

META-ANALYSIS

Comparing the Efficacy of Video-Assisted Thoracoscopic Surgery and Open Thoracotomy in Sleeve Lobectomy for the Treatment of Central-Type Non-small Cell Lung Cancer: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective • Central-type Non-small Cell Lung Cancer (NSCLC) treatment involves different surgical techniques, including Video-Assisted Thoracoscopic Surgery (VATS) and Open Thoracotomy Sleeve Lobectomy. However, there remains a lack of consensus on the most effective treatment modality.

Methods • This study strictly adhered to PRISMA guidelines. Four electronic databases were searched without time or language limitation, and studies comparing VATS and Open Thoracotomy in patients with central-type NSCLC undergoing sleeve lobectomy were included. Primary outcomes were perioperative outcomes (blood loss, operation time, intraoperative lymph node dissection count, postoperative hospital stay, and complication rates), 3-year Progression-Free Survival (PFS) rate, and Overall Survival (OS) rate.

Results • The meta-analysis included six studies with 569 patients. VATS was associated with longer operation time [SMD = 0.75, 95% CI (0.29, 1.21)], less intraoperative

blood loss [SMD = -0.23; 95% CI (-0.44, -0.01)], and shorter hospital stay [SMD = -0.53; 95% CI (-0.73, -0.34)]. There were no significant differences in the number of lymph nodes dissected, postoperative complications, and 3-year PFS and OS rates between the two groups.

Conclusions • VATS sleeve lobectomy for central-type NSCLC results in less surgical trauma and quicker postoperative recovery without adversely impacting tumor prognosis compared to open thoracotomy sleeve lobectomy. Despite a longer operation time, VATS could be considered an alternative to open thoracotomy sleeve lobectomy. VATS sleeve lobectomy is a safe and effective alternative to open thoracotomy in treating central-type NSCLC, as it results in less surgical trauma and quicker postoperative recovery without impacting tumor prognosis negatively. More well-designed randomized controlled trials are required to verify these findings. (*Altern Ther Health Med.* 2024;30(6):76-81).

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INTRODUCTION

Lung cancer continues to be a dominant global health concern, leading both in terms of incidence and mortality among all malignancies.¹ This disease is traditionally classified into small cell lung cancer and non-small cell lung cancer (NSCLC), with the latter encompassing the majority of cases. Despite extensive research and evolution in medical technologies over recent decades, the prognosis for NSCLC

remains dishearteningly poor. The five-year overall survival (OS) rate stands at a mere 19%, a statistic that starkly reveals the urgent need for improvements in detection and treatment modalities.² The low survival rate of NSCLC is primarily due to late-stage diagnosis, rapid spread, and limited treatment options. Early detection and innovative treatments like targeted therapies and immunotherapies are crucial for improving survival rates. Addressing risk factors like smoking and environmental exposures through public health initiatives is also vital. Enhanced survival rates will not only benefit individual patients but also lessen the disease burden and reduce healthcare costs, potentially boosting productivity in a country. Among the myriad of NSCLC subtypes, central-type NSCLC presents itself with relatively high frequency. To manage these tumors, current clinical guidelines endorse anatomical resections that preserve lung tissue, also known as sleeve lobectomy.³ Assuming anatomical feasibility and a

capacity to achieve margin-negative resection, sleeve lobectomy is usually favored over pneumonectomy due to its better preservation of pulmonary function.⁴

Historically, sleeve lobectomy was performed through an open thoracotomy approach, which, while effective, carries a considerable burden of morbidity due to its invasive nature. However, the dawn of the new millennium witnessed a significant evolution in surgical techniques with Santambrogio et al. reporting the first sleeve lobectomy through video-assisted thoracoscopic surgery (VATS) in 2002.⁵ This minimally invasive technique has potential advantages in reducing surgical trauma and promoting quicker recovery, yet it demands greater technical proficiency, particularly concerning bronchial anastomosis. The comparison between VATS and open thoracotomy for sleeve lobectomy has been the focus of numerous studies,⁶⁻⁸ aimed at elucidating the best practice in managing central-type NSCLC. However, the evidence generated by these studies has been hampered by the inherent limitations of small sample sizes and potential selection bias. These confounding factors engender uncertainty regarding the relative therapeutic benefits of the two surgical techniques and necessitate a more comprehensive review of the current evidence base.⁶

In response to this need, our study aims to compile and evaluate the existing body of research through a systematic review and meta-analysis. We intend to scrutinize the perioperative and long-term oncologic outcomes between VATS sleeve lobectomy and open thoracotomy sleeve lobectomy for the treatment of central-type NSCLC. This endeavor seeks to establish a more robust evidence base to guide clinical decision-making and to propel the application of VATS in this context. By comparing the two surgical methods, we aim to clarify the benefits, drawbacks, and overall efficacy of VATS as compared to traditional open thoracotomy, thereby informing surgical decision-making processes and enhancing patient outcomes. Furthermore, we anticipate that our findings will stimulate further research and innovation in this field, with the ultimate goal of improving survival and quality of life for patients diagnosed with central-type NSCLC.

MATERIALS AND METHODS

Search strategy

During the systematic review process, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.⁹ On May 16, 2023, a search was conducted in four electronic databases, namely, PubMed, Embase, Web of Science, and Cochrane Library, without imposing any temporal restrictions. The specific search terms used were: (“video-assisted thoracic surgery” OR “videoassisted” OR “thoracoscopic” OR “minimally invasive”) AND (“thoracotomy” OR “open”) AND (“lung cancer” OR “lung carcinoma”) AND (“sleeve” OR “bronchoplasty” OR “bronchoplastic”). There were no restrictions imposed on the language used. The manual screening of reference lists of pertinent articles was conducted to identify any potential additional records.

Inclusion criteria

The systematic review required that the studies met the specified criteria: 1) Studies that focus on patients with central-type NSCLC who have undergone sleeve lobectomy; 2) Studies that compare the efficacy of video-assisted thoracoscopic sleeve lobectomy and open thoracotomy sleeve lobectomy; 3) Studies that provide sufficient data for analysis.

The criteria for exclusion were as follows: 1) Literature that has been published multiple times; 2) Studies that have incomplete or unclear analytical data and inconsistent outcome indicators; 3) The types of literature that fall under the category of non-systematic reviews including case reports, commentaries, expert opinions, and narrative reviews.

Data extraction

A form for data collection that adhered to standardization was devised to extract pertinent information from the studies that were included in the analysis. The data extracted from each study encompassed the first author's name, year of publication, and patient age. Furthermore, the perioperative outcomes that were gathered include blood loss (measured in mL), duration of operation (measured in minutes), number of lymph nodes dissected during surgery, length of postoperative hospital stay (measured in days), and rates of complications. The text was utilized to extract the 3-year progression-free survival rate (PFS) and overall survival (OS) rate.

Quality assessment

Two independent reviewers assessed the included quality of the studies using the Newcastle-Ottawa Scale (NOS),¹⁰ which comprises nine components distributed across three categories, which evaluate potential sources of bias, including selection, comparability, and outcome. Subsequently, a quality score ranging from 0 to 9 was allocated to each study. Research works that obtained a score ranging from 0 to 3 were classified as studies of low quality, while those that scored between 4 and 6 were deemed to be of moderate quality. Studies that garnered a score of 7 to 9 were classified as high-quality research works. The implementation of a structured quality assessment approach guarantees a rigorous and uniform appraisal of the studies that have been incorporated.

Statistical analyses

The study employed a standardized mean difference (SMD) with a 95% confidence interval (CI) to compare continuous variables, such as blood loss, operation time, intraoperative lymph node dissection count, and postoperative hospital stay. Risk ratio (RR) with a 95% CI was utilized for dichotomous data, specifically for complication rates, 3-year progression-free survival rates, and overall survival rates. The variability among the studies was evaluated using the Q-statistic and I^2 test. In the cases where there was notable heterogeneity (indicated by $P < 0.1$ or an I^2 value greater than 50%), a random effects model was utilized. Conversely, a fixed effects model was applied when heterogeneity was not significant. To

Table 1. Characteristics of Studies Included in the Meta-Analysis

Author	Year	Patient Description	Age (Range, Years)	Follow-Up (Months)	VATS Sleeve Lobectomy Group	Open Thoracotomy Sleeve Lobectomy Group	Included Factors
Xie, Deng	2021	Patients undergoing sleeve lobectomy for stage I-IIIB central NSCLC	Median: 63 (38-83)	Median: 32.2	72	116	Age, gender, Charlson Comorbidity Index, FEV1, FEV1% predicted, smoking history, lung cancer histology, poorly differentiated cancer, surgeon, and all TNM stages
Xie, Zhang	2021	Patients undergoing sleeve lobectomy for stage I-IIIB central NSCLC	Mean: 61.3 (VATS group), 62.7 (Open group)	Median: 25 (both groups)	31	102	Age, gender, Charlson Comorbidity Index, FEV1, FEV1% predicted, smoking history, lung cancer histology, poorly differentiated cancer, surgeon, and all TNM stages
Qiu	2020	Patients undergoing sleeve lobectomy for stage I-IIIB central NSCLC	Mean: 61.7 (VATS group), 61.3 (Open group)	Median: 27.0 (VATS group), 24.0 (Open group)	38	39	Age, gender, body condition, CCI, BMI, FEV1, smoking history, histologic type, clinical T stage, and clinical N stage
Wu	2019	Patients undergoing single-port double sleeve lobectomy for stage IIIB central NSCLC	Mean: 62 (VATS group), 61 (Open group)	N/A	21	21	N/A
Zhou	2015	Patients undergoing sleeve lobectomy for stage I-IIIA central NSCLC	Mean: 60.5 (VATS group), 62.5 (Open group)	Median: 34 (both groups)	10	41	N/A
Cao	2019	Patients undergoing sleeve lobectomy for stage I-IIIA central NSCLC	Mean: 60.7 (VATS group), 60.5 (Open group)	Median: 44.0	39	39	Age, smoking history, tumor location, tumor size, BMI, FEV1, CO diffusing capacity, pleural and vascular invasion, histologic type, R0 resection, pathologic TNM stage, complications, and adjuvant therapy

conduct sensitivity analysis, we sequentially excluded individual studies to assess the resilience of our findings. Ultimately, the assessment of publication bias was conducted through the utilization of funnel plots, and subsequently evaluated via the Begg’s test and Egger’s test. A statistically significant result was defined as having $P < .05$. The data analysis was conducted using Stata version 17, developed by StataCorp (College Station, TX, USA).

RESULTS

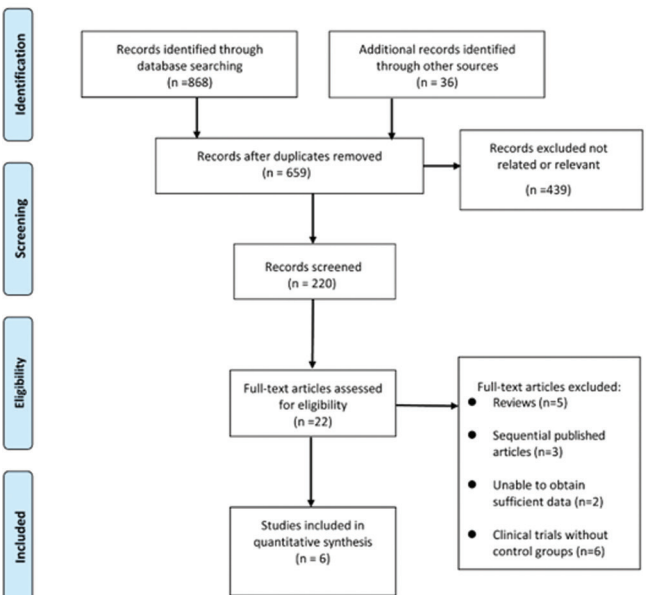
Search results and study selection

Upon conducting an initial search of electronic databases, a total of 904 relevant literature sources were identified. Following the elimination of redundant literature, careful examination of titles and abstracts, and rigorous adherence to the established inclusion and exclusion criteria, a total of 22 pertinent sources were identified, while 16 were deemed ineligible for further review. Ultimately, a total of six articles were incorporated. Figure 1 depicts the process and outcomes of the literature screening.

Study characteristics

The studies included in this meta-analysis consist of six papers, spanning from 2015 to 2021, all originating from China. The studies primarily examined patients undergoing sleeve lobectomy for stage I-IIIB central NSCLC, except for one study by Wu,⁷ which focused on patients undergoing single-port double sleeve lobectomy for stage IIIB central NSCLC. The age of the patients varied across the studies, with a median of 63 years (ranging from 38 to 83) in the oldest study by Xie,¹⁸ to means ranging from approximately 60.5 to 62 years in the remaining studies. Follow-up periods varied among studies, with medians ranging from 25 months to 44 months, except for the study by Wu, which did not provide follow-up data. Each study compared patients undergoing VATS sleeve lobectomy with those undergoing open thoracotomy sleeve lobectomy, with group sizes ranging from 10 to 116 patients in the VATS groups and from 21 to 116 in the open thoracotomy groups (Table 1).

Figure 1. Selection Process of the Included Studies



The included factors contributing to the difference between VATS and open thoracotomy sleeve lobectomy varied among studies as well. Factors considered across multiple studies included age, gender, Charlson Comorbidity Index, forced expiratory volume in 1 second (FEV1), FEV1% predicted, smoking history, lung cancer histology, body condition, body mass index (BMI), clinical T stage, and clinical N stage. Some unique factors were also considered in individual studies, such as surgeon, all TNM stages, TNM stage, complications, adjuvant therapy, and poorly differentiated cancer (Table 1).

Results of quality assessment

NOS was utilized to evaluate the methodological rigor of each study under consideration. Overall, three research studies obtained a score of 8 points, while another three studies achieved a score of 9 points. Blinding was not implemented in any of the studies, and there was a lack of indication of

Table 2. The Quality Assessment According to the NOS of Each Cohort Study

Study	selection				comparability	outcome			Total score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome		Assessment of outcome	Was follow-up long enough	Adequacy of follow-up of cohorts	
Xie, Deng	*	*	*	*	**	*	*	*	9
Xie, Zhang	*	*	*	*	**	*	*	*	8
Qiu	*	*	*	*	**	*	*	*	9
Wu	*	*	*	*	**	*	*	*	8
Zhou	*	*	*	*	**	*	*	*	9
Cao	*	*	*	*	*	*	*	*	8

Abbreviation: NOS: Newcastle-Ottawa Scale

Figure 2. Comparison of Operation Time Between VATS Group and Open Thoracotomy Group

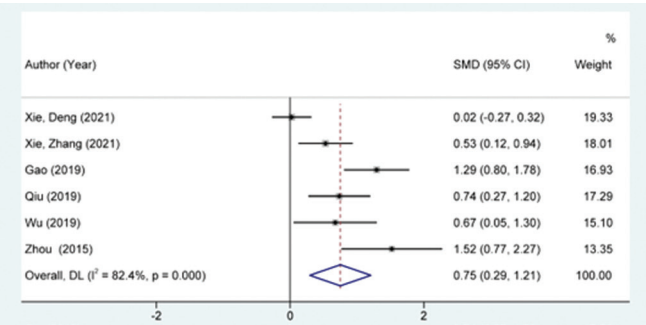


Figure 3. Comparison of Intraoperative Lymph Node Dissection Count Between VATS Group and Open Thoracotomy Group

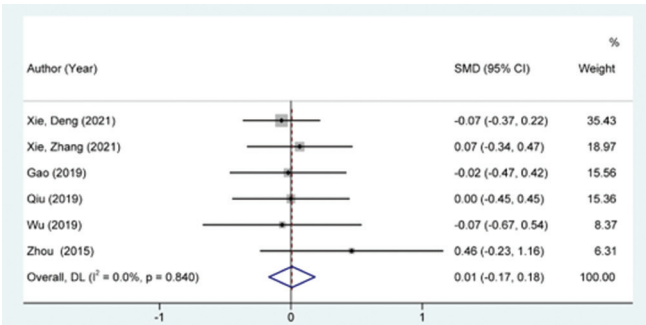


Figure 4. Comparison of Intraoperative Blood Loss Between VATS Group and Open Thoracotomy Group

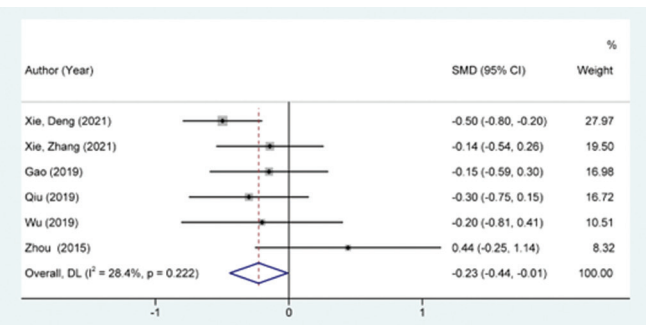


Figure 5. Comparison of Postoperative Hospital Stay Between VATS Group and Open Thoracotomy Group

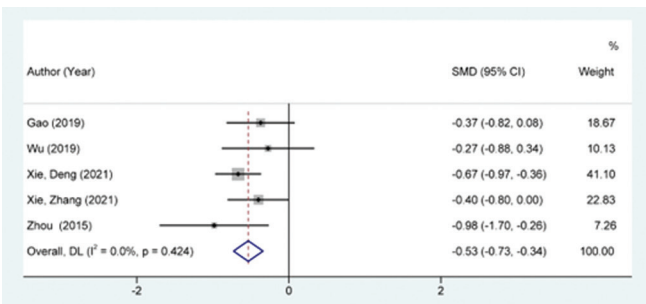
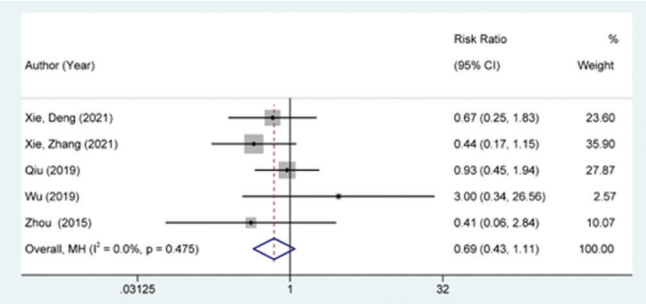


Figure 6. Comparison of Postoperative Complication Rates Between VATS Group and Open Thoracotomy Group

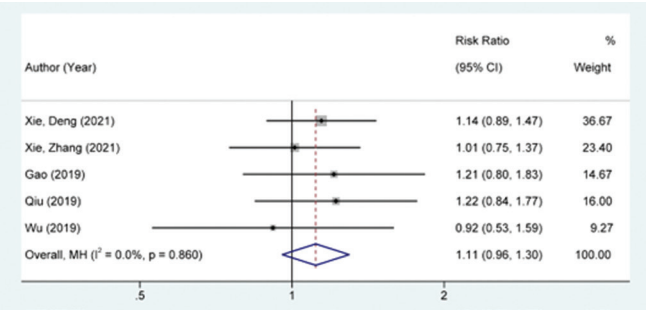


allocation concealment. There was no apparent presence of funding biases in any of the studies. No studies were found to have incomplete outcome data, early stoppage bias, or baseline imbalances. Table 2 provides a summary of the potential risks associated with bias and their corresponding ratios.

Short-term Efficacy

This meta-analysis incorporated six studies with a combined total of 569 patients, with 211 patients undergoing VATS sleeve lobectomy and 358 patients undergoing open thoracotomy sleeve lobectomy. In terms of intraoperative outcomes, the VATS group had a significantly longer operation time than the open thoracotomy group [SMD = 0.75; 95% CI = (0.29, 1.21); $P < .001$, Figure 2]. However, there was no statistically significant difference in the number of lymph nodes dissected during surgery between the two groups [SMD = 0.01; 95% CI = (-0.17, 0.18); $P = .65$, Figure 3]. Furthermore, the VATS group demonstrated a significant reduction in intraoperative blood loss [SMD = -0.23; 95% CI = (-0.44, -0.01); $P < .05$, Figure 4]. In postoperative outcomes, the VATS group exhibited a significantly shorter hospital stay compared to the open thoracotomy group [SMD = -0.53; 95% CI = (-0.73, -0.34); $P < .001$, Figure 5]. The occurrence of postoperative complications was not statistically different between the VATS and open thoracotomy groups [RR = 0.69; 95% CI = (0.43, 1.11); $P = .36$, Figure 6].

Figure 7. Comparison of 3-Year Disease Progression Rate Between VATS Group and Open Thoracotomy Group



Long-term Efficacy

As for long-term efficacy, the three-year OS rates and PFS rates were compared between the VATS and open thoracotomy groups. The VATS group exhibited a three-year OS rate of 72.6% and a PFS rate of 61.5%, whereas these rates were 68.1% and 58.6% respectively in the open thoracotomy group. However, there were no significant differences detected between the two groups in terms of the three-year disease progression rate [Odds Ratio (OR) = 1.11; 95% CI = (0.96, 1.30); $P = .35$, Figure 7] and the three-year survival rate [OR = 1.06; 95% CI = (0.95, 1.19); $P = .58$, Figure 8].

Publication bias

The funnel plots generated from the observed study exhibited symmetry, and no statistically significant evidence of publication bias was observed in the corresponding funnel plots (Figure 9). The absence of significant publication bias was also observed through Begg's and Egger's tests ($P_{\text{Begg}} = .651$, $P_{\text{Egger}} = .786$).

DISCUSSION

Sleeve lobectomy has become a mainstay in the treatment of central-type NSCLC. Historically, the procedure has been conducted via open thoracotomy. However, with the advent of minimally invasive thoracic surgery, there has been a shift towards performing sleeve lobectomy via VATS and even robot-assisted surgery.¹¹⁻¹³ Yet, the current body of literature is insufficient in terms of comparing the efficacy of VATS sleeve lobectomy and open thoracotomy sleeve lobectomy. This inadequacy gives rise to inquiries regarding the feasibility of VATS sleeve lobectomy as a substitute for the conventional approach.^{14,15} In light of the necessity for substantiation, our investigation aimed to conduct a methodical review and meta-analysis of current research about the application of VATS sleeve lobectomy for the management of central-type NSCLC. Our meta-analysis comprised six cohort studies, encompassing a total of 569 patients. The study revealed that the group subjected to VATS exhibited a statistically significant reduction in blood loss and shorter duration of hospitalization compared to the group that underwent open thoracotomy. The study found no statistically significant distinctions between VATS and open thoracotomy concerning intraoperative lymph node dissection, complication rates,

Figure 8. Comparison of 3-Year Survival Rate Between VATS Group and Open Thoracotomy Group

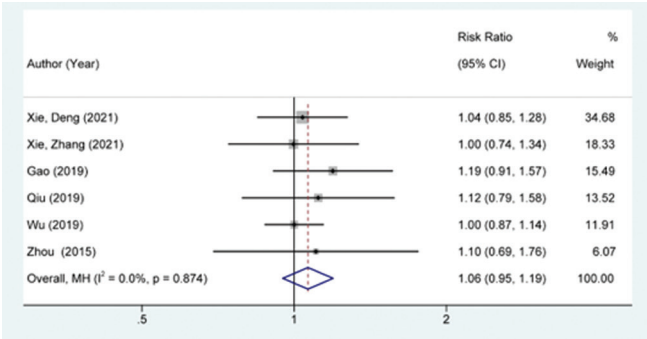
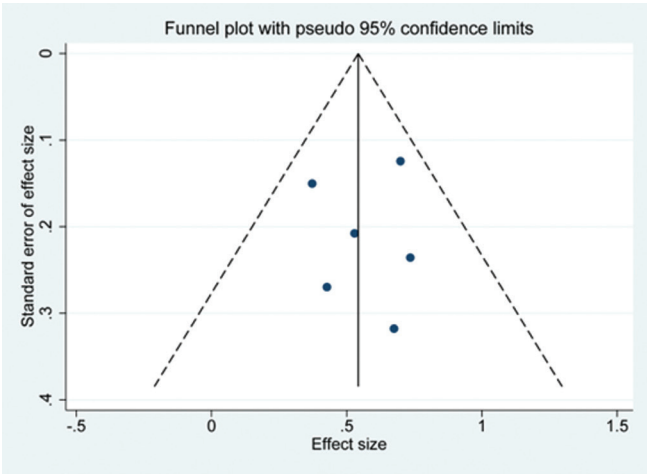


Figure 9. Funnel Plot for Publication Bias in All Included Studies



3-year OS, and PFS rates. However, the VATS group might require a longer operative time.

Our results highlight that while VATS sleeve lobectomy is more technically demanding compared to open thoracotomy sleeve lobectomy, it can result in less surgical trauma and enhanced postoperative recovery without compromising long-term tumor outcomes. This is congruent with previous evidence suggesting that VATS for lung cancer surgery can lead to lower postoperative complication rates, shorter hospital stays, and quicker functional recovery compared to open thoracotomy lung surgery. Furthermore, VATS has additional advantages over open thoracotomy, including reduced incisional pain, better preservation of thoracic and respiratory function, shortened hospital stays, decreased postoperative morbidity, and improved adherence to adjuvant chemotherapy.¹⁶

Meanwhile, studies have indicated that VATS sleeve lobectomy can significantly reduce blood loss during the operation, aligning with the findings of most previous research. This reduced blood loss suggests that VATS sleeve lobectomy can remarkably diminish surgical trauma for patients with central-type NSCLC. In addition, patients undergoing VATS sleeve lobectomy have demonstrated a notably reduced hospital stay post-surgery, indicating an improved recovery speed facilitated by this procedure. The

quality of lymph node dissection, a crucial component of lung cancer surgery, is a primary concern in minimally invasive thoracic oncology procedures.¹⁷ In our study, the total number of lymph nodes removed during VATS sleeve lobectomy was comparable to that in open thoracotomy.^{6,18,19} Moreover, the occurrence of major postoperative complications, such as bronchopleural fistula and pneumonia, showed no statistically significant difference between the two procedures. Therefore, the quality and therapeutic efficacy of sleeve lobectomy conducted via VATS are similar to those achieved by open thoracotomy.

Additionally, patients undergoing VATS sleeve lobectomy have shown a comparable long-term survival rate to those undergoing open sleeve lobectomy. This further suggests that VATS sleeve lobectomy satisfies the same surgical quality and therapeutic effectiveness as open sleeve lobectomy, making it a recommendable procedure for central-type NSCLC.²⁰ Nevertheless, a disadvantage associated with VATS sleeve lobectomy is that it may necessitate a greater amount of surgical time in contrast to open sleeve lobectomy. Prior research suggests that an extended duration of surgery is a standalone factor in forecasting pulmonary complications following a surgical procedure.²¹ Hence, it appears crucial to decrease the duration of the VATS sleeve lobectomy procedure. In our experience, the time required for VATS sleeve lobectomy was indeed longer initially but as surgeons performed more of these procedures, the operation time significantly decreased. Prior studies found that the operation time for VATS sleeve lobectomy was significantly prolonged, due to their limited sample sizes (N <40). However, a study by Dr. Xie et al. on 103 cases of VATS sleeve lobectomy found similar operation times to open sleeve lobectomy, possibly indicating a learning curve for VATS sleeve lobectomy.¹⁹

Our study had several limitations. The meta-analysis conducted was hindered in terms of quality and validity as it relied on retrospective cohort studies that provided low-quality evidence. Furthermore, the restricted sample size within our meta-analysis may potentially impact the outcomes. Moreover, the retrospective comparisons between VATS sleeve lobectomy and open sleeve lobectomy may potentially lead to patient selection bias. Subgroup analyses based on the type of sleeve lobectomy, TNM stage, and Charlson Comorbidity Index were not feasible due to the absence of pertinent data in the studies that were incorporated.

CONCLUSION

VATS sleeve lobectomy leads to less surgical trauma, quicker postoperative recovery, and does not adversely impact tumor prognosis compared to open thoracotomy sleeve lobectomy. Although VATS sleeve lobectomy might require longer operative time, it can serve as an alternative to open thoracotomy sleeve lobectomy for central-type NSCLC. However, more well-designed randomized controlled trials are required to verify these findings.

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AUTHOR DISCLOSURE STATEMENT

The authors have no potential conflicts of interest to report relevant to this article.

CONTRIBUTION OF AUTHORS

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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