Preoperative prediction of the risk of pulmonary complications after esophagectomy for cancer

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Objectives: Pulmonary complication is a frequent morbid event after esophagectomy for cancer. Its prediction may help select patients for preoperative rehabilitation.

Methods: We performed a retrospective review of 292 patients (231 men and 61 women; mean age, 60.1 years) who underwent esophagectomy for cancer between 1980 and 2000. Data were analyzed to identify factors associated with the development of pulmonary complications (reintubation for isolated respiratory failure and pneumonia). A scoring system was developed, and its ability to predict complications was assessed.

Results: Resection was performed for squamous cancer ($n = 100$), adenocarcinoma ($n = 186$), and other histologic types ($n = 6$) in patients with stages 0 or I ($n = 53$), II ($n = 94$), III ($n = 114$), and IV ($n = 23$) disease. Pulmonary complications, which developed in 78 (27%) patients, were associated with a 4.5-fold increase in operative mortality (7%-32%). Multivariable analysis identified independent predictors of pulmonary complications to be patient age (odds ratio [OR], 1.31; 95% confidence interval [CI], 0.99-1.74; $P = .059$), percentage forced expiratory volume in 1 second (OR, 1.21; 95% CI, 1.07-1.38; $P = .003$), and possibly performance status (OR, 1.48; 95% CI, 0.88-2.50; $P = .14$). A scoring system using these 3 covariates was developed, which predicted incremental risk of pulmonary complications ($P = .013$). The incremental risks of cardiovascular and overall cardiopulmonary complications were also predicted with this scoring system ($P < .01$ for each).

Conclusions: A scoring system using patient age, spirometry, and performance status helps predict the likelihood of pulmonary and cardiovascular complications after esophagectomy and can help select patients who may benefit from preoperative cardiopulmonary rehabilitation.

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Pulmonary complications such as pneumonia and respiratory insufficiency are among the most frequent complications that develop after esophagectomy. Their occurrence is associated with prolongation of postoperative hospital stay, increased cost of care, and substantial operative mortality. Despite the recognition of this fact for more than 2 decades, efforts at predicting the risk of pulmonary complications have been only moderately successful. Alterations in intraoperative and postoperative management of patients undergoing esophageal resection have failed to reduce the incidence of pulmonary complications to desirable levels.

Figure 1. The number of patients undergoing transthoracic resection (open bars) and transhiatal resection (filled bars) of esophageal cancer grouped by 2-year intervals. The numbers above the columns indicate the percentages of patients undergoing transhiatal resection during each interval.

We performed a review of patients undergoing esophagectomy to determine the incidence of pulmonary complications and whether the incidence has changed over time. We sought to identify risk factors associated with the development of pulmonary complications to develop a scoring system on the basis of preoperative parameters that would permit the estimation of the likelihood of pulmonary complications. The identification of factors that predict which patients are at excess risk for pulmonary complications might permit the development of methods for preventing such complications through preoperative rehabilitation or changes in operative techniques.

Patients and Methods

We performed a retrospective review of consecutive patients undergoing esophagectomy for malignancy in the Thoracic Surgery Service at The University of Chicago Medical Center from January 1980 through December 2000. Preoperative, operative, and postoperative data were obtained from chart reviews for patients operated on through 1989 and from a prospective database that was initiated in 1990. Operations included either transthoracic or transhiatal resections. Transthoracic approaches were used more often during the early years of the period of review, and the frequency of transhiatal resection increased during the latter portion of the period of review (Figure 1). Postoperative complications were categorized as pulmonary, cardiovascular, cardiopulmonary, surgical, infectious, other complications, and death. Pulmonary complications included the need for reintubation for isolated respiratory insufficiency postoperatively and pneumonia (fever, elevated white blood cell count, and pulmonary infiltrate requiring antibiotic therapy). Cardiovascular complications included the need for inotropic support to maintain blood pressure and perfusion (excluding the need for renal dose dopamine), arrhythmia, myocardial infarction, and pulmonary embolism. Cardiopulmonary complica-

tions were any pulmonary or cardiovascular complication. Surgical complications included anastomotic leak, necrosis of the reconstructive organ, recurrent laryngeal nerve injury, and chylothorax. Infectious complications consisted of empyema, intra-abdominal abscess, and wound infection. Death was defined as mortality during hospitalization for esophagectomy or within 30 days of esophagectomy.

Data are expressed as means $\pm$ SD. Continuous data were analyzed with a 2-sided *t* test, and noncontinuous data were analyzed with χ^2 analysis. Variables that demonstrated an important difference comparing patients without and with pulmonary complications were examined with backwards stepwise multivariable logistic regression analysis to identify important covariates predicting such complications. Important covariates were then combined into a scoring system that was assessed for its utility in predicting postoperative complications. Sensitivity, specificity, and accuracy were calculated, and the utility of the scoring system was evaluated by using receiver operating characteristic analysis.^{1,2}

Results

During the reference period, 292 patients underwent esophagectomy for cancer. There were 231 men and 61 women, with a mean age of 60.1 ± 10.8 years (range, 30-84 years). Demographic and other preoperative characteristics are listed in Table 1. Baseline laboratory data and pulmonary function data demonstrate that patients had relatively normal serum chemistries, blood counts, and pulmonary functions (Table 2). Operations included exclusive left thoracotomy with intrathoracic anastomosis ($n = 83$), left thoracotomy with cervical anastomosis ($n = 33$), right thoracotomy and laparotomy with intrathoracic anastomosis (Ivor Lewis, $n = 21$), right thoracotomy and laparotomy with cervical anastomosis ($n = 73$), transhiatal resection with cervical anastomosis ($n = 74$), and "other" ($n = 8$, Table 3). The majority of patients underwent reconstruction with a gastric tube positioned in the bed of the resected esophagus. Adenocarcinoma was the most common histologic type and occurred in almost two thirds of patients. Most patients had pathologic stage II or III disease. Overall postoperative length of stay was 19 ± 15 days (range, 0-82 days), which decreased during successive 5-year intervals from 22.9 ± 3.5 days during 1980 to 1984 to 14.1 ± 2.0 days during 1996 to 2000 ($P = .003$).

Because a substantial proportion (21%) of patients did not have pulmonary function tests performed preoperatively, the groups of patients with and without pulmonary function tests were examined to determine whether there were important differences between them. The only significant differences were that the patients who did not undergo pulmonary function testing had lower serum albumin levels (3.8 ± 0.6 vs 4.0 ± 0.4 mg/dL, $P = .05$), a lower incidence of hypertension (21% vs 35%, $P = .039$), and a higher incidence of preoperative radiotherapy (25.8% vs 10.0%, $P = .001$). The incidence of pulmonary complications be-

TABLE 1. Preoperative characteristics of patients undergoing esophagectomy

Characteristic	Evaluable patients	Overall	No pulmonary complications (n = 214)	Pulmonary complications (n = 78)	P value
Men/women	292	231/61	173/41	58/20	.2
Age (y)	291	60.1 ± 10.8	59.3 ± 11.1	62.2 ± 9.9	.035
Height (cm)	233	173.5 ± 10.2	174.2 ± 10.3	171.6 ± 9.9	.07
Weight (kg)	260	75.5 ± 24.5	75.8 ± 16.7	70.9 ± 17.9	.05
BMI (kg · m ⁻²)	229	24.8 ± 4.8	25.1 ± 4.5	24.2 ± 5.6	.3
Weight loss (kg)	269	5.5 ± 6.5	5.6 ± 6.4	5.3 ± 6.9	.7
Dysphagia	283	222 (78.4%)	159 (76.4%)	63 (84.0%)	.17
Prior or current cigarette use	284	227 (79.9%)	160 (77.3%)	68 (88.3%)	.038
Current alcohol use	281	208 (74.0%)	147 (71.7%)	61 (80.3%)	.15
Diabetes mellitus	290	26 (9.0%)	14 (6.6%)	12 (15.4%)	.02
Hypertension	291	94 (32.3%)	64 (30.0%)	30 (38.5%)	.17
Preoperative chemotherapy	292	77 (26.4%)	58 (27.1%)	19 (24.4%)	.6
Preoperative radiotherapy	292	39 (13.4%)	32 (15.0%)	7 (9.0%)	.18
Prior MI	291	32 (11.0%)	22 (10.3%)	10 (12.8%)	.5
Performance status	284	1.1 ± 0.6	1.1 ± 0.6	1.3 ± 0.7	.004

MI, Myocardial infarction.

TABLE 2. Preoperative laboratory values of patients undergoing esophagectomy

Value	Evaluable patients	Overall	No pulmonary complications (n = 214)	Pulmonary complications (n = 78)	P value
Serum hemoglobin (g/dL)	279	13.1 ± 2.0	13.1 ± 1.9	13.0 ± 2.1	.7
White blood cell count (1000/μL)	275	7.3 ± 3.0	7.3 ± 3.2	7.5 ± 2.5	.7
Serum albumin (mg/dL)	241	3.9 ± 0.5	4.0 ± 0.4	3.9 ± 0.6	.6
Serum total protein (mg/dL)	231	6.9 ± 0.6	6.9 ± 0.6	7.0 ± 0.7	.3
Serum creatinine (mg/dL)	273	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.3	.9
Serum total bilirubin (mg/dL)	239	0.6 ± 0.3	0.6 ± 0.3	0.6 ± 0.3	.9
Po ₂ (mm Hg)	191	82.5 ± 10.7	82.4 ± 11.2	82.7 ± 9.4	.8
Pco ₂ (mm Hg)	193	38.3 ± 4.2	38.4 ± 4.6	38.1 ± 3.2	.5
FVC (L)	230	3.9 ± 1.2	4.1 ± 1.2	3.5 ± 0.9	.003
FVC (%)	226	95.7 ± 18.4	97.3 ± 19.0	91.4 ± 16.3	.024
FEV ₁ (L)	230	2.9 ± 1.0	3.0 ± 1.0	2.5 ± 0.8	.003
FEV ₁ (%)	225	96.1 ± 23.8	99.0 ± 23.3	88.1 ± 23.8	.003
FEV ₁ /FVC (%)	230	72.4 ± 10.5	73.1 ± 10.1	70.5 ± 11.5	.12
DLCO%	191	88.4 ± 20.0	89.3 ± 19.9	85.9 ± 20.4	.3

FVC, Forced vital capacity; DLCO %, diffusing capacity for carbon monoxide expressed as a percentage of predicted and corrected for lung volume.

tween the 2 groups was similar (29.0% vs 26.1%, $P = .6$). We concluded that the patients who underwent preoperative pulmonary function testing were representative of the entire population of patients undergoing resection.

Pulmonary complications occurred in 78 (26.7%) patients. These complications were associated with a significant increase in postoperative length of stay, other nonfatal postoperative complications, and operative mortality (Table 3). Pulmonary complications rarely occurred in the absence of other complications, and isolated pulmonary complications were identified in only 6 (2.0%) patients. The incidence of complications did not change significantly over the time period of the study (Figure 2) and did not appear to decrease, despite the increased use of transhiatal, rather than transthoracic, resections (Table 3).

On the basis of the results of the univariate analysis,

variables selected as being potentially associated with pulmonary complications were patient age, performance status (Eastern Cooperative Oncology Group scale, assessed just before the operation), percentage forced expiratory volume in 1 second (FEV₁%), body mass index (BMI) of less than 20 kg · m⁻², diabetes mellitus, and a history of cigarette smoking.^{3,4} Multivariable analysis (220 patients in the final model) identified the important covariates to be patient age (odds ratio [OR] of 1.31 for a 10-year increment; 95% confidence interval [CI], 0.99-1.74; $P = .059$), FEV₁% (OR of 1.21 for a 10-percentage point decrement; 95% CI, 1.07-1.38; $P = .003$), and possibly performance status (OR of 1.48 for a 1-point increment; 95% CI, 0.88-2.50; $P = .14$).

These 3 covariates were combined into a scoring system by assigning a point for each 10-year interval of age over 50 years (1 point for ages 51-60 years, 2 points for ages 61-70

TABLE 3. Operative and postoperative data for patients undergoing esophagectomy

	Evaluable patients	Overall	No pulmonary complications (n = 214)	Pulmonary complications (n = 78)	P value
Any thoracotomy	284	210 (73.9%)	149 (72.0%)	61 (79.2%)	.2
Any laparotomy	284	168 (59.2%)	116 (56.0%)	52 (67.5%)	.08
Thoracotomy and laparotomy	284	94 (33.1%)	58 (28.0%)	36 (46.8%)	.003
Transhiatal resection	287	74 (25.8%)	58 (27.6%)	16 (20.8%)	.2
Transthoracic resection only	287	116 (40.4%)	91 (43.3%)	25 (32.5%)	.1
Substernal reconstruction	285	8 (2.8%)	2 (1.0%)	6 (7.8%)	.002
EBL (mL)	272	1208 ± 1262	1168 ± 1332	1320 ± 1042	.3
Transfusion (units)	265	2.7 ± 3.8	2.5 ± 3.9	3.4 ± 3.8	.07
Histology	290				.001*
Squamous cell		100 (34.5%)	61 (28.8%)	39 (50.0%)	
Adenocarcinoma		186 (64.1%)	147 (69.4%)	39 (50.0%)	
Other		4 (1.4%)	4 (1.9%)	0 (0%)	
Stage	286				.16
0, I		53 (18.5%)	42 (20.1%)	11 (14.3%)	
II		94 (32.9%)	66 (31.6%)	28 (36.4%)	
III		115 (40.2%)	80 (38.3%)	35 (45.5%)	
IV		24 (8.4%)	21 (10.0%)	3 (3.9%)	
LOS (d)	291	19.0 ± 15.0	13.9 ± 9.6	32.9 ± 18.1	<.001
Complications					
Cardiovascular	292	106 (36.3%)	51 (23.8%)	55 (70.5%)	<.001
Infectious	292	55 (18.8%)	25 (11.7%)	30 (38.5%)	<.001
Surgical	292	76 (26.0%)	45 (21.0%)	31 (39.7%)	.001
Other	292	105 (36.0%)	59 (27.6%)	46 (59.0%)	<.001
Overall nonfatal	292	160 (54.8%)	107 (50.0%)	53 (68.0%)	.006
Mortality	292	40 (13.7%)	15 (7.0%)	25 (32.1%)	<.001

EBL, Estimated blood loss; LOS, length of postoperative hospital stay.

*Comparing squamous cell and adenocarcinoma histologies only.

years, 3 points for ages 71-80 years, and 4 points for age >80 years) and by assigning a point for each 10-percentage-point interval of FEV₁% under 90% (1 point for 80%-89.9%, 2 points for 70%-79.9%, 3 points for 60%-69.9%, and 4 points for values of <60%). These 2 values were added to the performance status value to achieve a final score (mean, 3.5 ± 2.0) that had a nearly normal distribution (Figure 3). This score predicted an incrementally increasing risk of complications ($P = .013$ for risk by score category, Figure 4). The scores for patients without and with pulmonary complications were 3.2 ± 1.9 and 4.2 ± 2.1, respectively ($P = .003$). Using a score of 4 as a cutoff value, the accuracy of prediction of pulmonary complications was 65.4%.

This scoring system was evaluated for its ability to predict other types of complications. Mean scores between groups of patients with and without complications demonstrated that, among cardiovascular, cardiopulmonary, infectious, surgical, and other complications, significant differences in scores were found only for cardiovascular (3.1 ± 1.8 vs 4.1 ± 2.2, $P < .001$) and cardiopulmonary (3.0 ± 1.8 vs 4.1 ± 2.2, $P < .001$) complications. The relative risk of cardiovascular and cardiopulmonary complications increased with increasing scores ($P = .005$ and $P = .001$, respectively; Figure 4). By using a score of 4 as a cutoff

value, the accuracy of this scoring system in predicting cardiovascular and cardiopulmonary complications was 64.5% and 60.9%, respectively. The scores for patients with and without any type of complication or nonfatal complication differed significantly, but this was due to the high incidence of pulmonary and cardiovascular complications among the affected patients. Mortality was not predicted by the scoring system (3.4 ± 2.0 vs 3.9 ± 1.9, $P = .2$).

The decision threshold characteristics of the scoring system for pulmonary, cardiovascular, and cardiopulmonary complications were examined by using receiver operating characteristic analysis (Figure 5). Although all curves exhibit a good fit relative to the data points, this is largely a function of the small number of decision thresholds available in the scoring system. The relatively small deviation of the curves from the line of unity (representing no discrimination) suggests that the scoring system is good but not optimal as a means for predicting the likelihood of these complications.

Because pulmonary function test results are an important element in the scoring system, an examination of preoperative variables was undertaken to determine whether the risk of poor pulmonary function test results could be determined. Univariate analyses identified possible covariates to be sex, amount of weight loss, current or past cigarette use,

Figure 2. The number of patients without (open bars) and with (filled bars) pulmonary complications after esophagectomy for cancer grouped by 2-year intervals. The numbers above the columns are the percentages of patients who had postoperative pulmonary complications during each interval.

Figure 3. Distribution of risk scores for pulmonary complications.

alcohol consumption, BMI of less than $20 \text{ kg} \cdot \text{m}^{-2}$, hypertension, serum creatinine level, and performance status. Backwards stepwise multivariable logistic regression analysis identified the significant covariates for FEV₁% of less than 90% to be weight loss (OR for a 2-kg decrement, 1.03; 95% CI, 1.00-1.05; $P = .034$), alcohol use (OR, 3.92; 95% CI, 1.58-9.69; $P = .003$), and BMI of less than $20 \text{ kg} \cdot \text{m}^{-2}$ (OR, 8.36; 95% CI, 2.54-27.51; $P < .001$).

The role of the operative approach in the development of postoperative pulmonary complications was evident on the basis of the large influence of combined thoracotomy and laparotomy. This technique was significantly more likely to

Figure 4. The incidence of pulmonary ($P = .013$), cardiovascular ($P = .005$), and cardiopulmonary ($P = .001$) complications in relation to the predictive score.

Figure 5. Receiver operating characteristic curves for the scoring system relative to pulmonary complications (circles, $r^2 = 0.99$), cardiovascular (triangles, $r^2 = 0.99$), and cardiopulmonary complications (inverted triangles, $r^2 = 0.99$). The line of unity (no discrimination) is depicted as a dashed line.

be associated with such complications than was either an exclusive transthoracic approach or a transthiatal approach ($P = .012$). When combined thoracotomy and laparotomy as the operative approach was added as a variable in the multivariable analysis of factors associated with pulmonary complications, the important covariates that emerged were FEV₁% (10-percentage-point decrement: OR, 1.20; 95% CI, 1.05-1.37; $P = .006$), operative approach (OR, 2.49; 95%

CI, 1.30-4.76; $P = .006$), and age (10-year increment: OR, 1.34; 95% CI, 0.99-1.81; $P = .06$).

Discussion

The risk of pulmonary complications after esophagectomy is higher than after any other common operation, including major lung resection. The reasons posited for this high risk include surgical entry into 2 separate body cavities; disruption of bronchial innervation and lymphatic circulation; postoperative dysfunction of muscles of respiration, including the diaphragm; placement of a reconstructive organ in the substernal space; cachexia; advanced age; poor airway protection resulting from recurrent laryngeal nerve injury and discoordinated deglutition; tobacco and alcohol abuse; and poor performance status. The high incidence of pulmonary complications after esophagectomy has been recognized for decades, and a variety of intraoperative and postoperative techniques have been used in attempts to reduce the frequency of this problem. Unfortunately, the potential salutary effects of these interventions have not been fully realized. Although incentive spirometry, intermittent positive-pressure breathing, and chest physiotherapy substantially reduce the incidence of pulmonary complications after major abdominal surgery, similar efforts combined with more careful patient selection have succeeded in reducing the incidence of pulmonary complications after esophagectomy in relatively few institutions.⁵⁻⁸

The incidence of pulmonary complications was relatively stable in our institution over 2 decades, despite the introduction of routine postoperative epidural analgesia, a growing emphasis on early extubation, the increasingly vigorous use of pulmonary toilet exercises, and a more frequent use of the transhiatal approach for resection. The incidence of pulmonary complications we identified is within the 20% to 35% range reported by others.⁹⁻¹⁶ Direct comparisons between reports are sometimes difficult because of the differing definitions of what a pulmonary complication is and the natural attrition in the number of complications identified through retrospective, rather than prospective, studies. In addition, the substantial overlap between organ system complications suggests that identifying true pulmonary complications is often an inexact science.

Attempts to develop systems for predicting which patients are at increased risk of development of pulmonary complications have been only partially successful. In addition, many studies identify factors (intraoperative blood loss, use of epidural analgesia, use of bronchoscopy postoperative to clear secretions, tumor stage, and duration of the operation) that cannot be used to preoperatively predict the risk of complications.^{8,11,17} As a result, their focus is on identifying which patients should experience altered operative and postoperative management, and in most instances

they do not address the potential for preoperative intervention in limiting pulmonary complications.

The relative lack of utility of other perioperative predictive systems and the absence of adequate benefit provided by changes in operative and postoperative management have led to the concept of identification of and intervention for high-risk patients in the preoperative period. We identified 3 preoperative factors that were associated with an increased risk of pulmonary complications: age, spirometric values, and performance status. Others have demonstrated that advanced age and preoperative respiratory dysfunction are associated with postoperative pulmonary complications.^{11,12,14,17} It may be intuitively apparent that the factors we identified are predictive of the relative risk of development of pulmonary complications. The benefit of this analysis does not lie in the uniqueness of our observations. Instead, it directs the clinician to focus on a few specific factors and provides the ability to quantitate the relative effect of these factors before making treatment recommendations.

Age, spirometry, and performance status have several advantages in their use in a preoperative system for predicting postoperative complications. Age and spirometry are objective measurements, and performance status is based on a method of clinical observation that has been validated during 2 decades of use.¹⁸⁻²⁰ Only a brief patient interview and a single test, which can be performed in a physician's office, are necessary to enable the clinician to compile the required information. Combining these factors into a scoring system permits the assessment of relative risk on the basis of all 3 factors simultaneously. The intent of developing such a scoring system is so that preoperative interventions can be recommended that may reduce the risk of postoperative complications. That this is a potentially effective approach is evidenced by significant improvements demonstrated in patients who undergo a short period of cardiopulmonary rehabilitation in preparation for lung resection for cancer or lung volume reduction surgery for severe emphysema.^{21,22} Whether the risk of postoperative pulmonary complications can be reduced in patients undergoing esophagectomy by means of improving respiratory muscle strength and performance status has yet to be investigated.

A good predictive scoring system should be easy to use, have low cost, require little or no special testing, be a good predictor of outcomes for a given population, be a good predictor of outcome for an individual, provide meaningful results that guide clinical behavior, and either provide a specific value that separates low-risk from high-risk groups or provide a continuous incremental estimate of risk. Our scoring system fulfills many of these criteria. It is easy to use: To calculate a risk score, no complex formulas or transformations are necessary, and the score can be calcu-

lated in one's head. The cost is low because only one clinical test is required, and this is often obtained routinely. The system provides an incremental estimate of risk with which outcomes for a population can be predicted. It also uses 2 factors that can potentially be modified to reduce risk once it is identified. However, the system does not have the power to accurately predict outcome for an individual, and there is no specific cutoff value that clearly demarcates standard-risk and high-risk populations.

There are limitations to the use of this algorithm. It is unclear whether a demonstrated improvement in spirometry is necessary to confer benefits on patients. The time necessary to produce measurable improvement in performance is unknown and may differ among patients. Any delay in resection or other therapy mandated by the need for preoperative cardiopulmonary rehabilitation may permit tumor growth, resulting in increased symptoms and decreasing performance status. It is unclear as to how neoadjuvant chemotherapy, radiotherapy, or both affect performance status and spirometry and whether such interventions have any effect on the scoring system and its potential utility.

Although many surgeons obtain preoperative pulmonary function tests routinely on their patients undergoing esophagectomy, there is no standard clinical practice in this regard. Thus, it would be helpful to the clinician to know which patients should be sent for pulmonary function testing. The accuracy of predicting poor pulmonary function with any available algorithm other than clinical acumen is low. However, some guidance is available from our analyses, which demonstrate that the combination of alcohol use, excessive weight loss, and, most important, a BMI of less than $20 \text{ kg} \cdot \text{m}^{-2}$ should alert the clinician to the possibility of a greater than average risk of poor pulmonary function.

We also analyzed the effect of the operative approach on the development of pulmonary complications postoperatively. The combination of a thoracotomy and a laparotomy, such as is used in performing an Ivor Lewis esophagectomy, was highly predictive of the development of such complications. The effect of thoracoabdominal incisions on postoperative complications was not assessed because of the small number of such operations in our database, but it is likely that such an approach would have a similar negative effect on the incidence of pulmonary complications. In light of this finding, it is interesting to speculate about how alterations in the operative approach, including the use of minimally invasive surgical procedures, might diminish the incidence of postoperative pulmonary complications. Given the inherent bias engendered by the surgeon's selection of operative approaches on the basis of preoperative assessment of patients, it is not possible to formulate an algorithm that would assist in decisions about the optimal surgical approach for an individual patient.

Pulmonary complications remain among the most com-

mon problems that confront the esophageal surgeon. Current efforts to minimize these complications have not been completely successful. A new scoring system identifies populations at excess risk for pulmonary complications and may permit preoperative intervention, which reduces the risk of such problems. However, before its use can be recommended, this system requires validation through retrospective analyses of data from other centers and through prospective clinical trials.

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Discussion

Dr Richard I. Whyte (Stanford, Calif). A close look at the data suggests that if you have one of these complications there is a 4-fold higher incidence of death, so I wonder why it predicts one but not the other.

I have 2 questions. First of all, your preoperative data set did not appear to include the year of the operation. If you include the year of the operation, do you see a significant change in the patient population as time goes on? In other words, are you now operating on older, sicker patients?

The second question relates to the use of preoperative chemotherapy and radiation. I think a number of us who have used preoperative chemotherapy and radiation in patients undergoing esophagectomy have seen an incidence of people with an early postoperative adult respiratory distress syndrome-like pattern that can significantly complicate their postoperative hospitalization and even result in mortality. You did not identify patients in your series that had preoperative chemotherapy and radiation. Do you think this also is a risk factor?

Dr Ferguson. Thank you for your kind comments. I agree that it is obvious to most that these types of factors would likely predict the risk of pulmonary complications. I think the potential advantage in what we have identified is the ability to quantitate the individual risk for these patients.

Our series is not different than most in finding that there has been no difference in the incidence of pulmonary complications over time. In fact, only 2 reports in the literature have identified a reduction in pulmonary complications in the last decade or so: Wong's group from Hong Kong and Heitmiller's group from Hopkins. In fact, most of the studies comparing transthoracic with transhiatal resection have also shown no difference in the incidence of pulmonary complications, so it is not surprising that the increased use of this technique has not resulted in a decrease in the number of complications.

You asked whether there has been a change in the patient population on the basis of age, other risk factors, or perhaps the use of preoperative chemotherapy and radiation therapy. We could identify no change in the patients that we have operated on over this roughly 2-decade period. We looked specifically at preoperative chemotherapy and radiation therapy and found that they were not even close to being predictors for the likelihood of complications, so I think, intuitively, that once again this is a potential risk factor but does not bear out in the statistical analysis.

We also did look at the year of operation as a confounding variable, and this did not create any significant difference in the population, so it did not enter into the multivariable analysis.

Dr Alden Harken (Denver, Colo). This is a thoughtful review of a complex and very high-risk group of patients. I was struck, as

you were, by the link between the cardiac and the pulmonary complications, and I think we have all seen that once the first domino goes down, they all spiral.

I was interested that your cardiac complications were greater than your pulmonary complications: 36% versus 27%. I was struck that, for the past 15 years, we have all recognized that patients around a myocardial infarction on β -blockers do much better. Poulderman's multi-institutional review in the *New England Journal of Medicine* 2 years ago took very high-risk vascular patients and, by placing them on β -blockers, was able to cut down the cardiac complications in this dobutamine stress echocardiography high-risk vascular surgical group from 34% down to 3.4% with β -blockers alone. Do you use β -blockers, or have you looked at this group as to whether they were on β -blockers? There is progressively persuasive evidence that noncardiac surgical patients probably should be on—or at least the moderate and high-risk surgical groups should be on— β -blockers. Is the cardiovascular advantage of β -blockers offset by the bronchospastic disadvantage of β -blockers? What would be your recommendations in this group for the use of what appears to be a rational preventive perioperative cardiovascular risk program? Have you looked at perioperative β -blockers, and what would be your recommendation for the future?

Dr Ferguson. Thank you. It is an interesting problem. I do not know that it has been specifically studied in patients undergoing esophagectomy with regard to the relative risk of pulmonary versus cardiovascular complications. It all depends on definition. In fact, we excluded a number of patients who most would consider as having pulmonary complications, requiring reintubation for respiratory failure, because we believe the respiratory failure was associated with other problems, such as sepsis and massive myocardial infarction. We did not exclude patients in the cardiovascular risk group, and so that is why it may appear somewhat artificially higher than that in the pulmonary complication group. The vast majority of the complications in the cardiovascular group were relatively benign. We had few that affected mortality—maybe 6 myocardial infarctions, I think 2 or 3 pulmonary emboli, very few patients requiring inotropic support for something other than sepsis—and so almost all those patients had arrhythmias that are relatively benign. One could consider the use of β -blockers, particularly the more selective blockers, but I am still quite concerned about the risk of increasing pulmonary complications in these patients. We do not have data on it, so I have not been able to specifically look at the potential benefit of β -blockers in this patient population.

Dr Douglas E. Wood (Seattle, Wash). I have a couple of questions for you. One question relates to the second analysis that you did on the type of operative approach and its effect on complications. I guess I would like to rechallenge you on what you think the validity of that analysis is. You are presumably comparing very different patient populations—a group of patients that have bulky squamous carcinomas of the midesophagus, potentially of a different tumor stage group as well—from those I am presuming to have gastroesophageal-junction tumors with or without Barrett esophagus. Do you think it is fair to ignore those factors that led to your selection of an approach, which may be the most important component of determining complications?

Second, you propose that the reason for doing this is to identify a high-risk group of patients that could potentially benefit from pulmonary rehabilitation. Do we have time to do pulmonary rehabilitation in patients that have esophageal cancer? Pulmonary rehabilitation programs are generally 6 weeks to 3 months. These patients may be getting induction therapy and may have difficulty doing pulmonary rehabilitation during that, or they may have issues that prevent them from being able to wait that period of time before having a definitive procedure. Is it really going to help?

Dr Ferguson. Time prevented my discussing most of these issues during the talk, but you are right. There are certain issues with the approach to the operation that are very specific and may have also influenced the outcome in these patients. I do not know that there is a good way to sort it out, so I would caution accepting that finding without looking further into it. On the other hand, it

still indicates the potential for a different operative approach, such as a minimally invasive resection. This could accomplish the same resection as the 3-hole esophagectomy if our techniques improve and thus has the potential for limiting complications without compromising the approach to the operation.

With regard to rehabilitation, yes, there are certain disadvantages. One is that the performance status of the patient could actually worsen because of worsening dysphagia. It may interrupt preoperative chemotherapy and radiation therapy. It may provide too long of an interval between the radiation and the operation. Those are all potential disadvantages. On the other hand, some benefit has been seen in patients who got even a minimum of 2 weeks of fairly intensive cardiopulmonary rehabilitation, so I think something like that could still be considered in the majority of these patients who are thought to be at high risk.