All grades of severity of postoperative adverse events are associated with prolonged length of stay after lung cancer resection

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ABSTRACT

Objective: To determine whether all grades of severity of postoperative adverse events are associated with prolonged length of stay in patients undergoing pulmonary cancer resection.

Methods: This was a retrospective cohort study of all patients who underwent pulmonary resection with curative intent for malignancy at The Ottawa Hospital, Division of Thoracic Surgery (January 2008 to July 2015). Postoperative adverse events were collected prospectively with the Thoracic Morbidity & Mortality System, based on the Clavien-Dindo severity classification. Patient demographics, comorbidities, preoperative investigations, cardiopulmonary assessment, pathologic staging, operative characteristics, and length of stay were retrospectively reviewed. Prolonged hospital stay was defined as >75th percentile for each procedure performed (wedge resection 6 days, segmentectomy 6 days, lobectomy 7 days, extended lobectomy 8 days, pneumonectomy 10 days). Univariable and multivariable logistic regression analyses were conducted to identify factors associated with prolonged hospital stay.

Results: Of 1041 patients, 579 (55.6%) were female, 610 (58.1%) were >65 years old, 232 (22.3%) experienced prolonged hospital stay, and 416 (40.0%) patients had ≥ 1 postoperative adverse event. Multivariable analyses identified significant ($P < .05$) factors associated with prolonged hospital stay to be (odds ratio; 95% confidence interval): lower diffusion capacity of the lung for carbon monoxide (0.99; 0.98-0.99), surgical approach: open thoracotomy (1.8; 1.3-2.5), and presence of any postoperative adverse event: Grade I (5.8; 3.3-10.2), Grade II (6.0; 4.0-8.9), Grade III (11.4; 7.0-18.7), and Grade IV (19.40; 7.1-55.18).

Conclusions: Lower diffusion capacity of the lung for carbon monoxide, open thoracotomy approach, and the development of any postoperative adverse event, including minor events that required no additional therapy, were factors associated with prolonged hospital stay. (J Thorac Cardiovasc Surg 2018;155:798-807)

Association between Thoracic Morbidity & Mortality adverse event grade and odds ratio for prolonged length of stay.

Central Message

All adverse events, including minor ones, are associated with prolonged hospital stay after lung cancer resection.

Perspective

Along with lower diffusion capacity of the lung for carbon monoxide and open thoracotomy, multivariable analyses of 1041 cases at a single institution found that the occurrence of any postoperative adverse event, including minor events that require no treatment (Grade I) or pharmacological therapy only (Grade II), significantly increased the odds of having prolonged length of stay in patients undergoing pulmonary resection for lung cancer.

See Editorial Commentary page 808.

Pulmonary resection for lung cancer carries significant risks of postoperative adverse events (AEs) and prolonged length of stay (PLOS). Patients with cancer who have undergone

lobectomy and have a PLOS were found to have greater rates of postoperative AEs and mortality and lower 5-year survival rates.^{1,2} In addition, PLOS leads to greater costs

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Abbreviations and Acronyms

AE	= adverse event
CI	= confidence interval
COPD	= chronic obstructive pulmonary disease
DLCO	= diffusion capacity of the lung for carbon monoxide
ERAS	= enhanced recovery after surgery
%FEV ₁	= forced expiratory volume for 1 second expressed as a percentage of the forced vital capacity
IQR	= interquartile range
LOS	= length of stay
OR	= odds ratio
PFT	= pulmonary function test
PLOS	= prolonged length of stay
TM&M	= Thoracic Morbidity & Mortality
VATS	= video-assisted thoracoscopic surgery

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for hospital per patient.³ Given the important impact of PLOS on hospital costs, determining predisposing factors associated with PLOS can be used to improve quality of care for patients undergoing pulmonary resection. Several previous studies have identified risk factors for PLOS to be older age, male sex, comorbid illnesses, cardiopulmonary status, and postoperative complications.¹⁻⁶ However, most studies do not include minor AEs in their analyses or thoracic surgery-specific AEs. The impact of minor AEs on thoracic surgery length of stay (LOS) remains unknown.

The Thoracic Morbidity & Mortality (TM&M) classification system has been used to report and monitor the incidence of thoracic surgery-specific AEs classified by grades according to the degree of treatment required to manage the AEs.⁷ The TM&M system is reliable and reproducible,⁸ has been implemented by several groups internationally,^{9,10} and provides a simple and objective method to classify severity of AEs.¹¹⁻¹³

The objective of this study was to identify perioperative factors associated with increased odds of PLOS after pulmonary resection with curative intent. We used the TM&M classification system, including all grades of AEs independently, to determine their individual effect on PLOS.

PATIENTS AND METHODS

Study Design, Setting, and Population

This was a retrospective cohort study. All consecutive patients who underwent pulmonary resection with curative intent for malignant disease at

TABLE 1. Patient demographics, medical history, preoperative evaluation, staging, procedure performed, and approach

	Expected LOS, n = 809	PLOS, n = 232	P value
Patient characteristics			
Sex			
M	343 (42.4%)	119 (51.3%)	.016
F	466 (57.6%)	113 (48.7%)	
Age	809 (77.7%)	232 (22.3%)	.089
Medical history			
Comorbidities			
Diabetes	137 (16.9%)	39 (16.8%)	.965
Coronary artery disease	123 (15.2%)	48 (20.6%)	.047
Peripheral vascular disease	49 (5.9%)	17 (7.3%)	.484
Cerebrovascular history	33 (4.1%)	10 (4.3%)	.876
Hypercholesterolemia	161 (19.9%)	49 (21.1%)	.683
Hypertension	373 (46.1%)	105 (45.3%)	.819
Pulmonary hypertension	0 (0%)	2 (0.9%)	.008
Congestive heart failure	0 (0%)	2 (0.9%)	.008
Renal failure	12 (1.5%)	1 (0.4%)	.203
COPD	173 (21.4%)	65 (28.0%)	.034
Lung function tests			
%FEV ₁	809 (77.7%)	232 (22.3%)	<.001
DLCO	809 (77.7%)	232 (22.3%)	<.001
Pathologic staging	n = 803	n = 230	.885
Stage 0	4 (0.6%)	1 (0.4%)	
Stage I	539 (67.1%)	148 (64.3%)	
Stage II	170 (21.2%)	49 (21.3%)	
Stage III	87 (10.8%)	30 (13.0%)	
Stage IV	5 (0.6%)	2 (0.9%)	
Procedure performed			.880
Wedge	132 (16.3%)	35 (15.1%)	
Segmentectomy	34 (4.2%)	10 (4.3%)	
Lobectomy	586 (72.4%)	166 (71.6%)	
Extended lobectomy	18 (2.2%)	7 (3.0%)	
Pneumonectomy	39 (4.8%)	14 (6.0%)	
Approach			
VATS vs thoracotomy			<.001
VATS	488 (60.3%)	109 (47.0%)	
Thoracotomy	320 (39.7%)	123 (53.0%)	
Nonconverted vs converted			.022
Nonconverted	771 (95.3%)	212 (91.4%)	
Converted	38 (4.7%)	20 (8.6%)	
Resection margin	n = 798	n = 228	.175
R0	761 (95.4%)	215 (94.3%)	
R1	36 (4.5%)	11 (4.8%)	
R2	1 (0.1%)	2 (0.9%)	
Adverse events	n = 809	n = 232	
No	570 (70.5%)	55 (23.7%)	<.001
Yes	239 (29.5%)	177 (76.3%)	
Grade I vs none	n = 619	n = 80	
No adverse event	570 (92.1%)	55 (68.8%)	<.001
Grade I only	49 (7.9%)	25 (31.2%)	
Minor vs major	n = 239	n = 177	
Minor (Grade I + II)	184 (77.0%)	107 (60.5%)	<.001
Major (Grade III + IV)	55 (23.0%)	70 (39.5%)	

(Continued)

TABLE 1. Continued

	Expected LOS, n = 809	PLOS, n = 232	P value
TM&M grades	n = 809	n = 232	
No adverse event	570 (70.5%)	55 (23.7%)	<.001
Grade I	49 (6.1%)	25 (10.8%)	
Grade II	135 (16.7%)	82 (35.3%)	
Grade III	49 (6.1%)	54 (23.3%)	
Grade IV	6 (0.7%)	16 (6.9%)	

Mann-Whitney *U* test used for all non-normal distributed continuous variables. Values in bold are statistically significant at $P < .05$. *LOS*, Length of stay; *PLOS*, prolonged length of stay; *M*, male; *F*, female; *COPD*, chronic obstructive pulmonary disease; %*FEV*₁, forced expiratory volume for 1 second expressed as a % of the forced vital capacity; *DLCO*, diffusion capacity of the lung for carbon monoxide; *VATS*, video-assisted thoracoscopic surgery; *TM&M*, Thoracic Morbidity & Mortality.

The Ottawa Hospital between January 2008 and July 2015 were considered for inclusion. Pediatric patients younger than the age of 18 years, patients who underwent pulmonary resection for nonmalignant disease, and patients who suffered in-hospital mortality or were listed as having a Grade V AE (ie, mortality) were excluded. This study was approved by The Ottawa Hospital Research Ethics Board.

Data Source and Data Collection

Morbidity and mortality data were prospectively collected daily by senior thoracic surgical residents using an electronic TM&M form. Lists of procedures and the associated AEs were compiled weekly and further reaffirmed by staff surgeons and residents. AEs were presented and discussed monthly at divisional morbidity and mortality conferences, which further ensured that all the collected data were as accurate and transparent as possible.¹⁴

Additional data on patient demographics, comorbidities, preoperative investigations and cardiopulmonary assessment, pathologic staging, and LOS were retrieved from The Ottawa Hospital's electronic medical record system and retrospectively added to a TM&M-derived database of patient information—the Thoracic Surgery Quality monitoring, Information management, and Clinical documentation system. The Thoracic Surgery Quality monitoring, Information management, and Clinical documentation system contains information on the type of surgery performed, surgical approach, and TM&M-classified AEs.¹¹

Patient demographics included patients' sex and age at the time of the surgery. Comorbidities were collected for diabetes, coronary artery disease, hypercholesterolemia, congestive heart failure, pulmonary hypertension, hypertension, peripheral vascular disease, renal failure, cerebrovascular history, and chronic obstructive pulmonary disease (COPD). Preoperative investigations included imaging studies, investigative procedures, and pulmonary function tests (PFTs). Forced expiratory volume for 1 second expressed as a percentage of the forced vital capacity (%*FEV*₁) and diffusion capacity of the lung for carbon monoxide (DLCO) were values recorded from the PFT. %*FEV*₁ and DLCO were used because they have been shown to be predictive of morbidity and mortality after pulmonary resection.¹⁵ Pathologic staging and surgical margins were obtained from pathology reports on the resected tumor specimens. LOS data were calculated from patient record dates.

Defining Procedure-Specific PLOS

The primary outcome of this study was LOS, defined as the number of calendar days from the operation to hospital discharge. PLOS was defined as postoperative hospital stay greater than the 75th percentile of the specific procedure—wedge resection 6 days, segmentectomy 6 days, lobectomy 7 days, extended lobectomy 8 days, pneumonectomy 10 days—that the

TABLE 2. Summary statistics for continuous variables and test of normality

Variable	Mean ± SD/median (IQR)
All (n = 1041)	
Age	66.47 ± 9.27
Lung function tests	
% <i>FEV</i> ₁	79.26 ± 18.54
DLCO	71.67 ± 16.02
Expected LOS (n = 809)	
Age	66.20 ± 9.17
Lung function tests	
% <i>FEV</i> ₁	80.49 ± 18.23
DLCO	72.73 ± 16.09
PLOS (n = 232)	
Age	67.42 ± 9.57
Lung function tests	
% <i>FEV</i> ₁	74.0 (23)
DLCO	67.5 (19)

SD, Standard deviation; *IQR*, interquartile range; %*FEV*₁, forced expiratory volume for 1 second expressed as a % of the forced vital capacity; *DLCO*, diffusion capacity of the lung for carbon monoxide; *LOS*, length of stay; *PLOS*, prolonged length of stay.

patient underwent.¹⁶ We defined extended lobectomy to be pulmonary resection greater than single-lobe resection and less than pneumonectomy (ie, lobectomy + wedge). Because the postoperative recovery pathways employed can vary for patients between surgical centers and depending on the patient's extent of lung resection, it is more accurate to categorize PLOS as the top 75th percentile of the patients categorized by procedure in the center, as other have done.¹⁷ In addition, for the duration of this study, our postoperative pathways were defined by procedure, regardless of surgical approach.

Classification of Postoperative AEs

Postoperative AEs were reported using the TM&M classification system. Based on the Clavien-Dindo classification system, the TM&M defines all thoracic surgery AEs into the following grades: Grade I AE, requiring no pharmacologic intervention (eg, transient atrial fibrillation); Grade II AE, requiring pharmacologic intervention only (eg, atrial fibrillation requiring beta-blocker); Grade III AE, requiring further intervention without (IIIA) (eg, atrial fibrillation requiring cardioversion or device) or with general anesthesia (IIIB) (eg, atrial fibrillation requiring operative intervention under general anesthesia); Grade IV, AE requiring single-organ (IVA) or multiorgan life support (IVB); and Grade V, AE causing death.⁷ The TM&M defines Grade I prolonged alveolar air leak as air leak lasting >5 days or air leak present on discharge from hospital with planned follow-up >POD 6 with no intervention required.

Statistical Analysis

Comparison of baseline demographics, comorbidities, and operative variables between the expected LOS and PLOS cohorts were analyzed with the independent sample *t* test or Mann-Whitney *U* test for continuous variables and the χ^2 test or Fisher exact test for categorical variables, respectively. Continuous data were assessed for normality via the Shapiro-Wilk test and reported as either mean (standard deviation) or median (interquartile range [IQR]) depending on the result of the normality test. Univariable and multivariable logistic regression models were built to evaluate the association of patient- and treatment-related parameters on odds ratios (ORs) with 95% confidence intervals (95% CIs) for

TABLE 3. Consecutive pulmonary resection for cancer cases categorized base on procedure, mortality status, LOS status, and AE grade

Total pulmonary resection	Procedure		LOS status		AE grade	
n = 1062	Wedge resection	167 (15.7%)	Expected LOS (LOS ≤6 d)	132 (79.0%)	No AE	106 (80.0%)
					Grade I	5 (3.8%)
					Grade II	12 (9.1%)
					Grade III	7 (5.3%)
					Grade IV	2 (1.5%)
			PLOS (LOS > 6 d)	35 (21.0%)	No AE	13 (37.0%)
					Grade I	3 (8.6%)
					Grade II	8 (22.9%)
					Grade III	9 (25.0%)
					Grade IV	2 (5.7%)
	Segmentectomy	44 (4.1%)	Expected LOS (LOS ≤6 d)	34 (77.3%)	No AE	31 (91.2%)
					Grade I	1 (2.9%)
					Grade II	1 (2.9%)
					Grade III	1 (2.9%)
					Grade IV	0 (0%)
			PLOS (LOS >6 d)	10 (22.7%)	No AE	5 (50.0%)
					Grade I	2 (20.0%)
					Grade II	3 (30.0%)
					Grade III	0 (0%)
					Grade IV	0 (0%)
	Lobectomy	766 (72.1%)	Expected LOS (LOS ≤7 d)	586 (76.5%)	No AE	402 (68.6%)
					Grade I	37 (6.2%)
					Grade II	105 (17.9%)
					Grade III	39 (6.7%)
					Grade IV	3 (0.5%)
			PLOS (LOS >7 d)	166 (21.7%)	No AE	34 (20.5%)
					Grade I	20 (12.0%)
					Grade II	64 (38.6%)
					Grade III	38 (22.9%)
					Grade IV	10 (6.0%)
	Extended lobectomy	26 (2.4%)	Mortality	14 (1.8%)		
			Expected LOS (LOS ≤8 d)	18 (69.2%)	No AE	7 (38.9%)
					Grade I	3 (16.7%)
					Grade II	7 (38.9%)
					Grade III	1 (5.6%)
					Grade IV	0 (0%)
			PLOS (LOS >8 d)	7 (26.9%)	No AE	2 (28.6%)

(Continued)

TABLE 3. Continued

Total pulmonary resection	Procedure	LOS status		AE grade	
Pneumonectomy	59 (5.5%)	Mortality	1 (3.8%)	Grade I	0 (0%)
				Grade II	2 (28.6%)
				Grade III	3 (42.9%)
				Grade IV	0 (0%)
		Expected LOS (LOS ≤10 d)	39 (66.1%)	No AE	24 (61.5%)
				Grade I	3 (7.7%)
				Grade II	10 (25.6%)
				Grade III	1 (2.6%)
				Grade IV	1 (2.6%)
				No AE	1 (7.1%)
				Grade I	0 (0%)
				Grade II	5 (35.7%)
				Grade III	4 (28.6%)
				Grade IV	4 (28.6%)
		Mortality	6 (10.2%)		

LOS, Length of stay; AE, adverse event; PLOS, prolonged length of stay.

PLOS. The multivariable logistic regression model was created with stepwise variable selection using SPSS binary logistic function with the forward: conditional method. Missing %FEV₁ (n = 97) and DLCO (n = 167) data were added using multivariable imputation. A new data set was created using the Mersenne Twister random number generator to impute missing data values. The constraints were set to the observed minimum and maximum from the collected data—%FEV₁ (21, 169) and DLCO (28, 146). The model was assessed using the Omnibus test. *P* value < .05 was considered statistically significant. Data analyses were conducted with IBM SPSS Statistics Version 18 software (SPSS, Chicago, Ill).

RESULTS

Patient Demographics and Clinical Characteristics

A total of 1062 cases of consecutive pulmonary resection for cancer were identified, and of those, 21 (2.0%) were excluded due to in-hospital patient mortality, leaving 1041 cases meeting inclusion criteria for this study. A total of 97 (9.3%) missing %FEV₁ and 167 (16.0%) missing DLCO data were generated by the use of multiple imputation and were included in baseline analyses. A summary of patient characteristics in expected LOS versus PLOS group can be found in Table 1. In the cohort of patients with PLOS, there was a significant increased proportion of male patients (51.3% vs 42.4%), and comorbid illnesses, including history of coronary artery disease (20.6% vs 15.2%), pulmonary hypertension (0.9% vs 0%), congestive heart failure (0.9% vs 0%), COPD (28.0% vs 21.4%), and lower %FEV₁ and DLCO.

A test of normality was performed for all continuous variables, and the result is available in Table 2.

Volume of Procedures Performed

The majority of the pulmonary resections were lobectomies (n = 766; 72.1%). A breakdown of proportion of procedures performed is available in Table 3. Video-assisted thoracoscopic surgery (VATS) was favored for less-extensive lung resection (595/963 cases; 61.8%), whereas open operations were performed for the majority of extended lobectomies (19/25 cases; 76.0%) and almost all pneumonectomies (52/53 cases; 98.1%). In the PLOS group, there were significantly less VATS (47.0% vs 60.3%, *P* < .01), more thoracotomy (44.4% vs 35.0%, *P* < .01), and more intraoperative conversion from VATS to thoracotomy (8.6% vs 4.7%, *P* < .01) performed (Table 1).

Procedure-Specific Postoperative PLOS

LOS ranged from 1 to 66 days; the median LOS in patients without PLOS was 4 (IQR 2) days and the median PLOS was 11 (IQR 7) days. Based on the definition of PLOS as greater than or equal to the 75th percentile LOS for each procedure type, 232 patients (22.3%) were categorized as having PLOS. The PLOS group was not made up of the exactly top 25th percentile because LOS was reported as days in whole numbers.

TABLE 4. Ten most common AE in expected LOS and PLOS groups

	Total AE	Ten most common AE	n (% of total AE)
Expected LOS (n = 809)	n = 229	Atrial arrhythmia	67 (29.3)
		Prolonged air leak	44 (19.2)
		Subcutaneous emphysema	21 (9.2)
		Confusion	11 (4.8)
		Atelectasis	10 (4.4)
		Pneumothorax	9 (3.9)
		Pneumonia	7 (3.1)
		Urinary retention	7 (3.1)
		Urinary tract infection	7 (3.1)
		Pleural effusion	6 (2.6)
PLOS (n = 232)	n = 177	Prolonged air leak	54 (30.5)
		Atrial arrhythmia	28 (15.8)
		Pneumonia	11 (6.2)
		Subcutaneous emphysema	9 (5.1)
		Confusion	7 (4.0)
		Myocardial infarction	7 (4.0)
		Atelectasis	5 (2.8)
		Pleural effusion	5 (2.8)
		Empyema	4 (2.3)
		Bronchopleural fistula	3 (1.7)

AE, Adverse event; LOS, length of stay; PLOS, prolonged length of stay.

Postoperative TM&M Classification

A total of 416 (40.0%) patients had 1 or more postoperative AEs. The PLOS group had a significantly greater proportion of AEs (76.2% vs 29.5%, $P < .01$), Grade I AE (10.8% vs 6.1%, $P < .01$), Grade II AE (35.3% vs 16.7%, $P < .01$), Grade III AE (23.3% vs 6.1%, $P < .01$), and Grade IV AE (6.9% vs 0.7%, $P < .01$) (Table 1). The most common AEs in expected LOS and PLOS groups are listed in Table 4.

Univariable Analyses to Identify Factors Associated With PLOS After Pulmonary Resection

Univariable logistic regression models were used to analyze perioperative factors associated with PLOS. Significant factors included (in OR; 95% CI) male sex (1.4; 1.1-1.9), having a history of coronary artery disease (1.5; 1.0-2.1) or COPD (1.4; 1.0-2.0), lesser value of % FEV₁ (0.99; 0.98-0.99) or DLCO (0.98; 0.98-0.98), more invasive surgical approach—either open thoracotomy (1.7; 1.3-2.3) or those requiring intraoperative conversion (1.9; 1.1-3.4) and any stage of AE—stage I (5.3; 3.1-9.2), stage II (6.3; 4.3-9.3), stage III (11.4; 7.1-18.4), or stage IV (27.6; 10.4-73.5) (Table 5).

TABLE 5. Results of univariable logistic regression to identify perioperative factors associated with PLOS

Variable	Odds ratios (95% CI)	P value
Demographics		
Sex		
Female	1.00	
Male	1.43 (1.07-1.92)	.016
Age	1.01 (1.00-1.03)	.079
Comorbidities		
Diabetes	0.99 (0.67-1.46)	.965
Coronary artery disease	1.46 (1.00-2.11)	.048
Hypercholesterolemia	1.08 (0.75-1.54)	.683
Hypertension	0.97 (0.72-1.30)	.819
Pulmonary hypertension	Insufficient incidence	.999
Peripheral vascular disease	1.23 (0.69-2.17)	.484
Congestive heart failure	Insufficient incidence	.999
Renal failure	0.29 (0.04-2.22)	.232
Cerebrovascular history	1.06 (0.51-2.18)	.876
COPD	1.43 (1.03-2.00)	.035
Lung function tests		
%FEV1	0.985 (0.981- 0.988)	<.001
DLCO	0.979 (0.976-0.983)	<.001
Operative characteristics		
Procedure performed		
Lobectomy	1.00	
Wedge	0.94 (0.62-1.41)	.752
Segmentectomy	1.04 (0.50-2.15)	.919
Extended lobectomy	1.37 (0.57-3.34)	.485
Pneumonectomy	1.27 (0.67-2.39)	.464
Approach		
Conversion vs nonconversion		
Nonconversion	1.00	
Conversion	1.91 (1.09-3.36)	.024
VATS vs open		
VATS	1.00	
Open	1.72 (1.29-2.31)	<.001
Resection margin		
R0	1.00	
R1	1.18 (0.60-2.31)	.633
R2	Insufficient incidence	.999
Pathologic staging		
Stage 0	1.00	
Stage I	0.82 (0.09-7.98)	.867
Stage II	0.87 (0.09-8.50)	.901
Stage III	1.03 (0.10-10.33)	.977
Stage IV	1.20 (0.07-19.63)	.898
Adverse events		
None	1.00	
Grade I	5.29 (3.03-9.22)	<.001
Grade II	6.30 (4.26-9.30)	<.001
Grade III	11.42 (7.10-18.38)	<.001
Grade IV	27.64 (10.39-73.51)	<.001

Values in bold are statistically significant at $P < .05$. CI, Confidence interval; COPD, chronic obstructive pulmonary disease; %FEV₁, forced expiratory volume for 1 second expressed as a % of the forced vital capacity; DLCO, diffusion capacity of the lung for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

FIGURE 1. Association between Thoracic Morbidity & Mortality adverse event grade and odds ratio for prolonged length of stay.

Multivariable Analyses to Identify Factors Associated With PLOS After Pulmonary Resection

Multivariable logistic regression using stepwise variable selection was performed to identify perioperative factors associated with PLOS. Significant factors included (in OR; 95% CI): lower DLCO (0.99; 0.98-0.99); surgical approach: thoracotomy (1.8; 1.3-2.5) versus VATS; and presence of any postoperative AE: Grade I (5.8; 3.3-10.2), Grade II (6.0; 4.0-8.9); Grade III (11.4; 7.0-18.7), and Grade IV (19.4; 7.1-55.2) (Figure 1). The final model had an Omnibus test of model coefficient P value = .03 (Table 6). Sensitivity analysis was performed excluding patients with missing %FEV₁ and DLCO data, and the resulting estimates of effect did not change significantly (Table 7).

DISCUSSION

Our study identified several factors associated with increased odds of PLOS (defined as staying longer than

TABLE 6. Results of multivariable logistic regression model for odds ratio of having PLOS

Variable	Odds ratios (95% CI)	<i>P</i> value
Lung function tests		
DLCO	0.985 (0.975-0.995)	.005
Approach (VATS vs open)		
VATS	1.00	
Open	1.77 (1.26-2.48)	.001
Adverse events		
None	1.00	
Grade I	5.80 (3.28-10.24)	<.001
Grade II	5.97 (4.02-8.88)	<.001
Grade III	11.44 (6.99-18.71)	<.001
Grade IV	19.40 (7.07-55.18)	<.001
Omnibus tests of model coefficients <i>P</i> value		.032
Hosmer and Lemeshow test <i>P</i> value		.271

Congestive heart failure not included in final model due to low number of patients recorded to have the condition at the time of surgery ($n = 2$). Values in bold are statistically significant at $P < .05$. CI, Confidence interval; DLCO, diffusion capacity of the lung for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

TABLE 7. Sensitivity analysis of multivariable logistic regression performed excluding patients with missing PFT data

Variable	Odds ratios (95% CI)	<i>P</i> value
Lung function tests		
DLCO	0.982 (0.970-0.994)	.004
Approach (VATS vs open)		
VATS	1.00	
Open	2.04 (1.39-2.99)	.001
Adverse events		
None	1.00	
Grade I	8.64 (4.68-15.94)	<.001
Grade II	6.17 (3.88-9.81)	<.001
Grade III	10.31 (5.88-18.10)	<.001
Grade IV	23.62 (7.66-72.89)	<.001
Omnibus tests of model coefficients <i>P</i> value		.029
Hosmer and Lemeshow test <i>P</i> value		.048

Congestive heart failure not included in final model due to low number of patients recorded to have the condition at the time of surgery ($n = 2$). Values in bold are statistically significant at $P < .05$. CI, Confidence interval; DLCO, diffusion capacity of the lung for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

the 75th percentile for their surgical procedure) after pulmonary resection for lung cancer. These factors included lower DLCO, thoracotomy, and presence of any postoperative AE as defined by the TM&M classification system. Patient's sex, age, comorbidities, %FEV₁, resection margin, and pathologic stage were not found to have significant association with PLOS after pulmonary resection with curative intent.

A recent study of 490 patients from Institutional Society of Thoracic Surgery data also found DLCO as a factor for PLOS.¹⁸ In addition, previous studies also demonstrated that decreasing DLCO is associated with increased rate of pulmonary complications.¹⁹ Specifically, DLCO has a greater correlation with postoperative mortality than %FEV₁.²⁰ This correlation in morbidity and mortality also could be indirectly reflected in PLOS. In regard to surgical approach, previous studies have shown that VATS resulted in a significantly lower LOS than the thoracotomy approach in patients undergoing lobectomy.²¹⁻²³ Both approaches result in a similar rate of 5-year survival,²⁴ but VATS appears to offer the benefit of less postoperative AE, reduced pain, earlier mobility, and discharge.

Before the TM&M classification system was used to identify perioperative factors for increased odds of PLOS in pulmonary resection patients, the effect of minor AEs on patients has been controversial. Several previous studies have delineated predictive factors for PLOS using large databases of patients, such as the Society of Thoracic Surgeons' General Thoracic Surgery Database,¹ the American College of Surgeons' National Surgical Quality Improvement Program,³ or stand-alone institutional databases.⁴⁻⁶ Most studies did not classify or report the severity of AEs or simply omitted minor AEs

VIDEO 1. Explanation of the Thoracic Morbidity & Mortality system and the important effect of minor adverse events on patient length of stay. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)32135-9/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)32135-9/fulltext).

altogether.^{3,4} However, our study showed that even Grade I AEs significantly increased the odds of PLOS (95% CI) by 5.8 times (3.3-10.2). The most common Grade I AEs were air leaks (62% of Grade I AEs). We found the presence of any AE has a greater OR than surgical approach used, such as thoracotomy (1.8; 1.3-2.5). AEs experienced by patients postoperatively can prolong LOS due to required treatments and interventions, delayed recovery, and increased time needed for observation. Other previous studies have also found an association between AEs and PLOS in patients who underwent lung resection.^{1,3,5} Thus, reducing the rate of postoperative AEs may represent an important modifiable means to decrease LOS. In addition, decreased LOS may also lead to decreased costs. A recent study on factors associated with postoperative costs after anatomic lung resection without major AEs showed that even minor AEs (TM&M Grade I and II) are significantly associated with increased cost.¹⁰

We used different 75th percentile cut-off marks for PLOS for different pulmonary resections because increasing extent of pulmonary resection is a known risk factor for PLOS. Other studies have found that pneumonectomy was associated with a greater risk of major AEs and PLOS.¹⁷ The postoperative care pathway in the division has been largely determined by the type of procedure and extent of pulmonary resection.

A similar study using data from 4979 lobectomies for lung cancer found a greater number of significant predictors of PLOS. The predictors were age, Eastern Cooperative Oncology Group score, male sex, American Society of

Anesthesiologists score, insulin-dependent diabetes, renal dysfunction, induction therapy, %FEV₁, and smoking status.¹ However, the study used a more extended cut-off for PLOS at 14 days or longer, which included only 7% of the patients. They also did not account for the variable extent of pulmonary resections. Despite this, the National Surgical Quality Improvement Program study found similar results, where older age, thoracotomy, and various complications to be significant for increasing the risk of PLOS.³ Other additional studies looking at the effect of postoperative AEs on LOS also found that the presence of AEs was associated with PLOS.^{1,4,5} However, no previous studies used an AEs severity grading system similar to TM&M. The reporting of AEs in the literature is lacking. For example, a single-center study of 7457 noncardiac surgical patients, albeit not specific to thoracic surgery, found that AEs occurred only in 6.9%,⁴ which was much lower than the 40.0% AE rate found in our study. Minor AEs may not be included in the other studies.

Our study has several limitations. It is a single-center study, and practice patterns governing LOS vary greatly between institutions and health care systems. For example, flexibility for deviation from clinical pathways may vary from institution to institution. As a more specific example, response to prolonged air leaks can be managed without prolonged admission if there is a lower or rigid threshold to send patients home with chest tubes. Second, we were unable to collect data on variables that other studies have found to be significant, such as preoperative smoking status, induction status, and performance status. Some of the retrospective data obtained from patient charts have incomplete data set (eg, PFTs). However, the missing PFT data (12%) were substituted using multiple imputation methods and data analysis was checked with sensitivity analysis. In addition, despite the fact that TM&M data were collected in a prospective manner, this study remained a retrospective review and was subjected to difficulty controlling bias and establishing temporal cause/effect relationships. Finally, it should be noted that enhanced recovery after surgery (ERAS) pathways have been demonstrated to significantly reduce LOS in a thoracic surgery population.²⁵ During the inclusion period of our study, the ERAS pathway was not in use. However, our division is currently in the process of implementing ERAS pathway after all thoracic surgery.

Our study has several strengths. First, it included for the first time the use of an AE severity classification system to compare the relative impact of AEs on LOS. The TM&M data collection was performed daily and went through a weekly review by residents and staff.¹⁴ We perceive the 75th percentile procedure-specific definition for PLOS was clinically relevant, reflecting the majority of patients, and helped reflect expected procedure-specific differences in LOS. Lastly, the patients were risk adjusted for their

sex, age, comorbidities, and preoperative lung function scores.

Implications and Future Directions

Preventing AEs, including minor ones, may be helpful in reducing LOS. Factors indicating patients with high odds for PLOS could be provided targeted customized pre- and postoperative recovery pathways to minimize their stay and improve their hospital experience. Particularly, our finding of minor AEs being a factor for increased odds of PLOS further validates the importance of tracking all AEs, including minor ones. In addition, due to the interplaying relationship found between AEs, LOS, and costs, minimizing AEs and LOS may also lower the cost of care.^{10,26,27} Similar to TM&M, the adaptation of the original Clavien-Dindo AE classification system has been used in various other surgical subspecialties such as orthopedics, urology, and general surgery.²⁸⁻³⁰ It would be interesting to explore whether the same relationship between AE classification and PLOS exists in other surgical subspecialties.

CONCLUSIONS

Our study identified perioperative factors significantly associated with increased odds of PLOS, namely lower DLCO, thoracotomy, and the presence of any postoperative AE as reported by TM&M, including minor AEs such as Grade I, which require no new intervention, and Grade II, which require a new medication therapy only. This information may be useful for discharge planning where patients without identified factors may have fast tracking recovery pathway and patients with identified factors for PLOS can have additional support arranged to expedite return to function (Video 1).

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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