Short Communication

Predictive value of pulmonary function measures for short-term outcomes following lung resection: analysis of a single high-volume institution

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Abstract: Despite the importance of preoperative risk-stratification, there is a lack of consensus on how to identify high-risk patients for pulmonary resection. Enrollment criteria for national trials propose one definition based on preoperative pulmonary function tests. We sought to examine the value of preoperative forced expiratory volume in 1 second (FEV1) and diffusion capacity for carbon monoxide (DLCO) to predict short-term outcomes following pulmonary resection. Using our institutional Society of Thoracic Surgeons (STS) database we identified 419 consecutive lung cancer patients who presented to our institution for pulmonary resection between 2012 and 2016. We identified patients as "high risk" based on the national trial criteria of FEV1 or DLCO ≤50%. Our primary outcome was any postoperative complication within 30 days of surgery. Secondary outcomes included cardiac and pulmonary complications, 30-day readmission, and discharge disposition. DLCO ≤50% was associated with any postoperative complication (P=0.03), but not predictive of cardiac events, pulmonary complications, or 30-day readmission. There were no significant differences in any of these short-term outcomes for patients with FEV1 ≤50%. On multivariable analysis, neither FEV1 nor DLCO ≤50% were significantly associated with occurrence of postoperative complication (OR =1.67, 95% CI: 0.60–4.63; OR =1.66, 95% CI: 0.96–2.86, respectively). Notably, DLCO ≤50%—but not FEV1—was associated with discharge to a skilled facility on univariate (P=0.01) and multivariable analysis (OR =2.54; 95% CI: 1.08–5.99; P=0.03). This association between DLCO and discharge to a skilled facility persisted when DLCO was used as a continuous variable. For all-comers presenting to our institution for lung cancer resection, classification based on FEV1 or DLCO ≤50% may not reliably identify those at highest risk for short-term postoperative complications. While our findings suggest caution when using pulmonary parameters in isolation, the potential value of DLCO as a proxy for underlying comorbidity warrants further investigation.

Keywords: Lobectomy; pulmonary function; outcomes

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Introduction

The importance of preoperative risk-stratification is undisputed, particularly in the setting of major surgery. This information is critical not only for optimal patient selection and preoperative counseling, but also to evaluate outcomes of new minimally invasive alternatives. Yet, consensus on precise measures to identify high-risk patients for pulmonary resection remains elusive.

Table 1 Cohort characteristics

Variable	Value
Age, mean ± SD (years)	66.3±10.3
Male gender, n (%)	166 (39.5)
Current smoker, n (%)	99 (23.6)
Diabetes, n (%)	79 (18.8)
Coronary artery disease, n (%)	103 (24.5)
COPD, n (%)	122 (29.0)
Steroid use, n (%)	14 (3.3)
Neoadjuvant chemo or radiation therapy	39 (9.3)
FEV 1, average (range)	85.6% (29–140%)
DLCO, average (range)	70.1% (20–145%)
Pathologic stage, n (%)	
0–I	256 (61.0)
II	102 (24.3)
III	59 (14.0)
IV	2 (0.5)
Thoracoscopic procedure, n (%)	345 (82.1)
Procedure, n (%)	
Sub-lobar resection	90 (21.4)
Lobectomy	302 (71.9)
Pneumonectomy	27 (6.4)
Length of hospital stay, mean ± SD (days)	3.99±3.10
Any postoperative complication, n (%)	151 (36.0)
Postoperative pulmonary event[a], n (%)	20 (4.8)
Postoperative cardiac event[b], n (%)	31 (7.4)
Death within 30 days, n (%)	3 (0.7)
Readmission within 30 days, n (%)	32 (7.6)
Discharge to skilled facility, n (%)	32 (7.6)

[a], pneumonia, atelectasis requiring bronchoscopy, reintubation, tracheostomy, adult respiratory distress syndrome, initial ventilator support >24 hours; [b], myocardial infarction, atrial arrhythmia, ventricular arrhythmia.

The predictive value of pulmonary function tests (PFTs) was established in a cohort of patients who underwent resection through a thoracotomy incision. The appeal of such an easy to interpret objective measure by which to risk stratify patients is obvious. However, prior investigation into the ability of pulmonary parameters to forecast poor clinical outcomes has yielded conflicting results. For lung resection there is no clear consensus on how to define "high risk" patients.

Recently, enrollment criteria for several national multicenter trials led by the American College of Surgery Oncology Group (ACOSOG) established forced expiratory volume in 1 second (FEV1) or diffusion capacity for carbon monoxide (DLCO) of ≤50% predicted as major high-risk criteria (1). However, this definition reflects expert opinion rather than empirical data. Due to the high visibility of these trials there is concern that this approach to risk assessment could be widely disseminated and deny patients potentially curative surgery. We sought to investigate the relationship between pulmonary function using the national study cooperative group definition of high risk and short-term postoperative outcomes in a cohort from a single high-volume institution.

Methods

Using our institutional Society of Thoracic Surgeons (STS) database, we identified 419 consecutive patients who underwent pulmonary resection for cancer between 2012 and 2016. We evaluated postoperative 30-day complications and discharge disposition based on patients with predicted FEV1 or DLCO ≤50% as compared to >50% using Pearson's chi-squared or Fisher's exact tests. We also performed multivariable logistic regression to assess characteristics associated with postoperative complications and discharge disposition. We chose covariates a priori based on previously identified risk factors (2,3) and performed analyses using SPSS 23 (SPSS, Chicago, IL) with significance level (P=0.05).

Results

Table 1 describes the cohort characteristics. Overall, 36% of the cohort experienced any postoperative complication. Average FEV1 was 85.6% (range, 29–140%) and average DLCO was 70.1% (range, 20–145%). Average length of stay was 3.99 days. On univariate analysis, DLCO ≤50% was associated with any postoperative complication (P=0.03), but not predictive of cardiac events, pulmonary complications, or 30-day readmission. There were no significant differences in any of these short-term outcomes for patients with FEV1 ≤50% as compared to >50% (P>0.05 for all). On multivariable analysis, neither FEV1 nor DLCO ≤50% were significantly associated with occurrence of

Table 2 Multivariable analysis of factors predictive of any postoperative complication following pulmonary resection

Variable	Any postoperative event, n (%)	Adjusted odds ratio (95% confidence interval)	P value
Age		1.02 (1.00–1.05)	0.04
ASA			0.35
I–II	51 (31.7)	Reference	
III–IV	100 (38.8)	1.23 (0.80–1.90)	
Smoking status			0.02
Never or former	106 (33.0)	Reference	
Current	45 (45.5)	1.78 (1.11–2.86)	
Approach			0.83
Open	27 (36.5)	Reference	
Thoracoscopic	124 (35.9)	1.06 (0.61–1.85)	
Procedure			0.08
Sub-lobar resection	26 (28.9)	Reference	
Lobectomy or pneumonectomy	125 (38.0)	1.61 (0.95–2.72)	
Stage			0.41
0–1	90 (35.2)	Reference	
2	36 (35.3)	1.01 (0.61–1.65)	
3–4	25 (41.0)	1.48 (0.82–2.67)	
Preoperative predicted FEV1			0.33
≤50%	8 (47.1)	1.67 (0.60–4.63)	
>50%	143 (35.6)	Reference	
Preoperative predicted DLCO			0.07
≤50%	32 (47.8)	1.66 (0.96–2.86)	
>50%	119 (33.8)	Reference	

postoperative complication (OR =1.67, 95% CI: 0.60–4.63; OR =1.66, 95% CI: 0.96–2.86, respectively) (*Table 2*).

Notably, DLCO ≤50%—but not FEV1—was associated with discharge to a skilled facility on univariate (P=0.01) and multivariable analysis (OR =2.54, 95% CI: 1.08–5.99, P=0.03) (*Table 3*). Interestingly, when included in adjusted models as continuous variables, FEV1 (OR =0.99; 95% CI: 0.97–0.99, P=0.008) but not DLCO (OR =1.01, 95% CI: 0.99–1.02, P=0.4) was associated with postoperative complications. In contrast, the reverse held for discharge disposition in that there was an association with DLCO and discharge to a skilled facility but not FEV1 (FEV1 OR =1.01; 95% CI: 0.99–1.04, P=0.3; DLCO OR =0.96, 95% CI: 0.93–0.98, P=0.001).

Discussion

For all-comers presenting to our institution for lung cancer resection, classification based on FEV1 or DLCO ≤50% may not reliably identify those at highest risk for short-term postoperative complications. While more complex risk models exist to guide preoperative decision making (2), the ease of using discrete objective selection criteria is undeniably appealing. Nonetheless, reliance on these values as stand-alone measures for risk stratification may deny patients potentially curative resection.

Previous studies have challenged the prognostic value of pulmonary parameters, postulating that improved pain management and chest wall mechanics following thoracoscopic surgery blunt the sequelae of

Table 3 Multivariable analysis of factors predictive of discharge disposition following pulmonary resection

Variable	Adjusted odds ratio (95% confidence interval)	P value
Age	1.09 (1.0–1.1)	0.001
ASA		0.6
I–II	Reference	
III–IV	0.8 (0.4–1.7)	
Smoking status		0.8
Never or former	Reference	
Current	1.1 (1.5–2.9)	
Approach		0.02
Open	Reference	
Thoracoscopic	0.3 (0.1–0.8)	
Procedure		0.9
Sub-lobar resection	Reference	
Lobectomy or pneumonectomy	0.9 (0.4–2.6)	
Stage		0.5
0–1	Reference	
2	0.9 (0.3–2.4)	
3–4	1.7 (0.6–4.7)	
Preoperative predicted FEV1		0.6
≤50%	0.6 (0.1–5.1)	
>50%	Reference	
Preoperative predicted DLCO		0.03
≤50%	2.5 (1.1–6.0)	
>50%	Reference	

poor preoperative lung function (3). In our analysis, the significance of FEV1 and DLCO as continuous measures suggests that preoperative pulmonary function may influence postoperative events, even when controlling for operative approach. However, a cutoff value of 50% may be too high to adequately capture this effect. Our findings build upon prior work reporting acceptable early outcomes for stage I patients based on this "high-risk" definition (4,5). Furthermore, our cohort offers a more diverse selection with respect to patient, disease, and operative characteristics.

Notably, we observed a significant association between discharge to a skilled facility and DLCO as either a binary or continuous measure. The need for postoperative skilled nursing care may be more heavily influenced by preoperative factors such as chronic conditions and underlying frailty. A recent competing risks analysis examining cause-specific mortality for patients with early stage non-small cell lung cancer describes an inverse relation between DLCO and 1-year mortality, non-cancer specific mortality and overall survival (6). This finding suggests that DLCO may serve as a valuable proxy for comorbid disease with potential to forecast longer-term outcomes. Further investigation into the relationship between DLCO and other markers of chronic cardiopulmonary conditions and frailty such as a 6-minute walk test is warranted.

Our single-institution study has both strengths and limitations. We deliberately chose to include all-comers during our study period which allowed us to assess the

ACOSOG criteria in a more comprehensive group of patients than prior studies. Analysis of this cohort enables us to use our results to caution providers when applying this "high risk" definition broadly in preoperative assessment of patients with lung cancer. However, analyzing a heterogeneous cohort introduces a bias into our study that should be acknowledged when interpreting our findings. Furthermore, this study is underpowered to detect differences in specific outcomes including 30-day mortality and pulmonary complications as well as outcomes in subgroups of patients. Importantly, we operate at a high-volume center for lung volume reduction surgery, affording us extensive experience managing patients with poor pulmonary function that is not available at many facilities.

In conclusion, when applied to a diverse set of patients with lung cancer at a single institution, classification based on FEV1 or DLCO ≤50% may not accurately predict "high risk" patients for short term complications following pulmonary resection. This has significant implications for patient management, as surgical resection remains the gold standard of care and allows for nodal upstaging which is not possible with non-operative management. Our findings advocate for caution when interpreting "high-risk" criteria in isolation and offer an opportunity to better characterize postoperative risk following pulmonary resection.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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