Factors and outcomes associated with successful minimally invasive pneumonectomy

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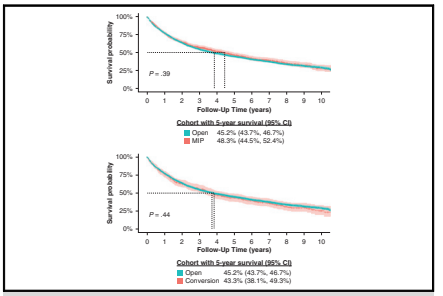
ABSTRACT

Objective: To test the hypothesis that patients undergoing minimally invasive pneumonectomy at high-volume minimally invasive lung surgery centers have improved survival compared with patients who undergo open pneumonectomy.

Methods: Patients from the National Cancer Database who underwent pneumonectomy for lung cancer between 2010 and 2020 were stratified into 3 groups according to surgical technique (open, minimally invasive, converted from minimally invasive to open). Institutions were categorized as low-, mid-, or high-volume minimally invasive lung surgery centers according to percentage of total anatomic lung resections performed by video-assisted or robotic-assisted thoracoscopic surgery. Outcomes were compared using Cox regression, Kaplan-Meier survival analysis, and propensity score matching.

Results: In total, 5750 patients from 850 facilities were included, with 4597 (79.9%) undergoing upfront open pneumonectomy. Among the 1153 attempted minimally invasive pneumonectomies, 364 (31.6%) required conversion to open pneumonectomy. Surgery at a non–high-volume center was associated with greater conversion risk (adjusted odds ratio, 4.16; $P < .001$), whereas neoadjuvant therapy was associated with lower risk (adjusted odds ratio, 0.60; $P = .015$). Similar 5-year overall survival was seen among the 3 groups (open 45.2%, minimally invasive 48.3%, converted 43.3%); however, conversion from minimally invasive to open pneumonectomy demonstrated a trend towards increased risk of death (hazard ratio, 1.16; $P = .058$).

Conclusions: Minimally invasive pneumonectomy for lung cancer had similar 5-year survival compared with open pneumonectomy. However, conversion from minimally invasive to open pneumonectomy showed a trend toward increased risk of death, and conversion rates were high irrespective of institutional minimally invasive lung surgery volume. Careful patient selection is necessary when considering minimally invasive pneumonectomy so that long-term outcomes are not compromised. (JTCVS Open 2025;24:423-37)



Survival of patients in the study cohort, stratified by surgical approach.

CENTRAL MESSAGE

Minimally invasive pneumonectomy has similar overall survival compared with upfront open pneumonectomy; however, conversion to open surgery may be associated with worse long-term outcomes.

PERSPECTIVE

Minimally invasive pneumonectomy had similar 5-year survival compared with open pneumonectomy; however, conversion to open surgery was common among all centers. A trend toward increased risk of death was seen in patients who required intraoperative conversion. Careful patient selection is necessary when considering minimally invasive pneumonectomy so that long-term outcomes are not compromised.

Operative techniques have improved over time, but pneumonectomy remains a high-risk procedure.[1-3] A broad range of 90-day and 5-year mortality rates have been reported in the literature, with factors such as patient age, disease stage, pulmonary function, resection laterality, and neoadjuvant therapy status correlating with short- and

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Abbreviations and Acronyms

CI = confidence interval
MIP = minimally invasive pneumonectomy
NCDB = National Cancer Database
OR = odds ratio
RATS = robotic-assisted thoracoscopic surgery
VATS = video-assisted thoracoscopic surgery

long-term outcomes.[3-7] Although it is critical to understand how patient-focused variables can impact outcomes, it is also important to consider institutional factors such as operative volume and surgeon expertise. Provider-centered variables include experience of the treating facility, surgical technique, and available medical technology. For example, it has been shown that hospital volume can impact patient outcomes in pulmonary resection.[8,9] The importance of surgeon volume has also been demonstrated with minimally invasive surgery techniques.[10]

As minimally invasive techniques have become more common, efforts have been made to characterize their impact on pneumonectomy outcomes. Hennon and colleagues[11] demonstrated the noninferiority of minimally invasive approaches for pneumonectomy relative to traditional open techniques. There have been more recent analyses, which have redemonstrated the safety of minimally invasive pneumonectomy (MIP) while providing insight into patient selection considerations.[12-15] However, there are limited data analyzing the association between institutional minimally invasive lung surgery volume and MIP outcomes despite the steady adoption of minimally invasive techniques for lung cancer surgery over the last 20 years. This study tests the hypothesis that patients who underwent MIP at high-volume centers had improved survival compared with patients who underwent open pneumonectomy.

METHODS

Data Source

The National Cancer Database (NCDB) is a large national database maintained by the American College of Surgeons and the American Cancer Society. The dataset captures approximately 70% of newly diagnosed cancer cases, with survival follow-up and more than 80 deidentified fields per patient.[16] The 2020 Participant User File, comprising more than 30 million records from North American Commission on Cancer–approved sites, was used for this analysis. The study was conducted in accordance with the 2013 amendment of the Declaration of Helsinki. This study was exempt from the Stanford University Institutional Review Board, as patients were deidentified in NCDB.

Patient Selection

The NCDB was queried for patients who underwent pneumonectomy for primary lung cancer between 2010 and 2020 (Figure 1). Patients with adenocarcinoma, squamous cell carcinoma, and large cell carcinoma histology were included. Patients recorded as having benign tumors and those with incomplete pathologic staging data were excluded. Patients with stage IV disease, N3 disease, and previous or subsequent malignancies were also excluded as the impact of other cancers and their treatments may confound survival analyses. In an effort to eliminate patients who likely were not originally planned to undergo pneumonectomy, patients with pT1N0M0 disease who did not receive neoadjuvant therapy were excluded. Patients who underwent sleeve resection were also excluded. Furthermore, patients in the NCDB who underwent pneumonectomy were presumed to be de novo pneumonectomy operations rather than completion pneumonectomy. Cases in which the surgical approach was not specified were excluded. Finally, to address missing data, we conducted a complete case analysis, excluding all patients with missing data in the key demographic and perioperative variables.

Cohort Classification

The study cohort was stratified into 3 groups according to surgical approach: open pneumonectomy, MIP, and conversion from MIP to open. MIP procedures were defined as pneumonectomies coded as either video-assisted or robotic-assisted thoracoscopic surgery (VATS and RATS, respectively) in the NCDB. Institutions were categorized as low-, mid-, or high-volume minimally invasive lung surgery centers according to the percentage of total anatomic lung resections performed via VATS or RATS. In this study, low-volume centers were defined as institutions performing fewer than 25% of total anatomic lung resections using minimally invasive approaches. Centers were considered mid-volume if 25% to 75% of total anatomic lung resections were performed with VATS or RATS. Centers that performed greater than 75% of anatomic lung resections minimally invasively were considered high-volume centers. Outcomes were compared according to surgical technique and minimally invasive lung surgery volume.

Statistical Analysis

The primary outcome was long-term survival, with surgical approach and center volume being the main exposures. No predictors or effect modifiers were identified a priori. Discrete variables between the 3 study groups were compared using the Pearson χ^2 test. Continuous variables were compared with the Kruskal-Wallis rank sum test. Multivariable logistic regression with backward selection was used to estimate independent predictors of conversion from MIP to open pneumonectomy. Variables assessed included race, Charlson-Deyo score, facility type, institutional minimally invasive lung surgery volume, household income, laterality, tumor histology, neoadjuvant status, tumor size, and clinical lymph node disease status. Postestimation tests were used to evaluate the model fit, check for collinearity, and exclude modes that did not improve the model.

To assess survival after pneumonectomy, multivariable Cox proportional hazards modeling and Kaplan-Meier curves were used. Variables assessed in the Cox model included age, sex, race, Charlson-Deyo score, facility type, facility minimally invasive lung surgery volume, insurance type, household income, county type, laterality, tumor histology, neoadjuvant status, adjuvant status, lymph node disease status, lymphovascular invasion, surgical margin status, and pneumonectomy approach. Kaplan-Meier analysis was used to compare 5-year overall survival and log-rank test was used to quantify the difference. Although survival is the primary outcome, loss to follow-up is accounted for in the Kaplan-Meier analyses censoring. Subgroup analyses were performed to assess overall survival according to institutional minimally invasive lung surgery volume.

We conducted a 1:1 propensity score matching analysis using the nearest neighbor method to reduce bias between the intent-to-treat surgical approach groups: open and MIP. We generated propensity score–matched groups using logistic regression on the basis of potential confounding baseline characteristics including age, sex, Charlson-Deyo score, facility type, insurance, income, county type, neoadjuvant therapy, adjuvant therapy,

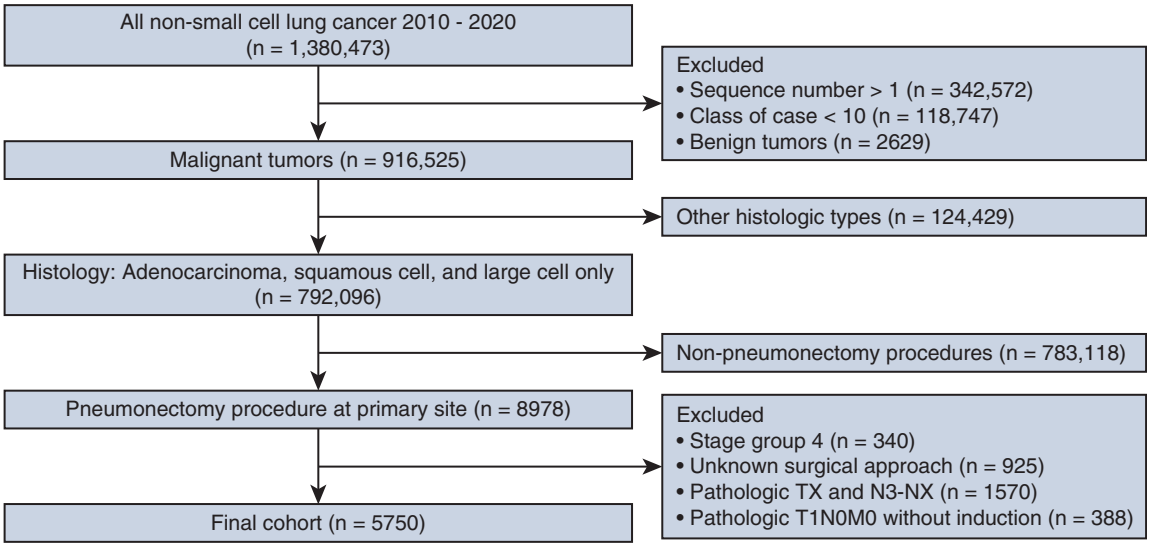


FIGURE 1. CONSORT diagram. This CONSORT diagram lays out our exclusion criteria for our cohort. *CONSORT*, Consolidated Standards of Reporting Trials.

clinical T and N stage, and tumor size. The propensity score–matched group distributions were compared using χ^2 test for categorical variables and Wilcoxon rank sum tests for continuous variables. All analyses were performed in R, version 4.3.2 (R Foundation for Statistical Computing).

RESULTS

Baseline Characteristics

This study cohort consisted of 5750 pneumonectomy cases that met inclusion criteria (Figure 1), with 4597 (79.9%) patients who underwent upfront open pneumonectomy. Among the 1153 attempted MIP cases, 789 (13.7%) were successfully performed by VATS or RATS, whereas 364 (6.3%) required conversion from attempted MIP to open pneumonectomy. Throughout the study period, the proportion of attempted and successful MIP increased while the overall incidence of pneumonectomy decreased (Figure 2). Patients in the open pneumonectomy cohort were slightly younger compared with MIP and patients who were converted (median age: open 62 vs MIP 64 vs converted 64 years, $P < .001$). The open pneumonectomy cohort had a lower proportion of patients undergoing treatment at an academic or research facility (open 40% vs MIP

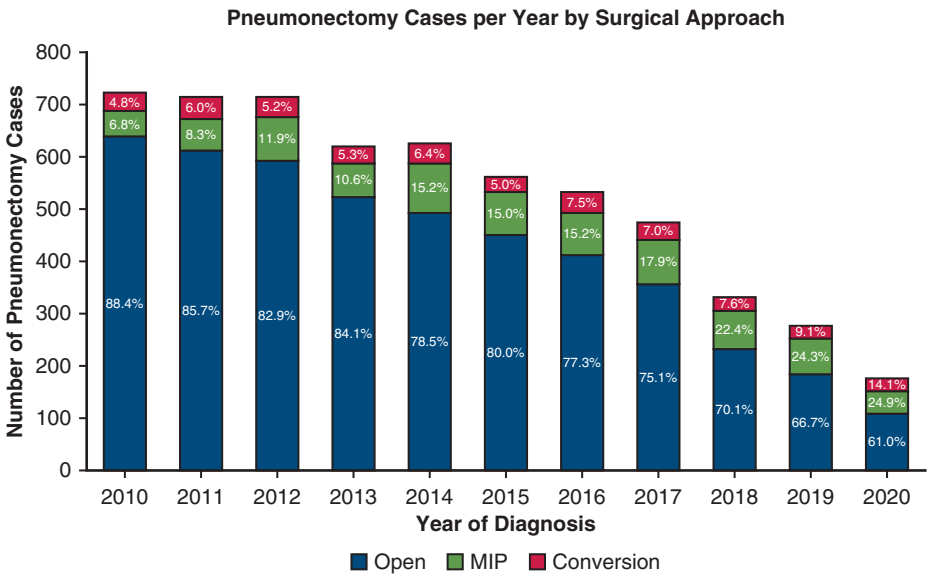


FIGURE 2. Pneumonectomies per year by surgical approach This bar graph shows the number of pneumonectomies performed per year in the study period, stratified by surgical technique (open, minimally invasive, converted from minimally invasive to open). *MIP*, Minimally invasive pneumonectomy.

49% vs converted 47%, $P < .001$) and a greater proportion of patients residing in rural counties (open 2.5% vs MIP 0.9% vs converted 0.6%, $P < .001$). Patients who underwent open pneumonectomy also had the lowest incidence of household income level above the median (open 55% vs MIP 60% vs converted 63%, $P = .002$). No differences were noted among the 3 study groups with respect to sex, race, Charlson-Deyo comorbidity score, insurance type, education level, or distance traveled to treating facility (Table 1).

Surgeries were performed at 850 different facilities, with most being academic/research programs or comprehensive community cancer programs. Regarding institutional minimally invasive lung surgery volume, 284 centers (33.4%) were categorized as low-volume, 283 (33.3%) as mid-volume, and 283 (33.3%) as high-volume minimally invasive lung surgery centers. Most patients who received open pneumonectomy underwent surgery at mid-volume centers (47%), followed by high-volume (32%) and low-volume centers (21%). In contrast, most patients who underwent MIP had surgery at high-volume centers (84%). Notably, among the 48 attempted MIPs at low-volume minimally invasive lung surgery centers, all 48 patients required conversion to open pneumonectomy (Table 1). Conversion rates for mid- and high-volume centers were 52.1% and 21.3%, respectively.

TABLE 1. Demographic characteristics

Characteristic	Overall N = 5750	Open n = 4597	MIS n = 789	MIS to open conversion n = 364	*P* value*
Age, y†	63 (56, 69)	62 (56, 69)	64 (57, 70)	64 (57, 71)	<.001
Female, n (%)	2019 (35%)	1581 (34%)	302 (38%)	136 (37%)	.070
Race, n (%)					.5
White	5016 (87%)	4026 (88%)	682 (86%)	308 (85%)	
Black	479 (8.3%)	377 (8.2%)	68 (8.6%)	34 (9.3%)	
Asian	174 (3.0%)	134 (2.9%)	24 (3.0%)	16 (4.4%)	
Other	81 (1.4%)	60 (1.3%)	15 (1.9%)	6 (1.6%)	
Charlson-Deyo score, n (%)					.6
0	3148 (55%)	2513 (55%)	445 (56%)	190 (52%)	
1	1763 (31%)	1404 (31%)	238 (30%)	121 (33%)	
2+	839 (15%)	680 (15%)	106 (13%)	53 (15%)	
Facility type, n (%)					<.001
Academic/research program	2357 (41%)	1801 (40%)	386 (49%)	170 (47%)	
Community cancer program	217 (3.8%)	192 (4.2%)	16 (2.0%)	9 (2.5%)	
Comprehensive community cancer program	2057 (36%)	1702 (37%)	225 (29%)	130 (36%)	
Integrated network cancer program	1054 (19%)	846 (19%)	156 (20%)	52 (14%)	
Center MIS volume, n (%)					<.001
Low MIS volume	991 (17%)	943 (21%)	0 (0%)	48 (13%)	
Mid MIS volume	2442 (42%)	2179 (47%)	126 (16%)	137 (38%)	
High MIS volume	2317 (40%)	1475 (32%)	663 (84%)	179 (49%)	
Insurance type, n (%)					.063
Private	2357 (41%)	1906 (42%)	314 (40%)	137 (38%)	
Medicaid	544 (9.6%)	440 (9.7%)	65 (8.3%)	39 (11%)	
Medicare	2487 (44%)	1959 (43%)	353 (45%)	175 (48%)	
Other government	98 (1.7%)	73 (1.6%)	21 (2.7%)	4 (1.1%)	
Uninsured	209 (3.7%)	174 (3.8%)	28 (3.6%)	7 (1.9%)	
Above median education, n (%)	2360 (47%)	1874 (47%)	325 (47%)	161 (52%)	.2
Above median household income, n (%)	2778 (56%)	2177 (55%)	407 (60%)	194 (63%)	.002
County type, n (%)					.001
Metropolitan	4434 (80%)	3505 (80%)	644 (85%)	285 (82%)	
Rural	117 (2.1%)	108 (2.5%)	7 (0.9%)	2 (0.6%)	
Urban	964 (17%)	791 (18%)	111 (15%)	62 (18%)	
Distance to facility, miles†	15 (6, 36)	16 (6, 37)	15 (7, 34)	14 (6, 32)	.6

This table shows baseline demographic data for the 3 primary study groups. There were significant differences in age, facility type, facility MIS volume, patient income level, and patient location between the 3 groups. There were no differences in the other demographic fields. *MIS*, Minimally invasive. *Kruskal-Wallis rank sum test; Pearson χ^2 test. †Described as median (interquartile range)

TABLE 2. Tumor characteristics and perioperative outcomes

Characteristic	Overall N = 5750	Open n = 4597	MIS n = 789	MIS to open conversion n = 364	*P* value*
Right-sided pneumonectomy, n (%)	2110 (37%)	1687 (37%)	296 (38%)	127 (35%)	.7
Tumor histology, n (%)					.046
Adenocarcinoma	2127 (37%)	1662 (36%)	321 (41%)	144 (40%)	
Large cell neuroendocrine	151 (2.6%)	120 (2.6%)	25 (3.2%)	6 (1.6%)	
Squamous	3472 (60%)	2815 (61%)	443 (56%)	214 (59%)	
Neoadjuvant therapy, n (%)					.013
Systemic therapy	396 (6.9%)	303 (6.6%)	70 (8.9%)	23 (6.3%)	
Systemic therapy plus radiation	508 (8.8%)	409 (8.9%)	79 (10%)	20 (5.5%)	
No neoadjuvant therapy	4846 (84%)	3885 (85%)	640 (81%)	321 (88%)	
Number of lymph nodes examined†	16 (10, 23)	16 (10, 23)	16 (10, 25)	16 (11, 24)	.034
Clinical lymph node disease (cN+), n (%)	2886 (50%)	2315 (50%)	392 (50%)	179 (49%)	.9
Clinical T stage					.1
cT0	5 (<0.1%)	5 (0.1%)	0 (0%)	0 (0%)	
cT1	661 (12%)	505 (11%)	97 (13%)	59 (17%)	
cT2	2019 (36%)	1644 (37%)	258 (34%)	117 (33%)	
cT3	1694 (30%)	1327 (30%)	252 (33%)	115 (32%)	
cT4	730 (13%)	594 (13%)	98 (13%)	38 (11%)	
cTIS	3 (<0.1%)	3 (<0.1%)	0 (0%)	0 (0%)	
cTX	452 (8.1%)	360 (8.1%)	64 (8.3%)	28 (7.8%)	
Clinical N stage					.9
cN0	2864 (51%)	2282 (51%)	397 (52%)	185 (52%)	
cN1	1422 (25%)	1136 (26%)	188 (24%)	98 (27%)	
cN2	928 (17%)	743 (17%)	129 (17%)	56 (16%)	
cN3	51 (0.9%)	40 (0.9%)	9 (1.2%)	2 (0.6%)	
cNX	315 (5.6%)	252 (5.7%)	46 (6.0%)	17 (4.7%)	
Pathologic T stage					.2
0/Pathologic complete response	181 (3.1%)	134 (2.9%)	35 (4.4%)	12 (3.3%)	
1	503 (8.7%)	404 (8.8%)	73 (9.3%)	26 (7.1%)	
2	1786 (31%)	1450 (32%)	220 (28%)	116 (32%)	
3	2243 (39%)	1793 (39%)	307 (39%)	143 (39%)	
4	1037 (18%)	816 (18%)	154 (20%)	67 (18%)	
Pathologic N stage					.068
0	1987 (35%)	1558 (34%)	309 (39%)	120 (33%)	
1	2690 (47%)	2171 (47%)	345 (44%)	174 (48%)	
2	1073 (19%)	868 (19%)	135 (17%)	70 (19%)	
Lymphovascular invasion, n (%)	2176 (43%)	1750 (43%)	282 (40%)	144 (46%)	.2
Tumor size, mm†	50 (35, 75)	50 (35, 75)	50 (35, 75)	50 (35, 76)	.4
Surgical margins, n (%)					.7
R0	5036 (88%)	4025 (88%)	693 (89%)	318 (88%)	
R1	383 (6.7%)	303 (6.6%)	50 (6.4%)	30 (8.3%)	
R2	18 (0.3%)	15 (0.3%)	2 (0.3%)	1 (0.3%)	
Positive NOS	280 (4.9%)	233 (5.1%)	33 (4.2%)	14 (3.9%)	
Positive margins, n (%)	681 (12%)	551 (12%)	85 (11%)	45 (12%)	.6
Adjuvant therapy, n (%)					.2
Systemic therapy	2003 (35%)	1595 (35%)	264 (33%)	144 (40%)	
Systemic therapy plus radiation	565 (9.8%)	456 (9.9%)	70 (8.9%)	39 (11%)	
No adjuvant therapy	3182 (55%)	2546 (55%)	455 (58%)	181 (50%)	
Immunotherapy, n (%)	104 (1.8%)	75 (1.6%)	23 (2.9%)	6 (1.6%)	.043

(Continued)

TABLE 2. Continued

Characteristic	Overall N = 5750	Open n = 4597	MIS n = 789	MIS to open conversion n = 364	*P* value*
Postoperative length of stay†	5.0 (4.0, 8.0)	5.0 (4.0, 8.0)	5.0 (4.0, 7.0)	6.0 (4.0, 8.0)	<.001
Unplanned readmission, n (%)	377 (6.6%)	304 (6.6%)	45 (5.7%)	28 (7.7%)	.4
30-d mortality, n (%)	401 (7.2%)	326 (7.3%)	49 (6.6%)	26 (7.7%)	.8
90-d mortality, n (%)	657 (12%)	535 (12%)	80 (11%)	42 (12%)	.6

This table shows tumor characteristics and perioperative variables for the 3 primary study groups. There were significant differences in tumor histology, neoadjuvant therapy use, examined lymph nodes, immunotherapy use, and postoperative length of stay between the 3 groups. There were no differences in the other pathologic fields and perioperative variables. *MIS*, Minimally invasive; *NOS*, not otherwise specified. *Kruskal-Wallis rank sum test; Pearson χ^2 test. †Described as median (interquartile range).

Tumor Characteristics and Perioperative Outcomes

Regarding histology, patients who underwent open pneumonectomy had the greatest proportion of squamous cell carcinoma (open 61% vs MIP 56% vs converted 59%, $P = .046$). Patients who underwent MIP had the greatest incidence of neoadjuvant chemotherapy (open 6.6% vs MIP 8.9% vs converted 6.3%) and neoadjuvant chemoradiation use (open 8.9% vs MIP 10% vs converted 5.5%) ($P = .013$). Patients who underwent MIP also had the greatest proportion of immunotherapy use (open 1.6% vs MIP 2.9% vs converted 1.6%, $P = .043$). The median number of lymph nodes examined for all 3 cohorts was 16; however, there was statistical difference because of variability in the interquartile range (open 16 [10, 23] vs MIP 16 [10, 25] vs converted 16 [11, 24], $P = .034$). No differences in tumor size, laterality, pathologic T stage, pathologic N stage, lymphovascular invasion, margin status, adjuvant therapy use were seen among the 3 study groups (Table 2). Patients who underwent MIP and open pneumonectomy had a lower median postoperative length of stay compared with patients

TABLE 3. Multivariable predictors of conversion from MIP to open pneumonectomy

Characteristic	Full model			Model after backward selection		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age (per decade)	0.99	0.84-1.15	.9			
Female (ref = male)	0.94	0.69-1.26	.7			
Non-White race (ref = White)	1.40	0.94-2.08	.094	1.33	0.90-1.95	.15
Charlson-Deyo score ≥2 (ref = <2)	0.85	0.56-1.28	.5	0.94	0.62-1.39	.7
Academic facility (ref = nonacademic)	1.07	0.81-1.41	.7	1.09	0.82-1.43	.6
Midvolume MIS center (ref = high-volume MIS center)	4.16	3.08-5.65	<.001	4.10	3.05-5.52	<.001
Private insurance type (ref = nonprivate)	0.97	0.70-1.33	.8			
Household income above median (ref = below median)	1.21	0.90-1.63	.2	1.19	0.91-1.58	.2
Metropolitan county type (ref = nonmetropolitan county)	0.98	0.68-1.43	>.9			
Right-sided pneumonectomy (ref = left-sided pneumonectomy)	0.87	0.64-1.16	.3	0.86	0.64-1.15	.3
Adenocarcinoma (ref = nonadenocarcinoma)	0.89	0.66-1.21	.5	0.91	0.68-1.21	.5
Neoadjuvant therapy (ref = no neoadjuvant therapy)	0.60	0.39-0.90	.015	0.61	0.40-0.90	.015
Tumor size (per 1 cm)	1.00	0.97-1.04	>.9			
Clinical lymph node disease (ref = clinical N0)	1.13	0.85-1.50	.4	1.12	0.85-1.48	.4

Multivariable predictors of MIP conversion were determined on the basis of logistic regression are shown in this table. Midvolume minimally invasive facility was associated with greater risk of conversion, whereas neoadjuvant therapy was associated with reduced risk of conversion. *MIP*, Minimally invasive pneumonectomy; *OR*, odds ratio; *CI*, confidence interval; *MIS*, minimally invasive.

who required conversion (open 5.0 vs MIP 5.0 vs converted 6.0 days, $P < .001$); however, unplanned readmissions and 30-day and 90-day mortality rates were similar.

Predictors of Conversion on Multivariable Analysis

On the basis of multivariable logistic regression model assessing predictors of conversion from MIP to open approach, mid-volume minimally invasive lung surgery centers had greater risk of conversion compared to high-volume centers (odds ratio [OR], 4.16; 95% confidence interval [CI], 3.08-5.65; $P < .001$). This increased risk remained following model adjustment with backward selection (OR, 4.10; 95% CI, 3.05-5.52; $P < .001$). In contrast, patients who received neoadjuvant therapy were less likely to require conversion compared to those who did not (OR, 0.60; 95% CI, 0.39-0.90; $P = .015$). This reduced risk also remained after model adjustment with backward selection (OR, 0.61; 95% CI, 0.40-0.90; $P = .015$). Notably, tumor size, clinical lymph node disease, laterality, and histology were not independently associated with risk of conversion (Table 3).

Survival Analysis

Patients who underwent MIP had the greatest median 5-year survival (48.3%) compared with patients who underwent open pneumonectomy (45.2%) and patients requiring conversion (43.3%) on the basis of Kaplan-Meier analysis; however, these differences were not statistically significant (Figure 3, *A-D*). In addition, MIP was not associated with lower risk of death compared with open pneumonectomy according to Cox proportional hazards model (hazard ratio, 0.91; 95% CI, 0.80-1.02; $P = .11$). However, conversion from MIP to open pneumonectomy demonstrated a trend toward increased risk of death compared with upfront open pneumonectomy (hazard ratio, 1.16; 95% CI, 1.00-1.35; $P = .058$). Other factors associated with increased risk of death

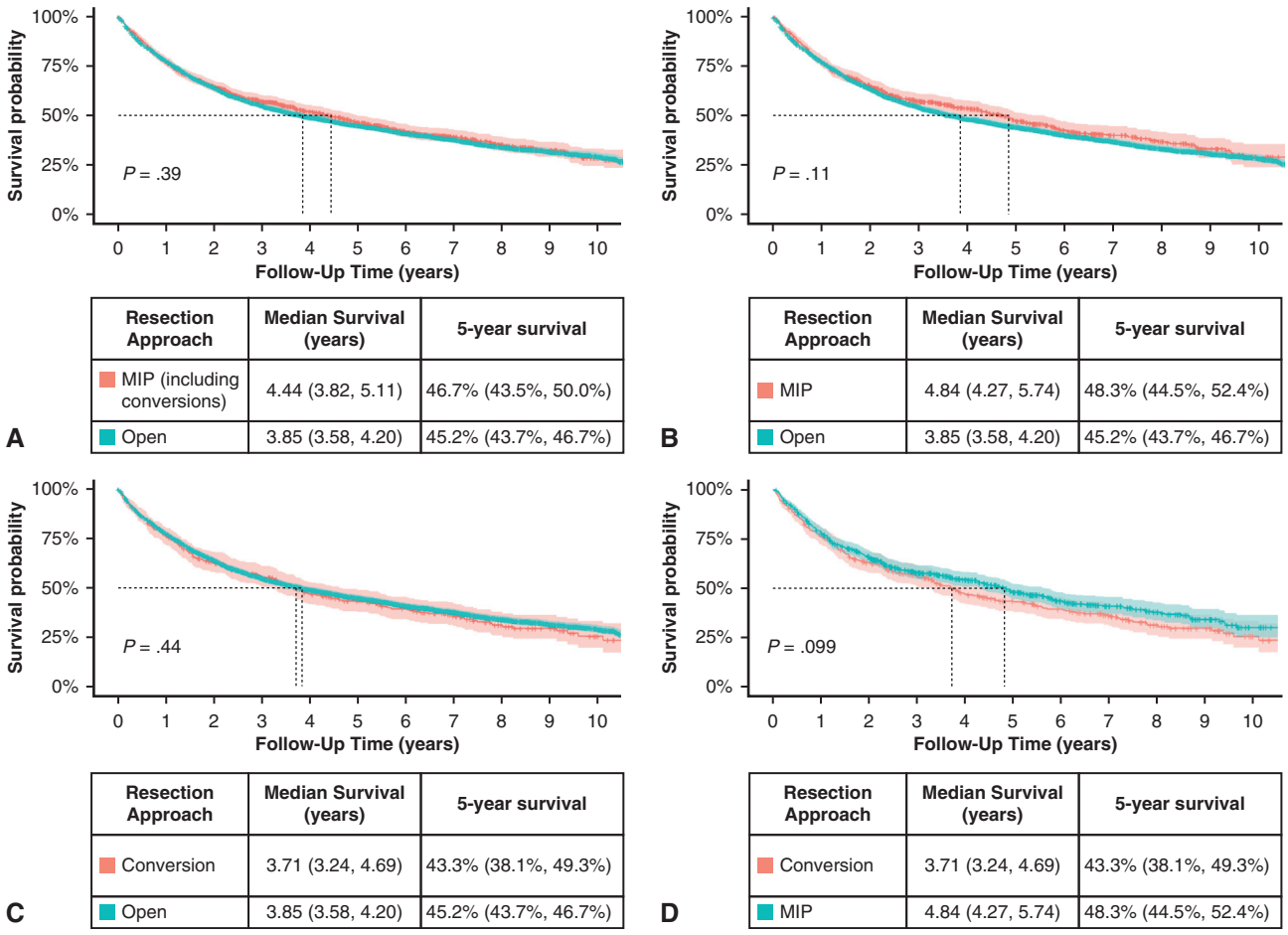


FIGURE 3. Kaplan-Meier survival curve for patients in the study cohort. This panel of Kaplan-Meier curves demonstrates 5-year survival in the surgical technique study groups. Inset (A) compares open pneumonectomies with MIP in an intent-to-treat setup. Inset (B) compares MIP without conversions with open. Inset (C) compares conversions with open pneumonectomies. Inset (D) compares conversions to MIP. All curves overlap, showing no improved survival in any subsets relative to another (all $P > .05$). *MIP*, Minimally invasive pneumonectomy.

included increasing age, Charlson-Deyo score of 2 or greater, right-sided pneumonectomy, lymph node disease, lymphovascular invasion, and positive surgical margins. Female sex, surgery performed at an academic or research facility, private insurance status, and receiving adjuvant therapy were associated with reduced risk of death (Table 4).

Subgroup analyses were performed to examine overall survival among all patients who underwent pneumonectomy according to institutional minimally invasive lung surgery volume. Patients who underwent pneumonectomy at high-volume centers using any surgical technique had improved 5-year survival compared with patients who underwent pneumonectomy at low-volume centers (46.4% vs 43.2%, $P = .045$) (Figure E1, *A*); however, increased risk of death was not seen in low-volume centers after adjustment using Cox proportional hazards method (Table 4). No other differences were noted among the subgroups (Figure E1, *B* and *C*).

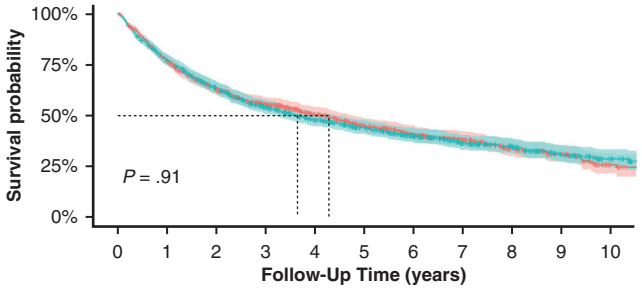
Propensity Score–Matched Analysis

Propensity score matching was performed to create matched cohorts on an intent-to-treat basis. Patients who were planned to undergo open pneumonectomy were matched to patients who were planned to undergo MIP in a 1:1 fashion. Matched cohorts of 904 patients who underwent open pneumonectomy patients were compared against 904 patients who underwent MIP. Patient were well matched with absolute standard mean differences across the analyzed variables between 0 and 0.1 (Table E1). In this matched analysis, patients who underwent MIP were primarily treated at high MIS volume centers (74%), and patients who underwent open pneumonectomy were mostly treated at mid-volume centers (45%) ($P < .001$). The median number of lymph nodes examined was lower in open pneumonectomy patients (open 15 vs MIP 16, $P = .008$). No other differences were noted between the matched cohorts with respect to demographic, tumor, and perioperative variables (Table E1). On Kaplan-Meier survival analysis, no differences in long-term survival were noted among patients in the open pneumonectomy, MIP, and converted pneumonectomy groups (Figure 4, *A-D*). Subgroup analyses examining overall survival according to institutional minimally invasive lung surgery volume were similar (Figure E2, *A-C*).

TABLE 4. Cox proportional hazards method

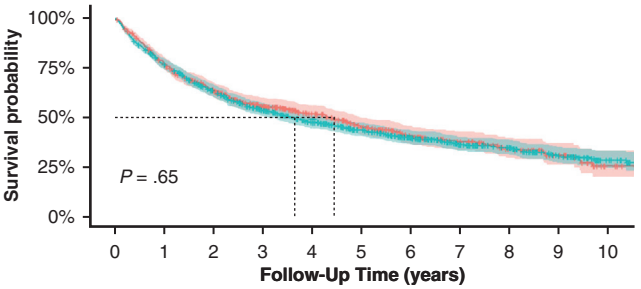
Characteristic	HR	95% CI	*P* value
Age (per decade)	1.11	1.07-1.16	<.001
Female sex (ref = male)	0.79	0.73-0.86	<.001
Non-White race (ref = White)	0.93	0.82-1.04	.2
Charlson-Deyo score ≥2 (ref = <2)	1.20	1.08-1.32	<.001
Academic/research facility (ref = nonacademic facility)	0.86	0.79-0.93	<.001
Center MIS volume (ref = high-volume MIS center)			
Mid-volume MIS center	1.00	0.92-1.09	>.9
Low-volume MIS center	1.01	0.90-1.13	>.9
Private insurance type (ref = nonprivate insurance)	0.75	0.69-0.82	<.001
Household income above median (ref = below median income)	0.95	0.88-1.03	.2
Metropolitan county type (ref = nonmetropolitan county)	0.95	0.87-1.04	.2
Right-sided pneumonectomy (ref = left-sided pneumonectomy)	1.27	1.18-1.37	<.001
Adenocarcinoma histology (ref = nonadenocarcinoma)	1.05	0.97-1.14	.2
Neoadjuvant therapy (ref = no neoadjuvant therapy)	0.87	0.78-0.98	.017
Adjuvant therapy (ref = no adjuvant therapy)	0.57	0.52-0.62	<.001
Clinical lymph node disease (ref = clinical N0)	1.26	1.17-1.36	<.001
Lymphovascular invasion (ref = no lymphovascular invasion)	1.31	1.21-1.41	<.001
Positive surgical margin (ref = negative margin)	1.41	1.26-1.56	<.001
Pneumonectomy approach (ref = open pneumonectomy)			
Minimally invasive	0.91	0.80-1.02	.11
Conversion from MIS to open	1.16	1.00-1.35	.058

Factors associated with survival after using regression analysis are shown in this table. Female sex, treatment at an academic/research facility, private insurance, adjuvant therapy, and minimally invasive resection were associated with improved survival. Increased patient age, elevated Charlson-Deyo score, right-sided pneumonectomy, clinical nodal disease, lymphovascular invasion, and positive surgical margins were associated with reduced survival. *HR*, Hazard ratio; *CI*, confidence interval; *MIS*, minimally invasive.



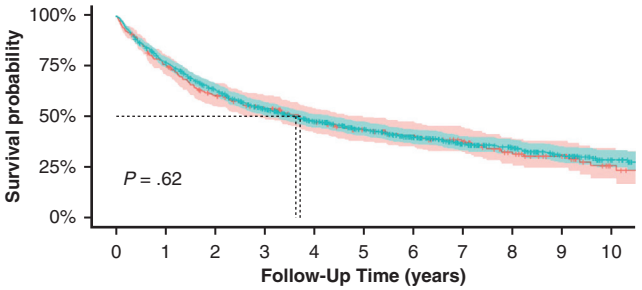
Resection Approach	Median Survival (years)	5-year survival
MIP (including conversions)	4.27 (3.65, 4.84)	45.0% (41.5%, 48.8%)
Open	3.64 (3.20, 4.45)	44.4% (41.1%, 48.0%)

A



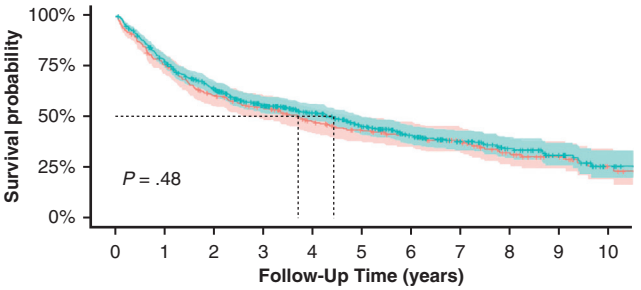
Resection Approach	Median Survival (years)	5-year survival
MIP (no conversions)	4.44 (3.67, 5.17)	45.7% (41.4%, 50.4%)
Open	3.64 (3.20, 4.45)	44.4% (41.1%, 48.0%)

B



Resection Approach	Median Survival (years)	5-year survival
Conversion	3.71 (2.66, 5.22)	43.6% (37.7%, 50.4%)
Open	3.64 (3.20, 4.45)	44.4% (41.1%, 48.0%)

C



Resection Approach	Median Survival (years)	5-year survival
Conversion	3.71 (2.66, 5.22)	43.6% (37.7%, 50.4%)
MIP (no conversions)	4.44 (3.67, 5.17)	45.7% (41.4%, 50.4%)

D

FIGURE 4. Kaplan-Meier survival curve for propensity-matched patients. This panel of Kaplan-Meier curves demonstrates 5-year survival in the propensity-matched analysis study group. Inset (A) compares open pneumonectomies with MIP in an intent-to-treat setup (open, *blue*; MIP, *red*). Inset (B) compares MIP without conversions with open. Inset (C) compares conversions with open pneumonectomies. Inset (D) compares conversions with MIP. All curves overlap, showing no improved survival in any subsets relative to one another (all $P > .05$). *MIP*, Minimally invasive pneumonectomy.

DISCUSSION

With the increased use of VATS and RATS in lung cancer surgery, more complex resections are being attempted minimally invasively. Although avoiding a thoracotomy incision may lead to improved perioperative outcomes on the basis of a plethora of data supporting VATS lobectomy over open surgery,[17-20] it is important to study the potential long-term impact of minimally invasive techniques in these complex lung cancer resections. In our study, MIP was not associated with reduced postoperative length of stay or unplanned readmissions compared with open pneumonectomy but demonstrated similar overall survival both on unadjusted and adjusted analysis. Furthermore, possible downsides of requiring conversion from minimally invasive to open pneumonectomy are important to consider, including longer postoperative admissions and the potential for increased risk of death. Although conversions in our Cox model did not reach the threshold for statistical significance, this may have been impacted by patients included in the conversion cohort who underwent a planned diagnostic thoracoscopy followed by a planned open pneumonectomy rather than a true intraoperative conversion. Using NCDB data, such patients could not be eliminated from the study cohort. Nonetheless, the trend toward increased risk of death after intraoperative conversion is notable. Importantly, the current analysis demonstrates that rates of conversion nationally were relatively high, ranging from 20% to 50% among institutions that perform greater than 25% of lung resections using minimally invasive techniques. Furthermore, there was a 4-fold increased risk of conversion when comparing mid-volume centers with high-volume centers. Patients who underwent conversion procedures had the greatest rates of unplanned readmissions and 30-day mortality, although the differences were not statistically significant.

Currently, there are several existing publications that have assessed the overall utility of minimally invasive approaches in pneumonectomy. It is important to highlight that in many of these studies, including the current manuscript, the incidence of pneumonectomy overall has decreased substantially over time while long-term outcomes for locally advanced lung cancer continue to improve. Taken together, these trends are likely related to a combination of improved surgical experience and technique that allows more opportunities for lung preservation, and the impact that novel neoadjuvant strategies have had on the surgery itself and overall survival. The largest published study to date on MIP, which was undertaken with NCDB data, demonstrated noninferiority of MIP for short- and long-term outcomes compared with open pneumonectomy.[11] In a smaller multi-institutional cohort, Yang and colleagues[15] found no significant differences in perioperative morbidity and mortality, postoperative length of stay, and median overall survival between minimally invasive and open pneumonectomy patients. Findings from the current study are consistent with those demonstrated by Hennon and colleagues[11] and Yang and colleagues,[15] although neither study examined the impact of intraoperative conversion from MIP or institutional minimally invasive lung surgery volume to the extent presented here. Thus, the novelty of the current analysis relates to our data demonstrating high rates of conversion nationally, irrespective of institutional minimally invasive lung surgery experience, and the potential for increased risk of death if conversion is required. These results indicate that, although overall survival is similar between MIP and open surgery, minimally invasive approaches for pneumonectomy may not confer the same benefits of improved postoperative recovery seen in minimally invasive lobectomy but carry the potential increased risk of death in cases of intraoperative conversion.

The fact that neoadjuvant therapy was associated with reduced risk of conversion may in part be related to lymph node status, as many patients receiving neoadjuvant therapy likely had lymph node disease discovered on clinical staging. Notably, clinical lymph node status was not a significant factor for conversion on the basis of our multivariable analysis, suggesting that the use of neoadjuvant therapy may have had an impact. Previous publications examining conversion from VATS to open lobectomy indicate that the presence of lymph node disease is a significant factor.[21-23] In the current series, patients who underwent MIP had the greatest incidence of pN0 disease while open pneumonectomy and converted patients had similar incidence of pN1 and pN2 disease, although this difference did not quite reach statistical significant ($P = .068$). Nonetheless, these results suggest that surgeons should pay particular attention to lymph node status when considering the suitability of a minimally invasive approach. The NCBD, unfortunately, does not capture reasons for conversion, which is a limitation of this study.

Additional limitations of this study relate to the retrospective nature of the analysis, as causality cannot be established between variables and outcomes. This study includes cases between 2010 and 2020, with minimally invasive pneumonectomy comprising up to a quarter of annual cases in recent years. As such, our cohort analyzes a timeframe where there has been evolution in surgical practice as well as an increase in the use of targeted agents and immunotherapy, which may have had an impact on the survival analysis. Although the use of the NCDB confers the benefits of a large nationwide dataset, our study is limited to analysis of variables captured within the database. For example, details pertaining to the extent of lymph node disease (eg, single-station vs multi-station, occult vs bulky), tumor location (eg, central vs peripheral), or response to neoadjuvant therapy are not captured in the NCDB despite being important factors related to surgical approach and prognosis. Although the Charlson-Deyo comorbidity score provides some index for pre-existing conditions, specific comorbidities are not tabulated in the NCDB. Certain comorbidities, such as baseline cardiac or pulmonary conditions, could have impacted perioperative outcomes, long-term survival, and the choice of surgical approach. Some previous institutional studies contain more granular data, but do not assess outcomes of patients who required conversion. Regarding conversions, it is unknown whether a proportion of patients coded in the NCDB as converted from MIP may in fact have had a diagnostic thoracoscopy followed by a planned open pneumonectomy. Furthermore, neither the duration of minimally invasive approach nor estimated blood loss are tabulated in the NCDB, which could potentially serve as surrogate indicators of a planned diagnostic thoracoscopy. Despite this possibility, there was a trend toward worse outcomes in the converted cohort compared with patients who underwent upfront open pneumonectomy, and this difference may have been more profound if diagnostic thoracoscopy patients could be eliminated from the conversion cohort. Specific postoperative complications are not tabulated in the NCDB, which may have provided additional insights on the impact of conversions and associated perioperative outcomes as well as the overall survival analysis. The relatively smaller sample size of the conversion cohort may have impacted our ability to detect statistically significant differences. Finally, it is conceivable that there are patients within this study cohort who were scheduled to have a lesser resection, but intraoperatively it was determined that pneumonectomy was necessary because of the extent of the cancer or the occurrence of an intraoperative event. This possibility could not be accounted for in our analysis and has the potential to impact our findings.

CONCLUSIONS

MIP for lung cancer had similar overall survival compared with upfront open pneumonectomy; however, using minimally invasive techniques was not associated with reduced postoperative length of stay or unplanned readmissions. Furthermore, intraoperative conversion from minimally invasive to open pneumonectomy occurred 20% to 50% of the time in mid- and high-volume minimally invasive lung surgery centers and may be associated with increased risk of death. Neoadjuvant therapy increases the likelihood of successful minimally invasive pneumonectomy, whereas surgery at a non−high-volume center is associated with a 4-fold risk of conversion. Careful patient selection is necessary when considering MIP so that long-term outcomes are not compromised.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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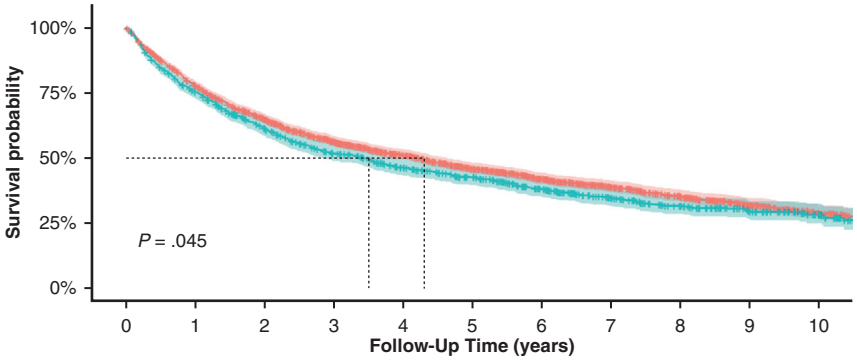
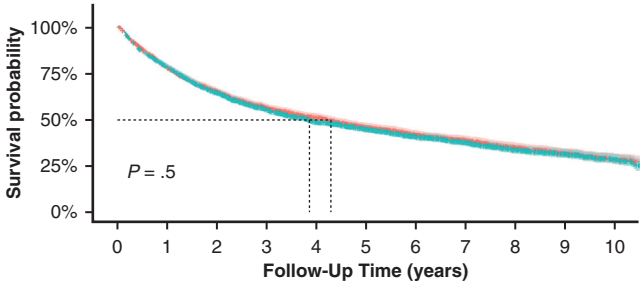
Key Words: pneumonectomy, surgery, operative planning, surgical volume, neoadjuvant therapy



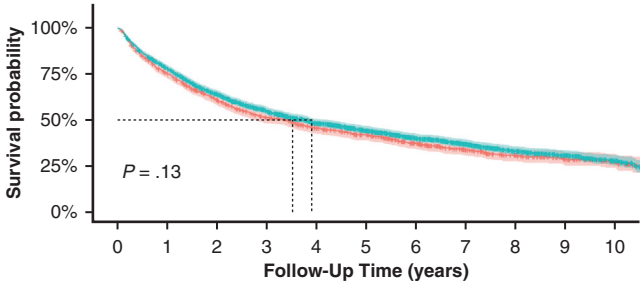
Center MIS Volume	Median Survival (years)	5-year survival
High volume	4.30 (3.85, 4.70)	46.4% (44.2%, 48.6%)
Low volume	3.50 (2.86, 4.02)	43.2% (40.0%, 46.6%)

A



Center MIS Volume	Median Survival (years)	5-year survival
High volume	4.30 (3.85, 4.70)	46.4% (44.2%, 48.6%)
Mid volume	3.87 (3.57, 4.47)	45.5% (43.5%, 47.7%)

B



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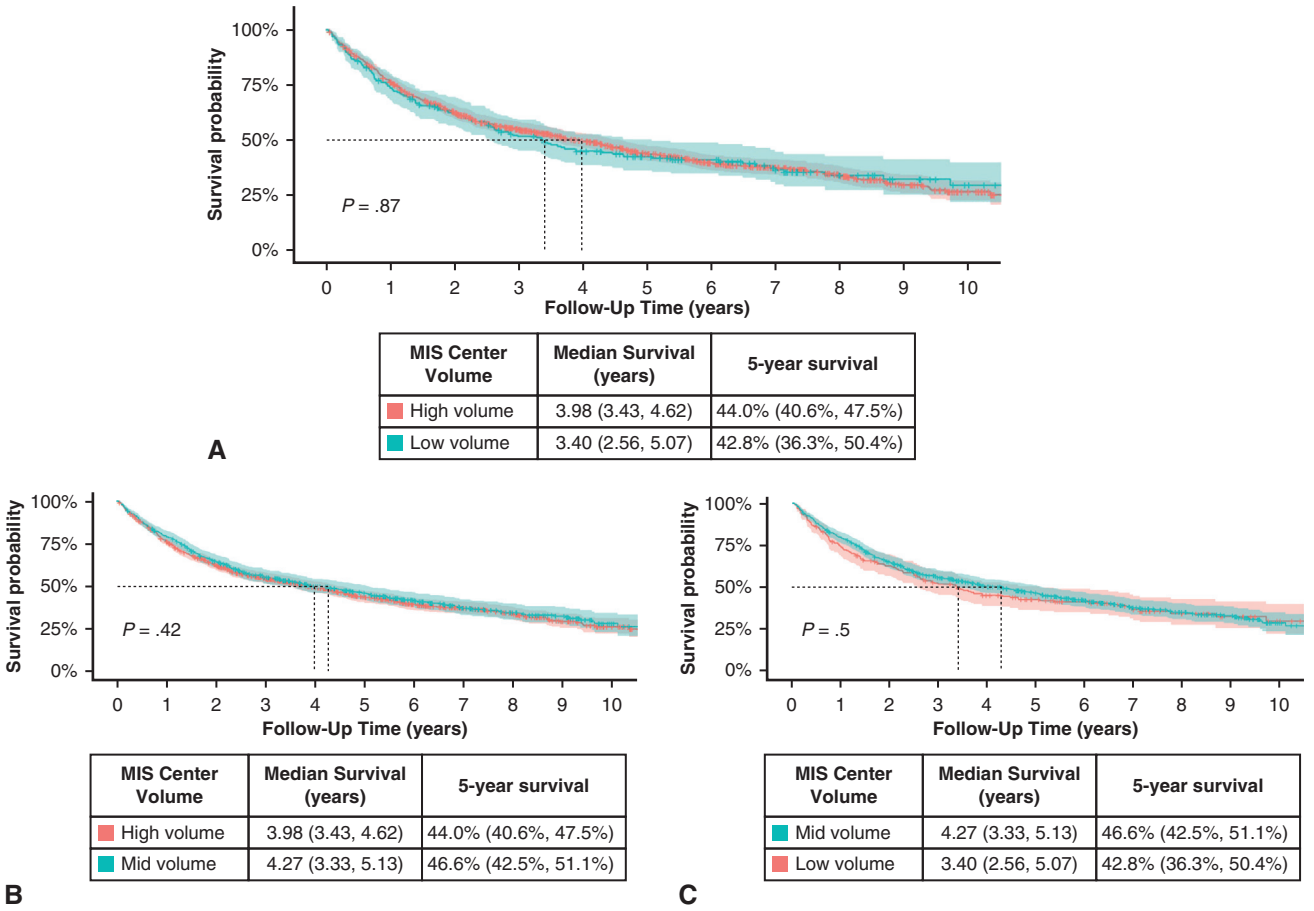
Low volume	3.50 (2.86, 4.02)	43.2% (40.0%, 46.6%)

C

FIGURE E1. Kaplan-Meier survival curves for patients who underwent MIP on the basis of center minimally invasive volume. This panel of Kaplan-Meier curves demonstrates 5-year survival for patients who underwent MIP, stratified by whether their MIP was completed at a high-, mid-, or low-volume center. Inset (A) compares MIP survival at high-volume with low-volume centers. Inset (B) compares MIP survival at high-volume with midvolume centers. Inset (C) compares MIP survival at midvolume with low-volume centers. The low-volume group had lower survival than the high-volume group at 5 years ($P = .045$) (inset A). *MIP*, Minimally invasive pneumonectomy.



MIS Center Volume	Median Survival (years)	5-year survival
High volume	3.98 (3.43, 4.62)	44.0% (40.6%, 47.5%)
Low volume	3.40 (2.56, 5.07)	42.8% (36.3%, 50.4%)

MIS Center Volume	Median Survival (years)	5-year survival
High volume	3.98 (3.43, 4.62)	44.0% (40.6%, 47.5%)
Mid volume	4.27 (3.33, 5.13)	46.6% (42.5%, 51.1%)

MIS Center Volume	Median Survival (years)	5-year survival
Mid volume	4.27 (3.33, 5.13)	46.6% (42.5%, 51.1%)
Low volume	3.40 (2.56, 5.07)	42.8% (36.3%, 50.4%)

FIGURE E2. Kaplan-Meier survival curves for propensity-matched patients who underwent MIP on the basis of center minimally invasive volume. This panel of Kaplan-Meier curves demonstrates 5-year survival for patients in the propensity-matched analysis who underwent MIP, stratified by whether their MIP was completed at a high-, mid-, or low-volume center. Inset (A) compares MIP survival at high-volume with low-volume centers. Inset (B) compares MIP survival at high-volume with midvolume centers. Inset (C) compares MIP survival at midvolume with low-volume centers. All curves overlap, showing no improved survival in any subsets relative to one another (all $P > .05$). *MIP*, Minimally invasive pneumonectomy.

TABLE E1. Demographic characteristics, tumor characteristics, and perioperative outcomes after propensity score matching for intent-to-treat open versus MIP

Characteristic	Open, N = 904	MIP, n = 904	Absolute SMD	*P* value*
Surgical approach				
MIS to open conversion		280 (31%)		
Minimally invasive		624 (69%)		
Open	904 (100%)			
Age, y†	64 (57, 70)	64 (57, 71)	0.0022	.8
Female	343 (38%)	329 (36%)	0.0322	.5
Race				.7
White	776 (86%)	775 (86%)	–	
Asian	36 (4.0%)	34 (3.8%)	–	
Black	80 (8.8%)	77 (8.5%)	–	
Other	12 (1.3%)	18 (2.0%)	–	
Charlson-Deyo score, n (%)				.7
0	479 (53%)	489 (54%)	0.0222	
1	307 (34%)	291 (32%)	0.0379	
2+	118 (13%)	124 (14%)	0.0193	
Facility type				>.9
Academic/research program	430 (48%)	437 (48%)	0.0155	
Community cancer program	21 (2.3%)	20 (2.2%)	0.0075	
Comprehensive community cancer program	288 (32%)	288 (32%)	0.0000	
Integrated network cancer program	165 (18%)	159 (18%)	0.0174	
Center MIS volume				<.001
Low MIS volume	174 (19%)	40 (4.4%)	–	
Mid MIS volume	410 (45%)	197 (22%)	–	
High MIS volume	320 (35%)	667 (74%)	–	
Insurance type				>.9
Private	340 (38%)	354 (39%)	0.0317	
Medicaid	84 (9.3%)	82 (9.1%)	0.0077	
Medicare	437 (48%)	430 (48%)	0.0155	
Other government	22 (2.4%)	18 (2.0%)	0.0317	
Uninsured	21 (2.3%)	20 (2.2%)	0.0075	
Above median education	430 (48%)	439 (49%)		.7
Above median household income	553 (61%)	547 (61%)	0.0136	.8
County type				.7
Metropolitan	754 (83%)	765 (85%)	0.0337	
Rural	7 (0.8%)	5 (0.6%)	0.0298	
Urban	143 (16%)	134 (15%)	0.0280	
Distance to facility, miles†	14 (6, 32)	14 (6, 31)	–	.6
Right-sided pneumonectomy	338 (37%)	332 (37%)	–	.8
Tumor histology				.7
Adenocarcinoma	363 (40%)	358 (40%)	0.0113	
Large cell carcinoma	20 (2.2%)	26 (2.9%)	0.0397	
Squamous cell	521 (58%)	520 (58%)	0.0022	
Neoadjuvant therapy				>.9
Systemic therapy	63 (7.0%)	63 (7.0%)	0.0000	
Systemic therapy plus radiation	74 (8.2%)	73 (8.1%)	0.0041	
No neoadjuvant therapy	767 (85%)	768 (85%)	0.0031	
Lymph nodes examined†	15 (10, 22)	16 (11, 24)	–	.008
Clinical lymph node disease	438 (48%)	442 (49%)	–	.9

(Continued)

TABLE E1. Continued

Characteristic	Open, N = 904	MIP, n = 904	Absolute SMD	*P* value*
Clinical T stage				>.9
cT0/IS	0 (0%)	0 (0%)	0.0000	
cT1	126 (14%)	121 (13%)	0.0162	
cT2	302 (33%)	302 (33%)	0.0000	
cT3	300 (33%)	299 (33%)	0.0024	
cT4	106 (12%)	108 (12%)	0.0068	
cTX	70 (7.7%)	74 (8.2%)	0.0161	
Clinical N stage				>.9
cN0	466 (52%)	462 (51%)	0.0089	
cN1	230 (25%)	235 (26%)	0.0126	
cN2	151 (17%)	149 (16%)	0.0060	
cN3	9 (1.0%)	7 (0.8%)	0.0252	
cNX	48 (5.3%)	51 (5.6%)	0.0144	
Pathologic T stage				.2
0/CR	27 (3.0%)	28 (3.1%)	–	
1	96 (11%)	72 (8.0%)	–	
2	280 (31%)	271 (30%)	–	
3	359 (40%)	365 (40%)	–	
4	142 (16%)	168 (19%)	–	
Pathologic N stage			–	.2
0	300 (33%)	332 (37%)	–	
1	437 (48%)	404 (45%)	–	
2	167 (18%)	168 (19%)	–	
Lymphovascular invasion	347 (44%)	334 (42%)	–	.6
Tumor size, mm†	50 (35, 75)	50 (35, 75)	0.0163	>.9
Surgical margins				.5
R0	796 (88%)	798 (89%)	–	
R1	55 (6.1%)	60 (6.7%)	–	
R2	5 (0.6%)	2 (0.2%)	–	
Positive NOS	45 (5.0%)	37 (4.1%)	–	
Positive margins	105 (12%)	99 (11%)	–	.7
Adjuvant therapy				.8
Systemic therapy	330 (37%)	328 (36%)	0.0046	
Systemic therapy plus radiation	79 (8.7%)	88 (9.7%)	0.0336	
No adjuvant therapy	495 (55%)	488 (54%)	0.0155	
Immunotherapy	14 (1.5%)	23 (2.5%)	–	.13
Postoperative length of stay	5.0 (4.0, 8.0)	5.0 (4.0, 7.0)	–	.081
Unplanned readmission	52 (5.8%)	58 (6.4%)	–	.6
30-d mortality	69 (7.8%)	58 (6.8%)	–	.4
90-d mortality	107 (12%)	93 (11%)	–	.5

This table shows baseline demographic data for the 2 primary groups in the propensity score–matched analysis. There were significant differences in facility MIS volume and number of lymph nodes examined between the 2 groups. There were no differences in the other demographic fields. *MIP*, Minimally invasive pneumonectomy; *SMD*, standard mean difference; *MIS*, minimally invasive; *NOS*, not otherwise specified. *Pearson χ^2 test; Wilcoxon rank sum test; Fisher exact test. †Described as having as median (interquartile range).