



Does single-port video-assisted thoracic lobectomy have favorable perioperative results for non-small cell lung cancer compared with multi-port approach? A systematic review and meta-analysis

Shiyou Wei, Nan Chen, Chengwu Liu, Kejia Zhao, Longfei Zhu, Lunxu Liu

Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu 610041, China

Contributions: (I) Conception and design: S Wei, N Chen, L Liu; (II) Administrative support: L Liu; (III) Provision of study materials or patients: S Wei, N Chen; (IV) Collection and assembly of data: S Wei, N Chen; (V) Data analysis and interpretation: S Wei, N Chen, C Liu, K Zhao, L Zhu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Lunxu Liu, Department of Thoracic Surgery, West China Hospital, Sichuan University, No. 37, Guoxue Alley, Chengdu 610041, China. Email: lunxu_liu@aliyun.com.

Background: The preliminary clinical outcomes and short-term results of single-port video-assisted thoracic surgery (VATS) are encouraging. This study was aimed to assess whether single-port VATS lobectomy have favorable perioperative results for non-small cell lung cancer (NSCLC) compared with multi-port approach.

Methods: An electronic search of five databases was performed to find out relevant comparative studies. Outcome measures included operative time, perioperative blood loss, conversion rate, the number of lymph nodes dissection, postoperative pain, chest drainage duration, length of hospital stay, overall postoperative morbidity and mortality. Relative risk (RR) and standard mean difference (SMD) with their 95% confidence intervals (CI) were calculated by means of Stata version 12.0.

Results: Eight retrospective observational studies met the inclusion criteria, with a total of 1,257 patients (482 in single-port group and 775 in multi-port group). Meta-analysis showed that single-port VATS lobectomy was associated with less blood loss (SMD = -0.24, 95% CI: -0.48 to 0, P=0.047) and lower overall postoperative morbidity (RR=0.64, 95% CI: 0.45 to 0.92, P=0.015), but higher conversion rate (RR =2.02, 95% CI: 1.10 to 3.73, P=0.024) when compared to multi-port approach. However, when propensity-matched data were analyzed, single-port approach was only associated with less blood loss (SMD = -0.48, 95% CI: -0.69 to -0.25, P<0.001) and postoperative pain (SMD = -0.59, 95% CI: 0.23 to 0.95, P=0.001) when compared to multi-port approach.

Conclusions: Single-port VATS lobectomy is a safe and feasible procedure for patients with NSCLC in selected cases. But based on the present findings, there is still insufficient evidence to prove its superior short-term effects than multi-port approach.

Keywords: Single-port surgery; video-assisted thoracic surgery (VATS); lobectomy; non-small cell lung cancer (NSCLC)

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Introduction

Lung cancer was the first cause of cancer death among male and female worldwide (1). Surgical resection remains the mainstay therapy for patients with early stage non-small cell lung cancer (NSCLC). Soon after the first adoption

of video-assisted thoracic surgery (VATS) lobectomy in early 1990s (2,3), growing evidence has demonstrated that VATS lobectomy is an alternative surgical approach for patients with early stage NSCLC, with regards to reduced postoperative pain, short length of hospital stay

and even improved long-term survival when compared with open lobectomy (4-7). Even though, no standardized thoroscopic technique has been established yet. Generally, most thoracic surgeons would like to take two, three or four ports VATS to perform lobectomy.

With the development of surgical techniques and instruments, single-port or uniportal VATS was introduced to the minimally invasive thoracic surgery gradually. Since the first report of single-port VATS lobectomy in 2011 (8,9), several studies have suggested that single-port VATS lobectomy is a safe and feasible surgical procedure for patients with lung cancer (10-13). Besides, some studies even showed that single-port VATS decreased postoperative pain and improved patients' satisfaction when compared to conventional multi-port VATS (14,15). The preliminary clinical outcomes and short- and mid-term results of single-port VATS are encouraging (16,17). But whether single-port VATS lobectomy has favorable perioperative results for NSCLC compared with multi-port approach is still controversial. Thus, we take an attempt to perform the present systematic review and meta-analysis to evaluate the safety and perioperative efficacy of single-port VATS lobectomy for patients with NSCLC.

Methods

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (18).

Search strategy

Published studies comparing single-port VATS to multi-port VATS lobectomy were identified by a comprehensive electronic search of PubMed, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and *ClinicalTrials.gov* up to December 2016. The search terms 'single port' OR 'single incision' OR 'uniport' OR 'single access' OR 'single hole' OR 'one port' OR 'one incision' AND 'video-assisted thoracic surgery' OR 'VATS' OR 'thoroscopic surgery' were used to identify eligible comparative studies. In addition, we reviewed the reference lists of articles to identify further relevant citations.

Study selection

After removing the duplicates, the titles, abstracts and full-

texts of references were evaluated by two reviewers (Shiyu Wei and Nan Chen) independently to find out the relevant studies. Studies were included if they were randomized controlled trials (RCT) or nonrandomized comparative studies comparing single-port VATS lobectomy to multi-port procedure for patients with NSCLC. Studies pertaining to single-port segmentectomy or wedge resection were excluded, since segmentectomy was technically more demanding than lobectomy. We also excluded studies that didn't include a comparative group or didn't provide at least one outcome of interest. Regarding duplicate data from the same center or hospital, we only included the latest and most updated article.

Data extraction and quality assessment

Two reviewers (Shiyu Wei and Nan Chen) independently assessed each included study and conducted data abstraction and quality assessment. Patients undergoing thoroscopic lobectomy through a single incision were defined as single-port group and those who received thoroscopic lobectomy performed by three or two incisions were defined as multi-port group. The outcome measures for this meta-analysis were operative time, perioperative blood loss, conversion rate, the number of lymph nodes dissection, postoperative pain, chest drainage duration, length of hospital stay, overall postoperative morbidity and mortality. The Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias for each included observational study. Studies with scores more than 7 were considered to be high quality; conversely, those with scores less than 3 were thought to be low quality. Any disagreements between the two reviewers were resolved by group discussion and the final determinations were performed by a senior reviewer (LLX).

Statistical analysis

Meta-analysis was performed by pooling the results of included studies. Pooled analysis for dichotomous variables such as overall postoperative morbidity, and conversion rate, was conducted by using the relative risks (RR) and their 95% confidence intervals (CI) with the Mantel-Haenszel method. And the standard mean differences (SMD) and their 95% CIs with Inverse-Variance method were calculated as the summary statistic for continuous variables such as operative time, perioperative blood loss and length of hospital stay. But if pooled analysis was impossible to perform as a result of heterogeneity in

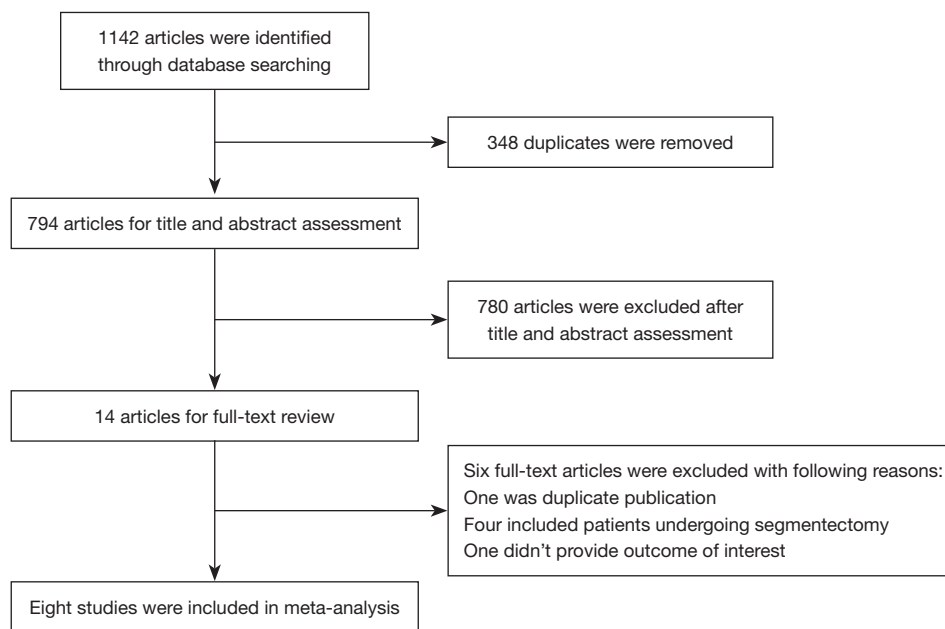


Figure 1 Flow chart summarizing the systematic literature selection.

measurement methods among studies, descriptive analysis would be used to present the results of studies. And when studies reported results as median and range or interquartile range, these data were not included to conduct pooled analysis. All pooled outcome measures were determined by using random-effect models since the interventions varied among included studies. Statistical heterogeneity among the studies was assessed by means of a standard Cochrane's Q test with a significance level of $\alpha=0.10$. The I^2 statistic test was performed to further examine clinical heterogeneity. $I^2 \geq 50\%$ was considered to indicate substantial heterogeneity. All P values were two-tailed, with $P < 0.05$ suggesting statistical significant. All statistical analysis was carried out using Stata version 12.0 (StataCorp, College Station, TX, USA).

Results

Summary of included studies

A flow chart summarizing the systematic literature selection is shown in *Figure 1*. A total of 1,142 publications (PubMed 934 publications, Embase 201 publications, Cochrane library three publications, and *ClinicalTrials.gov* four publications) were identified through the electronic searches and 348 of those were removing as a result of duplicates. After titles and abstracts review, 14 articles were selected for

further evaluation. Finally, eight retrospective observational studies were included in this meta-analysis (19-26). A total of 1,257 patients were included in this meta-analysis, 482 (38.4%) in single-port group and 775 (61.6%) in multi-port group. Of these studies, seven studies were conducted in Asia and only one study in Europe. Two of these studies presented propensity-matched data. The quality of included studies assessed by the NOS was acceptable, with mean NOS scores of 6.5. For most studies, the methodological quality with regard to cohort selection and comparability was adequate. However, the follow-up periods were limited for all studies. The detailed characteristics and risk of bias assessment of included studies were shown in *Table 1*.

Assessment of perioperative outcomes

There was a statistically significant less perioperative blood loss for patients in single-port group compared to multi-port group (SMD = -0.24, 95% CI: -0.48 to 0, $P=0.047$, *Figure 2*). And single-port VATS lobectomy was significantly associated with lower overall postoperative morbidity rate than multi-port approach (RR=0.64, 95% CI: 0.45 to 0.92, $P=0.015$, *Figure 3*). But single-port approach was significantly associated with higher conversion rate than multi-port approach (RR =2.02, 95% CI: 1.10 to 3.73, $P=0.024$, *Figure 4*).

Table 1 Characteristics and risk of bias assessment of included trials

Author and year	Location	Study design	Study period	No. of patients	Age (years old)	Gender (male/female)	Surgical techniques	Lebo distribution (left/right)	Pathologic stage (I/II/III/IV)	Surgeons	Quality scores
Meelhay 2015	UK	ROS	August 2012 to December 2013	S: 15 M: 95	S: 70 M: 69	S: 8/7 M: 49/46	S: single 4–5 cm incision M: three 1–5 cm incisions	S: NA M: NA	S: NA M: NA	Three surgeons	6
Zhu 2015	China	ROS	August 2014 to October 2014	S: 33 M: 49	S: 62 M: 59	S: 11/22 M: 19/30	S: single 3.5–4.5 cm incision M: three 1.4–4 cm incisions	S: 14/19 M: 20/29	S: 23/8/2/0 M: 34/11/4/0	NA	7
Liu 2016	Taiwan	ROS	May 2005 to December 2014	S: 100 M: 342	NA	S: 39/61 M: 150/192	S: single incision M: two or three incisions	S: 29/71 M: 100/241	S: 62/–/– M: 230/–/–	Two surgeons	6
Shen 2016	China	ROS	October 2013 to October 2014	S: 100 M: 100	S: 62 M: 61	S: 56/44 M: 55/45	S: single 3.5 cm incision M: three 1–4 cm incisions	S: NA M: NA	S: NA M: NA	Different surgeons	7
Chung 2015	Korea	ROS	January 2013 to February 2014	S: 90 M: 60	S: 61 M: 63	S: 50/40 M: 34/26	S: single 3.5–5 cm incision M: three 0.5–5 cm incisions	S: 46/44 M: 29/31	S: 53/10/14/13 M: 36/8/8/6	single surgeon	6
Hirai 2016	Japan	ROS	March 2011 to December 2014	S: 60 M: 20	S: 73 M: 66	S: 33/27 M: 12/8	S: single <5 cm incision M: three or four incisions	S: 34/26 M: 11/9	S: 60/0/0/0 M: 20/0/0/0	Single surgeon	7
Lin 2016	China	ROS	October 2013 to April 2014	S: 21 M: 46	S: 59 M: 62	S: 13/18 M: 29/17	S: single 3–5 cm incision M: two incisions	S: 11/10 M: 19/27	S: NA M: NA	NA	6
Dai 2016	China	ROS	January 2013 to June 2015	S: 63 M: 63	S: 58 M: 57	S: 40/23 M: 46/17	S: single 3–5 cm incision M: two incisions	S: NA M: NA	S: 30/16/17/0 M: 20/14/19/0	Single surgeon	7

ROS, retrospective observational study; RCT, randomized controlled trial; S, single-port VATS; M, multi-port VATS; NA, not available.

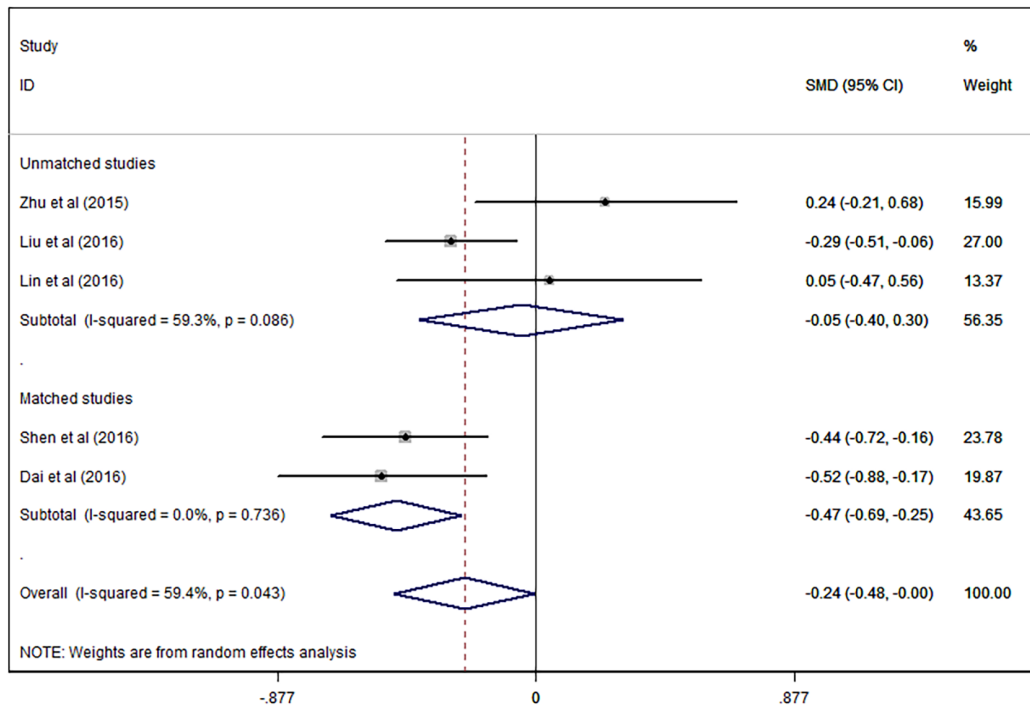


Figure 2 Forest plot outcome of blood loss for patients with NSCLC undergoing single-port versus multi-port VATS lobectomy. NSCLC, non-small cell lung cancer; VATS, video-assisted thoracic surgery.

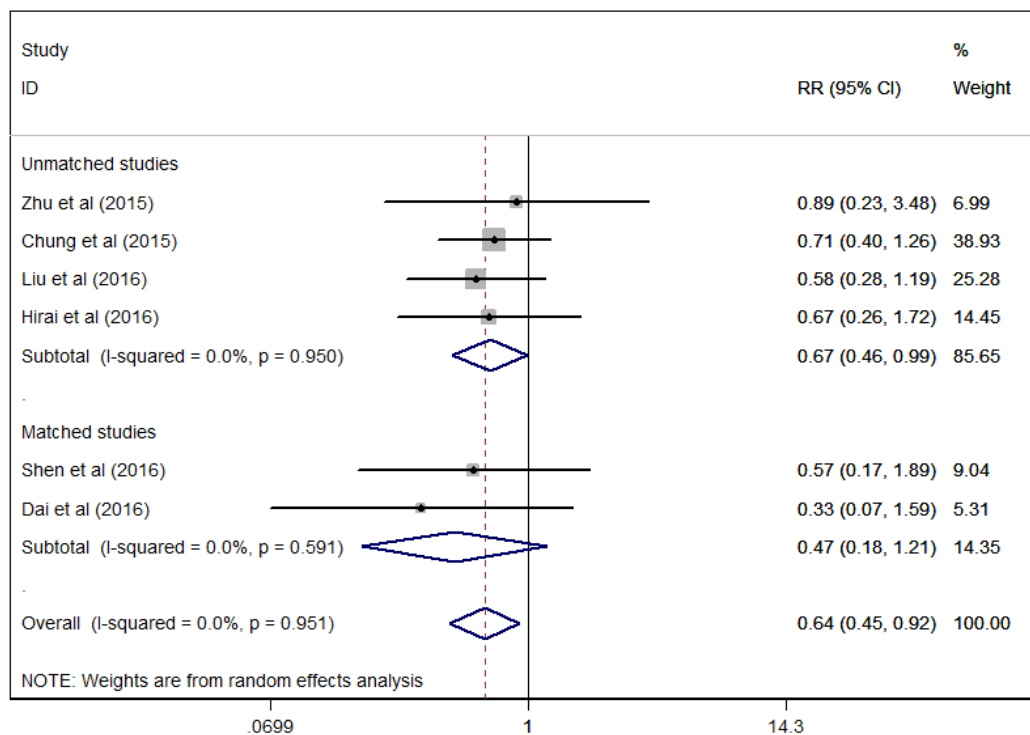


Figure 3 Forest plot outcome of postoperative morbidity for patients with NSCLC undergoing single-port versus multi-port VATS lobectomy. NSCLC, non-small cell lung cancer; VATS, video-assisted thoracic surgery.

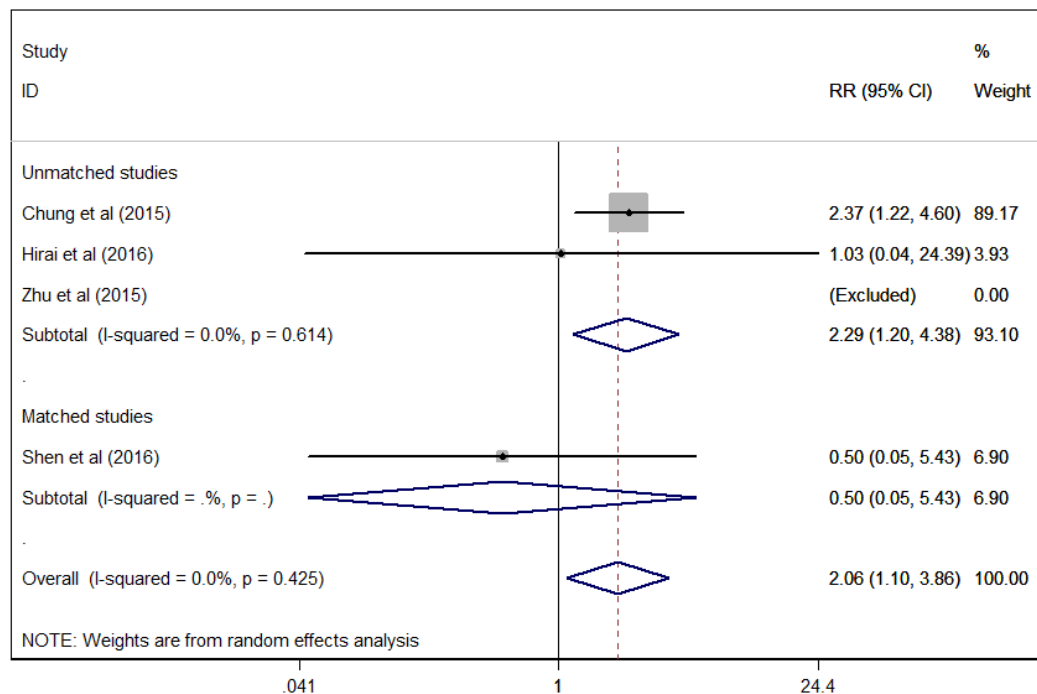


Figure 4 Forest plot outcome of conversion rate for patients with NSCLC undergoing single-port versus multi-port VATS lobectomy. NSCLC, non-small cell lung cancer; VATS, video-assisted thoracic surgery.

There were no statistically significant differences between single-port and multi-port VATS in regards to operative time (SMD =0.37, 95% CI: -0.20 to 0.93, P=0.204), the number of lymph nodes dissection (SMD =0.03, 95% CI: -0.18 to 0.25, P=0.763), postoperative pain (SMD =1.35, 95% CI: -0.16 to 2.85, P=0.08), chest drainage duration (SMD =-0.10, 95% CI: -0.43 to 0.22, P=0.535), and length of hospital stay (SMD =-0.17, 95% CI: -0.38 to -0.04, P=0.113). We failed to perform a pooled analysis on mortality between the two groups, since no deaths were reported in single-port group and only one death was shown in multi-port group (*Table 2*).

Assessment of propensity-matched data

When propensity-matched data were analyzed, there were no statistically significant differences between single-port and multi-port VATS in regards to overall morbidity, length of hospital stay, operative time, the number of lymph nodes dissection, conversion rate and chest drainage duration, but single-port approach was associated with less blood loss (SMD =-0.48; 95% CI: -0.69 to -0.25, P<0.001) and postoperative pain (SMD =-0.59, 95% CI: 0.23 to

0.95, P=0.001) when compared to multi-port approach (*Table 2*).

Discussion

The first description of single-port VATS took place in 1998 and concerned a series of six consecutive patients with pneumothorax (27). Later, Rocco and colleagues (28) reported their first experience of pulmonary wedge resection with single-port VATS in 2004. With the improvement of surgical techniques, Gonzalez-Rivas and colleagues reported complex single-port VATS lung resections including lobectomy (8), bronchial sleeve lobectomy (29), segmentectomy (30), pneumonectomy (31), and pulmonary vascular reconstruction and bronchoplasty (32) subsequently. And according to the latest reports (33,34), single-port VATS can be applied to lobectomy and wedge resection in non-intubated patients. Indeed, it is a challenging technique for most thoracic surgeons, since three or four thoracoscopic items were placed through a single incision at the same time, which may restrict surgeons' maneuvering (10,35). However, advocates of single-port VATS emphasize that this approach has close

Table 2 Unmatched and matched outcome measures for observational studies

Outcomes	No. of studies	I ² (%)	Pooling model	Effect size	95% CI		P
Operative time							
Overall estimate	6	94.0	Random	0.37	-0.20	0.93	0.204
Unmatched study	4	96.3	Random	0.61	-0.35	1.57	0.213
Matched study	2	60.3	Random	-0.05	-0.41	0.30	0.771
Blood loss							
Overall estimate	5	59.4	Random	-0.24	-0.48	0.00	0.047
Unmatched study	3	59.3	Random	-0.05	-0.40	0.30	0.779
Matched study	2	0	Random	-0.48	-0.69	-0.25	<0.001
Conversion rate							
Overall estimate	4	0	Random	2.06	1.10	3.86	0.024
Unmatched study	3	0	Random	2.28	1.2	4.36	0.012
Matched study	1	NA	Random	0.5	0.05	4.36	0.569
Lymph nodes dissection							
Overall estimate	5	58.1	Random	0.03	-0.18	0.25	0.763
Unmatched study	3	78.8	Random	-0.04	-0.45	0.36	0.831
Matched study	2	0	Random	0.106	-0.11	0.32	0.338
Chest drainage duration							
Overall estimate	4	61.1	Random	-0.10	-0.43	0.22	0.535
Unmatched study	3	69.7	Random	-0.14	-0.59	0.30	0.528
Matched study	1	NA	Random	-0.18	-0.46	0.10	0.862
Postoperative pain							
Overall estimate	2	95.3	Random	1.35	-0.16	2.85	0.08
Unmatched study	1	NA	Random	2.13	1.58	2.68	<0.001
Matched study	1	NA	Random	0.59	0.23	0.95	0.001
Length of hospital stay							
Overall estimate	6	56.5	Random	-0.17	-0.38	0.04	0.113
Unmatched study	4	57.7	Random	-0.11	-0.39	0.16	0.422
Matched study	2	73.9	Random	-0.25	-0.69	0.19	0.265
Postoperative morbidity							
Overall estimate	6	0	Random	0.64	0.45	0.92	0.015
Unmatched study	4	0	Random	0.67	0.46	0.99	0.046
Matched study	2	0	Random	0.47	0.18	1.21	0.117

resemblance to open approach in terms of dissecting, isolating, and dividing hilar structures, which provides a direct view for surgeons to target structures (10,12,16).

To our knowledge, this is the first systematic review and meta-analysis comparing single-port VATS to multi-port VATS lobectomy for patients with NSCLC. This

meta-analysis indicated that single-port VATS lobectomy was associated with less blood loss and lower overall postoperative morbidity, but higher conversion rate than multi-port approach. However, these findings should be interpreted with caution, as high selection of patients at the beginning of a new surgical technique should be taken into consideration. Moreover, when propensity-matched data were analyzed, single-port approach was associated with less blood loss and postoperative pain. Overall, these findings suggested that single-port VATS lobectomy is a safe and feasible procedure for NSCLC in selected cases, but there has been insufficient evidence to prove its superior short-term effects than multi-port approach so far.

Single-port VATS lobectomy was associated with higher conversion rate among unmatched studies in this meta-analysis, but there was no significant difference among matched studies. Chung and colleagues (23) reported a conversion rate as high as 35.5% in patients undergoing single-port VATS lobectomy, but Shen and colleagues (22) just reported one conversion to two-port VATS lobectomy and another conversion to open thoracotomy; and Hirai and colleagues (24) also showed only one conversion to open lobectomy. This can be explained in part by the learning curve that is associated with a new surgical approach. With the improvement of surgeons' experience and surgical technique, the conversion rate single-port VATS lobectomy can be comparable to multi-port approach. On the other hand, Chung and colleagues (23) noted the reasons for conversion. In their study, most conversions were two-port VATS mainly due to diffuse, tight pleural adhesions and hilar lymph nodes, and the main reasons for conversion to three-port VATS or open lobectomies were due to tumor location and bronchial injury occurred in the initial single-port approach. And this indicated that single-port VATS lobectomy may be still difficult to deal with highly complex cases when compared with multi-port approach.

Previous studies have showed that when compared with multi-port VATS, single-port approach was associated with less postoperative pain in patients with pneumothorax (36-38). This superiority may benefit from the reduction in the number of intercostal spaces and avoiding the use of a trocar in the procedure, which minimized the risk of intercostal nerve injury (16). That is to say, less postoperative pain may be a potential advantage for single-port VATS when compared to multi-port approach. In our meta-analysis, decreased postoperative pain in single-port VATS lobectomy was observed among matched studies, but there was no significant difference among unmatched

studies. Since pain was assessed at various time points with different scales in most included studies, only two studies with same time points and scales were included for meta-analysis and there was significant heterogeneity between the two studies. Thus, this finding should be interpreted with caution, and further studies with standardized pain management protocols are necessary.

There are several limitations existing in this systematic review and meta-analysis. Firstly, only eight retrospective studies were included to conduct this meta-analysis. Considering the quantity and quality of included studies, our results should be interpreted with caution. Secondly, specific criteria for the definition of outcomes, such as conversion and morbidity, were not clearly stated in most included studies. Thirdly, we failed to pool the analysis of outcomes in terms of quality of life, cost-effectiveness, and long-term survival outcomes of single-port VATS versus multi-port VATS lobectomy.

In summary, single-port VATS lobectomy is a safe and feasible procedure for patients with NSCLC in selected cases, but there has been insufficient evidence to prove its superior short-term effects than multi-port approach so far. And further well designed studies with long-term follow-up outcomes are necessary to assess each advantages and indications for single-port and multi-port VATS lobectomy.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/vats.2017.05.04>). Liu L serves as the Editor-in-Chief of *Video-Assisted Thoracic Surgery*. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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