Robotic anatomic pulmonary resection—the data

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Abstract: Robot-assisted pulmonary resection, specifically robotic-assisted lobectomy (RL), has gained increasing popularity worldwide due to its high-resolution three-dimensional visualization and precise wristed instrumentation. This adoption aligns with current society guidelines recommending minimally invasive resection for early-stage lung cancer. RL serves as an excellent alternative to thoracoscopic or open approaches, and this article reviews the comprehensive data available on RL. This review gathered papers that examined and compared the outcomes, lymph node yield, cost, and survival associated with open lobectomy (OL), video-assisted thoracoscopic surgery (VATS) lobectomy, and RL. With a specific focus on the outcomes of RL, including its impact on perioperative outcomes, cost-effectiveness, lymph node yield, and long-term survival. Existing data suggest that RL offers numerous advantages, such as reduced complications, minimal blood loss, shorter hospital stays, and lower conversion rates to open surgery compared to traditional OL. Furthermore, RL exhibits improved lymph node yield and equivalent long-term survival outcomes, further supporting its efficacy. As RL continues to evolve, the need for ongoing research becomes increasingly important. This includes conducting randomized clinical trials (RCTs) to refine our understanding of RL and further enhance patient outcomes. With a focus on accumulating and analyzing contemporary data, this article underscores the continuous progression of RL within the field of robotic-assisted pulmonary resection.

Keywords: Robotic-assisted; lobectomy; minimally-invasive; video-assisted thoracoscopic surgery (VATS); thoracotomy

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Introduction

Robot-assisted pulmonary resection has become an increasingly common surgical approach in the United States. The robotic platform provides superior three-dimensional visualization, dexterity, and stabilization that has drawn surgeons to increasingly adopt this technique. In 2008, approximately 1% of lobectomies were performed utilizing a robotic platform (1). In 2020, this number grew to 33% (2). The 2021 update of the Society of Thoracic Surgery (STS) database showed a 328% increase use of robotic-assisted lobectomy (RL) in the last 6 years (3). RL is an excellent alternative to video-assisted thoracoscopic surgery (VATS) particularly as the landscape shifts away from open lobectomy (OL) to a minimally invasive approach (4). Current CHEST and National Comprehensive Cancer Network (NCCN) guidelines recommend minimally invasive resection for early-stage lung cancer (5,6). Long-term data continues to be reported about the efficacy and safety for robotic pulmonary resection. Here we review the current data available on RL.

Current landscape of outcomes data

Both RL and VATS lobectomy (VL) have been associated with decreased complications and length of stay (LOS) when compared to OL (1,7-11). Outcomes studies now increasingly compare all three surgical modalities together (*Table 1*) (12-35). As such, data are accumulating on the relationship of surgical approach and its impact on perioperative outcomes, LOS, cost, nodal harvest, and survival. Most publications are single-center retrospective series which were conducted during the use of older generation robotic systems. There are relatively few randomized clinical trials (RCTs) and meta-analyses on the topic. This highlights the need for modern data encompassing the most recent generation of robotic technology, enhanced recovery after surgery (ERAS) pathways, and a surgeon workforce that is overcoming the learning curve.

Perioperative outcomes, LOS, and conversion rates

RL has shown equivalent safety outcomes to VL (4,36,37). As with VL, RL is associated with decreased blood loss, blood transfusion, air leaks, mortality, pain, and LOS compared to OL (1,30,36-39). For example, an analysis of the State Inpatient Database (SID) between the years of 2009–2010 (33,095 patients) found that RL had decreased complications (43.8% *vs.* 54.1%, P=0.016), in-hospital mortality (0.2% *vs.* 2.0%, P=0.016), and LOS (7.4 *vs.* 5.9, P=0.015) when compared to OL (1).

Analyses of large databases show mixed results. The STS database, Surveillance, Epidemiology, and End Results (SEER) database, and the Premier Healthcare database have found similar morbidity and mortality rates between RL and VL (1,27,40). However, there are large database analyses that show better postoperative outcomes with RL as compared to VL. A Premier Healthcare Database analysis from 2011–2015 found that RL was associated with lower postoperative complications (P=0.006), shorter hospital stay (P=0.006), and lower conversion rate to open (P<0.0001) when compared to VL (9). Another study including the Premier Healthcare Database comparing RL to VL amongst surgeons who completed more than 20 lobectomies per year found that RL had lower 30-day complication rates (33.4% *vs.* 39.2%) and conversion rates to open thoracotomy (4.8% *vs.* 8.0%, P=0.007) when compared to VL (41). Earlier reports showed higher iatrogenic bleeding complications and conversion to open rates with RL as compared to VL, but we suspect this is reflective of the initial learning curve (42). Conversion rates of less than 1% have now been achieved even during the initial learning curve (43).

Updated studies reviewing 5,721 cases published more recently [2022] demonstrate even more favorable outcomes than previously noted demonstrating RL had shorter operative time than VL (P<0.0001) and OL (P=0.0004), lower conversion rate (11.9% *vs.* 6%, P<0.0001), shorter hospital stay (P<0.0001), and lower postoperative transfusion rate (P=0.01) (13).

However, this initial data set excluded those with advanced disease and neoadjuvant therapy. To elicit possible sources of conversion, a multivariable regression model was run on the same data set now including those with advanced disease and neoadjuvant therapy. This cohort showed similar trends in conversion rates with RL having a lower conversion rate than VL (3.6 *vs.* 12.9%, P<0.0001) (14). When comparing VL to RL conversions, pulmonary artery injury was observed in RL more often than VL (25% *vs.* 14%, P<0.01), however, these conversions took place after bleeding was adequately controlled without hemodynamic compromise. No difference in these groups was noted between estimated blood loss or blood transfusions, and there was no intraoperative mortality in either group. Whereas VL had more conversions for anatomical reasons (66.6 *vs.* 45.6%, P=0.0002) (14).

Operative time

Most data during the initial learning curve, including data from early meta-analyses, indicate longer operative time for RL when compared to both VL and OL (10,37,44). However, with newer robotic systems and formation of proficient robotic teams, contemporary operative times between VL and RL are not as drastic as initially described (34). Amongst high volume surgeons the mean time difference was 20–25 minutes (9,40,41). This negligible variation in operative time between RL and VL was also seen in a contemporary meta-analysis (176 *vs.* 162 minutes, P=0.08) (45). A modern analysis of operative times between VATS *vs.* robotic segmentectomy also found no statistical difference (148±52 *vs.* 149±50 minutes; P=0.773) (46).

Cost data

The cost of robotic surgery has been a point of criticism since its early use. Earlier cost analysis showed significantly

Table 1 Publications regarding outcomes data for RL, VL, and OL

Author	Year	n	Data source	Groups	Survival	Lymph nodes	LOS	30-day morbidity	Conversion to open (RL *vs.* VL)
Kent (12)	2023	6,646	Multicenter	RL, VL, OL	RL > VL; OL > VL	RL > VL; RL > OL	RL < OL; VL < OL	N/A	RL < VL
Kent (13)	2023	5,721	Multicenter	RL, VL, OL	N/A	N/A	RL < OL; VL < OL	N/A	RL < VL
Herrera (14)	2023	7,216	Multicenter	RL, VL, OL	N/A	N/A	RL < VL	N/A	RL < VL
Merritt (15)	2023	24,257	Administrative (NCDB)	RL, VL, OL	RL > OL; VL > OL	Equal	RL < OL; VL < OL	N/A	N/A
Jin (16)	2022	320	Randomized clinical trial	RL, VL	N/A	RL > VL	Equal	Equal	Equal
Hennon (17)	2020	64,676	Administrative (NCDB)	RL, VL, OL	RL > OL; VL > OL	Equal	RL < OL; VL < OL	N/A	RL < VL
Kneuertz (18)	2020	514	Administrative (STS)	RL, VL, OL	Equal	Equal	RL < OL; VL < OL	RL < OL; VL < OL	Equal
Cui (19)	2020	18,908	Administrative (NCDB)	RL, VL	VL > RL	N/A	N/A	Equal	RL < VL
Sesti (20)	2020	4,307	Administrative (SEER-Medicare)	RL, VL	Equal	N/A	N/A	N/\A	N/A
Li (21)	2019	121	Single center	RL, VL	Equal	RL > VL	RL < VL	Equal	Equal
Li (22)	2019	1,075	Single center	RL, VL	N/A	RL > VL	RL < VL	Equal	Equal
Kneuertz (23)	2019	514	Single center	RL, VL, OL	Equal	N/A	RL < OL; VL < OL	RL = VL < OL	N/A
Huang (24)	2019	166	Single center	RL, VL	Equal	Equal	RL > VL	Equal	Equal
Nelson (25)	2019	831	Single center	RL, VL, OL	Equal	RL > VL	RL < VL	Equal	N/A
Spaggiari (26)	2019	1,139	Single center	RL, OL	Equal	N/A	N/A	N/A	N/A
Veluswamy (27)	2020	2,766	Administrative (SEER-Medicare)	RL, VL, OL	Equal	Equal	N/A	Equal	N/A
Cerfolio (28)	2018	1,339	Multicenter	RL	N/A	N/A	N/A	N/A	N/A
Worrell (29)	2019	98	Single center	RL, VL	Equal	Equal	Equal	Equal	Equal
Yang (30)	2017	470	Single center	RL, VL, OL	Equal	RL > VL	RL < OL; VL < OL	Equal	Equal
Park (31)	2017	29	Single center	RL, VL	Equal	Equal	Equal	Equal	Equal
Martin (32)	2016	2,830	Administrative (KCR)	VL, OL	VL > OL	Upstaging with RL	N/A	N/A	N/A
Yang (33)	2016	18,780	Administrative (NCDB)	RL, VL, OL	RL > OL; VL > OL	Equal	RL < OL; VL < OL	Equal	RL < VL
Bao (34)	2016	184	Single center	RL, VL	N/A	Equal	Equal	Equal	Equal
Lee (35)	2015	211	Single center	RL, VL	Equal	Equal	Equal	Equal	N/A

RL, robot-assisted lobectomy; VL, video-assisted thoracoscopic surgery lobectomy; OL, open lobectomy; LOS, length of stay; NCDB, National Cancer Data Base; STS, Society of Thoracic Surgery; SEER, Surveillance, Epidemiology, and End Results; KCR, the Kentucky Cancer Registry; N/A, not applicable.

increased costs amongst RL as compared to VL and OL (27,43). The average RL is estimated to cost $3,000–5,000 per case due to disposable instruments and cost of the robotic console (29,36,40,43). A SEER database analysis found that costs for RL were similar to OL ($54,702 and $57,104, P=0.08), but higher when compared to VL ($48,729, P=0.02) (27). Recent data from a prospective randomized study as well as a meta-analysis also show higher cost for RL as compared to VL (16,47).

However, some contemporary studies have found no statistical difference in cost calculations between RL, OL, and VL (23,25). Nelson *et al.* found no difference in cost between RL and VL following adjustments such as institutional robotic case volume (25). Kneuertz *et al.* additionally found no difference in cost between RL, VL ($17,260), and OL ($18,075, P=0.48) when propensity-weighted adjusted cost analysis was performed on direct, indirect, and total hospital costs (23). Although these more contemporary data are from institutions with dedicated robotic teams and higher case volume which may not be easily replicated; these are still encouraging findings.

Lymph node yield

Recent single-center analyses have noted a higher lymph node yield with the robotic approach (*Table 1*) (21,22,25,30). Li *et al.* reported more lymph node counts with RL as compared to VL (13 *vs.* 10, P<0.01) (21). Yang *et al.* found that the robotic approach harvested a higher median number of lymph node stations (5 for RL) as compared to VL and OL (4, P<0.001) (30). In a larger retrospective single-center study of 831 patients, Nelson *et al.* found that RL has improved N1 and N2 sampling when compared to both VL and RL (25).

A contemporary multi-institutional retrospective comparison of robotic and VATS segmentectomies also found that the robotic approach attained a greater number of N1 nodes and N1 stations (46). An additional multi-institutional analysis by Wilson *et al.* found superior pathologic up-staging of pN1 (6.6%) and pN2 (4.3%) with RL as compared to historical controls for VL; RL was equivalent to OL historical controls (48). Most recently, a prospective RCT and contemporary meta-analysis demonstrated superior lymph node yield with RL when compared to VL (16,47). This meta-analysis also found that RL was associated with more harvested lymph nodes [weighted mean difference (WMD) 1.72, 95% confidence interval (CI): 0.63–2.81, P=0.002] and lymph node stations (WMD 0.51, 95% CI: 0.15–0.86, P=0.005) (47). Although meta-analysis shows improved yield, when looking at long-term survival, a large retrospective review showed RL and VL had similar upstage rates and lymph node yield (17). This was further confirmed in a more recent study in which inverse probability of treatment weighting (IPTW) was applied and showed no significant difference in N1 and N2 lymph node upstaging rates between RL, VL, and OL [N1 upstaging RL: 11.79%, VL: 11.49%, OL: 11.85% (P=0.274)] with clinical T2–3N0 non-small cell lung cancer (NSCLC); however, RL and VL did confer an overall survival benefit over OL (P<0.001) (15).

Survival

Numerous retrospective and large database studies demonstrate equivalent survival following lobectomy regardless of a robotic, VATS, or open surgical approach (*Table 1*) (19-21,23-33,35). The majority of these are single-center, retrospective studies, which did not utilize propensity-score matching to compare survival between different groups. Nevertheless, the trend of at least equivalent survival has been consistent in multi-center analysis and large database analysis (18,20,27,28).

Cerfolio *et al.* reported 5-year survival for NSCLC in one of the largest multi-institutional robotic series from four institutions (28). In this study, 1,339 patients were analyzed. The 5-year stage-specific survival was 83% (stage IA), 77% (stage IB), 68% (stage IIA), 70% (stage IIB), 62% (stage IIIA), and 31% (stage IIIB) (28). The cumulative incidence of local recurrence in the ipsilateral chest was 3% (95% CI: 2–5%) (19). These stage-specific survival results were comparable, and in fact superior, to historical controls (28,49). Notably this multi-center study did not have a VL or OL arm for comparison.

A 2020 large database analysis of the STS outcomes database found no difference in overall or disease-free stage-specific 5-year survival in patients who underwent RL for stage I–IIIA NSCLC as compared to both OL and VL (18). Similarly, a large contemporary multicenter retrospective study of 6,646 cases showed that patients undergoing RL and OL have statistically similar overall survival; however, they found that the VATS group was associated with shorter overall survival [OL *vs.* VATS: hazard ratio (HR) 0.64, P<0.001 and RL *vs.* VATS: HR 0.79; P=0.007] (12). A SEER-Medicare patient propensity-matched analysis of patients with NSCLC who underwent VL and RL between 2008–2013 also found no difference in 3-year survival between the two modalities (71.4% *vs.* 73.1%, P=0.366) (20). A separate SEER analysis comparing all three modalities (RL, VL, and OL) additionally found no significant difference in overall survival or lymph node sampling (27).

A larger analysis of 30,040 lobectomies for the National Cancer Data Base (NCDB) found that the minimally invasive approaches (VL and RL) had improved 2-year survival when compared to OL (33). Although the majority of data indicate similar survival between RL and VL (*Table 1*), an additional analysis of the NCDB from 2010–2014 by Cui *et al.* found that RL had higher long-term mortality risk than VL at 1-year post-surgery amongst patients with stage I NSCLC (HR 1.33, 95% CI: 1.15–1.55) (19). No statistically significant 1-year survival difference was found for tumors larger than 2 cm (19).

Conversely, a meta-analysis by Wu *et al.* has suggested that RL has long-term survival benefits over VL (4). RL had a longer disease-free survival than the VL group (HR 0.76; 95% CI: 0.59–0.97, P=0.03) (4). The overall survival had a similar trend but was not statistically significant (4). Overall survival was also equal between RL and VL in the meta-analysis by Ma *et al.* (47). Notably these meta-analyses do not include the study by Cui *et al.*, as it was published following the completion of these meta-analyses (19).

Clinical trials

There are no RCTs comparing all three surgical modalities in lung cancer. The only prospective RCT, the RVlob trial, was recently published in April 2021 (16). The RVlob trial is a single-center prospective RCT conducted in China that compared short-term outcomes between RL and VL (16). This trial enrolled 320 patients (RL n=157, VL n=163). Perioperative outcomes such as conversion to thoracotomy, blood loss, operative time, LOS, visual analog pain scales, and complications were similar between the two groups (P<0.05) (16). The RL group had a statistically significantly higher number of harvested lymph nodes (11 *vs.* 10, P=0.02), higher number of N1 lymph nodes (6 *vs.* 5, P=0.005), and more lymph nodes examined (6 *vs.* 5, P<0.001) (16). Total hospitalization cost was notably higher in the RL group ($12,821 *vs.* $8,009, P<0.001) (29). Unfortunately, the primary outcome measure of 3-year overall survival has not yet been reached and is expected to be available in 2023 (16).

Other prospective RCTs are ongoing. The Belgian NCT03152071 trial was completed in July 2018 and randomized patients to VATS *vs.* robotic resection for lung cancer (50). The primary outcome of this study is postoperative pain (50). Unfortunately, results are not yet published. A multi-institutional RCT (Canada, United States, and France, NCT02617186) randomizing patients with early-stage lung cancer to VATS or robotic resection is planned to be completed in 2031 (51). This trial's primary outcome is difference in health-related quality of life (HRQOL) scores (51). The Italian ROMAN study (prospective, randomized, multicenter study on video thoracoscopic *vs.* robotic approach for lobectomy or anatomical segmentectomy in patients affected with lung cancer) is currently enrolling patients and is planned to be completed in 2023 (52). The ROMAN trial's primary outcomes are intraoperative and postoperative complications (52). Finally, the Brazilian "Prospective analysis of robot-assisted surgery" trial (NCT02292914) is a prospective RCT recruiting from 5 different specialties including the digestive system, urology, gynecology, head/neck, and thoracic surgery (53). Specifically, within the thoracic category, the RCT is recruiting patients who undergo lobectomy (53). The primary outcome is postoperative complications (53).

Meta-analyses

There are some meta-analyses comparing RL, VL, and OL (*Table 2*). Most of these analyses showed equivalent or better perioperative outcomes for patients undergoing RL as compared to VL or OL. An early meta-analysis by O'sullivan *et al.* analyzed the three surgical approaches in a pairwise comparison (OL *vs.* VL, OL *vs.* RL, RL *vs.* VL) (10). This study found that RL was superior OL in terms of complications [odds ratio (OR) 0.67, 95% CI: 0.58–0.76, P<0.005] and hospital stay (WMD −1.4, 95% CI: −1.96 to 0.85, P<0.005) (10). A systematic review and meta-analysis by Aiolfi *et al.* found that RL and VL had less perioperative morbidity and 30-day mortality when compared to OL (11). Amongst the meta-analyses comparing all three modalities, only Aiolfi *et al.* studied long-term survival and found that the modalities had equivalent 5-year overall survival (11). This was also confirmed in two recent meta-analyses comparing RL to VL (4,47).

The included studies within these more recent meta-analyses comparing RL and VL have significant overlap; however, Ma *et al.* analyzed a more contemporary core group of studies (between publication years 2015–2020) (47). In contrast, Wu *et al.* included studies published from 2011–

Table 2 Meta-analyses comparing RL, VL, and OL

Author	Year	Groups	Number of studies	Overall survival	Disease-free survival	30-day mortality	Postoperative complications	Lymph node harvest	Conversion to open (RL *vs.* VL)
Ma (47)	2021	RL, VL	18	Equal	Equal	Equal	RL < VL	RL > VL	RL < VL
Wu (4)	2021	RL, VL	25	Equal	RL > VL	RL < VL	Equal	Equal	Equal
Aiolfi (11)	2021	RL, VL, OL	34	Equal	N/A	RL < OL; VL < OL	RL = VL < OL	RL > VL; OL > VL	Equal
Hu (54)	2020	RL, VL, OL	32	N/A	N/A	N/A	RL < VL; RL = OL	Equal	Equal
O'Sullivan (10)	2019	RL, VL, OL	13	N/A	N/A	RL < VL; RL < OL	RL = VL < OL	RL < VL; RL = OL	Equal
Liang (45)	2018	RL, VL	14	N/A	N/A	RL < VL	Equal	Equal	Equal
Wei (44)	2017	RL, VL	12	N/A	N/A	RL < VL	Equal	Equal	Equal

RL, robotic-assisted lobectomy; VL, video-assisted thoracoscopic surgery lobectomy; OL, open lobectomy.

2020 (4). Both studies found equivalent overall survival but diverged in disease-free survival (4,47). Wu *et al.* found RL had longer disease-free survival as compared to VL (HR: 0.76; 95% CI: 0.59–0.97, P=0.03) (4). This trend was also found in overall survival; however, this did not reach statistical significance. Wu *et al.* also found decreased 30-day mortality in the RL group, which was found to be equivalent in Ma *et al.*'s analysis (4,47).

Interestingly, the more contemporary analysis by Ma *et al.* found that RL was associated with less blood loss (WMD 50.40, P=0.01), lower conversion rate (OR 0.50, P<0.001), more harvested lymph node and stations (WMD 1.72, P=0.002; WMD 0.51, P=0.005), shorter chest tube drainage (WMD −0.61, P>0.001), shorter hospital stay (WMD −1.12, P<0.001), lower complication rate (OR 0.90, P=0.02), and lower recurrence rate (OR 0.51, P<0.001) (47). As with the RVlob trial, this meta-analysis did note a higher cost with RL as compared to VL (WMD $3,909, P<0.001) (47). In another comprehensive meta-analysis conducted by Hu *et al.*, they observed a reduced occurrence of postoperative complications in the RL group as compared to the VATS group (54).

Conclusions

The superiority of a minimally invasive approach (RL and VL) to OL is well established. Minimally invasive approaches have less complications and decreased LOS. As such, current society guidelines recommend a minimally invasive approach, when possible, particularly for early-stage NSCLC. RL is a safe alternative to VL and OL with equivalent oncologic long-term survival outcomes and likely improved lymph node removal. Compared to VL, some data indicate that RL may also have decreased conversion to open, decreased complications, decreased recurrence, and improved disease-free survival. The increased operative time appears negligible after an initial learning curve. Cost is still a concern; however, some encouraging data are showing similar costs between RL and VL. As technology evolves and there are additional robotic platforms on the market, it is expected that cost will ultimately decrease. We look forward to additional contemporary outcomes data pertaining to robotic lung resection, particularly future RCTs to further inform the data available.

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