Optimizing selection of patients for major lung resection

Objectives: **It is not known whether a normal diffusing capacity for carbon monoxide permits safe lung resection in patients with marginal spirometric values, or whether normal spirometric values negate the adverse effects of a low diffusing capacity. The purposes of this study were (1) to determine the best predictors of morbidity and mortality and (2) to assess whether interactions exist between diffusing capacity and spirometry that help estimate outcome after major lung resection.** *Design:* **A retrospective analysis of 376 patients who underwent lung resection was performed. Three hundred three had lung cancer and 73 had other disease. Two hundred eighty-four underwent lobectomy/bilobectomy and 92 had pneumonectomy. We assessed the relationship of 23 preoperative variables to 18 postoperative events classified into categories as pulmonary or cardiac complications, overall morbidity, and operative mortality.** *Results:* **The best single predictor of complications was the percent predicted postoperative diffusing capacity. The incidences of pulmonary and cardiac complications, morbidity, and mortality were inversely related to predicted postoperative diffusing capacity percent ($p < 0.004$ for each). Multivariate logistic regression analyses identified only predicted postoperative diffusing capacity percent and age as significant independent predictors of pulmonary complications, morbidity, and death, and these with prior myocardial infarction predicted cardiac complications. There were no interactions between percent predicted postoperative forced expiratory volume in 1 second and predicted postoperative diffusing capacity percent in estimating risks of complications.** *Conclusion:* **Predicted postoperative diffusing capacity percent is the strongest single predictor of risk of complications and mortality after lung resection. There is little interrelationship of predicted postoperative diffusing capacity percent and predicted postoperative forced expiratory volume in 1 second, indicating that these values should be assessed independently in estimating operative risk. (J THORAC CARDIOVASC SURG 1995;109:275-83)**

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Operative risk for lobectomy and pneumonectomy is traditionally estimated by assessment of cardiac function, evaluation of spirometric measurements, and analysis of arterial blood gas values. Only moderate correlations have been reported between any of these variables and the prevalence of complications after lung resection.[1, 2] The diffusing capacity of the lung for carbon monoxide ($D_{L_{CO}}$) recently has been shown to be an independent predictor of operative morbidity and mortality after

Table I. *Preoperative and operative factors examined in evaluating risk of pulmonary resection*

General
Year of operation
Age
Sex
Diagnosis
Stage (where applicable)
Diabetes mellitus
Serum creatinine
Cardiopulmonary, qualitative
NYHA class
Hypertension
Prior myocardial infarction
Tobacco use
Cardiopulmonary, quantitative
FVC, FVC%
FEV_1, FEV_1%, ppoFEV_1, ppoFEV_1%
DL_{CO}, DL_{CO}%, ppoDL_{CO}, ppoDL_{CO}%
ppoPROD
Extent of resection

NYHA, New York Heart Association; *FVC,* forced vital capacity; *FEV_1,* forced expiratory volume in 1 second; *DL_{CO},* diffusing capacity for carbon monoxide; See text for explanation of pulmonary function test values expressed as a percent of predicted normal and for calculation of predicted postoperative (ppo) values and product (ppoPROD).

Table II. *Categories of postoperative events evaluated in estimating risk of pulmonary resection*

Death
Morbidity
Pulmonary
Postoperative ventilatory support >24 hours
Reintubation
New bronchodilator use
Pneumonia
Lobar collapse
Cardiac
Myocardial infarction
New β-adrenergic blocker use
Vasodilator administration
Inotropic support
Arrhythmia
Other
Wound infection
Empyema
Air leak >7 days
Pulmonary embolus
Bronchopleural fistula
Recurrent laryngeal nerve injury
Miscellaneous

major pulmonary resection.[3, 4] The use of this measurement as a preoperative screening tool has not been widespread. It is not known whether normal DL_{CO} permits safe resection in patients with marginal spirometric values or whether normal spirometric values negate the adverse effects of a low diffusing capacity. The purposes of this study were to determine the best predictors of risk of morbidity and mortality after major lung resection and to assess whether interactions exist between DL_{CO} and spirometry that help estimate outcomes after major lung resection.

Patients and methods

A retrospective review was conducted of the records of 406 patients who underwent lobectomy, bilobectomy, or pneumonectomy at the University of Chicago Medical Center from January 1980 through December 1992. Thirty patients were excluded from analysis because they had undergone urgent thoracotomy for trauma or prior lung resection. The analysis was performed on the remaining 376 patients. Data were recorded for 23 preoperative and operative risk factors (Table I). Spirometry and measurement of total lung capacity and DL_{CO} were performed as previously described.[3] Normal values for lung volumes were taken from regression equations of Morris, Koski, and Johnson (men)[5] and Goldman and Becklake (women).[6] Prediction equations for DL_{CO} were those of Gaensler and Wright.[7] Diffusing capacity was corrected for hematocrit value, and the results were corrected further for lung volume by the equation of Gelb and associates.[8] Predicted postoperative function was calculated for the forced expiratory volume in 1 second (FEV_1) and DL_{CO} (ppoFEV_1, ppoDL_{CO}) and for FEV_1 and DL_{CO} expressed as a percent of predicted normal values (ppoFEV_1%, ppoDL_{CO}%) by multiplying the raw values or percent of predicted normal values of observed measurements by the fraction of functional lung segments remaining after resection. Functional lung segments were assigned as calculated previously[9, 10]: right upper lobe 3; right middle lobe 2; right lower lobe 5; left upper lobe 5; left lower lobe 4. The product of ppoDL_{CO} and ppoFEV_1 was calculated (ppoPROD).[11] Data on 18 postoperative complications were recorded as previously defined.[3]

Descriptive summary statistics were produced to characterize the 376 cases in terms of baseline variables. Five binary outcome variables (present/absent) were constructed on the basis of operative complications: mortality (death during hospitalization for operation or within 30 days of operation), pulmonary, cardiac, other, and overall morbidity (an aggregation of all complications) (Table II). In cases in which patient outcome data could not be scored reliably, the outcomes were classified as missing. Univariate associations with each of the five outcome variables were performed by means of contingency table analyses (χ^2 test) for categoric predictive variables and Student's t tests for continuous predictive variables.[12] Because of the exploratory nature of this retrospective study and the multiple statistical tests performed, the significance of the results was interpreted with caution. Two-sided significance levels less than 0.05 were deemed to be of modest statistical significance. Significance levels less than 0.001 were judged to be highly significant and worthy of clinical consideration.

Recoding of three continuous measures (ppoFEV_1%, ppoDL_{CO}%, and ppoPROD) was used to create ordinal

categoric variables. These were correlated with each of the five outcome variables by either an exact or an asymptotic computation of the Cochran-Armitage trend test for a one-sided alternative (i.e., $P_1 \geq P_2 \geq \ldots \geq P_n$, where P_n denotes the proportion of patients with the complication in the nth level of the categorized variable).[13]

Forward stepwise logistic regression was performed to identify variables that were significant and independent predictors of each particular type of complication.[14] Likelihood ratio tests were used to determine significance. Because of both the large number of predictor variables that were considered and the extent of missing data for some variables, the pool of candidate covariates for stepwise regression was carefully selected on the basis of the significance of the univariate results across all five outcomes. To avoid problems with multicollinearity among the pulmonary function measurements, we constructed three pools of covariates that included both measured preoperative and estimated postoperative values expressed as (1) raw values (FVC, DL_{CO}, FEV_1, $ppoDL_{CO}$, $ppoFEV_1$), (2) percent of predicted normal values (FVC%, DL_{CO}%, FEV_1%, $ppoDL_{CO}$, $ppoFEV_1$%), or (3) a combination of these (FVC, DL_{CO}, FEV_1, ppoPROD). Each group was tested separately. Four of the 10 baseline patient variables (age, sex, New York Heart Association score, and prior myocardial infarction) were selected to be included in these pools of covariates on the basis of univariate correlations.

All data checking, descriptive statistics, χ^2 tests, Student's t tests, and stepwise logistic regression analyses were performed in Number Cruncher Statistical System (NCSS, Jerry Hintze, Kaysville, Utah). All exact and asymptotic Cochran-Armitage trend tests were performed in StatXact (CYTEL Software, Cambridge, Mass.).

Results

The group comprised 221 men and 155 women with a mean age of 60 years (median 62 years, range 17 to 87 years). There was a smoking history in 339 patients (90%), 44 (12%) had diabetes, 110 (29%) had hypertension, and 10% (14/134) had a serum creatinine concentration greater than 1.4 mg/dl. The majority of patients (358/369; 97%) were in New York Heart Association class I or II, 3% (11/369) were in class III, and none were in class IV. Forty-seven (13%) patients had a history of prior myocardial infarction, none of which had occurred in the 3 months before resection. Spirometric values, diffusing capacity measurements, the predicted postoperative values for these determinations, and the calculated ppoPROD are listed in Table III.

Operations performed were lobectomy (246; 65%), bilobectomy (38; 10%), and pneumonectomy (92; 25%). Three hundred three patients (80%) underwent resection for lung cancer, of whom 128 had stage I disease, 55 were stage II, and 119 stage IIIA-B. The stage was unknown in one patient. Twenty patients had resection for metastatic disease, 6 for carcinoid tumor, and 47 for benign problems. The prevalence of complications is listed in Table IV. Information regarding complications other than death was not available for all patients. The hospital mortality rate for major pulmonary resection in patients with lung cancer was 7.6%. The mortality for those undergoing lobectomy or bilobectomy was 5.6% and was 12.5% for pneumonectomy. Pulmonary complications occurred in 20.1% (60/298), cardiac complications in 22.6% (65/287), and other complications in 33.1% (96/290), for an overall morbidity of 48.3% (141/292) in patients with lung cancer.

Table III. *Pulmonary function data**

	Preop. value	*Predicted postop. value*
FVC (L)	3.25 ± 0.92	—
FVC%	86.3 ± 18.1	—
FEV_1 (L)	2.29 ± 0.71	1.64 ± 0.63
FEV_1%	83.7 ± 20.7	61.0 ± 20.0
DL_{CO} (ml/min/torr)	20.5 ± 6.3	14.8 ± 5.3
DL_{CO}%	86.3 ± 21.8	62.1 ± 18.5
ppoPROD	—	4014 ± 2052

For abbreviations see Table I.
*Values are mean ± standard deviation.

Univariate analysis demonstrated that age, sex, New York Heart Association class, and prior myocardial infarction were the only demographic variables that were at least of moderate statistical significance ($p < 0.05$) as predictors of morbidity and/or mortality. In contrast, the preoperative and predicted postoperative values for all of the pulmonary function tests except FVC% were statistically significant predictors of most of these complications (Table V). Logistic regression used to test the univariate models demonstrated that the best single predictor of mortality was $ppoDL_{CO}$%. The incidences of mortality and other complications (pulmonary, cardiac, overall morbidity) were inversely related to $ppoDL_{CO}$% (Cochran-Armitage trend test; Fig. 1). According to the percent predicted covariate pool described earlier, stepwise logistic regression analysis identified only $ppoDL_{CO}$% and age as predictors of pulmonary complications ($p < 0.0001$), morbidity ($p = 0.0005$), and mortality ($p < 0.0001$), and these along with a history of prior myocardial infarction predicted cardiac morbidity ($p < 0.0001$) (see appendix).

The respective contribution of $ppoFEV_1$% and $ppoDL_{CO}$% to the prediction of mortality were examined by constructing both a main effects model with only these variables and a main effects plus

Table IV. *Morbidity and mortality after pulmonary resection (%)*

	Lobectomy/bilobectomy		*Pneumonectomy*		*Total*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Mortality	18/284	6.3	11/92	12.0	29/376	7.7
Morbidity	140/271	52	37/88	42	168/359	47
Pulmonary	55/279	20	16/89	18	71/368	19
Cardiac	52/264	20	23/86	27	75/350	21
Other	94/269	35	23/88	26	117/357	33

Table V. *Results of univariate analysis**

		Morbidity			
Variable	*Mortality*	*Pulmonary*	*Cardiac*	*Other*	*Overall*
Operation year	0.41	0.10	0.76	0.017	0.03
Age	0.13	0.85	0.02	0.92	0.02
Sex	0.45	0.02	0.0002	0.97	0.77
Diagnosis	0.59	0.69	0.55	0.37	0.34
Stage	0.016	0.25	0.44	0.76	0.68
Tobacco use	0.70	0.48	0.61	0.27	0.13
Diabetes mellitus	0.30	0.11	0.82	0.58	0.67
Hypertension	0.44	0.92	0.23	0.22	0.22
Prior myocardial infarction	0.13	0.10	<0.0001	0.44	0.006
NYHA class	0.02	0.016	0.01	0.75	0.37
Serum creatinine	0.32	0.39	0.33	0.14	0.15
FVC	0.09	0.003	0.23	0.08	0.02
FVC%	0.29	0.19	0.09	0.49	0.42
DL_{CO}	0.0004	<0.0001	0.016	0.02	0.0001
DL_{CO}%	0.002	0.006	0.08	0.08	0.002
FEV_1	0.005	<0.0001	0.014	0.0011	0.0001
FEV_1%	0.22	0.013	0.02	0.06	0.05
ppoDL_{CO}	<0.0001	<0.0001	0.002	0.06	0.0002
ppoDL_{CO}%	<0.0001	0.0003	0.007	0.19	0.004
ppoFEV_1	0.0009	<0.0001	0.01	0.015	0.003
ppoFEV_1%	0.02	0.02	0.01	0.20	0.14
ppoPROD	0.0006	0.0008	0.004	0.05	0.005

*See Table I for definitions.

interaction model including these variables and ppoPROD. In the two-variable model, only ppoDL_{CO}% was significant ($p = 0.0013$), whereas ppoFEV_1% had no significant influence on mortality ($p = 0.70$) (Fig. 2). In the interaction model ppoPROD was not a significant variable. These data indicate that there is little interaction between ppoFEV_1% and ppoDL_{CO} in predicting mortality and that ppoDL_{CO}% is the strongest single predictor of mortality after major lung resection.

Discussion

Despite the fact that the accurate estimate of risk of complications after major lung resection is vital, the use of traditional methods of assessing operative risk provides only a modest ability to predict postoperative morbidity and mortality.[1, 2] Because many physicians find this extent of risk assessment insufficient, others have investigated the utility of preoperative exercise testing or measurement of physiologic variables such as oxygen consumption and arterial oxygen saturation during exercise.[15-19] These tests have not met with widespread use because they are expensive and labor intensive, and few data are available with which to assess their accuracy. In 1988 we[3] determined that the assessment of pulmonary gas exchange, expressed as preoperative single-breath DL_{CO} independently predicts risk of mortality and pulmonary morbidity after lobectomy or pneumonectomy. Others confirmed these findings and suggested that the use of a postoperative predicted value of DL_{CO} (ppoDL_{CO}%), calculated by means of functional data from quantitative ventilation/perfusion scans, offers an improved ability to predict such complications.[4] However, it is unclear whether a normal diffusing

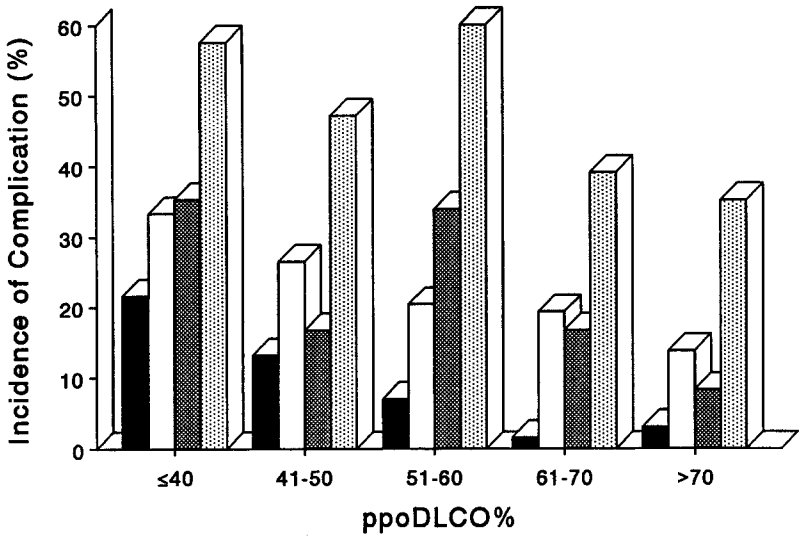

Fig. 1. The incidence of mortality *(shaded bars)*, cardiac morbidity *(open bars)*, pulmonary morbidity *(cross-hatched bars)*, and overall morbidity *(stippled bars)* versus ppoDL_{CO}% (see text for explanation). Mortality and complications are inversely related to ppoDL_{CO}% (Cochran-Armitage trend test; $p \leq 0.004$ for each).

capacity permits safe major lung resection in patients with marginal spirometric values or whether an abnormal diffusing capacity suggests high operative risk despite adequate spirometric values. Using data collected during the generation of our original report, we have added information from patients operated on in the intervening years and performed a more rigorous statistical analysis of our data to address these questions.

Our findings confirm those of our previous report that diffusing capacity is a strong and independent predictor of risk of mortality after major lung resection.[3] In addition to its ability to estimate the risks of mortality and pulmonary morbidity, we also found that diffusing capacity was strongly predictive of cardiac complications and overall morbidity. The association of diffusing capacity and cardiac morbidity is not surprising because of the known increase in pulmonary vascular resistance that results from major lung resection.[20, 21] An increase in pulmonary vascular resistance causes right heart strain, contributing to the relatively high frequency of cardiovascular complications evident in our study and in reports by others.[22-24] The strong correlation between ppoDL_{CO}% and the overall risk of morbidity is likely due to the contribution of cardiopulmonary complications to overall morbidity. The lack of correlation between diffusing capacity and other complications that were unrelated to cardiopulmonary morbidity helps confirm its value in the physiologic assessment of patients considered for major lung resection.

A strong correlation has been identified by others between predicted postoperative expiratory volumes (ppoFEV_1 and ppoFEV_1%) and morbidity and mortality.[4, 25-27] In contrast, all determinations of FEV_1 in our study, including preoperative and predicted postoperative values, were significant predictors of morbidity and mortality on univariate analysis but failed to approach significance when joined with multiple variables during stepwise logistic regression analysis. There are many possible explanations for this finding. Because of the retrospective nature of the study, patients were carefully selected before the operation, largely on the basis of ppoFEV_1 ($\geq$900 ml) and, in recent years, ppoFEV_1% ($\geq$40). In such a highly selected group, the predictive ability of FEV_1 is substantially reduced. In addition, there is a statistical correlation between FEV_1 and diffusing capacity, and some of the predictive ability of FEV_1 may be duplicated by the inclusion of diffusing capacity values in the analysis.

Our primary interest in performing this analysis was to determine whether a normal diffusing capacity permits safe resection in patients with a marginal FEV_1 and whether a normal FEV_1 negates the effects of a suboptimal diffusing capacity. Such a finding would have the potential effect of increasing the pool of individuals eligible for potentially curative resection. It has been suggested by others that the product of ppoFEV_1% and ppoDL_{CO}%, the so-called ppoPROD, may be a universal value that includes the important elements of both of these measurements.[11] When combined with ppoFEV_1%

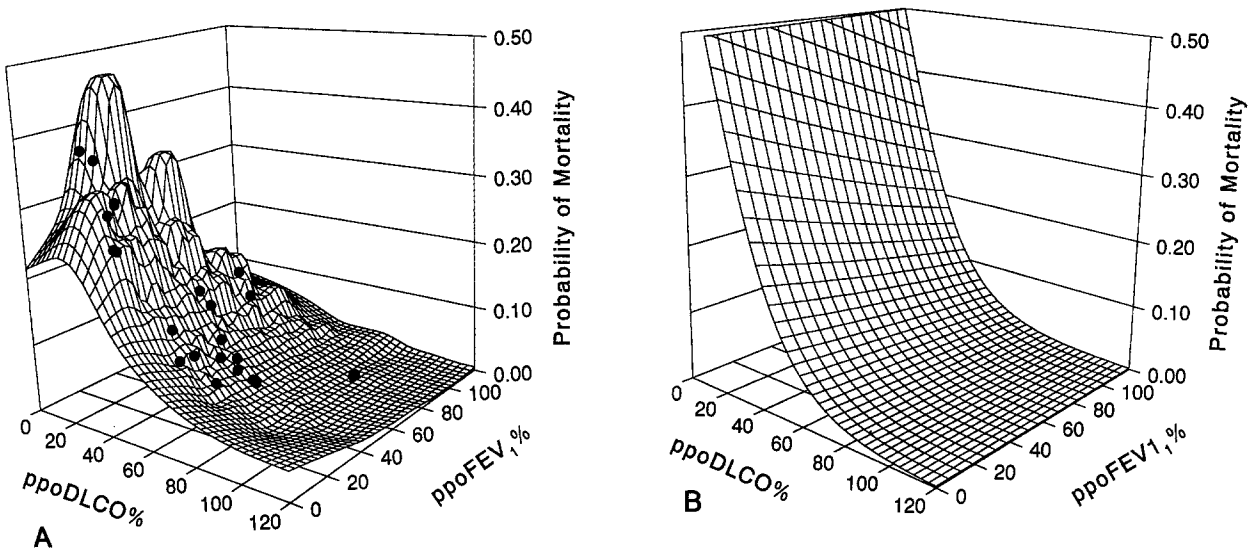

Fig. 2. The probability of mortality expressed as a function of ppoDL_{CO}% and ppoFEV_1%, where probability = 1/[1 + exp(−[0.703 − (0.0559 × ppoDL_{CO}%) − (0.00557 × ppoFEV_1%)])]. *Left,* A surface constructed by calculating the estimated probability of mortality using ppoDL_{CO}% and ppoFEV_1% data from 287 patients. Actual operative mortalities are indicated by *black dots. Right,* A theoretical surface of predicted risk of mortality generated by the equation alone demonstrates that almost all of the risk is dependent on ppoDL_{CO}%.

and ppoDL_{CO}% and subjected to stepwise logistic regression analysis, ppoPROD had no predictive power in our patient population. A similar analysis comparing ppoDL_{CO}% and ppoFEV_1% determined that nearly all of the predictive power of these two variables was contained in ppoDL_{CO}%. As illustrated in Fig. 2, there is only a modest increment in the probability of mortality as ppoFEV_1% declines, assuming ppoDL_{CO}% remains in a normal range. Conversely, as ppoDL_{CO}% decreases, mortality increases substantially, with little apparent influence of ppoFEV_1%. These data indicate that there is no important interaction between ppoFEV_1% and ppoDL_{CO}% in the prediction of risk of mortality after major lung resection and suggest that each should be assessed independently in formulating recommendations regarding resection.

From our data we were able to generate formulas that estimate the probabilities of mortality and pulmonary, cardiac, and overall complications for individual patients (see appendix). The specific equations developed from our patient data may not be directly applicable to other patient groups or individuals, however, and are provided only as suggested guidelines.

It is important to remember that our conclusions are based on a retrospective analysis of patients operated on during a 13-year interval. There is no doubt that biases are reflected both in the patients who were referred for potential operation and in the selection of patients who eventually received an operation. Such biases are most strongly grounded in preoperative assessment of cardiovascular status and pulmonary function, the latter being based primarily on spirometry. Rather than using measurement of diffusing capacity to override selection bias based on these factors, we embrace their continued use, because they have a proven record in predicting operative risk. However, dependence on spirometry alone in estimating the extent of pulmonary dysfunction is unreliable in many patients, particularly considering that many patients with lung cancer have a reduction of DL_{CO} that is out of proportion to changes in their spirometric values.[28] We advocate the routine use of diffusing capacity assessment as an additional test that improves estimates of mortality and morbidity, both in an overall patient population and, potentially, in an individual patient.

One of the authors (R.M.) was primarily responsible for the statistical analyses included in this study.

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Discussion

Dr. Joseph I. Miller *(Atlanta, Ga.).* For those of us interested in the physiologic evaluation of the lung resection candidate, I believe that this paper will become a major landmark in using values for resectability.

There are several things I would like to mention. In the group of patients described by the authors, 75% underwent either lobectomy or bilobectomy and 25% underwent pneumonectomy, with mortality rates ranging from 5.6% to 12.5% for the two groups, or a total of 7.7%.

Several conclusions were reached from which I will ultimately raise several questions: First, the authors pointed out that there was little interreaction between the ppoFEV_1 and the ppoDL_{CO} in predicting mortality and

that the ppoDL_{CO}% was the strongest indicator of postoperative morbidity and mortality. It is interesting that in their correlation there was no relationship between the FEV_1, the FEV_1%, and the estimated postoperative values of these as identified as predictors of morbidity and mortality. Also, their primary interest was in performing an analysis to determine whether the DL_{CO} would permit safe resection in patients with normal spirometric values or whether it is an adverse indicator despite normal values.

In review of their manuscript, I would make the following statements: Block and Olsen in 1972 used a DL_{CO} of "greater than 50% of predicted" as one of the criteria for pneumonectomy.

In a paper presented before the Association 2 years ago, based on 2340 patients in whom spirometric values were applied to resection, these values were suggested as being the lower limits of normal below which a resection could be carried out. Again, in the lobectomy category there is a wide physiologic variable that will permit the majority of patients to undergo lobectomy when assessed carefully. In the pneumonectomy group the degree of variability that one can apply is much less.

In that group of patients we looked also at DL_{CO}, particularly in the pneumonectomy group. In the majority of those undergoing pneumonectomy, the preoperative DL_{CO} was greater than 50% of predicted, which went with the original criteria.

I would raise the following questions for Dr. Ferguson; Do you believe there is a specific cutoff value of DL_{CO} below which pneumonectomy should not be performed? Could you define a spectrum of parameters of DL_{CO} during which lobectomy could safely be carried out? Is there a DL_{CO} below which elective resection should not be carried out?

A third statement that I would make is that the DL_{CO} is probably the most specific indicator in anticipating complications in the emphysematous lung, particularly when combined with review of high-resolution computed tomographic scanning.

Dr. Ferguson. We have not separated out the effects of measuring diffusing capacity in predicting risk in patients undergoing lobectomy versus those undergoing pneumonectomy. Part of the value in measuring the ppoDL_{CO}% is that it takes into account the amount of lung one is anticipating resecting. In general, at least on a mathematical basis, one could use the same limiting value of ppoDL_{CO}% in making a decision about patients being considered for lobectomy as one does in those being considered for pneumonectomy. However, that having been said, pneumonectomy is certainly a more morbid operation than lobectomy. Other factors are probably involved in determining morbidity and mortality in those patients in addition to simply the amount of lung that is resected.

In looking at patients who have very acceptable FEV_1 values (one could take, for example, a postoperative predicted FEV_1 of 60%, which is well above the generally accepted limiting value of 40%), we find that the diffusing capacity is still a good predictor of mortality. For example, for patients with ppoDL_{CO}% of less than 50, the mortality rate is about 15%, which compares with the whole group of patients with a ppoFEV_1% greater than 60% in which the mortality rate is only about 3%.

In general, we believe that a reasonable value to use for predicting high-risk patients is a ppoDL_{CO}% of 50. That is not a hard and fast rule. In fact, we will operate on patients who have predicted postoperative values of less than 50. It is just an indicator that those patients are probably at higher risk.

Dr. James B. D. Mark *(Stanford, Calif.).* You have made some presumptions, one of which is that the portion of lung that you are removing is functioning just as well as the portion of lung that you are leaving in. Thus you are using your preoperative predictors as predictors of postoperative function based on percentage of lung removed. Have you done any postoperative pulmonary function testing to either prove or disprove that preoperative presumption?

Dr. Ferguson. We have not consistently tested these patients after the operation. In the studies in which postoperative tests were done, the values sometimes do not correlate closely with the predicted values. Part of the reason for that is that in many patients the resected lung is not adequately functioning. In some patients there is airflow obstruction or decreased pulmonary artery flow to those lobes. Thus our estimates of ppoDL_{CO}%, in fact, turn out to be relatively conservative estimates. If one wishes to increase the accuracy of the estimate, quantitative ventilation/perfusion scans help to determine how much functional lung is going to be removed.

Appendix

Multivariate analysis of risk factors influencing the development of pulmonary events, cardiac events, morbidity, or mortality was performed by means of stepwise logistic regression. With the formulas developed through this analysis, we report one optimal model for each of four categoric outcomes based on parsimony and the goodness-of-fit χ^2 statistic. Using these logistic regression models, we estimated the probability of mortality and other complications as a function of variables from the percent predicted postoperative value covariate pool using the logistic function:

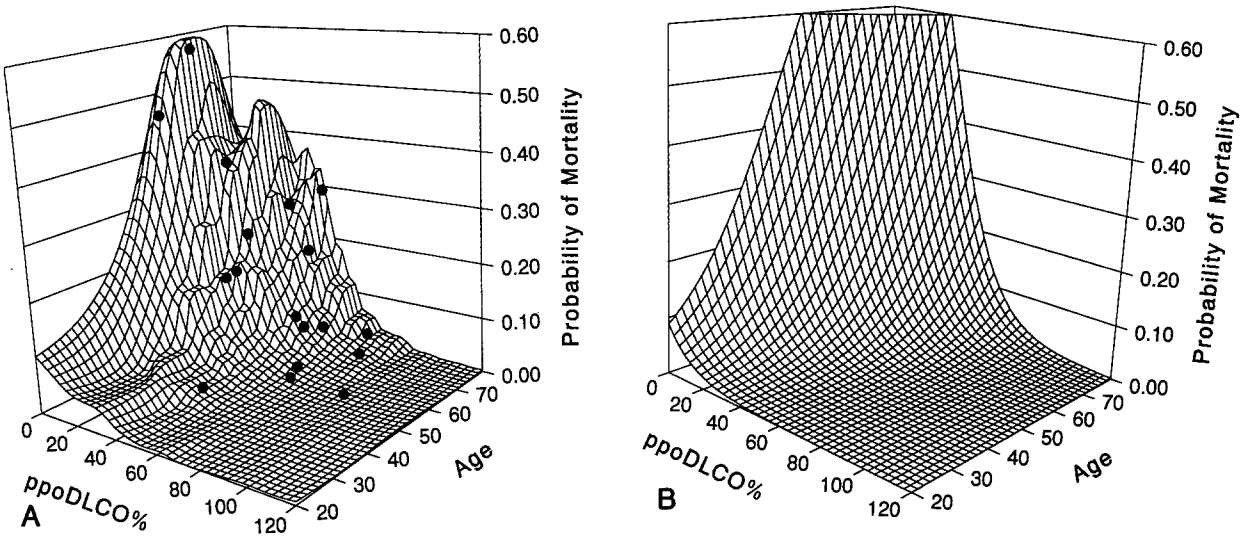
$$P(\text{mortality}) = 1/(1 + \exp[-(\text{BO} + \text{B1X1} + \text{B2X2} + \text{B3X3})])$$

where BO is a constant, B1 is the slope of the regression line describing the risk of mortality as a function of variable X1, B2 is the slope of the regression line describing the risk of mortality as a function of variable X2, etc. On the basis of our data,

$$\text{Logit}_{\text{Mortality}} = -4.033 - (0.0767 \times \text{ppo}DL_{CO}\%) + (0.0852 \times \text{Age})$$

and the probability of mortality for an individual is therefore calculated as

$$P_{\text{Mortality}} = 1/(1 + \exp[-(-4.033 - [0.0767 \times \text{ppo}DL_{CO}\%] + [0.0852 \times \text{Age}])]).$$



Appendix Fig. 1. The probability of mortality expressed as a function of ppoDL_{CO}% and age, where probability = 1/[1 + exp(−[−4.033 − (0.0767 × ppoDL_{CO}%) + (0.0852 × age)])]. *Left,* A surface constructed by calculating the estimated probability of mortality using ppoDL_{CO}% and age data from 275 patients. Actual operative mortalities are indicated by *black dots. Right,* A theoretical surface of predicted risk of mortality generated using the equation only demonstrates the interaction of ppoDL_{CO}% and age in estimating risk.

For example, assuming that a low-risk patient has ppoDL_{CO}% = 70 and age = 50 years, then

$$P_{\text{Mortality}} = 1/(1 + \exp[-(-4.033 - [0.0767 \times 70] + [0.0852 \times 50])])$$

$$P_{\text{Mortality}} = 1/(1 + \exp[-(-5.142)]), \text{ or } 0.58\%$$

For moderate-risk patients who deviate from these relatively favorable values, the calculations are similar. For a patient with ppoDL_{CO}% = 55 and age = 50 years,

$$P_{\text{Mortality}} = 1/1(1 + \exp[-(-3.995)]), \text{ or } 1.8\%,$$

and for a patient with ppoDL_{CO}% = 70 and age = 65 years,

$$P_{\text{Mortality}} = 1/(1 + \exp[-(-3.864)]), \text{ or } 2\%.$$

Patients are at higher risk if they deviate further from the relatively favorable values. For example, for a patient with ppoDL_{CO}% = 45 and age = 65 years,

$$P_{\text{Mortality}} = 1/(1 + \exp[-(-1.9465)]), \text{ or } 12.5\%,$$

and for a patient with ppoDL_{CO}% = 55 and age = 75 years,

$$P_{\text{Mortality}} = 1/(1 + \exp[-(-1.8615)]), \text{ or } 13.5\% \text{ (appendix Fig. 1).}$$

This formula also can be used to describe the increase in relative risk, or "odds," of mortality for a unit change in one variable, assuming that all other variables are held constant. For our data, a decrease in ppoDL_{CO}% of 10 units (10%) is estimated to increase the odds of mortality by a factor of 2.15. The 95% confidence interval for this factor = exp[B(10) ± 1.96 (standard error B)]. Since B = 0.0767 ± 0.0179 (standard error), the 95% confidence interval = 2.08 to 2.23.

Similar equations developed for estimating the probability of pulmonary morbidity, cardiac morbidity and overall morbidity are as follows:

$$\text{Logit}_{\text{Pulmonary}} = -2.408 - (0.0387 \times \text{ppo}DL_{CO}\%) + (0.0519 \times \text{Age})$$

$$\text{Logit}_{\text{Cardiac}} = -2.332 - (0.031 \times \text{ppo}DL_{CO}\%) + (1.212 \times \text{Prior myocardial infarction}) + (0.0406 \times \text{Age})$$

$$\text{Logit}_{\text{Overall morbidity}} = -0.228 - (0.0193 \times \text{ppo}DL_{CO}\%) + (0.0276 \times \text{Age}).$$

A statistically significant stepwise logistic regression model could not be constructed for predicting other complications.