Pulmonary complications after lung resection in the absence of chronic obstructive pulmonary disease: The predictive role of diffusing capacity

Mark K. Ferguson, MD,[a] Henning A. Gaissert, MD,[b] Joshua D. Grab, MS,[c] and Shubin Sheng, MS[c]

Objective: Diffusing capacity is not routinely used in assessing risk of lung resection, perhaps owing to uncertainty as to whether patients with normal spirometric results require additional evaluation. We determined whether diffusing capacity is predictive of pulmonary complications after lung resection in patients with normal spirometric results.

Methods: We reviewed outcomes of major lung resection in The Society of Thoracic Surgeons General Thoracic Surgery Database from 2002 to 2008 to determine the relationship of diffusing capacity (expressed as percent of predicted) to postoperative pulmonary complications stratified by chronic obstructive pulmonary disease status.

Results: Percent of predicted diffusing capacity was measured in 7891 (57%) patients. There were 3905 women and 3986 men with a mean age of 66.3 ± 10.6 years who underwent lobectomy (6904; 87.5%), bilobectomy (463; 5.9%), and pneumonectomy (524; 6.6%). Chronic obstructive pulmonary disease was identified in 2711 (34.4%) patients. Pulmonary complications occurred in 13%, and the operative mortality was 1.9%. Percent of predicted diffusing capacity was strongly associated with the development of pulmonary complications (odds ratio, 1.12 per 10-point decrease; $P < .0001$). Decreasing percent of predicted diffusing capacity was incrementally related to an increased incidence of pulmonary complications regardless of chronic obstructive pulmonary disease status. There was no apparent interaction between percent of predicted diffusing capacity and chronic obstructive pulmonary disease status in the predictive model.

Conclusions: Percent of predicted diffusing capacity predicts pulmonary complications after lung resection in patients without chronic obstructive pulmonary disease. We recommend measurement of diffusing capacity in lung resection candidates, regardless of chronic obstructive pulmonary disease, as an important element in the accurate assessment of operative risk. (J Thorac Cardiovasc Surg 2009;138:1297-302)

Pulmonary complications are among the most common causes of postoperative morbidity after major lung resection. They are associated with increased operative mortality and hospital cost.[1] Although spirometry and diffusing capacity of the lung for carbon monoxide (D$_{LCO}$) were both shown in the 1950s to be importantly reduced after major lung resection,[2-4] the use of D$_{LCO}$ has not become routine in assessing operative risk for major lung resection. In the European Thoracic Surgery Database, 77% of patients underwent major lung resection without measurement of D$_{LCO}$.[5] It is not known whether this is owing to lack of access to qualified pulmonary function laboratories, cost concerns, or the impression that patients with normal spirometric results do not require the additional measurement of D$_{LCO}$.

Two recent reports demonstrate that D$_{LCO}$ is an important and independent predictor of postoperative complications after major lung resection, even in patients without chronic obstructive pulmonary disease (COPD).[6,7] Both reports were based on review of outcomes from single institutions, raising concerns about how generalized the findings and recommendations are. The recent advent of The Society of Thoracic Surgeons (STS) General Thoracic Surgery Database provides an ideal opportunity to explore the utility of D$_{LCO}$ measurement in the general population of patients undergoing major lung resection for cancer. Using the STS database, we sought to determine the relative predictive value of D$_{LCO}$ in patients with and without COPD.

METHODS

Outcomes of major lung resection in the STS General Thoracic Surgery Database from January 2002 through June 2008 were reviewed. Patients were selected who had a diagnosis of primary lung cancer and who underwent major lung resection (lobectomy, sleeve lobectomy, bilobectomy, or pneumonectomy). Exclusion criteria were as follows: concomitant chest wall resection, extrapleural pneumonectomy, carinal sleeve pneumonectomy, completion pneumonectomy, and emergency or urgent operation. Demographic and surgical information was abstracted from the database for analysis. COPD was defined as FEV$_1$/FVC<0.7 (FEV$_1$, forced expiratory volume in the first second; FVC, forced vital capacity) *and* FEV$_1$% < 80, which corresponds to moderate to severe COPD by international criteria.[8] Patients without COPD were classified

Abbreviations and Acronyms
ASA = American Society of Anesthesiolgists
COPD = chronic obstructive pulmonary disease
D_{LCO} = diffusing capacity of the lung for carbon monoxide
FEV_1 = forced expiratory volume in the first second
FVC = forced vital capacity
STS = The Society of Thoracic Surgeons

as ''normal'' ($FEV_1/FVC \geq 0.7$ *and* $FEV_1\% > 80$) or ''not normal/no COPD'' ($FEV_1/FVC < 0.7$ *or* $FEV_1\% < 80$, but not both). Some categorical variables (performance status, American Society of Anesthesiolgists [(ASA] score) were dichotomized, whereas resection type was organized into 3 categories: lobectomy, bilobectomy or sleeve lobectomy, and pneumonectomy. Staging was done according to the American Joint Commission on Cancer.[9] The study end point was pulmonary complications, defined as atelectasis necessitating bronchoscopy, pneumonia, adult respiratory distress syndrome, bronchopleural fistula, initial ventilator support necessary for more than 48 hours, tracheostomy, reintubation for any reason, or any other pulmonary complication.

Patients with insufficient data, primarily D_{LCO} (expressed as a percent of predicted), were omitted from the analysis. Univariate analyses were performed by χ^2 analysis for categorical variables and the unpaired Student *t* test for continuous variables. Mulitvariable analyses included logistic regression methods using generalized estimating equations to account for within-site (ie, hospital) correlation of patients. Interaction terms were constructed to explore independence of variables in the models. Continuous data are expressed as mean $\pm$ SD.

A waiver for this study was granted by The University of Chicago Internal Review Board.

RESULTS

Records were available for 14,160 patients operated on at 107 participating sites during the period of study. Of these, 2.3% had spirometric data that were considered inaccurate. Of the remaining 13,839 patients, 7891 (57%) had sufficient D_{LCO} data and were used in the analyses. Criteria for COPD were present in 2711 (34.4%) patients, 2672 (33.8%) patients had normal spirometric data, and 2508 (31.8%) were classified as not normal/no COPD. There were few clinically important differences between the groups of patients with and without values for D_{LCO} (Table 1). Patients with D_{LCO} measurement were more advanced in mean age, more likely to have hypertension and to receive induction therapy, and had higher mean FVC and FEV_1 values. D_{LCO} measurement, however, was also associated with a lower mean FEV_1/FVC ratio and a greater proportion of patients with COPD. Operations in the study group included lobectomy in 6904 (87.5%), sleeve lobectomy or bilobectomy in 463 (5.9%), and pneumonectomy in 524 (6.6%). The majority of patients in the study group had T1 or T2 tumors (84.5%) and no nodal involvement (69.1%). The incidence of pulmonary complications in the study group was 13%, and 1.9% of patients had operative

mortality (Table 2). The incidences of pulmonary complications and operative mortality did not differ between groups with and without D_{LCO} measurements.

Univariate analyses identified a number of variables that were associated with pulmonary complications, including age, sex, performance status, ASA class, cardiovascular disease, pulmonary dysfunction, other organ dysfunction, and the extent of the operation (Table 3). Logistic regression analysis identified age, performance status, ASA class, congestive heart failure, renal insufficiency, a recent smoking history, induction therapy, the extent of resection, $FEV_1\%$, and D_{LCO} as significant predictors of pulmonary complications (Table 4). Age, induction therapy, the extent of surgery, and $D_{LCO}\%$ were the preoperative clinical variables most strongly associated with the development of

TABLE 1. Comparison of patient populations with and without measurement of D_{LCO}

Parameter	D_{LCO} not measured (5948 patients)	D_{LCO} measured (7891 patients)	P value
Mean age (y)	65.8 ± 11.0	66.3 ± 10.6	.018
Male	3000 (50.4%)	3986 (50.5%)	.93
Performance status 0 or 1	5063/5427 (93.9%)	7177/7682 (93.4%)	.76
ASA class I to III	4905/5443 (90.1%)	6860/7580 (90.5%)	.46
BMI	27.2 ± 5.9	27.2 ± 6.0	.18
Hypertension	3161/5927 (53.3%)	4383/7855 (55.8%)	.004
Coronary artery disease	1206/5894 (20.5%)	1633/7781 (21.0%)	.45
Congestive heart failure	171/5880 (2.9%)	247/7743 (3.2%)	.35
Diabetes mellitus	824/5867 (14.0%)	1122/7805 (14.4%)	.58
Renal insufficiency	129/5899 (2.2%)	192/7854 (2.4%)	.32
Recent smoking history	1662/5911 (28.1%)	2154/7828 (27.5%)	.44
Preoperative chemotherapy	408/5805 (7.0%)	633/7700 (8.2%)	.01
Preoperative radiotherapy	292/5864 (5.0%)	444/7703 (5.8%)	.046
FVC%	85.8 ± 20.6	88.8 ± 18.1	<.001
$FEV_1\%$	78.8 ± 21.7	80.3 ± 20.9	.01
FEV_1/FVC	0.69 ± 0.12	0.68 ± 0.11	<.001
COPD	686/2165 (31.7%)	2711/7891 (34.4%)	.02
Procedure			.31
Pneumonectomy	357 (6.0%)	524 (6.6)	
Bilobectomy/sleeve lobectomy	356 (6.0%)	463 (5.9%)	
Lobectomy	5235 (88.0%)	6904 (87.5%)	
Pulmonary complications	723/5948 (12.2%)	1028/6863 (13.0%)	.13
Operative mortality	130/5948 (2.2%)	152/7891 (1.9%)	.29

Performance status, Zubrod performance status; *D_{LCO},* diffusing capacity of the lung for carbon monoxide; *ASA,* American Society of Anesthesiology; *BMI,* body mass index; *recent smoking history,* quit cigarette use less than 30 days before the operation; *FVC,* forced vital capacity; *FEV_1,* forced expiratory volume in the first second; *COPD,* chronic obstructive pulmonary disease, defined as FEV_1/FVC ratio<0.7 and $FEV_1\% < 80$.

TABLE 2. Incidence of pulmonary complications

Category	Affected	Percent
Any pulmonary complication	1028/7891	13.0
Atelectasis requiring bronchoscopy	321/7828	4.1
Pneumonia	326/7826	4.2
Adult respiratory distress syndrome (ARDS)	97/7815	1.2
Bronchopleural fistula	34/7812	0.4
Air leak>5 d	798/7790	10.2
Initial ventilator support>48 h	50/7816	0.6
Reintubation	282/7821	3.6
Tracheostomy	101/7819	1.3
Other pulmonary complication	387/7824	4.9

these complications ($P < .0001$ for each). After addition of an interaction variable to explore the relationship between DLCO and COPD status, the strongest predictors of pulmonary complications (including DLCO%) were unchanged, indicating COPD status did not influence the predictive ability of DLCO% with regard to pulmonary complications. A parsimonious model of pulmonary complications was developed using backward selection ($P = .05$) and accounting for interactions between DLCO%, FEV_1%, and FVC%. Independent predictors of pulmonary complications and their odds ratios were similar to the nonparsimonious model. The variables with the greatest statistical significance were age, induction therapy, FEV_1%, DLCO%, extent of resection, and a recent smoking history.

The incidence of DLCO% less than 60 was 25.7% overall and was 12.4%, 26.3%, and 42.3% in the normal, not normal/no COPD, and COPD groups, respectively. Figure 1 illustrates the incidence of pulmonary complications by DLCO group for patients related to COPD status. The frequency of pulmonary complications increased markedly as DLCO% decreased ($P < .001$ for all patients and for each COPD status group). At the extremes of DLCO (DLCO% > 90 or DLCO% < 60), there were no differences in the risk of pulmonary complications within each COPD status category. However, for the DLCO% categories 60 to 74 and 75 to 89, there was a significant, increasing risk of pulmonary complications progressing from patients with normal spirometric data to those with COPD ($P = .003$ for each).

COMMENT

The ability to predict complications after an operation as common as major lung resection has important ramifications for patients, caregivers, medical research, and the health care industry. Accurate predictive models can enhance communication between patients and their surgeons, may indicate when preoperative intervention is indicated to reduce risk, can help determine whether parenchyma-sparing procedures rather than anatomic lobectomy are appropriate, and may

TABLE 3. Univariate analysis of factors associated with pulmonary complications

Parameter	No complications (6863 patients)	Complications (1028 patients)	P value
Mean age (y)	66.1 ± 10.6	67.7 ± 10.3	<.001
Male	49.0%	52.8%	.022
Zubrod performance status			
0	44.9%	40.4%	<.001
1	49.0%	49.4%	
2	4.8%	8.2%	
3 or 4	1.3%	2.0%	
ASA class			
I	1.8%	0.7%	<.001
II	24.1%	15.3%	
III	65.3%	69.8%	
IV or V	8.8%	14.2%	
BMI	27.3 ± 5.8	26.8 ± 5.8	.002
Hypertension	55.2%	59.5%	.011
Coronary artery disease	20.2%	26.0%	<.001
Congestive heart failure	2.8%	5.8%	<.001
Diabetes mellitus	13.9%	17.5%	.003
Renal insufficiency	2.1%	4.4%	<.001
Recent smoking history	26.7%	33.0%	<.001
Preoperative chemotherapy	7.8%	11.3%	<.001
Preoperative radiotherapy	5.3%	8.6%	<.001
FVC%	89.2 ± 18.1	86.1 ± 17.8	<.001
FEV_1%	81.1 ± 20.9	75.0 ± 19.8	<.001
FEV_1/FVC	0.68 ± 0.11	0.66 ± 0.12	<.001
COPD status			
Normal spirometry	35.3%	23.9%	<.001
Not normal/no COPD	31.8%	31.8%	
COPD	32.9%	44.3%	
DLCO%	75.0 ± 22.2	67.4 ± 20.5	<.001
Procedure			
Pneumonectomy	6.7%	6.1%	<.001
Bilobectomy/sleeve lobectomy	5.5%	8.5%	
Lobectomy	87.8%	85.4%	

ASA, American Society of Anesthesiology; *FVC*, forced vital capacity; *FEV₁*, forced expiratory volume in the first second; *BMI*, body mass index; *recent smoking history*, quit cigarette use less than 30 days before the operation; *COPD*, chronic obstructive pulmonary disease defined as FEV₁/FVC<0.7 and FEV₁% < 80; *normal spirometry*, FEV₁/FVC≥0.7 and FEV₁% > 80; *DLCO*, diffusing capacity of the lung for carbon monoxide.

improve patient selection. Such models also permit risk stratification for quality improvement and clinical research and allow improved allocation of limited clinical resources.

Risk modeling for major lung resection is a burgeoning and increasingly complex field. Until recently, relatively small databases that were usually based at a single institution

TABLE 4. Logistic regression analysis of pulmonary complications

Parameter	Odds ratio	Lower CI	Upper CI	P value
Age	1.01	1.01	1.02	<.0001
Male	1.13	0.97	1.32	.13
Performance status ≥2	1.56	1.10	2.21	.014
ASA class IV or V	1.26	1.04	1.51	.017
Hypertension	1.01	0.88	1.17	.84
Coronary artery disease	1.11	0.93	1.34	.25
Congestive heart failure	1.58	1.20	2.10	.0014
Diabetes mellitus	1.18	0.98	1.41	.079
Renal insufficiency	1.53	1.10	2.15	.012
Recent smoking history	1.30	1.14	1.50	.0001
Preoperative chemotherapy and/or radiotherapy	1.51	1.27	1.8	<.0001
FVC%	1.00	1.00	1.01	.22
FEV$_1$%	0.99	0.98	1.00	.005
Spirometry not normal/no COPD	1.09	0.91	1.31	.36
COPD	1.16	0.94	1.43	.16
D$_{LCO}$% (10 point decrease)	1.12	1.09	1.16	<.0001
Pneumonectomy	0.92	0.71	1.20	.56
Bilobectomy or sleeve lobectomy	1.62	1.28	2.06	<.0001

CI, Confidence interval; *ASA,* American Society of Anesthesiology; *recent smoking history,* quit cigarette use less than 30 days before the operation; *COPD,* chronic obstructive pulmonary disease defined as FEV$_1$/FVC<0.7 and FEV$_1$% > 80; *D$_{LCO}$,* diffusing capacity of the lung for carbon monoxide.

FIGURE 1. Risk of pulmonary complications relative to diffusing capacity *(D$_{LCO}$)* and chronic obstructive pulmonary disease *(COPD)* status.

STS General Thoracic Surgery Database, we found that D$_{LCO}$ was reported for fewer than 60% of patients undergoing major lung resection. This attitude is supported by published algorithms that do not include D$_{LCO}$ as an initial screening measure for lung resection candidates.[17,18]

Possible reasons for omitting D$_{LCO}$ as part of routine preoperative evaluation include limited access to testing facilities, concerns about cost-effectiveness, lack of awareness of the predictive ability of this test, use of other predictive tests such as exercise capacity in lieu of D$_{LCO}$, perceived lack of impact on clinical recommendations, and perceived lack of utility in the setting of normal spirometry. This study explored the question of whether D$_{LCO}$ has predictive ability for pulmonary complications after major lung resection in patients with normal spirometric results. Recent publications from single institutional data found that risk associated with D$_{LCO}$ was independent of whether patients had COPD.[6,7] Because findings from such reports may not be applicable to the general population, in this study a national database was queried to determine whether D$_{LCO}$ independently predicts risk regardless of COPD status.

The data for this study came from 107 centers that may represent a self-selected group of surgeons and medical centers with interest in tracking clinical activity and outcomes. Reasons for why some patients had D$_{LCO}$ reported and others did not are unclear; the population of patients with D$_{LCO}$ measured was somewhat older with a higher incidence of risk factors such as hypertension, induction therapy, and COPD. Interestingly, the patients without D$_{LCO}$ measurements had worse spirometric data, suggesting that the decision to measure D$_{LCO}$ is not based on the clinical impression or actual measurement of lung volumes and flows. Outcomes of surgery were quite good, with 13% of patients having postoperative pulmonary complications and only 1.9% of patients having operative mortality. We found that, regardless of COPD status, D$_{LCO}$ was a strong

provided limited insight into risk prediction. Models based on these data were characterized by poor predictive ability because of limited statistical power, missing clinical variables, or small numbers of complications. Their applicability to more general populations was therefore questioned. The recent creation of national and international databases for thoracic surgery, such as the European Thoracic Surgery Database, Epithor (French Society of Thoracic and Cardio-Vascular Surgery), and the STS General Thoracic Surgery Database, opens the field to new possibilities of risk prediction and improved outcomes for major lung resection.

As these databases grow and predictive modeling based on their data improves, how will this information be used? It is interesting to note how the development of other models of risk of pulmonary surgery has affected surgeon behavior in the recent past. Until the 1990s, models for risk of major lung resection accounted for only 12% to 22% of operative mortality.[10,11] D$_{LCO}$ was identified in 1988 as a strong, independent predictor of morbidity after major lung resection.[12] The utility of D$_{LCO}$ in assessing risk was confirmed by a number of other authors.[13-16] Despite the recognition of D$_{LCO}$ as the single strongest predictor of pulmonary morbidity and operative mortality after major lung resection, surgeons have been slow to adopt its use in the routine assessment of patients for lung resection. In the European Thoracic Database, less than 25% of patients undergoing lung resection had a preoperative D$_{LCO}$ measured.[5] In the
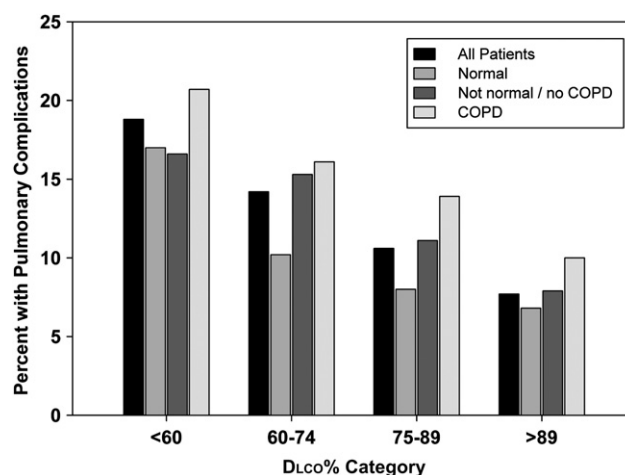
preoperative clinical predictor of pulmonary complications after major lung resection. The results are similar to those reported from independent centers.[6,7] The results of this study confirm the general applicability of using DLCO as a routine measure of risk in the preoperative assessment of lung resection candidates regardless of COPD status.

There are several potential weaknesses in this study. The data set may not be reflective of the general population of patients who undergo major lung resection in the United States. Because the STS General Thoracic Surgery Database does not have an auditing feature, whether the data are accurate and reflect all of the patients treated at participating sites are unknown. A large number of patients were excluded from this study because information on DLCO was lacking. Whether this information was lacking because it was never obtained or because it was not entered into the database is not certain. A number of differences existed between the groups of patients with and without DLCO measurements, some of which were important in the predictive models for pulmonary complications.

In summary, we found that DLCO is an independent and strong predictor of the risk of pulmonary complications in patients undergoing major lung resection for cancer and that this predictive ability exists regardless of COPD status. The lack of DLCO measurement was associated with worse spirometric results, suggesting the possibility that physicians who do not measure DLCO routinely before major lung resection may have indications for its measurement other than or in addition to spirometric findings. Surgeons who elect to forego measurement of DLCO on the basis of the absence of classic findings of COPD will fail to identify an important abnormality in this factor in up to 25% of patients. We recommend measurement of DLCO in candidates for lung resection as an important element in the accurate assessment of operative risk.

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Discussion

Dr Kemp Kernstine *(Duarte, Calif)*. This is a very important study using the STS database, our database, to demonstrate that the DLCO measurement is correlated with complications after lung resection. This correlation was not solely in patients with COPD, but in patients without COPD as well. What your findings tell us is that DLCO should be measured in all patients whether they have COPD or not, because DLCO independently is correlated with the postoperative lung resection complication rate.

I have a couple of questions or comments. Currently, the cardiac and congenital heart surgery databases have a quality assurance system that is a component of each and the thoracic database does not. Do you think that this might affect your results?

Dr Ferguson. It is true that there can be concerns raised by the quality of the data submitted and the selection of data submitted, and we have no way of assessing that. I think it is appropriate to keep those concerns in mind when interpreting the data and the results of our analysis.

Dr Kernstine. Do you recommend then that we should encourage the STS to have a quality assurance system in our thoracic data base?

Dr Ferguson. Absolutely.

Dr Kernstine. Then is the DLCO sufficiently standardized across hospitals to make a generalized recommendation that all thoracic surgeons should be performing DLCO routinely?

Dr Ferguson. It is a bit of an issue. We have found anecdotally that the occasional patient comes to us with marginal DLCO and when we measure it, it is actually a little bit better. There are a number of potential explanations for that. One is that there are differences in

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techniques or reliability of results between institutions; in addition, some patients have had improvement, for example, in the pneumonia that they presented with to the outside physicians that led to the investigation for possible lung cancer, resulting in an improved D_{LCO} on remeasurement. At least a couple of studies have performed repeated measurements on healthy patients over time, demonstrating that, on average, the difference in D_{LCO} measurement was about 1 percentage point. I think, in general, measurements of D_{LCO} are very reliable. It is not effort related on the part of the patient and it is not subject to interpretation by someone who is reporting the results, so on the basis of that I think it is very reliable.

Dr David Follette (*Sacramento, Calif*). Dr Ferguson, I completely agree with your conclusions. I do have 3 questions for you.

In a patient with COPD, it is not only D_{LCO} but the corrected D_{LCO}. Is there any way through the database that you can tell whether these were just the numbers or whether they were the corrected numbers, because it can make a difference in a COPD population.

Dr Ferguson. It does make a difference and there is no way of telling in the database which it is. If there is a difference, it is primarily related to hemoglobin of the patient and generally gets better if you use the corrected value than the uncorrected value, but we have no way of distinguishing which value was reported.

Dr Follette. I found that the second and more useful test, especially coupled with the D_{LCO}, is the carbon dioxide level on a blood gas. A slight carbon dioxide retention and marked depression in D_{LCO}, in my view, is the highest risk pulmonary resection candidate that I deal with. In the database, do they report blood gas data and did you happen to correlate P_{CO_2} levels with the D_{CLO}?

Dr Ferguson. That is a good question and I agree with your general assessment, but I do not recall whether there were blood gas values. Certainly we did not perform any correlation between those two. In my own institution, for example, we probably get blood gas information on only about 30% of patients, so it is not done routinely.

Dr Follette. I know you did not present it, but I would like your guideline as to what D_{LCO} level puts a big red flag up in Chicago. I have used one that is less than 40% with the red flag up for me. The data you presented only showed a 10-point drop from normal. What guideline do you use before you tell the patient and the referring doctors that this is a very high-risk patient?

Dr Ferguson. I try to be cautious when I am talking about specific numbers. In Alex Brunelli's study, they used a predicted postoperative D_{LCO} cutoff of 40% for distinguishing high-risk patients. That is what we use in general to distinguish between much higher risk than so-called average risk, but it is really incremental all the way. We will go so far as to operate on patients with a postoperative predicted D_{LCO} of maybe 30% if they seem otherwise pretty vigorous. Everything else has to be taken into account as well as this one number.

Dr Carolyn Reed (*Charleston, SC*). I think that also pertains to my question. A couple weeks ago we had a patient with FVC/FEV_1 80% of predicted, D_{LCO} less than 40% of predicted, maximum oxygen consumption 20, and the patient had to have a lobectomy to get the cancer out. Would you offer that patient a lobectomy?

Dr Ferguson. Given that D_{LCO}, exercise testing is the additional test I would do, and if that was as good as 20, yes, I would go with the lobectomy.

Dr Richard Whyte (*Stanford, Calif*). Dr Ferguson, I have 1 question. You used the term a couple of times that the D_{LCO} was the strongest predictor of increased morbidity. You looked at the P value on that. The P value was very low, but you had other issues there that had a much higher relative risk that were still highly statistically significant. I am wondering why you say this is the most sensitive or this is the least likely to be a random predictor. I would say that perhaps it is not the most important predictor of a bad outcome. Could you comment on that?

Dr Ferguson. I am not a statistician. The P value is substantially less than .0001, and that is the only reason we say it is the strongest predictor. In our work with our own database in doing backward elimination multivariable analysis, it does arise oftentimes as the only predictor because most of those other things fall out. You have to be a little careful about looking at the odds ratios and comparing them because they are based on a variety of different incremental changes for continuous variables. Somehow, those have to be matched up to enable a head-to-head comparison. What we have elected to do sometimes is to measure effects of a 10-year change in age, a 10-point difference in D_{LCO}, and so on. Whether those changes are equal to a 1-point increase in creatinine or to a change from no hypertension to hypertension is very hard to determine.

Dr Tara Karamlou (*Portland, Ore*). If I understand your findings, you advocate that D_{LCO} is able to be generalized to the entire population. Yet in one of your earlier slides, you showed that induction chemotherapy and radiotherapy as well as, I believe, mortality, were significantly different although you mention not importantly different from a clinical perspective between the patients who had D_{LCO} measured and the subgroup who did not. Can you defend that statement? Could it be more accurate to say that D_{LCO} might be more useful in patients who perhaps are going to be getting neoadjuvant therapy or within the subgroup where you are actually measuring it from your study?

Dr Ferguson. We do not have numbers of 5.5 million as in the cardiac database, but 5500 patients is a large enough group of patients to demonstrate statistically significant differences between the D_{LCO} and no D_{LCO} groups but not important clinical differences. For example, there is difference in FEV_1, but it was only 2 percentage points. I do think, though, it is important that we focus on D_{LCO} measurement in patients undergoing induction therapy, because a number of people have demonstrated a substantial decrease in D_{LCO} as a result of induction chemotherapy and radiation therapy. In our population, we measure D_{LCO}, sometimes on multiple occasions, until the D_{LCO} gets back toward normal before we will subject them to surgery.