Outcomes for Elective Open and Thoracoscopic Surgical Lung Biopsies in the United States and Temporal Trends

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Abstract

Objective: To elucidate the outcomes of surgical lung biopsies (SLBs) performed for indications other than interstitial lung disease (ILD) and stratify outcomes according to procedural approach (open vs thoracoscopic).

Patients and Methods: Using the Nationwide Inpatient Sample database (January 1, 2008, through December 31, 2014), we identified elective hospitalizations with *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for open (33.28) and thoracoscopic (33.20) SLB. We stratified cases by the presence/absence of ILD. Our primary outcome was in-hospital mortality.

Results: There were 47,469 hospitalizations for elective SLB (26,540 [55.9%] thoracoscopic) during the study period; 23,930 patients (50.5%) were women, 17,019 (35.9%) had ILD, and the mean ± SD age was 62.6±13.0 years. Over the study period, thoracoscopic increasingly replaced open SLB, and in-hospital mortality declined (3.5% [308 of 8678] in 2008 vs 2.5% [130 of 5215] in 2014; *P*<.001). Mortality following thoracoscopic SLB was 2.1% (550 of 26,519; 1.9% [214 of 11,513] in ILD and 2.2% [336 of 15,006] in non-ILD), and mean ± SD length of stay was 5.1±6.9 days. Open SLBs had worse outcomes; mortality was 3.7% (782 of 20,914; 3.9% [214 of 5487] in ILD and 3.7% [568 of 15,427] in non-ILD), and mean ± SD length of stay was 8.2±12 days. On multivariable analysis, male sex, advanced age, ILD, and higher comorbidity index correlated with higher mortality. Conversely, lower mortality was observed among individuals with obesity (odds ratio, 0.73; 95% CI, 0.60-0.88) and those who had their thoracoscopic SLBs performed at high-volume centers (top quartile) (odds ratio, 0.73; 95% CI, 0.57-0.94).

Conclusion: Surgical lung biopsy is more often performed for non-ILD indications. Interstitial lung disease was an independent predictor of poor outcomes, but the unadjusted outcomes were worse in the non-ILD cohort due to differences in patient characteristics. Thoracoscopic SLBs performed at high-volume centers had superior outcomes.

Recent advancements in chest imaging modalities have improved clinicians' ability to establish pulmonary diagnoses noninvasively. Nonetheless, clinicians continue to encounter pulmonary disorders wherein a diagnosis cannot be established without obtaining lung tissue specimens. Of lung biopsy techniques, surgical lung biopsy (SLB) is the criterion standard and is often favored over other approaches not only for its superior diagnostic yield[1-4] but also for its therapeutic role, eg, in the management of high-risk pulmonary nodules.[5,6]

The approach to SLB can be open (ie, thoracotomy) or thoracoscopic (video-assisted thoracoscopic surgery [VATS]). The choice of SLB method is generally determined by the individual surgeon's expertise, experiences, and preference in the absence of special situations such as the presence of extensive pleural adhesions for which thoracotomy may be preferred. Most earlier studies assessing SLB outcomes did not distinguish these 2 separate approaches but instead reported the results of these procedures together. This issue is partly related to the recent introduction of an *International Classification of Diseases, Ninth*

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Revision, Clinical Modification (ICD-9-CM) code that corresponds to thoracoscopic lung biopsy (2006 in England; late 2007 in the United States).[7,8]

Coutinho et al[9] reported that diffuse parenchymal abnormalities on computed tomography, suggestive of interstitial lung disease (ILD), accounted for only 38.1% of SLBs, while nodular lesions comprised the majority of non-ILD cases. Despite this data, previous studies have focused on the outcomes of SLBs performed for ILD,[7,8,10] while the outcomes of SLBs performed for non-ILD indications remain understudied.

Two recent advancements have added to the preexisting complexity surrounding decisions to pursue SLB[11]: (1) nintedanib, an antifibrotic agent, may slow lung function decline in all progressive fibrosing ILDs[12-15] and (2) stereotactic ablative radiotherapy has proven effective in long-term control of localized, clinically diagnosed lung cancer (ie, diagnosed on clinicoradiologic grounds without histopathologic confirmation).[16-20]

The availability of such management options that do not require a precise histopathologic diagnosis emphasizes the necessity of weighing the benefits of SLB against its risks. Based on individualized risk-benefit analyses, well-informed patients will make decisions that align with their values. To inform such clinician-patient conversations, we conducted this population-based study with the following aims: (1) delineate the outcomes of SLBs, stratified by approach (open vs thoracoscopic) and indication (ILD vs non-ILD), (2) specify the patient-related factors that can predict in-hospital mortality, (3) ascertain whether SLB exhibits a surgical volume−outcome relationship, and (4) describe the temporal trends in SLB utilization.

PATIENTS AND METHODS

We used the Nationwide Inpatient Sample (NIS), which is the largest publicly available database that contains information on hospital discharges in the United States.[21] Each record within the NIS represents a hospital discharge and contains information on the diagnoses and procedures related to that hospitalization.

We searched all hospital discharges between January 1, 2008, and December 31, 2014, for ICD-9-CM procedure codes 33.28 (open biopsy of lung) and 33.20 (thoracoscopic lung biopsy); records including both codes simultaneously were excluded. We sought to characterize the outcomes of elective SLBs; hence, we only included hospitalizations designated as "elective." Based on the presence/absence of an ICD-9-CM code for ILD (Supplemental Table 1, available online at http://www.mcpiqojournal.org), we divided records into 2 groups: "ILD" and "non-ILD," respectively (Supplemental Figure, available online at http://www. mcpiqojournal.org).

In accordance with the methodology recommended by the developers of the NIS database, we used weighted data to produce national estimates.[22,23] Changes in trend analyses spanning the transition period 2011-2012 in the NIS data set were accounted for. We recorded patient characteristics (age, sex, ethnicity, presence of ILD, obesity, and comorbidities), procedure characteristics (open vs thoracoscopic), and outcomes.

For assessment of comorbidities, we used the Charlson comorbidity index (CCI),[24] which is the most commonly used comorbidity index in administrative databases,[25] includes 17 comorbidities, and is calculated on the basis of ICD-9-CM codes.[26] A more detailed description of the CCI scoring can be found in Supplemental Table 2 (available online at http://www.mcpiqojournal.org).[27,28]

Before 2012, the NIS had linked unique hospital identifiers to discharge records. Thus, we used data from 2008 to 2011 to estimate the number of SLBs performed at each center. To assess volume-outcome relationship, we divided centers according to their SLB procedural volume into high volume (top quartile) and low volume (remainder 3 quartiles). Because open and thoracoscopic SLBs require different surgical skills, we performed additional analyses examining the procedural volume−outcome relationship for each approach separately.

Our primary outcome was in-hospital mortality. Secondary outcomes were length of hospital stay, cost of hospitalization, rate of in-hospital pneumothorax, and chest tube insertion.

We performed a sensitivity analysis assessing hospitalization outcomes after excluding

TABLE 1. Characteristics of Patients Who Underwent Elective Surgical Lung Biopsy, Stratified by Procedural Approach (Open vs VATS)[a,b,c,d]

Variable	VATS (n=26,540 [55.9%])	Open (n=20,929 [44.1%])	Total (N=47,469)	P value
Sex				<.001
Male	12,665 (47.8)	10,838 (51.8)	23,503 (49.5)	
Female	13,854 (52.2)	10,076 (48.2)	23,930 (50.5)	
Age (y), mean ± SD	62.0±13.4	63.3±12.5	62.6±13.0	<.001
Race				<.001
White	18,513 (80.6)	14,727 (81.8)	33,240 (81.1)	
Black	1993 (8.7)	1526 (8.5)	3519 (8.6)	
Hispanic	1280 (5.6)	1034 (5.7)	2314 (5.6)	
Asian/Pacific Islander	521 (2.3)	273 (1.5)	794 (1.9)	
Native American	106 (0.5)	111 (0.6)	217 (0.5)	
Other	543 (2.4)	337 (1.9)	880 (2.1)	
Indication				<.001
ILD	11,517 (43.4)	5502 (26.3)	17,019 (35.9)	
Non-ILD	15,023 (56.6)	15,427 (73.7)	30,450 (64.1)	
Charlson comorbidity index				<.001
0-1	13,201 (49.7)	6541 (31.3)	19,742 (41.6)	
2-3	8012 (30.2)	7802 (37.3)	15,814 (33.3)	
≥4	5327 (20.1)	6586 (35.5)	11,913 (25.1)	
Obesity	3112 (11.7)	2617 (12.5)	5729 (12.1)	0.01

[a]ILD, interstitial lung disease; VATS, video-assisted thoracic surgery.
[b]Data are presented as No. (percentage) of patients unless indicated otherwise.
[c]Numbers may not always add up to the total due to weighted and missing data.
[d]Percentages may not always add up to 100% due to rounding.

records that, besides the SLB codes mentioned previously, had *ICD-9-CM* codes describing more extensive procedures: segmentectomy (32.30, 32.39), lobectomy (32.41, 32.49), and pneumonectomy (32.50, 32.59).

For statistical analyses, we used 2-sample *t* tests to compare means of continuous variables and Pearson χ^2 tests to measure associations between categorical variables. Potential predictors of SLB outcomes were selected based on the findings reported by previous studies (age, sex, CCI),[8] in addition to other variables of interest, such as obesity, procedural indication (ILD vs non-ILD) and approach (thoracoscopic vs open), and the center's SLB procedural volume (high volume vs low volume). Univariate analysis was performed to evaluate the association of these variables with our primary outcome (ie, in-hospital mortality). Multivariable logistic regression analysis that included the previously mentioned variables was then applied to predict the odds of in-hospital mortality. Statistical analysis was performed using SPSS Statistics for Windows, version 26 (IBM Corp). Statistical significance was defined as *P*<.05.

RESULTS

Over the period 2008-2014, 47,469 hospitalizations for elective SLB were included; 26,540 of the SLBs (55.9%) were thoracoscopic (Table 1). Of patients who underwent these procedures, 23,930 (50.5%) were women, 33,240 (81.1%) were white, and 27,727 (58.4%) had a CCI score of 2 or higher. The mean ± SD age was 62.6±13.0 years.

Over the study period, the total number of SLBs declined by 40% (8678 in 2008 vs 5215 in 2014) (Figure). Although the number of SLBs performed for both indications (ILD and non-ILD) declined, the decline was steeper in the non-ILD cohort, as evidenced by the increasing proportion of ILD-related SLBs over time (32.6% [2829 of 8678] in 2008 vs 41.2% [2150 of 5215] in 2014). Furthermore, the thoracoscopic technique increasingly replaced open SLB (VATS comprised 49.0% of SLBs [4253 of 8678] in 2008 vs 64.0% [3335 of 5215] in 2014), and the overall in-hospital mortality declined (3.5% [308 of 8678] in 2008 vs 2.5% [130 of 5215] in 2014).

Males and individuals with obesity and higher CCI scores (≥ 2) were more likely to undergo open rather than thoracoscopic SLB (odds ratio [OR], 1.18, 1.08, and 2.18, respectively; $P<.01$) (Table 1). Conversely, patients with ILD were twice as likely to undergo VATS than those without ILD (OR, 2.15; 95% CI, 2.07 to 2.24).

Evaluating the principal diagnosis in the ILD cohort revealed that the nonspecific *ICD-9-CM* code 515 ("postinflammatory pulmonary fibrosis") was the principal diagnosis in 66.9% of hospitalizations (11,390 of 17,019). In the non-ILD cohort, *ICD-9-CM* codes indicative of primary or secondary lung malignancy were the principal diagnosis in 56.4% (17,174 of 30,450) (Supplemental Table 3, available online at https://mcpiqojournal.org).

Thoracoscopic SLB (VATS)
Among the 26,540 hospitalizations for VATS, 52.2% of patients (13,854) were women and 80.6% (18,513) were white, with a mean age of 62.0±13.4 years (Table 1). The CCI score was 2 or higher in 50.3% of cases (13,339) . Most VATS procedures were performed for non-ILD indications (15,006 [56.6%]).

VATS outcomes varied according to the procedural indication (Table 2). Compared to patients with ILD, those who underwent VATS for non-ILD indications had generally worse outcomes, with higher in-hospital mortality (2.2% [336 of 15,006] vs 1.9% [214 of 11,513]; $P=.03$), hospital length of stay (5.8 vs 4.2 days; $P<.001$), cost of hospitalization (66 vs 49 thousand US dollars; $P<.001$), and rate of chest tube insertion (14.7% [2207 of 15,006] vs 12.3% [1417 of 11,513]; $P<.001$). Supplemental Table 4 (available online at https://mcpiqojournal.org) illustrates in-hospital mortality rate following VATS, stratified by age group, sex, and indication.

Open SLB
Of the 20,929 hospitalizations for open SLB, 48.2% of patients (10,076) were women, 81.8% (14,727) were white, and 72.8% (14,390) had a CCI score of 2 or higher; the mean ± SD age was 63.3±12.5 years (Table 1). Most open SLBs (73.7% [15,427]) were performed for non-ILD indications.

Compared to patients with ILD, those in the non-ILD cohort had a longer hospital stay (8.5 vs 7.5 days; $P<.001$) and higher cost of hospitalization (88 vs 79 thousand US dollars; $P<.001$) (Table 3). In-hospital mortality and rate of pneumothorax and chest tube insertion were not significantly different ($P=.49$, $P=.68$ and $P=.11$, respectively).
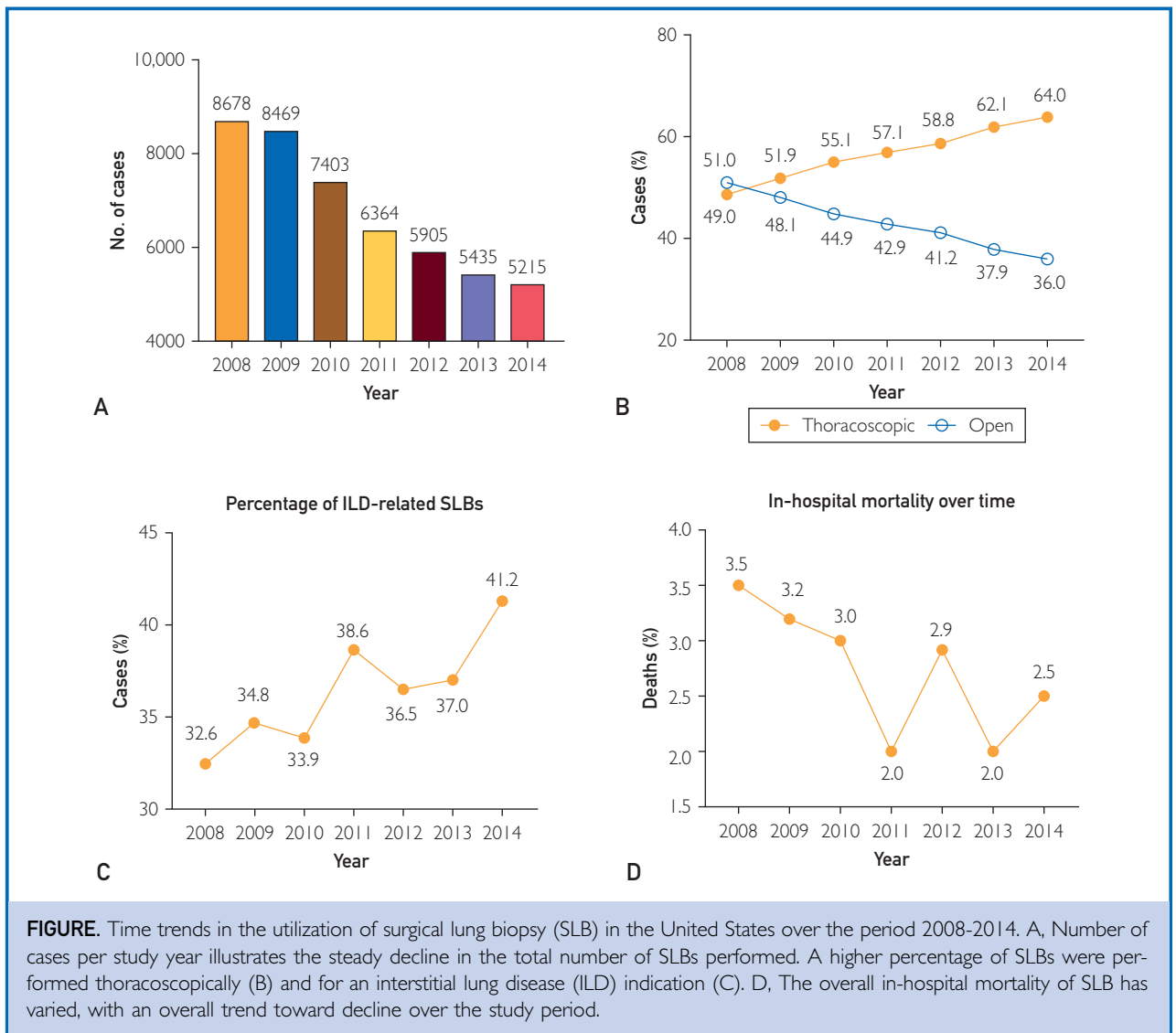
Surgical Volume—Outcome Analysis
In this analysis, we included 20,500 SLBs performed from 2008 to 2011. Of those, 12,890 (62.9%) were performed at high-volume centers and 11,588 (56.4%) were thoracoscopic (Supplemental Table 5, available online at https://mcpiqojournal.org). Among these patients, 10,449 (51.0%) were women, 6944 (33.9%) had ILD, and 12,173 (59.4%) had a CCI score of 2 or higher; the mean age was 62.8 years.

Compared to individuals who underwent SLB at low-volume centers, those who had their procedures performed at high-volume centers had slightly fewer comorbidities (CCI ≥ 2 in 7508 of 12,890 [58.1%] vs 4665 of 7610 [61.2%]) and were less likely to undergo VATS (7196 of 12,890 [55.7%] vs 4392 of 7610 [57.6%]) (Supplemental Table 5). Patients with procedures performed at high-volume centers were more likely to have obesity (1489 of 12,890 [11.6%] vs 723 of 7610 [9.5%]) and ILD (4504 of 12,890 [34.9%] vs 2440 of 7610 [32.1%]; $P<.05$). Age and sex were not significantly different in the 2 groups ($P=.15$ and $P=.84$, respectively).

Hospitalization outcomes were better at high-volume than low-volume centers, with lower in-hospital mortality (318 of 12,890 [2.5%] vs 228 of 7610 [3.0%]; relative risk reduction, 16.7%), lower rates of chest tube insertion (1603 of 12,890 [12.4%] vs 1272 of 7610 [16.7%]; $P<.001$), and lower cost (63 vs 71 thousand US dollars; $P<.001$) (Supplemental Table 5).

Risk Factors of In-Hospital Mortality
As previously known,[7,8] advanced age, male sex, and higher CCI score were associated with in-hospital mortality on univariate analysis ($P<.05$) (Supplemental Table 6, available online at https://mcpiqojournal.org). When these and other variables of interest (obesity,

FIGURE. Time trends in the utilization of surgical lung biopsy (SLB) in the United States over the period 2008-2014. A, Number of cases per study year illustrates the steady decline in the total number of SLBs performed. A higher percentage of SLBs were performed thoracoscopically (B) and for an interstitial lung disease (ILD) indication (C). D, The overall in-hospital mortality of SLB has varied, with an overall trend toward decline over the study period.

procedural indication and approach, and the center's procedural volume) were incorporated into a multivariable logistic regression model, we found male sex, age older than 60 years, and CCI score of 2 or higher to be associated with increased odds of death (Table 4). Among these variables, CCI score of 4 or higher and age 80 years or older were the strongest risk factors for in-hospital mortality, with adjusted ORs of 2.38 and 2.41, respectively (both $P<.001$).

We found ILD to be associated with higher odds of in-hospital mortality (OR, 1.49; 95% CI, 1.31-1.71) (Table 4).

Accordingly, it is surprising that the unadjusted outcomes were worse in the non-ILD cohort (Table 2). To explain this discrepancy, we compared the characteristics of patients with and without ILD and found significant differences in patient selection. Patients with ILD were younger, more likely to be female, more likely to undergo thoracoscopic than open SLB, and had fewer comorbidities (all $P<.001$) (Supplemental Table 7, available online at http://www. mcpiqojournal.org).

Conversely, thoracoscopic approach and obesity were independently associated with

TABLE 2. Outcomes of Thoracoscopic SLBs, Stratified by Sex and Procedural Indication (N=26,5198)[a,b,c,d]				
Variable	ILD (n=11,513) (5166 M; 6347 F)	Non-ILD (N=15,006) (7499 M; 7507 F)	Total (N=26,519)	P value
In-hospital mortality	214 (1.9)	336 (2.2)	550 (2.1)	.03
Male	87 (1.7)	248 (3.3)		
Female	127 (2.0)	88 (1.2)		
Length of stay (d)	4.2±5.3	5.8±7.9	5.1±6.9	<.001
Male	4.2±5.7	6.0±7.9		
Female	4.1±4.9	5.6±7.9		
Chest tube	1417 (12.3)	2207 (14.7)	3624 (13.7)	<.001
Male	686 (13.3)	1123 (15.0)		
Female	731 (11.5)	1084 (14.4)		
Pneumothorax	1254 (10.9)	1664 (11.1)	2918 (11.0)	.63
Male	593 (11.5)	812 (10.8)		
Female	661 (10.4)	852 (11.3)		
Cost of hospitalization[e]	49±54	66±101	59±84	<.001
Male	48±53	71±126		
Female	50±54	61±654		

[a]F, female; ILD, interstitial lung disease; M, male; SLB, surgical lung biopsy.
[b]Data are presented as No. (percentage) of patients or mean ± SD.
[c]Numbers may not always add up to the total due to weighted and missing data.
[d]Percentages may not always add up to 100% due to rounding.
[e]Cost of hospitalization is presented as thousand US dollars (rounded to the nearest integer).

40% and 27% lower risk of death, respectively (P<.001 and P=.001, respectively) (Table 4). We performed similar analyses for VATS and open procedures separately and found similar results (Table 4).

Based on a multivariable analysis that included potential confounders (age, sex, CCI score, ILD, and procedural approach), we found that a center's procedural volume is independently associated with mortality. The SLBs performed at high-volume centers had 19% lower odds of mortality than those performed at low-volume centers (OR, 0.81; 95% CI, 0.68-0.97). Additional multivariable analyses exploring potential procedural volume—outcome relationship were performed for both SLB approaches separately and revealed that such a relationship exists for thoracoscopic (OR, 0.73; 95% CI, 0.57-0.94) but not open (OR, 0.94; 95% CI, 0.74-1.20) SLBs.

Sensitivity Analysis
We excluded 9147 of the 47,469 records (19.3%) with more extensive surgical procedures. Of those, lobectomy was performed in 7771 (16.4%), segmentectomy in 1045

(2.2%), and pneumonectomy in 399 (0.8%). In 68 of the 9147 hospitalizations (0.7%), more than one procedural ICD-9-CM code was present. The demographic characteristics of the remaining patients were similar to those of the original cohort (Supplemental Table 8, available online at http://www.mcpiqojournal.org). As expected, most patients with more extensive resections were in the non-ILD cohort. Aside from the surprising increase in mortality (3.7% to 4.4%) among those who underwent less extensive open SLBs, other outcomes appeared similar to those of the original cohort (Supplemental Tables 9 and 10).

DISCUSSION
This is the first population-based study to describe the outcomes of the 2 SLB approaches (open and thoracoscopic) for both ILD and non-ILD indications along with temporal trends. Our data show elective thoracoscopic SLB to be associated with lower in-hospital mortality than elective open SLB and that thoracoscopic SLBs may have better outcomes when undertaken at high-volume centers. Risk factors for in-hospital mortality

TABLE 3. Outcome of Open SLBs, Stratified by Sex and Procedural Indication[a,b]

Variable	ILD (n=5502) (2705 M; 2782 F)	Non-ILD (n=15,427) (8133 M; 7294 F)	Total (N=20,929)	P value
In-hospital mortality	214 (3.9)	568 (3.7)	782 (3.7)	.49
Male	141 (5.2)	359 (4.4)		
Female	73 (2.6)	209 (2.9)		
Length of stay (d)	7.5±12.9	8.5±11.7	8.2±12.0	<.001
Male	8.6±16.1	9.0±14.2		
Female	6.5±8.6	7.8±8.1		
Chest tube	689 (12.6)	2063 (13.4)	2752 (13.1)	.11
Male	356 (13.2)	1141 (14.0)		
Female	333 (12.0)	922 (12.6)		
Pneumothorax	654 (11.9)	1869 (12.1)	2523 (12.1)	.68
Male	323 (11.9)	939 (11.5)		
Female	331 (11.9)	930 (12.8)		
Cost of hospitalization[c]	79±111	88±149	85±140	<.01
Male	87±124	93±168		
Female	72±96	81±124		

F, female; ILD, interstitial lung disease; M, male; SLB, surgical lung biopsy.
[a]Numbers may not always add up to the total due to weighted and missing data.
[b]Percentages may not always add up to 100% due to rounding.
[c]Cost of hospitalization is presented as thousand US dollars (rounded to the nearest integer).

included male sex, advanced age, ILD (vs non-ILD indications), and high comorbidity index.

Concordant with a prior single-center study,[9] we found that SLBs are performed more often for non-ILD indications (64% in our study and 71% in the study by Coutinho et al[9]), most commonly, pulmonary nodules. This notion is supported by the finding that 56% of our non-ILD cohort had a provisional diagnosis of primary or secondary lung cancer.[29,30]

Over the period 2008-2014, several trends in the utilization of SLB have emerged. The number of SLBs performed annually for both ILD and non-ILD indications steadily declined. Also, the thoracoscopic gradually replaced the open approach throughout the study period, comprising nearly two-thirds of SLBs performed in 2014.

In our study, the in-hospital mortality was 2.1% (1.9% in ILD and 2.2% in non-ILD) following thoracoscopic SLB and 3.7% (3.9% in ILD and 3.7% in non-ILD) following open SLB. Considering this difference in in-hospital mortality between the 2 procedural approaches, the increasing utilization of thoracoscopic SLBs relative to open procedures likely contributed to the lower in-hospital mortality following SLBs performed during the later years of our study (2008-2010 vs 2011-2014).

The effect that the procedural approach, in and of itself, has on postoperative mortality following elective SLBs requires further clarification as previous studies have yielded inconsistent results.[7,8,10,31,32] Hutchinson et al[8] studied 32,022 SLBs performed in the United States between 2001 and 2011; all were performed for ILD. Based on the 11,146 elective hospitalizations that had "biopsy" ICD-9-CM codes and the procedural approach specified, univariate analysis showed that open SLB was associated with nearly triple the odds of death compared to thoracoscopic procedures. Such marked difference in mortality is surprising because other studies,[7,10,31,32] 2 of which were population-based,[7,10] did not reach a similar conclusion.

Our results suggest that biases in patient selection may confound the relationship between the procedural approach and mortality; males and those with higher CCI scores were more likely to undergo open rather than thoracoscopic SLBs. Therefore, in the absence of adjustment, it remains unclear whether the mortality difference noted by Hutchinson et al[8] is related to the procedural approach, per se, or if biases in patient selection are also at play.

TABLE 4. Results of Multivariate Logistic Regression Analysis Measuring Associations Between Variables and In-Hospital Mortality for the Entire Cohort (All SLBs), in Addition to Stratification by Procedural Approach (VATS and Open)[a,b]

Variable	VATS		Open SLB		Entire cohort	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Male sex	1.57 (1.32-1.87)	<.001	1.62 (1.39-1.88)	<.001	1.6 (1.43-1.79)	<.001
Age group (y)						
<50	1.00	…	1.00	…	1.00	…
50-59	1.45 (1.03-2.04)	.04	0.85 (0.62-1.18)	.32	1.1 (0.87-1.39)	.43
60-69	1.11 (0.80-1.56)	.53	1.49 (1.13-1.98)	.005	1.34 (1.08-1.66)	.008
70-79	1.71 (1.23-2.37)	.001	1.94 (1.46-2.56)	<.001	1.84 (1.49-2.27)	<.001
≥80	2.81 (1.95-4.05)	<.001	2.07 (1.46-2.92)	<.001	2.41 (1.88-3.09)	<.001
Charlson comorbidity index						
0-1	1.00	…	1.00	…	1.00	…
2-3	2.28 (1.81-1.89)	<.001	1.58 (1.29-1.94)	<.001	1.91 (1.64-2.22)	<.001
≥4	3.86 (3.00-4.96)	<.001	1.65 (1.33-2.05)	<.001	2.38 (2.02-2.81)	<.001
ILD	1.62 (1.32-1.98)	<.001	1.47 (1.23-1.75)	<.001	1.49 (1.31-1.71)	<.001
Obesity	0.72 (0.53-0.98)	.04	0.73 (0.56-0.93)	.01	0.73 (0.60-0.88)	.001
VATS	NA	…	NA	…	0.60 (0.54-0.67)	<.001

ILD, interstitial lung disease; NA, not applicable; OR, odds ratio; SLB, surgical lung biopsy; VATS, video-assisted thoracoscopic surgery.

[a]Numbers may not always add up to the total due to weighted and missing data.

[b]Percentages may not always add up to 100% due to rounding.

We found that open procedures were independently associated with higher odds of death than thoracoscopic, albeit with a lesser magnitude than reported by Hutchinson et al[8] (adjusted OR, 1.67 vs unadjusted OR, 2.72, respectively). Besides the statistical adjustments we performed, this difference between the 2 studies may be related to our inclusion of a larger number of SLBs that were not limited to ILD.

Certain patient-related factors correlated with SLB outcomes. Male sex, advanced age, and higher CCI score predicted higher mortality.[7,8,33] Interestingly, obesity was independently associated with lower mortality. Numerous studies have reported that obesity, which had been traditionally regarded as a risk factor for worse postoperative outcomes, is associated with lower mortality following many types of surgical procedures. This phenomenon has been termed *the obesity paradox* and is incompletely understood.[34]

Besides the surgical approach, 2 other procedure-related factors influenced outcomes: indication and the center's surgical volume. Ours is the first study to directly compare outcomes based on the procedural indication (ie, ILD vs non-ILD). The

unadjusted in-hospital mortality varied modestly between the 2 groups. Nevertheless, multivariable analysis revealed that ILD was independently associated with increased risk of mortality (62% for VATS; 47% for open SLBs).

An inverse relationship between hospital procedural volume and postoperative mortality (volume-outcome relationship) exists for multiple procedures.[35] Whether SLB exhibits such a surgical volume—outcome relationship has been unclear.[36] Fisher et al[10] conducted a population-based study to answer this question and reported that high-volume hospitals had superior outcomes following nonelective SLBs but failed to reach a similar conclusion for elective SLBs (OR, 0.94; 95% CI, 0.74-1.18). Our study found that elective SLBs performed at high-volume centers were associated with lower in-hospital mortality (17% relative risk reduction) and hospitalization costs. Interestingly, this volume-outcome relationship was observed in association with thoracoscopic but not open SLBs.

It is worth noting that *ICD-9-CM* codes describing more extensive procedures (eg, segmentectomy, lobectomy) were present in 19% of our cohort. Such codes were, expectedly,

primarily found in the non-ILD cohort. In the context of focal lung lesions (eg, high-risk pulmonary nodules), the extent of resection partly depends on the patient's baseline health status, the lesion's location, and intraoperative course and does not necessarily imply the procedure's intent (diagnostic vs therapeutic). For example, surgical sampling of a deeply situated nodule may only be feasible through a segmentectomy or lobectomy. Of essence, all records in our study had a "lung biopsy" code indicating a diagnostic intent in all cases.

To ascertain whether including patients who underwent more extensive resections substantially influenced our findings, we performed a sensitivity analysis excluding those patients. While most results remained unchanged, we observed a surprising increase in mortality among those who underwent less extensive open SLBs. This paradox suggests that a selection bias may have been introduced (eg, extensive surgeries could be completed in healthier individuals without intraoperative complications). Taken together, we believe that our decision to include all patients requiring an SLB (irrespective of the surgical extent) minimizes bias and therefore enhances the clinical applicability and generalizability of our findings.

Finally, our study had some limitations. First, we did not include SLBs performed later than 2014 given the shift to *International Classification of Diseases, Tenth Revision, Clinical Modification* codes in subsequent years, along with paucity of data; at the time of this analysis, the NIS database had data until 2017 only. However, we do not believe that our study period has substantially impacted our results for several reasons: (1) since 2014, no major changes have occurred in the management of high-risk pulmonary nodules and SLB remains the recommended approach,[5,6] (2) although enthusiasm has surrounded the role of transbronchial lung cryobiopsy as a potential alternative to SLB in the diagnosis of ILD, SLB remains the criterion standard diagnostic modality according to the most recent guidelines,[37,38] and (3) surgical techniques utilized in SLB have not witnessed major advances since the end of our study period.[39]

Because nonspecific *ICD-9-CM* codes were abundant, we could not discern the exact procedural indication. Rather, we classified patients into 2 categories that clinicians can readily distinguish (ILD and non-ILD). Finally, we could not always identify the final diagnoses. Nonetheless, our study aims to provide patients and clinicians with risk estimates using information known before the procedure, when the diagnosis is still unknown.

CONCLUSION

Through the period 2008-2014, the number of SLBs performed in the United States declined, and thoracoscopic gradually replaced open procedures. Thoracoscopic SLB was associated with 40% lower risk of in-hospital mortality and may be partly responsible for the down-trending SLB-related mortality over the same period. Male sex, advanced age, higher comorbidity index, and ILD were independently associated with poor outcomes, whereas obesity appeared protective. A relationship between higher hospital procedural volume and superior outcomes existed for thoracoscopic but not open SLBs.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

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