National Emphysema Treatment Trial (NETT), supported by the National Heart, Lung, and Blood Institute (NHLBI), the Health Care Financing Administration (HCFA, now the Center for Medicare and Medicaid Services), and the Agency for Health Care Policy and Research (AHCPR, now the Agency for Healthcare Research and Quality), is the first multicenter clinical trial designed to determine the role, safety, and effectiveness of surgery to reduce lung volume. Patient screening for entry into the study began in the fall of 1997. It is expected to run for a few more years, and multiple reports are anticipated that will help to define the altered physiology, the best diagnostic evaluations, the optimum rehabilitation, and the role of surgery in the long-term management of severe emphysema. This investigation, coupled with the Lung Health Study,⁷⁸ will continue to provide a focus on emphysema for years to come. In March of 2002, the NHLBI reported on a workshop on COPD.⁷⁹ The report discussed the new results, concepts, and opportunities in COPD research: protease functions, oxidant injury, viral infection, mucous hypersecretion, apoptosis, alveolar regulation, biomarkers, genetics, inflammation, imaging technologies, molecular characterization, and drug development. It recommended research into characterization of the disease process, pathogenesis, and therapy. However, it did not include the effects of trauma or surgery, or the additive effects of aging on patients with COPD.

Pneumonia *per se* is not a surgical condition, but the consequences and complications of pneumonia such as empyema require intervention. Gavazzi et al investigated empyema in elderly patients⁸⁰ and found that many very old patients present with a pleural effusion that is not associated with classic symptoms of pneumonia. Prompt attention to pleural drainage and institution of antibiotic therapy are the most important prognostic factors. These researchers recommended that, because of the diversity of clinical presentation in the elderly population and because of the efficiency of rapid treatment, physicians should perform an examination of pleural fluid when the cause of pleural effusion in an older patient is uncertain. Chu et al echoed the same sentiments, emphasizing that failure of early recognition leads to a protracted course.⁸¹

Although thoracotomy and decortication have been the mainstay of empyema management in all patients for many years, clinicians constantly look for less invasive methods to manage these very ill patients. Tube thoracostomy with the installation of fibrinolytic agents was introduced more than 30 years ago. It has met with some success, particularly for the frail patient or the patient who is too ill to undergo a major surgical procedure. Cameron reviewed the use of fibrinolytics, including several randomized trials.⁸² At this time, there is insufficient evidence to support routine use of intrapleural fibrinolytic

therapy in the treatment of parapneumonic effusion and empyema. Ongoing trials may shift the balance toward the use of fibrinolytic therapy.

Another technique that has been popularized is the use of VATS for the management of empyema. This technique specifically for empyema was first described in 1985.⁸³ Since then, there have been a number of reports verifying the usefulness of thoracoscopy.^{84,85} Coote reviewed the trials comparing thoracoscopy with tube thoracostomy and with tube thoracostomy plus fibrinolytic therapy.⁸⁶ This reviewer concluded that thoracoscopy seems to offer an advantage in terms of chest tube time and length of stay but that there is insufficient level I evidence to conclude that thoracoscopy is clearly superior.

ThoracicSurg 9: (Levels B, A): The effects of lung volume reduction procedures and their complications on elderly patients with chronic obstructive pulmonary disease need to be investigated in cohort studies that compare younger and older patients. Subsequently, a randomized controlled trial might be needed to compare outcomes in elderly patients who undergo a standard volume-reduction procedure with similar patients who do not.

ThoracicSurg 10 (Level A): Randomized trials are needed to evaluate the efficacy of minimally invasive techniques and compare them with standard thoracotomy for the management of empyema in elderly patients.

ESOPHAGEAL CANCER

Esophageal cancer is one of the 10 most common solid tumors in humans. There are approximately 12,500 cases per year in the United States.⁸⁷ Over 90% of these patients will die of their disease despite therapy.⁸⁸ Early symptoms of esophageal cancer may be subtle or entirely lacking. Intermittent dysphagia may be ignored by the patient or under-investigated by treating physicians. More than 60% of patients, at presentation, therefore have metastatic or unresectable disease. Of the patients who proceed on to surgery, 75% have locally advanced disease.^{89,90} In a study of the interval between onset of dysphagia and treatment, Rothwell et al found a median delay of 15 weeks for patients with dysphagia and 17 weeks for patients with other symptoms. The most frequent cause of delay was late presentation to the family doctor.⁹¹

The incidence of squamous cell cancers varies tremendously across the globe. Its incidence in Western countries is approximately 5 to 10 cases per 100,000 persons. Areas in Iran and China report an incidence of up to 500 cases per 100,000. Factors related to the development of squamous cell cancers include age, sex, race, diet, alcohol consumption, and tobacco abuse. The average age at presentation for squamous cell cancer of the esophagus in the United States is 67 years. The overall incidence is 4 to 6 times higher in men than in women.⁹² Tobacco and alcohol consumption are strong predisposing factors in the development of squamous cell carcinoma of the esophagus. Case studies have revealed a strong dose-related risk among smokers that is 5 to 10 times the risk among nonsmokers.⁹³ The same is true of alcohol, with the greatest increased risk among those consuming hard liquor as opposed to wine or beer.⁹⁴ The combination of smoking and heavy alcohol consumption appears to have a synergistic effect on the development of esophageal cancer and to cause a 100-fold increase in relative risk.⁹⁵ Nutritional deficien-

cies in vitamins A, B₂, and C also have been implicated in the development of squamous cell cancers of the esophagus, as have mineral deficiencies involving zinc and magnesium. The risk was found to be elevated with high meat intake, and protective effects were found with increased consumption of raw fruits and vegetables.⁹⁶ These risk factors are of specific importance to elderly patients and to their family physicians. High cumulative exposure to tobacco and alcohol, combined with nutritional deficiencies that are often seen among seniors, should prompt the physician to specifically ask questions on the quality of patient swallowing. There should be a low threshold for further investigations, such as a contrast esophagram and esophagoscopy.

Adenocarcinomas of the esophagus are generally not associated with any of the risk factors typically found among patients with squamous cell cancer.⁹⁷⁻¹⁰¹ Patients with adenocarcinomas usually are well-nourished middle- to upper-class men with no history of alcohol abuse. Obesity and gastroesophageal reflux have been linked to the subsequent development of esophageal adenocarcinoma.¹⁰²⁻¹⁰⁴ Benign columnar metaplasia of the esophagus (Barrett's esophagus) is found in 10% of patients with symptomatic gastroesophageal reflux and is present in 70% of resected adenocarcinomas of the gastric cardia and esophagus.^{105,106} Patients with Barrett's esophagus are at risk of developing dysplasia within the areas of columnar metaplasia. The presence of dysplasia in a columnar-lined esophagus represents a premalignant condition that substantially increases the risk for the subsequent development of invasive cancer.¹⁰⁷ The risk of developing adenocarcinoma in the presence of Barrett's esophagus is estimated to be 1/400 to 1/170 patient years. This is 40 times greater than that seen in patients without Barrett's esophagus.¹⁰⁸⁻¹¹⁰ The histologic progression of Barrett's esophagus to carcinoma may be related to mutations of the p53 tumor suppressor gene.¹¹¹ Growth factor mutations involving *erb-b2* and EGFR may further contribute to malignant transformation.¹¹² Other studies have suggested that destruction of cyclin kinase inhibitors may promote uninhibited growth of the cancers.¹¹³ The prevalence of gastroesophageal reflux and its influence on the subsequent development of Barrett's esophagus has resulted in a dramatic change in the epidemiology of esophageal cancer over the past 20 years in the United States. Adenocarcinomas of the gastroesophageal junction have become the predominant histologic subtype, now accounting for more than 70% of esophageal cancers. In the United States between 1976 and 1987, the average annual rate of increase in incidence of esophageal adenocarcinoma among white males was 9.4%, exceeding that of any other malignancy.¹¹⁴ Similar trends were noted in western European countries.¹¹⁵ This is in marked contrast to worldwide statistics, where squamous cell cancers still account for the majority of cases. Patients with a long history of reflux should be screened for Barrett's changes by esophagoscopy. The presence of dysplasia must be specifically sought, as it represents a premalignant condition. High-grade dysplasia is an indication for esophagectomy because of the prevalence of occult adenocarcinoma.¹¹⁶ Educational efforts must therefore be aimed toward the general public and health care personnel in order to enhance recognition of the relationship between reflux and esophageal cancer. This knowledge may lead to the early investigation of symptoms and improve patient acceptance of either surveillance or therapeutic procedures.

In the past few years, investigations into the possibility of preventing cancer with simple agents have borne fruit. Moran reviewed the use of anti-inflammatory drugs to decrease the risk of developing cancer in general.¹¹⁷ The Mayo Clinic group, working

with a well-established model of Barrett's cancer, demonstrated a decrease in the rate of cancer development in rats fed COX-2 inhibitors.¹¹⁸ Kaur et al gave patients with Barrett's esophagus COX-2 inhibitors and demonstrated a decrease in COX-2 and prostaglandin E₂ expression in mucosal biopsies.¹¹⁹ In a novel approach, Lin et al gave the Chinese herbal medicine zeng sheng ping to patients with high-grade dysplasia and riboflavin with calcium to patients with mild dysplasia.¹²⁰ The patients with high-grade dysplasia had a 50% reduction in relative risk, and the patients with mild dysplasia had an 80% reduction in relative risk. Clinical trials with COX-2 inhibitors are now starting in the United States.

Esophageal resection is the standard treatment of both squamous cell cancers and adenocarcinomas of the esophagus. Improvements in patient selection, anesthesia, operative technique, and peri-operative care have dramatically reduced operative mortality over the past 20 years.¹²¹ Surgical resection can provide an 80% 5-year survival in patients with stage I disease. The 5-year survival of patients after surgery for locally advanced disease is approximately 20% to 30%. Unfortunately, the majority of patients are unable to undergo surgery because they have extensive disease at the time of diagnosis. The formidable physiologic stress posed by the operation itself also renders many additional patients inoperable because of their comorbidities. Two surgical approaches are widely used for esophageal resection: trans-hiatal esophagectomy with cervical esophagogastric anastomosis and Ivor Lewis transthoracic esophagectomy. The major difference between the two techniques relates to the location of the anastomosis and the need for thoracotomy. The trans-hiatal esophagectomy involves an upper midline laparotomy and a left cervical neck incision. Mobilization of the esophagus is done through the hiatus, and a thoracotomy is not required. The esophagogastric anastomosis is placed in the left neck at the level of the clavicle. The Ivor Lewis esophagectomy is performed via a laparotomy incision and a right thoracotomy.¹²² The anastomosis is located in the chest at the level of the azygous vein. The equivalence of trans-hiatal esophagectomy to transthoracic esophagectomy for long-term survival has been well documented at different centers throughout the world in both retrospective case series and prospective clinical trials.¹²³⁻¹³⁰

Surgery may have its most important functional impact by changing the mode of recurrence in esophageal cancer. Autopsy findings comparing resected and nonresected patients treated for esophageal cancer found local residual cancer to be much more common among patients who had not undergone surgery as part of their therapy (94.4% versus 21.2%, $P < .0001$). The low incidence of localized disease suggests that esophagectomy, though often palliative in terms of overall survival benefit, may be very effective in minimizing the incidence of local recurrence and its attendant disabling symptoms.¹³¹ Recurrence patterns after trans-hiatal esophagectomy indicate that almost 40% of patients will later develop loco-regional disease, either alone or in combination with systemic metastases. In multivariate analysis, recurrence was found to be related to postoperative lymph node status and the radical nature of the operation.¹³² Surgery will result in better long-term control of local symptoms. The choice of operation may have some impact on the risk for local recurrence. The potential benefit of more radical forms of local resection, such as total thoracic esophagectomy with radical lymphadenectomy, must be balanced against the risk for increased peri-operative morbidity and mortality. Among elderly patients, the trans-hiatal esophagectomy is likely to be a less physiologically demanding

operation. It obviates the need for thoracotomy and therefore avoids the attendant pain and decline in respiratory performance associated with a second incision into the chest. The location of the anastomosis in the neck, as opposed to the right chest, maximizes the extent of the proximal margin and makes management of any potential leak less complicated.¹³³ Anastomotic leaks are generally well tolerated, as the cervical esophagogastric anastomosis is easily accessed and drained, and strictures are safely dilated.¹³⁴ The use of a side-to-side stapled anastomosis in the neck has resulted in a substantial reduction in frequency of anastomotic leaks and later strictures. It represents the latest in a series of technical refinements of this operation.¹³⁵ Orringer et al at the University of Michigan have provided benchmark data regarding the safety and efficacy of trans-hiatal esophagectomy. Data from 1085 patients were reported, with a hospital mortality rate of 4%.¹³⁶ Actuarial survival of patients with carcinoma equaled or exceeded that reported for transthoracic esophagectomy. Late functional results were good or excellent in 70% of patients. Greater safety, fewer complications, and comparable long-term survival have led many to consider trans-hiatal esophagectomy to be the approach of choice for patients with limited functional reserve.^{137,138}

Age-related declines in cardiopulmonary capacity are important in evaluating patients for esophagectomy. A multivariate analysis of postoperative complications after esophageal resection found age and volume of transfusion to be associated significantly with postoperative hypoxemia and the need for prolonged respiratory support.¹³⁹ In a study using the National Medicare claim database for patients aged 65 years and older, the operative mortality of 1.2 million patients who were hospitalized between 1994 and 1999 for major elective surgery was reviewed. Operative mortality was found to vary widely according to the type of procedure. Esophagectomy and pneumonectomy were associated with the highest risk of death, with mortality rates of 13.6% and 13.7%, respectively.¹⁴⁰ Operative mortality among patients 80 years and older was more than twice that observed for patients 65 to 69 years old. A retrospective analysis for risk factors associated with poor outcome after esophagectomy in a series of 269 patients found age ($P = .001$, relative risk [RR] = 2.6) and performance status ($P = .04$, RR = 1.9) to predict operative mortality. Multivariate analysis determined the optimal predictive model to be defined by age (RR = 3.9), intraoperative blood loss (RR = 1.7), pulmonary complications (RR = 6.6), and the need for inotropic support (RR = 10.2).¹⁴¹

Several authors specifically reviewed their experience with esophagectomy among elderly patients. Poon et al studied 167 patients over the age of 70 and compared the results of esophagectomy with that found in 570 younger patients.¹⁴² The resection rate in the elderly population was lower than that in younger patients (48% versus 65%, $P < .001$). No significant differences were observed in the rate of surgical complications. The 30-day mortality was higher in the elderly patients (7.2% versus 3.0%, $P = .02$), but the hospital mortality rate was not significantly different between the elderly and younger age groups (18.0% versus 14.4%, $P = .27$). Survival was similar between the two age groups when deaths from unrelated medical conditions were excluded from analysis. The authors concluded that in the elderly patient, esophagectomy for carcinoma of the esophagus could be carried out with acceptable risk and that intensive peri-operative support would be required. Alexiou et al reviewed 337 patients under the age of 70 and compared them with 150 patients aged 70 to 79 and 36 patients aged 80 to 86 undergoing esophagectomy at a specialty center for thoracic surgery in England. These three groups were analyzed with

regard to preoperative medical status, resectability, complications, operative mortality, and long-term survival. Patients over the age of 70 had fewer pre-existing respiratory problems than younger patients. No significant differences in resectability rate were detected among the three groups (80.8%, 77.7%, and 80%, respectively). Elderly patients had a higher incidence of overall (34% and 36.1%), respiratory (24.7% and 19.4%), and cardiovascular (7.3% and 11.1%) complications than did those aged under 70 years (24.6%, 16.3%, and 2.1%, respectively). However, operative mortality (4.7%, 6.7%, and 5.6%) and 5-year survivals inclusive of operative mortality (25.1%, 21.2%, and 19.8%) were similar among the three groups. Esophagectomy in this specialist thoracic unit was safe and associated with acceptable long-term survival in all age groups.¹⁴³ Jougon et al noted the same in a study that compared 89 patients over the age of 70 years with 451 younger patients. The older patients had a 24.7% morbidity rate and 7.8% mortality. No significant differences between the two groups were found in terms of morbidity, mortality, mean hospital stay, or long-term survival.¹⁴⁴ Chino et al reported a 60% incidence of postoperative complications in a series of 45 patients over the age of 80 years. Five-year survival after resection was 30.8% and comparable to that for younger patients.¹⁴⁵ Xijiang et al reported on a series of 63 elderly patients operated upon for esophageal cancer between 1978 and 1992. A complication rate of 25.4% was noted, with pulmonary problems being most commonly encountered. The 3-year survival rate among patients undergoing surgery with curative intent was 100%, 35%, and 25% in stages I, II, and III, respectively.¹⁴⁶ Naunheim et al described 38 patients over the age of 70 who underwent transthoracic (71%) or trans-hiatal (29%) esophagectomy. Pneumonia was again the most prevalent postoperative complication, occurring in 29% of patients.¹⁴⁷ Thomas et al reported on 56 patients over the age of 70 and compared them with 330 younger patients undergoing esophagectomy for cancer. Pulmonary function, as assessed by spirometry, was significantly worse among the older patients. Operative mortality was comparable in the two groups (10.7% versus 11.2%). Postoperative morbidity included anastomotic leak (10.7% versus 13.6%) and pulmonary complications (17.9% versus 20.6%) in both groups. Excellent palliation of dysphagia was achieved in 92% of the elderly patients who survived operation. Five-year survival was not different for elderly and younger patients (17% versus 18.9%).¹⁴⁸ Among even older patients, the report by Adam et al on 31 octogenarians undergoing esophagectomy demonstrated an elective operative mortality rate of 10.7%, with the successful palliation of dysphagia in 73%. The 5-year survival rate was 17%.¹⁴⁹ Emergency operation was associated with an increased risk of complications and death. Karl et al noted no significant difference in preoperative risk factors, operative mortality, length of stay, length of procedure, estimated blood loss, rate of major complication, or Kaplan-Meier survival rate between patients older than 70 years and those who were younger.¹⁵⁰

Minimally invasive esophagectomy holds the potential for further reducing operative morbidity and mortality.^{151,152} No prospective trials have directly compared traditional open esophagectomy with minimally invasive surgery among elderly patients. There are also no long-term data to determine whether the minimally invasive approach is equivalent to open procedures in terms of stage-specific long-term survival and patterns of tumor recurrence.^{153,154} The same is also true for endoscopic mucosal resection, a minimally invasive technique developed for the treatment of superficial esophageal carcinoma and high-grade dysplasia in Barrett's esophagus.^{155,156}

Improvement in pain control is an essential element in promoting early patient mobilization and preventing respiratory complications such as atelectasis or pneumonia. A multimodality approach to control postoperative pain and the physiologic stress response has led to earlier extubation, earlier discharge from intensive care, and improved patient mobilization.¹⁵⁷ A balanced program of preemptive and postoperative analgesia has been proposed for elderly high-risk patients undergoing esophagectomy.¹⁵⁸ A paravertebral block may be combined with general anesthesia, opioids, and nonsteroidal anti-inflammatory drugs prior to incision. Postoperative analgesia can be provided with either continuous extrapleural intercostal nerve block or thoracic epidural infusion. Regional analgesia in elderly patients may help reduce the need for systemic narcotics. The sedative and neuropsychologic side effects of these drugs may be avoided. Pain scores upon mobilization among patients in whom epidural analgesia was continued for 5 days were found to be significantly decreased in comparison with those from patients who were switched over to patient-controlled analgesia with intravenous morphine in the early postoperative period.¹⁵⁹ The increased use of advanced thoracoscopic and laparoscopic techniques for minimally invasive esophagectomy may further reduce the physiologic impact of the operation and resultant risk of complications related to inadequate analgesia.^{160,161}

One of the prime questions facing physicians caring for elderly patients relates to whether the proposed treatment will yield an acceptable quality of life for the patient. Esophageal obstruction related to tumor progression leads to multiple problems that are, in aggregate, devastating to the patients' sense of well-being. Oral food intake is severely limited, and many patients are unable to swallow their own saliva. This will lead to the persistent need to regurgitate the contents of an obstructed esophagus during the day and predispose to episodes of aspiration. Persistent pain may also result from stasis and inflammation within the obstructed esophagus. The need for tube feeding further limits patient autonomy. A consideration of esophagectomy in an elderly patient must therefore take into account survival benefit, functional outcome, and quality of life. Among patients of advanced age, for whom the potential for long life is quite limited, functional outcome is of paramount importance. Esophagectomy must be examined in terms of its ability to palliate dysphagia and to restore normal swallowing. The functional results after esophagectomy will have to be compared with results obtained after chemoradiation, stenting, or endoscopic ablation.¹⁶²

Comprehensive strategies have been devised to reduce the complications of esophagectomy. Gillinov and Heitmiller reported on a management program from 1990 to 1995 that was designed to maximize airway protection in the postoperative period and discussed their results with trans-hiatal esophagectomy. The clinical pathway consisted of overnight mechanical ventilation, chest physiotherapy, video pharyngo-esophagram on postoperative day 6 or 7, and graduated postesophagectomy therapeutic diet. Pulmonary complications were classified as major or minor, depending upon whether or not a change in therapy was required. Ten patients (10%) had 11 major pulmonary complications that included pneumonia, pleural effusion, exacerbation of pre-existing COPD, and mucus plug requiring bronchoscopy or mechanical ventilation. Patients with major pulmonary complications were older (69.3 ± 9.8 versus 59.2 ± 12.1 years, $P < .02$) and more likely to have pre-existing lung disease. Pneumonia was the most common cause of death following trans-hiatal esophagectomy.¹⁶³ The introduction of clinical care pathways was also associated with a 34% reduction in total hospital costs, with major decreases in pharmacy,

laboratory, radiology, and miscellaneous charges.¹⁶⁴ Orringer et al, in their large series of patients undergoing trans-hiatal esophagectomy at the University of Michigan, emphasized smoking cessation, preoperative incentive spirometry, and walking 1 to 2 miles per day prior to surgery as key elements for early postoperative mobilization and minimizing pulmonary complications.¹³⁶ Intensive-care monitoring was not routinely used in their series of trans-hiatal esophagectomies, as patients were usually extubated in the operating room, immediately after surgery. These strategies reflect the practices of highly experienced centers and may form the framework of clinical guidelines that will optimize the care of elderly patients.

Most clinical trials have focused on morbidity and mortality as measures of patient outcome. The physician's assessment of the relative harms or benefits of treatment may differ considerably from the patient's. Quality-of-life scores are patient based and more likely to accurately reflect the efficacy of various treatments. Complications such as vocal cord palsy may have marked detrimental effects on speech and comfortable swallowing that are difficult to quantify within the context of a clinical trial unless quality of life is taken into account.¹⁶⁵ Simple questionnaire studies have shown only 22% of patients to have no complaints after esophagectomy.¹⁶⁶ Gross measures, such as the ability to return to work, appear to indicate that the majority of patients can achieve a satisfactory quality of life after esophagectomy.¹⁶⁷ However, return to work may be an inappropriate endpoint for elderly patients. Less reflux, regurgitation, and esophagitis are associated with cervical esophagogastric anastomoses than with intrathoracic anastomoses.¹⁶⁸

Few studies have prospectively measured quality of life by using validated and appropriate instruments that are sufficiently sensitive to small but clinically important changes in quality of life. Disease-specific modules have been developed for use in conjunction with generic measures. The European Organization for Research and Treatment of Cancer (EORTC) QLQ-OES24 is an adjunct to the EORTC QLQ-C30 core quality-of-life instrument and was specifically designed for patients undergoing potentially curative treatment or palliation of malignant dysphagia.¹⁶⁹ There is evidence to suggest that these quality-of-life indices may help predict survival in patients with esophageal cancer. Blazeby et al reported on 89 consecutive patients with esophageal cancer who completed the EORTC QLQ-C30 questionnaire and the dysphagia scale from the esophageal cancer module. Univariate analysis revealed that better baseline physical and role function scores were significantly associated with increased survival, and that worse fatigue, appetite loss, and constipation scores were significantly associated with shorter survival ($P < .01$). Multivariate analysis, taking account of associations between the quality-of-life scores and adjusting for age, comorbidity, and tumor stage, showed that only physical function at baseline remained significantly associated with survival.¹⁷⁰ In a related study, consecutive patients undergoing potentially curative esophagectomy or purely palliative treatment were studied with the EORTC QLQ-C30 and the dysphagia scale from the QLQ-OES24 before treatment and at regular intervals for 3 years or until death. Six weeks after esophagectomy, patients reported worse functional, symptom, and global scores than before treatment. In patients who survived at least 2 years, quality-of-life scores returned to preoperative levels within 9 months, but patients who died within 2 years of surgery never regained their former quality of life. In both groups, dysphagia improved after surgery, and the improvement was maintained until death or for the duration of the study. Patients undergoing palliative treatment reported gradual deterioration in most aspects until death.

Esophagectomy was thus found to provide lasting palliation of dysphagia at the cost of a transient reduction in global quality-of-life scores among patients surviving more than 2 years.¹⁷¹

Studies on the functional outcome of esophageal resection have generally focused on patient symptoms. McLarty et al reported on 359 patients undergoing esophagectomy for stage I or stage II esophageal carcinoma. Long-term function and quality of life were measured in 107 patients who survived 5 or more years. Median age at operation was 62 years, with Ivor Lewis resection performed in 72% and trans-hiatal esophagectomy in 13%. Median survival was 10.2 years. Gastroesophageal reflux was present in 60%, symptoms of dumping in 50%, and dysphagia to solid food in 25%. Factors affecting late functional outcome were analyzed, and it was determined that a cervical anastomosis was associated with significantly fewer reflux symptoms and that dumping syndrome occurred more often in younger patients. Quality of life was assessed separately by the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) and compared with the national norm. Scores measuring physical functioning were decreased. Scores measuring ability to work, social interaction, daily activities, emotional dysfunction, perception of health, and levels of energy were similar to national norms, and mental health scores were higher.¹⁷²

Johansson and Walther compared 50 patients over the age of 70 with 89 younger patients at 3, 6, and 12 months after esophagectomy in an effort to determine the influence of age on survival and functional outcome after surgery. The overall hospital mortality rate was only 1.4%, with all deaths occurring in the younger age group. Between 71% and 77% of the patients experienced no dysphagia at the three evaluations during the first postoperative year. The 5-year survival rate was 31%. Survival correlated with tumor stage but not with age. Functional outcome, as measured by dysphagia scores, was equivalent in patients over and under 70 years of age.¹⁷³

Information regarding long-term functional outcome and quality of life after esophagectomy has also been collected from patients undergoing surgery for benign disease. These data are particularly relevant because the length of follow-up is not limited by the progression of malignancy. The Mayo Clinic published their results with esophagectomy for benign disease. Eighty-one patients completed a combined two-part questionnaire regarding esophageal function and quality of life (SF-36) a median of 9.8 years (range, 10 months to 18.9 years) after surgery. Median age at time of esophageal reconstruction was 51 years, and alimentary continuity was re-established with stomach in 71.6%. Dysphagia to solids was present in 59.3%, with one third requiring at least one postoperative dilatation. Heartburn was present in 61.7%. The number of bowel movements per day increased in 45.7% and was unchanged in 44.4%. Age, sex, and type of esophageal reconstruction did not affect late functional outcome. Physical functioning, social functioning, and health perception were decreased ($P < .05$). No significant change was observed in role-physical, mental health, bodily pain, energy or fatigue, and role-emotional scores.¹⁷⁴ Another study from the same institution found that 175 of 255 patients had functional improvement after esophagectomy for benign disease, with a median follow-up of 52 months. Functional results were classified as excellent in 31.8%, good in 10.2%, fair in 35.4%, and poor 22.6%.¹⁷⁵ These data indicate that esophagectomy is associated with an acceptable quality of gastrointestinal function and that the results are durable over time.

The effect of hospital volume on hospital mortality after esophagectomy in the Netherlands was studied over the period from 1993 to 1998. Fifty-two percent of the procedures were performed in low-volume centers averaging 1 to 10 resections per year, 6% were performed in medium-volume centers with 11 to 20 resections a year, and 42% were performed in two high-volume centers averaging more than 50 resections a year. Hospital mortality was found to be 12.1% in low-volume centers and 7.5% in medium-volume hospitals; a 4.9% mortality rate was found in high-volume centers, despite the observation that these specialty units appeared to manage slightly more advanced tumors than the low- and medium-volume centers.¹⁷⁶ The increased operative experience among specialty surgeons who perform high numbers of complex procedures at tertiary-care hospitals may be one of the most critical determinants of patient mortality. Familiarity with the technical pitfalls of procedure and their potential consequences in the postoperative period allows the experienced surgeon to either avoid complications or recognize them earlier once they occur. High-volume hospitals are also more likely to have a wider range of advanced diagnostic or therapeutic services that may salvage patients who become gravely ill after operation.

Studies in the United States have indicated that hospitals with a high volume of esophagectomy, and therefore more experienced surgical teams, can perform the procedure with lower costs and patient mortality rates than low-volume centers can achieve. Logistic regression analysis was used to determine the relationship between hospital volume and mortality in 1561 patients who had esophagectomy for cancer in California between 1990 and 1994.¹⁷⁷ An average of two or fewer resections was performed annually in 88% of hospitals. The mortality rate in hospitals performing more than 30 esophagectomies during the 5-year period was 4.8%. This compared with a mortality rate of 16% for hospitals that performed the procedure less frequently. These results strongly support the importance of an experienced surgical team for complex procedures associated with a high risk of complication. Similar conclusions came from a retrospective cohort study using the SEER-Medicare linked database that examined 5013 patients aged 65 years or older at diagnosis who underwent pancreatectomy, esophagectomy, pneumonectomy, liver resection, or pelvic exenteration between 1984 and 1993.¹⁷⁸ Thirty-day mortality in relation to procedure volume was adjusted for comorbidity, patient age, and cancer stage. Higher volume was linked with lower mortality for pancreatectomy ($P = .004$), esophagectomy ($P < .001$), liver resection ($P = .04$), and pelvic exenteration ($P = .04$), but not for pneumonectomy ($P = .32$). The most striking results were for esophagectomy, for which the operative mortality rose to 17.3% in low-volume hospitals, compared with 3.4% in high-volume hospitals. Adjustments for case mix and other patient factors did not change the finding that low volume is strongly associated with excess mortality. As age increases, other factors that are not controllable, such as delirium and other geriatric complications, may erode the advantage of the experienced surgeon. Mortality may be no different for the oldest-old patients.

The relationship between hospital volume and cost was recently evaluated for 1136 patients undergoing esophageal resection in Maryland. High hospital volume was associated with a fivefold reduction in the risk of death, a 6-day reduction in length of stay, and a savings of \$11,673 in hospital charges.¹⁷⁹ In a study on the relationship between operative volume, hospital size, and cancer specialization on morbidity, mortality, and hospital use after esophagectomy for cancer, data from the Health Care Utilization Project was

used to evaluate all Medicare-reimbursed esophagectomies for treatment of cancer from 1994 to 1996 in 13 national cancer institutions and 88 community hospitals. Complications, length of stay, hospital costs, and mortality were assessed according to hospital size, institutional specialization, and operative volume. Mortality was found to be lower in national cancer institution hospitals than in community hospitals (4.2% versus 13.3%, $P < .05$) or in hospitals performing a large number of esophagectomies (3.0% versus 12.2%, $P < .05$). Multivariate analysis revealed that the independent risk factor for operative mortality is the volume of esophagectomies performed and not the number of other operations, hospital size, or institutional specialization. Hospitals performing a large number of esophagectomies were found to show a tendency toward fewer complications (55% versus 68%, $P = .06$), decreased length of stay (14.7 days versus 17.7 days, $P = .006$), and lower charges (\$39,867 versus \$62,094, $P < .005$). The analysis indicated that the increased experience of the surgical team, and not merely hospital size or cancer specialization, can account for improved patient outcome with lower cost.¹⁸⁰ These data were not stratified by age and did not explicitly report on whether the improvement in overall patient mortality reflects a uniform improvement in all age groups or advances limited to patients of a specific age.

ThoracicSurg 11 (Level B): Screening endoscopic trials should be performed for elderly patients with longstanding reflux or a history of Barrett's esophagus to determine if early detection and treatment of high-grade dysplasia is cost-effective.

ThoracicSurg 12 (Levels B, A): Nonrandomized chemoprevention trials targeted specifically toward at-risk elderly patients should be continued, to be followed by a randomized controlled trial of chemoprevention using the most promising agent and comparing it with usual care.

ThoracicSurg 13 (Level B): The Society of Thoracic Surgeons database and other similar databases should be used to gather data on the impact of age-related comorbidities and other factors related to operative management on the outcomes of esophagectomy for elderly patients.

ThoracicSurg 14 (Level B): A national database for collecting morbidity and long-term survival rates of minimally invasive techniques for esophageal cancer should be established.

ThoracicSurg 15 (Level B): Esophagectomy needs to be evaluated for effectiveness as a procedure for improving quality of life and preventing complications of aspiration in elderly patients.

ThoracicSurg 16 (Level B): Instruments to measure age-specific outcomes of surgery for esophageal cancer need to be developed and validated. Functional status and quality of life should be among the outcomes assessed.

ThoracicSurg 17 (Level A): Large clinical esophageal cancer trials should incorporate the age-specific instruments described in ThoracicSurg 16.

ThoracicSurg 18 (Level B): Esophagectomy could be used as a model for highly complex surgical procedures in the elderly patient to answer the following questions:

- **What makes the high-volume center able to provide better care for elderly esophagectomy patients?**
- **Do high-volume centers achieve better surgical outcomes with the oldest-old patients?**
- **In what ways can care be improved for the elderly patient after esophagectomy?**
- **Once a formula for success is characterized, is it applicable to the care of elderly patients receiving other types of major operations?**

BENIGN ESOPHAGEAL DISEASE

Among elderly persons, disorders of deglutition are quite common.^{181,182} With increasing age, patients develop significant dysphagia, along with achalasia, gastroesophageal reflux disease (GERD), and constipation. Neurologic problems that accompany normal aging and the increased incidence of cerebrovascular accidents also add to dysphagia in the older population. Several swallowing clinics around the country have begun to concentrate the necessary interdisciplinary expertise in one location and have met with some success. The chapter on otolaryngology addresses issues surrounding dysphagia (see Chapter 8).

Disorders of digestion commonly require therapy. They are treated by a variety of nonsurgical methods but sometimes require surgical intervention. Some 750 references deal specifically with operations for achalasia and reflux in the geriatric population. Surgeons and gastroenterologists tend to disagree on the right approach to all patients with reflux regardless of age. Sarani et al performed a survey to understand the variation in approach to the patient with GERD.¹⁸³ Surveys were sent to 1000 randomly selected members of the American Gastroenterological Association (AGA) and to 1000 randomly selected members of the Society of American Gastrointestinal Endoscopic Surgeons (SAGES). Twenty percent of the AGA surveys and 33% of the SAGES surveys were completed and returned. The AGA group considered patients whose symptoms are not well controlled, those who have complications of disease, and those who require significant lifestyle changes to control their symptoms as the best candidates for surgical evaluation. As a group, gastroenterologists remain somewhat hesitant to refer patients for laparoscopic antireflux surgery. Surgeons considered patients whose symptoms have been well controlled with medical therapy, those who have complications of disease, and those who require significant lifestyle changes to control their symptoms as ideal candidates for fundoplication. As new, less invasive approaches emerge, the therapy for GERD will likely continue to be controversial.

Surgeons agree that the trend is to perform less invasive procedures and that results are equal to or better than open procedures. However, laparoscopic antireflux surgery is commonly denied to older patients with GERD because of a perceived higher operative complication rate, a decreased impact of the intervention on quality of life, and decreased cost-effectiveness. Several series of procedures on elderly patients are now available for

evaluation. These are either retrospective reviews or historical prospective studies. One of the first reviews to directly address the issues relating to elderly patients was reported by Trus et al in 1998.¹⁸⁴ They had operated upon 42 patients aged 65 years and over out of a total of 359 patients with GERD. These patients did as well as the younger patients. Brunt et al reported an almost identical study the following year from Washington University.¹⁸⁵ In 2001, Kamolz et al evaluated the quality-of-life issues in elderly patients who had antireflux operations.¹⁸⁶ They followed 72 elderly patients after surgery for 1 to 3 years. Three patients developed significant complications, and two required reoperation. The remaining patients did well, with a significant increase in their perceived quality of life.

In 2002, two prospective cohort studies were reported. Bammer et al examined the safety and long-term outcome of patients aged 80 years and older who were having laparoscopic antireflux surgery.¹⁸⁷ Immediate results were good, with two major complications and no deaths. At follow-up, 96% stated that their surgical outcome was satisfactory. Two patients were suffering from severe symptoms. Overall well-being at a mean follow-up time of 3.1 years was 7.5 (range 3 to 10) on a 10-point scale in comparison with 2.2 (range 1 to 5) before surgery ($P = .03$). Khajanchee et al culled from their database of 1100 patients 30 patients with a mean age of 71 years who had severe symptoms of GERD and compared them with a young cohort of patients from the same database.¹⁸⁸ All patients had at least 6 months of follow-up. Each group demonstrated a significant improvement in the postoperative symptom assessment scores and the esophageal functional studies ($P < .05$). No significant differences were found in postoperative complications, postoperative hospital stay, postoperative symptom scores, Demeester scores, or the quality-of-life data. Even reoperative procedures seem to be safe in experienced hands. Kamolz et al described their series of 11 patients aged 65 years and over who required reoperation.¹⁸⁹ There were no serious postoperative complications, and the 3- and 1-year follow-up demonstrated continued good results.

Newer techniques for even less invasive procedures than those now used are being developed. These will require some refinement before they can be considered to be appropriate for trials in the elderly population.

ThoracicSurg 19 (Level B): A structured literature review should be performed and a consensus conference between gastroenterologists and surgeons should be organized to establish criteria, based on symptoms and quality of life, for intervention in the management of gastroesophageal reflux disease, particularly in elderly patients.

ThoracicSurg 20 (Level A): A prospective trial of laparoscopic antireflux surgery comparing elderly patients with younger matched control patients operated on during the same period should be performed to determine the suitability of this operation for the elderly patient.

RESEARCH IN SUPPORT OF IMPROVED CARE

Thoracic surgeons have extended the indications for operation into the oldest segment of the population. This coincides with advances in the medical management of comorbidities and improvements in critical care. Operative interventions are an integral part of advanced therapy for the aging population. Technical improvements, including minimally invasive

approaches, continue to be investigated. Complex operations such as esophagectomies are performed routinely on older patients, with excellent results.

Accurate data are needed to determine the population at risk for the development of esophageal and chronic lung diseases and those who might benefit from surgical intervention. At the primary care level, surveys must be performed to identify age bias or aberration from evaluation protocols and to determine whether surgical candidates are referred appropriately. Surgeons using evidence-based protocols in conjunction with pulmonologists, gastroenterologists, and oncologists must collaborate to identify appropriate candidates for surgical intervention and to manage them successfully through the perioperative period.

Older patients undergoing operations require more advanced techniques to reduce morbidity. Preoperative preparation through organized care is important in preparing the older person for the stress of a large thoracic procedure. Safer anesthetic techniques and greater use of minimally invasive operations may yield better outcomes. The postoperative phase, which includes intensive care, hospital stay, and rehabilitation periods, require refinement in protocols and procedures to afford the best results. Thoracic surgeons require the latest data and educational support to be able to treat their older patients optimally.

KEY RESEARCH QUESTIONS IN GERIATRIC THORACIC SURGERY

The most important research areas identified in the specialty of geriatric thoracic surgery are the impact of preoperative preparation on improving the perioperative experience, the design and assessment of geriatric clinical management programs to accommodate the increasingly older and sicker patients who may require thoracic operations, and the analysis of short- and long-term quality-of-life outcomes among geriatric thoracic surgical patients. Studies to address these issues include clinical trials, observational studies, subgroup analyses, and expansion of databases to address key questions about the care of elderly thoracic surgical patients.

ThoracicSurg KQ1: How effective is preoperative preparation in improving the immediate surgical outcome for elderly patients?

Hypothesis-generating research studies should focus on the technical aspects of specific thoracic operations. Database analyses and observational studies of specific procedures for preoperative evaluation, education, and preparation of elderly patients should elucidate the risk factors and specific preparation necessary for thoracic surgical procedures. Newer methods of assessment may ultimately shape management decisions in thoracic surgery for the elderly patient, as they may alter practices of surgeons, revise risk stratification, and further clarify the expectations for postoperative recovery from thoracic surgery by the geriatric patient. Cohort studies to compare various preoperative preparation strategies for elderly patients are needed. Multivariate analyses of such studies may clarify the minimum functional capacity and the role of treatment techniques to achieve the desired outcome.

Hypothesis-testing research should include randomized trials of elderly patients with and without specific preoperative habilitation.

ThoracicSurg KQ2: What changes in perioperative care are needed to improve outcomes in the elderly thoracic surgical patient?

Hypothesis-generating research should include methodologic studies to identify high-risk elderly patients and devise clinical pathways for their care. Database analyses of the pre-hospital, in-hospital, and rehabilitative periods of elderly surgical patients should be performed to identify clinical management strategies that result in decreased morbidity and improved functional recovery. Prospective cohort studies of patients aged 75 and over treated by nonoperative means, standard operation, and minimally invasive modalities are needed to clarify the potential benefits of each therapy.

Hypothesis-testing research studies include randomized trials of perioperative management strategies, with emphasis on reduction in morbidity. Case-control or randomized studies of elder-specific pathways to elucidate the benefit of pathways in obtaining better functional outcomes and reducing in-hospital adverse events are needed. The aim of these studies would be to identify treatment strategies that reduce the incidence of perioperative pulmonary complications, wound-related problems, and end-organ failure, which have been shown to be especially prevalent in elderly thoracic patients.

ThoracicSurg KQ3: To what extent do thoracic surgical operations improve quality-of-life outcomes in the elderly patient population?

Hypothesis-generating research should include the expansion of current clinical databases to include short- and long-term quality-of-life outcomes of elderly thoracic surgical patients. The ability to satisfactorily gauge the success of thoracic operations in improving quality of life for elderly patients depends heavily on the accurate measure of preoperative and perioperative functional capabilities. Observational studies and database analysis should focus on the refinement of risk factors for poor outcomes in elderly surgically treated patients.

Hypothesis-testing research studies to address this question would be aimed at comparing surgical and medical therapy for lung and esophageal disease in older patients. Randomized trials of elderly patients treated for specific disease entities, particularly chronic lung disease and thoracic cancers, using age-specific instruments are needed to clarify the role of operative therapy in improving survival and quality of life.

REFERENCES

1. American Cancer Society: Cancer Facts and Figures. American Cancer Society, 2002. p 10.
2. Feinstein MB, Bach PB. Epidemiology of lung cancer. *Chest Surg Clin N Am* 2000;10:653-661.
3. Cooley ME, Kaiser LR, Abrahm JL, Giarelli E. The silent epidemic: tobacco and the evolution of lung cancer and its treatment. *Cancer Invest* 2001;19:739-751.
4. Fry WA, Phillips JL, Menck HR. Ten-year survey of lung cancer treatment and survival in hospitals in the United States: a national cancer data base report. *Cancer* 1999;86:1867-1876.
5. Haura EB. Treatment of advanced non-small-cell lung cancer: a review of current randomized clinical trials and an examination of emerging therapies. *Cancer Control* 2001;8:326-336.

6. Flehinger BJ, Kimmel M, Melamed MR. The effect of surgical treatment on survival from early lung cancer: implications for screening. *Chest* 1992;101:1013-1018.
7. Martini N, Beattie EJ, Jr. Results of surgical treatment in Stage I lung cancer. *J Thorac Cardiovasc Surg* 1977;74:499-505.
8. Williams DE, Pairolero PC, Davis CS, et al. Survival of patients surgically treated for stage I lung cancer. *J Thorac Cardiovasc Surg* 1981;82:70-76.
9. Pairolero PC, Williams DE, Bergstralh EJ, et al. Postsurgical stage I bronchogenic carcinoma: morbid implications of recurrent disease. *Ann Thorac Surg* 1984;38:331-338.
10. Harpole DH, Jr., Herndon JE, 2nd, Young WG, Jr., et al. Stage I nonsmall cell lung cancer: a multivariate analysis of treatment methods and patterns of recurrence. *Cancer* 1995;76:787-796.
11. Wada H, Tanaka F, Yanagihara K, et al. Time trends and survival after operations for primary lung cancer from 1976 through 1990. *J Thorac Cardiovasc Surg* 1996;112:349-355.
12. Mountain CF. Revisions in the International System for Staging Lung Cancer. *Chest* 1997;111:1710-1717.
13. Strauss GM. Screening for lung cancer: an evidence-based synthesis. *Surg Oncol Clin N Am* 1999;8:747-774, viii.
14. Sobue T, Suzuki T, Matsuda M, et al. Survival for clinical stage I lung cancer not surgically treated: comparison between screen-detected and symptom-detected cases. The Japanese Lung Cancer Screening Research Group. *Cancer* 1992;69:685-692.
15. Eddy DM. Screening for lung cancer. *Ann Intern Med* 1989;111:232-237.
16. Bailar JC, III. Early lung cancer detection: summary and conclusions. National Cancer Institute Early Lung Cancer Detection Program Cooperative Study Group. *Am Rev Respir Dis* 1984;130:565-570.
17. Will BP, Berthelot JM, Nobrega KM, et al. Canada's Population Health Model (POHEM): a tool for performing economic evaluations of cancer control interventions. *Eur J Cancer* 2001;37:1797-1804.
18. Tockman MS, Mulshine JL. The early detection of occult lung cancer. *Chest Surg Clin N Am* 2000;10:737-749.
19. Tockman MS, Mulshine JL, Piantadosi S, et al. Prospective detection of preclinical lung cancer: results from two studies of heterogeneous nuclear ribonucleoprotein A2/B1 overexpression. *Clin Cancer Res* 1997;3:2237-2246.
20. Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet* 1999;354:99-105.
21. Marshall D, Simpson KN, Earle CC, Chu CW. Economic decision analysis model of screening for lung cancer. *Eur J Cancer* 2001;37:1759-1767.
22. Hollen PJ, Gralla RJ, Kris MG, Cox C. Quality of life during clinical trials: conceptual model for the Lung Cancer Symptom Scale (LCSS). *Support Care Cancer* 1994;2:213-222.
23. Anderson H, Hopwood P, Stephens RJ, et al. Gemcitabine plus best supportive care (BSC) vs BSC in inoperable non-small cell lung cancer—a randomized trial with quality of life as the primary outcome. UK NSCLC Gemcitabine Group. *Non-Small Cell Lung Cancer. Br J Cancer* 2000;83:447-453.
24. Pater JL, Zee B, Palmer M, et al. Fatigue in patients with cancer: results with National Cancer Institute of Canada Clinical Trials Group studies employing the EORTC QLQ-C30. *Support Care Cancer* 1997;5:410-413.
25. Auchter RM, Scholtens D, Adak S, et al. Quality of life assessment in advanced non-small-cell lung cancer patients undergoing an accelerated radiotherapy regimen: report of ECOG study 4593. Eastern Cooperative Oncology Group. *Int J Radiat Oncol Biol Phys* 2001;50:1199-1206.

26. The Elderly Lung Cancer Vinorelbine Italian Study Group. Effects of vinorelbine on quality of life and survival of elderly patients with advanced non-small-cell lung cancer. *J Natl Cancer Inst* 1999;91:66-72.
27. Gridelli C. The ELVIS trial: a phase III study of single-agent vinorelbine as first-line treatment in elderly patients with advanced non-small cell lung cancer. Elderly Lung Cancer Vinorelbine Italian Study. *Oncologist* 2001;6 Suppl 1:4-7.
28. 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.
29. Berggren H, Ekroth R, Malmberg R, et al. Hospital mortality and long-term survival in relation to preoperative function in elderly patients with bronchogenic carcinoma. *Ann Thorac Surg* 1984;38:633-636.
30. Shirakusa T, Tsutsui M, Iriki N, et al. Results of resection for bronchogenic carcinoma in patients over the age of 80. *Thorax* 1989;44:189-191.
31. Evans EW. Resection for bronchial carcinoma in the elderly. *Thorax* 1973;28:86-88.
32. Ginsberg RJ, Hill LD, Eagan RT, et al. Modern thirty-day operative mortality for surgical resections in lung cancer. *J Thorac Cardiovasc Surg* 1983;86:654-658.
33. de Perrot M, Licker M, Reymond MA, et al. Influence of age on operative mortality and long-term survival after lung resection for bronchogenic carcinoma. *Eur Respir J* 1999;14:419-422.
34. Pagni S, McKelvey A, Riordan C, et al. Pulmonary resection for malignancy in the elderly: is age still a risk factor? *Eur J Cardiothorac Surg* 1998;14:40-44; discussion 44-45.
35. Harvey JC, Erdman C, Pisch J, Beattie EJ. Surgical treatment of non-small cell lung cancer in patients older than seventy years. *J Surg Oncol* 1995;60:247-249.
36. Hanagiri T, Muranaka H, Hashimoto M, et al. Results of surgical treatment of lung cancer in octogenarians. *Lung Cancer* 1999;23:129-133.
37. 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.
38. 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.
39. Bates M. Results of surgery for bronchial carcinoma in patients aged 70 and over. *Thorax* 1970;25:77-78.
40. Oliaro A, Leo F, Filosso PL, et al. Resection for bronchogenic carcinoma in the elderly. *J Cardiovasc Surg (Torino)* 1999;40:715-719.
41. Jensik RJ, Faber LP, Milloy FJ, Monson DO. Segmental resection for lung cancer: a fifteen-year experience. *J Thorac Cardiovasc Surg* 1973;66:563-572.
42. Sioris T, Salo J, Perhoniemi V, Mattila S. Surgery for lung cancer in the elderly. *Scand Cardiovasc J* 1999;33:222-227.
43. Tanita T, Hoshikawa Y, Tabata T, et al. Functional evaluations for pulmonary resection for lung cancer in octogenarians: investigation from postoperative complications. *Jpn J Thorac Cardiovasc Surg* 1999;47:253-261.
44. Ishida T, Yokoyama H, Kaneko S, et al. Long-term results of operation for non-small cell lung cancer in the elderly. *Ann Thorac Surg* 1990;50:919-922.
45. Wada H, Nakamura T, Nakamoto K, et al. Thirty-day operative mortality for thoracotomy in lung cancer. *J Thorac Cardiovasc Surg* 1998;115:70-73.
46. Bernet F, Brodbeck R, Guenin MO, et al. Age does not influence early and late tumor-related outcome for bronchogenic carcinoma. *Ann Thorac Surg* 2000;69:913-918.
47. Mane JM, Estape J, Sanchez-Lloret J, et al. Age and clinical characteristics of 1433 patients with lung cancer. *Age Ageing* 1994;23:28-31.
48. Aoki T, Yamato Y, Tsuchida M, et al. Pulmonary complications after surgical treatment of lung cancer in octogenarians. *Eur J Cardiothorac Surg* 2000;18:662-665.

49. Wada H, Nakamura T, Nakamoto K, et al. Thirty-day operative mortality for thoracotomy in lung cancer. *J Thorac Cardiovasc Surg* 1998;115:70-73.
50. 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.
51. Wang J, Olak J, Ultmann RE, Ferguson MK. Assessment of pulmonary complications after lung resection. *Ann Thorac Surg* 1999;67:1444-1447.
52. Holden DA, Rice TW, Stelmach K, Meeker DP. Exercise testing, 6-min walk, and stair climb in the evaluation of patients at high risk for pulmonary resection. *Chest* 1992;102:1774-1779.
53. Mizushima Y, Noto H, Sugiyama S, et al. Survival and prognosis after pneumonectomy for lung cancer in the elderly. *Ann Thorac Surg* 1997;64:193-198.
54. Bernard A, Deschamps C, Allen MS, et al. Pneumonectomy for malignant disease: factors affecting early morbidity and mortality. *J Thorac Cardiovasc Surg* 2001;121:1076-1082.
55. Magdeleinat P, Alifano M, Benbrahem C, et al. Surgical treatment of lung cancer invading the chest wall: results and prognostic factors. *Ann Thorac Surg* 2001;71:1094-1099.
56. Kirsh MM, Rotman H, Bove E, et al. Major pulmonary resection for bronchogenic carcinoma in the elderly. *Ann Thorac Surg* 1976;22:369-373.
57. 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.
58. Joo JB, DeBord JR, Montgomery CE, et al. Perioperative factors as predictors of operative mortality and morbidity in pneumonectomy. *Am Surg* 2001;67:318-321; discussion 321-312.
59. Breyer RH, Zippe C, Pharr WF, et al. Thoracotomy in patients over age seventy years: ten-year experience. *J Thorac Cardiovasc Surg* 1981;81:187-193.
60. Sherman S, Guidot CE. The feasibility of thoracotomy for lung cancer in the elderly. *JAMA* 1987;258:927-930.
61. O'Rourke MA, Crawford J. Lung cancer in the elderly. *Clin Geriatr Med* 1987;3:595-623.
62. von Knorring J, Lepantalo M, Lindgren L, Lindfors O. Cardiac arrhythmias and myocardial ischemia after thoracotomy for lung cancer. *Ann Thorac Surg* 1992;53:642-647.
63. Yano T, Yokoyama H, Fukuyama Y, et al. The current status of postoperative complications and risk factors after a pulmonary resection for primary lung cancer: a multivariate analysis. *Eur J Cardiothorac Surg* 1997;11:445-449.
64. Asamura H, Naruke T, Tsuchiya R, et al. What are the risk factors for arrhythmias after thoracic operations? A retrospective multivariate analysis of 267 consecutive thoracic operations. *J Thorac Cardiovasc Surg* 1993;106:1104-1110.
65. Ferguson TB, Jr., Hammill BG, Peterson ED, et al. A decade of change—risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990-1999: a report from the STS National Database Committee and the Duke Clinical Research Institute. Society of Thoracic Surgeons. *Ann Thorac Surg* 2002;73:480-489; discussion 489-490.
66. Tovar EA, Roethe RA, Weissig MD, et al. Muscle-sparing minithoracotomy with intercostal nerve cryoanalgesia: an improved method for major lung resections. *Am Surg* 1998;64:1109-1115.
67. McKenna RJ, Jr. Thoracoscopic lobectomy with mediastinal sampling in 80-year-old patients. *Chest* 1994;106:1902-1904.
68. Ishida T, Ishii T, Yamazaki K, et al. Thoracoscopic limited resection of bronchogenic carcinoma in patients over the age of 80. *Int Surg* 1996;81:237-240.
69. Kaga K, Park J, Nishiumi N, et al. Usefulness of video-assisted thoracic surgery (Two Windows Method) in the treatment of lung cancer for elderly patients. *J Cardiovasc Surg (Torino)* 1999;40:721-723.
70. Yim AP. Thoracoscopic surgery in the elderly population. *Surg Endosc* 1996;10:880-882.
71. Asamura H, Nakayama H, Kondo H, et al. Video-assisted lobectomy in the elderly. *Chest* 1997;111:1101-1105.

72. Shennib HA, Landreneau R, Mulder DS, Mack M. Video-assisted thoracoscopic wedge resection of T1 lung cancer in high-risk patients. *Ann Surg* 1993;218:555-558; discussion 558-560.
73. McKenna RJ, Jr., Fischel RJ, Wolf R, Wurnig P. Video-assisted thoracic surgery (VATS) lobectomy for bronchogenic carcinoma. *Semin Thorac Cardiovasc Surg* 1998;10:321-325.
74. Lewis RJ, Caccavale RJ. Video-assisted thoracic surgical non-rib spreading simultaneously stapled lobectomy (VATS(n)SSL). *Semin Thorac Cardiovasc Surg* 1998;10:332-339.
75. Jaklitsch MT, Bueno R, Swanson SJ, et al. New surgical options for elderly lung cancer patients. *Chest* 1999;116:480S-485S.
76. Lewis RJ, Caccavale RJ, Bocage JP, Widmann MD. Video-assisted thoracic surgical non-rib spreading simultaneously stapled lobectomy: a more patient-friendly oncologic resection. *Chest* 1999;116:1119-1124.
77. Kozak LJ, Hall MJ, Owings MF. National Hospital Discharge Survey: 2000 Annual Summary with detailed diagnosis and procedure data. *Vital Health Stat* 2002;Series 13.
78. Scanlon PD, Connett JE, Waller LA, et al. Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease. The Lung Health Study. *Am J Respir Crit Care Med* 2000;161:381-390.
79. Croxton TL, Weinmann GG, Senior RM, Hoidal JR. Future research directions in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2002;165:838-844.
80. Gavazzi G, Orliaguet O, Coume M, et al. [Thoracic empyema in very old patients: two types of clinical presentation]. *Rev Med Interne* 2001;22:1124-1127.
81. Chu MW, Dewar LR, Burgess JJ, Busse EG. Empyema thoracis: lack of awareness results in a prolonged clinical course. *Can J Surg* 2001;44:284-288.
82. Cameron R. Intra-pleural fibrinolytic therapy vs. conservative management in the treatment of parapneumonic effusions and empyema. *Cochrane Database Syst Rev* 2000;(3):CD002312.
83. Hutter JA, Harari D, Braimbridge MV. The management of empyema thoracis by thoracoscopy and irrigation. *Ann Thorac Surg* 1985;39:517-520.
84. Landreneau RJ, Keenan RJ, Hazelrigg SR, et al. Thoracoscopy for empyema and hemothorax. *Chest* 1996;109:18-24.
85. Angelillo-Mackinlay T, Lyons GA, Piedras MB, Angelillo-Mackinlay D. Surgical treatment of postpneumonic empyema. *World J Surg* 1999;23:1110-1113.
86. Coote N. Surgical versus non-surgical management of pleural empyema. *Cochrane Database Syst Rev* 2002;(2):CD001956.
87. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. *CA Cancer J Clin* 2000;50:7-33.
88. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF, Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991;265:1287-1289.
89. Lund O, Hasenkam JM, Aagaard MT, Kimose HH. Time-related changes in characteristics of prognostic significance in carcinomas of the oesophagus and cardia. *Br J Surg* 1989;76:1301-1307.
90. Forastiere AA, Heitmiller RF, Kleinberg L. Multimodality therapy for esophageal cancer. *Chest* 1997;112:195S-200S.
91. Rothwell JF, Feehan E, Reid I, et al. Delay in treatment for oesophageal cancer. *Br J Surg* 1997;84:690-693.
92. Kirby TJ, Rice TW. The epidemiology of esophageal carcinoma: the changing face of a disease. *Chest Surg Clin N Am* 1994;4:217-225.
93. Rogot E, Murray JL. Smoking and causes of death among U.S. veterans: 16 years of observation. *Public Health Rep* 1980;95:213-222.
94. Yu MC, Garabrant DH, Peters JM, Mack TM. Tobacco, alcohol, diet, occupation, and carcinoma of the esophagus. *Cancer Res* 1988;48:3843-3848.

95. Tuyns AJ. Oesophageal cancer in non-smoking drinkers and in non-drinking smokers. *Int J Cancer* 1983;32:443-444.
96. Kjaerheim K, Gaard M, Andersen A. The role of alcohol, tobacco, and dietary factors in upper aerogastric tract cancers: a prospective study of 10,900 Norwegian men. *Cancer Causes Control* 1998;9:99-108.
97. Brown LM, Silverman DT, Pottern LM, et al. Adenocarcinoma of the esophagus and esophagogastric junction in white men in the United States: alcohol, tobacco, and socioeconomic factors. *Cancer Causes Control* 1994;5:333-340.
98. Gammon MD, Schoenberg JB, Ahsan H, et al. Tobacco, alcohol, and socioeconomic status and adenocarcinomas of the esophagus and gastric cardia. *J Natl Cancer Inst* 1997;89:1277-1284.
99. Zhang ZF, Kurtz RC, Sun M, et al. Adenocarcinomas of the esophagus and gastric cardia: medical conditions, tobacco, alcohol, and socioeconomic factors. *Cancer Epidemiol Biomarkers Prev* 1996;5:761-768.
100. Kabat GC, Ng SK, Wynder EL. Tobacco, alcohol intake, and diet in relation to adenocarcinoma of the esophagus and gastric cardia. *Cancer Causes Control* 1993;4:123-132.
101. Gray JR, Coldman AJ, MacDonald WC. Cigarette and alcohol use in patients with adenocarcinoma of the gastric cardia or lower esophagus. *Cancer* 1992;69:2227-2231.
102. Brown LM, Swanson CA, Gridley G, et al. Adenocarcinoma of the esophagus: role of obesity and diet. *J Natl Cancer Inst* 1995;87:104-109.
103. Lagergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999;340:825-831.
104. Chow WH, Blot WJ, Vaughan TL, et al. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. *J Natl Cancer Inst* 1998;90:150-155.
105. Cameron AJ, Lomboy CT. Barrett's esophagus: age, prevalence, and extent of columnar epithelium. *Gastroenterology* 1992;103:1241-1245.
106. Altorki NK, Oliveria S, Schrupp DS. Epidemiology and molecular biology of Barrett's adenocarcinoma. *Semin Surg Oncol* 1997;13:270-280.
107. Spechler SJ, Robbins AH, Rubins HB, et al. Adenocarcinoma and Barrett's esophagus: an overrated risk? *Gastroenterology* 1984;87:927-933.
108. Skinner DB, Walther BC, Riddell RH, et al. Barrett's esophagus: comparison of benign and malignant cases. *Ann Surg* 1983;198:554-565.
109. Williamson WA, Ellis FH, Jr., Gibb SP, et al. Barrett's esophagus: prevalence and incidence of adenocarcinoma. *Arch Intern Med* 1991;151:2212-2216.
110. Cameron AJ, Ott BJ, Payne WS. The incidence of adenocarcinoma in columnar-lined (Barrett's) esophagus. *N Engl J Med* 1985;313:857-859.
111. Schneider PM, Casson AG, Levin B, et al. Mutations of p53 in Barrett's esophagus and Barrett's cancer: a prospective study of ninety-eight cases. *J Thorac Cardiovasc Surg* 1996;111:323-331; discussion 331-323.
112. D'Amico TA, Harpole DH, Jr. Molecular biology of esophageal cancer. *Chest Surg Clin N Am* 2000;10:451-469.
113. Singh SP, Lipman J, Goldman H, et al. Loss or altered subcellular localization of p27 in Barrett's associated adenocarcinoma. *Cancer Res* 1998;58:1730-1735.
114. Blot WJ, Fraumeni JF, Jr. Trends in esophageal cancer mortality among US blacks and whites. *Am J Public Health* 1987;77:296-298.
115. Bytzer P, Christensen PB, Damkier P, et al. Adenocarcinoma of the esophagus and Barrett's esophagus: a population-based study. *Am J Gastroenterol* 1999;94:86-91.
116. Heitmiller RF, Redmond M, Hamilton SR. Barrett's esophagus with high-grade dysplasia: an indication for prophylactic esophagectomy. *Ann Surg* 1996;224:66-71.
117. Moran EM. Epidemiological and clinical aspects of nonsteroidal anti-inflammatory drugs and cancer risks. *J Environ Pathol Toxicol Oncol* 2002;21:193-201.

118. Buttar NS, Wang KK, Leontovich O, et al. Chemoprevention of esophageal adenocarcinoma by COX-2 inhibitors in an animal model of Barrett's esophagus. *Gastroenterology* 2002;122:1101-1112.
119. Kaur BS, Khamnehei N, Iravani M, et al. Rofecoxib inhibits cyclooxygenase 2 expression and activity and reduces cell proliferation in Barrett's esophagus. *Gastroenterology* 2002;123:60-67.
120. Lin P, Chen Z, Hou J, et al. [Chemoprevention of esophageal cancer]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 1998;20:413-418.
121. Krasna MJ. Surgical staging and surgical treatment in esophageal cancer. *Semin Oncol* 1999;26:9-11.
122. Visbal AL, Allen MS, Miller DL, et al. Ivor Lewis esophagogastrectomy for esophageal cancer. *Ann Thorac Surg* 2001;71:1803-1808.
123. Jauch KW, Bacha EA, Denecke H, et al. Esophageal carcinoma: prognostic features and comparison between blunt transhiatal dissection and transthoracic resection. *Eur J Surg Oncol* 1992;18:553-562.
124. Bolton JS, Sardi A, Bowen JC, Ellis JK. Transhiatal and transthoracic esophagectomy: a comparative study. *J Surg Oncol* 1992;51:249-253.
125. Goldmanc M, Maddern G, Le Prise E, et al. Oesophagectomy by a transhiatal approach or thoracotomy: a prospective randomized trial. *Br J Surg* 1993;80:367-370.
126. Horstmann O, Verreet PR, Becker H, et al. Transhiatal oesophagectomy compared with transthoracic resection and systematic lymphadenectomy for the treatment of oesophageal cancer. *Eur J Surg* 1995;161:557-567.
127. Putnam JB, Jr., Suell DM, McMurtrey MJ, et al. Comparison of three techniques of esophagectomy within a residency training program. *Ann Thorac Surg* 1994;57:319-325.
128. Jacobi CA, Zieren HU, Muller JM, Pichlmaier H. Surgical therapy of esophageal carcinoma: the influence of surgical approach and esophageal resection on cardiopulmonary function. *Eur J Cardiothorac Surg* 1997;11:32-37.
129. Millikan KW, Silverstein J, Hart V, et al. A 15-year review of esophagectomy for carcinoma of the esophagus and cardia. *Arch Surg* 1995;130:617-624.
130. Gluch L, Smith RC, Bambach CP, Brown AR. Comparison of outcomes following transhiatal or Ivor Lewis esophagectomy for esophageal carcinoma. *World J Surg* 1999;23:271-275; discussion 275-276.
131. Mafune KI, Tanaka Y, Takubo K. Autopsy findings in patients with esophageal carcinoma: comparison between resection and nonresection groups. *J Surg Oncol* 2000;74:196-200.
132. Hulscher JB, van Sandick JW, Tijssen JG, et al. The recurrence pattern of esophageal carcinoma after transhiatal resection. *J Am Coll Surg* 2000;191:143-148.
133. Blewett CJ, Miller JD, Young JE, et al. Anastomotic leaks after esophagectomy for esophageal cancer: a comparison of thoracic and cervical anastomoses. *Ann Thorac Cardiovasc Surg* 2001;7:75-78.
134. Honkoop P, Siersema PD, Tilanus HW, et al. Benign anastomotic strictures after transhiatal esophagectomy and cervical esophagogastrotomy: risk factors and management. *J Thorac Cardiovasc Surg* 1996;111:1141-1146; discussion 1147-1148.
135. Orringer MB, Marshall B, Iannettoni MD. Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis. *J Thorac Cardiovasc Surg* 2000;119:277-288.
136. Orringer MB, Marshall B, Iannettoni MD. Transhiatal esophagectomy: clinical experience and refinements. *Ann Surg* 1999;230:392-400; discussion 400-393.
137. Tilanus HW, Hop WC, Langenhorst BL, van Lanschot JJ. Esophagectomy with or without thoracotomy: is there any difference? *J Thorac Cardiovasc Surg* 1993;105:898-903.

138. Bolton JS, Ochsner JL, Abdoh AA. Surgical management of esophageal cancer: a decade of change. *Ann Surg* 1994;219:475-480.
139. Tsutsui S, Moriguchi S, Morita M, et al. Multivariate analysis of postoperative complications after esophageal resection. *Ann Thorac Surg* 1992;53:1052-1056.
140. Finlayson EV, Birkmeyer JD. Operative mortality with elective surgery in older adults. *Eff Clin Pract* 2001;4:172-177.
141. Ferguson MK, Martin TR, Reeder LB, Olak J. Mortality after esophagectomy: risk factor analysis. *World J Surg* 1997;21:599-603; discussion 603-594.
142. Poon RT, Law SY, Chu KM, et al. Esophagectomy for carcinoma of the esophagus in the elderly: results of current surgical management. *Ann Surg* 1998;227:357-364.
143. Alexiou C, Beggs D, Salama FD, et al. Surgery for esophageal cancer in elderly patients: the view from Nottingham. *J Thorac Cardiovasc Surg* 1998;116:545-553.
144. Jougon JB, Ballester M, Duffy J, et al. Esophagectomy for cancer in the patient aged 70 years and older. *Ann Thorac Surg* 1997;63:1423-1427.
145. Chino O, Makuuchi H, Machimura T, et al. Treatment of esophageal cancer in patients over 80 years old. *Surg Today* 1997;27:9-16.
146. Xijiang Z, Xizeng Z, Xishan H, Hongjing J. Surgical treatment for carcinoma of the esophagus in the elderly patient. *Ann Thorac Cardiovasc Surg* 1999;5:182-186.
147. Naunheim KS, Hanosh J, Zwischenberger J, et al. Esophagectomy in the septuagenarian. *Ann Thorac Surg* 1993;56:880-883; discussion 883-884.
148. Thomas P, Doddoli C, Neville P, et al. Esophageal cancer resection in the elderly. *Eur J Cardiothorac Surg* 1996;10:941-946.
149. Adam DJ, Craig SR, Sang CT, et al. Esophagectomy for carcinoma in the octogenarian. *Ann Thorac Surg* 1996;61:190-194.
150. Karl RC, Smith SK, Fabri PJ. Validity of major cancer operations in elderly patients. *Ann Surg Oncol* 1995;2:107-113.
151. Luketich JD, Nguyen NT, Weigel T, et al. Minimally invasive approach to esophagectomy. *JSLs* 1998;2:243-247.
152. Watson DI, Davies N, Jamieson GG. Totally endoscopic Ivor Lewis esophagectomy. *Surg Endosc* 1999;13:293-297.
153. Peracchia A, Rosati R, Fumagalli U, et al. Thoracoscopic esophagectomy: are there benefits? *Semin Surg Oncol* 1997;13:259-262.
154. Luketich JD, Schauer PR, Christie NA, et al. Minimally invasive esophagectomy. *Ann Thorac Surg* 2000;70:906-911; discussion 911-902.
155. Noguchi H, Naomoto Y, Kondo H, et al. Evaluation of endoscopic mucosal resection for superficial esophageal carcinoma. *Surg Laparosc Endosc Percutan Tech* 2000;10:343-350.
156. Ell C, May A, Gossner L, et al. Endoscopic mucosal resection of early cancer and high-grade dysplasia in Barrett's esophagus. *Gastroenterology* 2000;118:670-677.
157. Brodner G, Pogatzki E, Van Aken H, et al. A multimodal approach to control postoperative pathophysiology and rehabilitation in patients undergoing abdominothoracic esophagectomy. *Anesth Analg* 1998;86:228-234.
158. Sabanathan S, Shah R, Tsiamis A, Richardson J. Oesophagogastrrectomy in the elderly high risk patients: role of effective regional analgesia and early mobilisation. *J Cardiovasc Surg (Torino)* 1999;40:153-156.
159. Flisberg P, Tornebrandt K, Walther B, Lundberg J. Pain relief after esophagectomy: thoracic epidural analgesia is better than parenteral opioids. *J Cardiothorac Vasc Anesth* 2001;15:282-287.
160. Nguyen NT, Follette DM, Wolfe BM, et al. Comparison of minimally invasive esophagectomy with transthoracic and transhiatal esophagectomy. *Arch Surg* 2000;135:920-925.

161. Fernando HC, Christie NA, Luketich JD. Thoracoscopic and laparoscopic esophagectomy. *Semin Thorac Cardiovasc Surg* 2000;12:195-200.
162. Chan A, Wong A. Is combined chemotherapy and radiation therapy equally effective as surgical resection in localized esophageal carcinoma? *Int J Radiat Oncol Biol Phys* 1999;45:265-270.
163. Gillinov AM, Heitmiller RF. Strategies to reduce pulmonary complications after transhiatal esophagectomy. *Dis Esophagus* 1998;11:43-47.
164. Zehr KJ, Dawson PB, Yang SC, Heitmiller RF. Standardized clinical care pathways for major thoracic cases reduce hospital costs. *Ann Thorac Surg* 1998;66:914-919.
165. Baba M, Aikou T, Natsugoe S, et al. Quality of life following esophagectomy with three-field lymphadenectomy for carcinoma, focusing on its relationship to vocal cord palsy. *Dis Esophagus* 1998;11:28-34.
166. Suzuki H, Abo S, Kitamura M, et al. An evaluation of symptoms and performance status in patients after esophagectomy for esophageal cancer from the viewpoint of the patient. *Am Surg* 1994;60:920-923.
167. Collard JM, Otte JB, Reynaert M, Kestens PJ. Quality of life three years or more after esophagectomy for cancer. *J Thorac Cardiovasc Surg* 1992;104:391-394.
168. De Leyn P, Coosemans W, Lerut T. Early and late functional results in patients with intrathoracic gastric replacement after oesophagectomy for carcinoma. *Eur J Cardiothorac Surg* 1992;6:79-84; discussion 85.
169. Blazeby JM, Alderson D, Farndon JR. Quality of life in patients with oesophageal cancer. *Recent Results Cancer Res* 2000;155:193-204.
170. Blazeby JM, Brookes ST, Alderson D. Prognostic value of quality of life scores in patients with oesophageal cancer. *Br J Surg* 2000;87:362-373.
171. Blazeby JM, Farndon JR, Donovan J, Alderson D. A prospective longitudinal study examining the quality of life of patients with esophageal carcinoma. *Cancer* 2000;88:1781-1787.
172. McLarty AJ, Deschamps C, Trastek VF, et al. Esophageal resection for cancer of the esophagus: long-term function and quality of life. *Ann Thorac Surg* 1997;63:1568-1572.
173. Johansson J, Walther B. Clinical outcome and long-term survival rates after esophagectomy are not determined by age over 70 years. *J Gastrointest Surg* 2000;4:55-62.
174. Young MM, Deschamps C, Allen MS, et al. Esophageal reconstruction for benign disease: self-assessment of functional outcome and quality of life. *Ann Thorac Surg* 2000;70:1799-1802.
175. Young MM, Deschamps C, Trastek VF, et al. Esophageal reconstruction for benign disease: early morbidity, mortality, and functional results. *Ann Thorac Surg* 2000;70:1651-1655.
176. van Lanschot JJ, Hulscher JB, Buskens CJ, et al. Hospital volume and hospital mortality for esophagectomy. *Cancer* 2001;91:1574-1578.
177. Patti MG, Corvera CU, Glasgow RE, Way LW. A hospital's annual rate of esophagectomy influences the operative mortality rate. *J Gastrointest Surg* 1998;2:186-192.
178. Begg CB, Cramer LD, Hoskins WJ, Brennan MF. Impact of hospital volume on operative mortality for major cancer surgery. *JAMA* 1998;280:1747-1751.
179. Dimick JB, Cattaneo SM, Lipsett PA, et al. Hospital volume is related to clinical and economic outcomes of esophageal resection in Maryland. *Ann Thorac Surg* 2001;72:334-339; discussion 339-341.
180. Swisher SG, Deford L, Merriman KW, et al. Effect of operative volume on morbidity, mortality, and hospital use after esophagectomy for cancer. *J Thorac Cardiovasc Surg* 2000;119:1126-1132.
181. Wade PR. Aging and neural control of the GI tract. I. Age-related changes in the enteric nervous system. *Am J Physiol Gastrointest Liver Physiol* 2002;283:G489-G495.
182. Schindler JS, Kelly JH. Swallowing disorders in the elderly. *Laryngoscope* 2002;112:589-602.

183. Sarani B, Scanlon J, Jackson P, Evans SR. Selection criteria among gastroenterologists and surgeons for laparoscopic antireflux surgery. *Surg Endosc* 2002;16:57-63.
184. Trus TL, Laycock WS, Wo JM, et al. Laparoscopic antireflux surgery in the elderly. *Am J Gastroenterol* 1998;93:351-353.
185. Brunt LM, Quasebarth MA, Dunnegan DL, Soper NJ. Is laparoscopic antireflux surgery for gastroesophageal reflux disease in the elderly safe and effective? *Surg Endosc* 1999;13:838-842.
186. Kamolz T, Bammer T, Granderath FA, et al. Quality of life and surgical outcome after laparoscopic antireflux surgery in the elderly gastroesophageal reflux disease patient. *Scand J Gastroenterol* 2001;36:116-120.
187. Bammer T, Hinder RA, Klaus A, et al. Safety and long-term outcome of laparoscopic antireflux surgery in patients in their eighties and older. *Surg Endosc* 2002;16:40-42.
188. Khajanchee YS, Urbach DR, Butler N, et al. Laparoscopic antireflux surgery in the elderly. *Surg Endosc* 2002;16:25-30.
189. Kamolz T, Granderath FA, Bammer T, et al. Failed antireflux surgery: surgical outcome of laparoscopic refundoplication in the elderly. *Hepatogastroenterology* 2002;49:865-868.

