Uniportal versus multiportal video-assisted thoracoscopic surgery for non-small cell lung cancer: a meta-analysis

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Abstract

Background Uniportal video-assisted thoracoscopic surgery (U-VATS) has recently emerged as an alternative procedure for non-small cell lung cancer (NSCLC); however, whether U-VATS has advantages over multiportal VATS (M-VATS) remains unknown.

Methods We performed a systematic review of two databases (Pubmed and Web of Science) to search comparative studies of U-VATS and M-VATS anatomical pulmonary resection for NSCLC. Parameters of continuous variables (operative time, blood loss, number of resected lymph nodes, drainage duration, length of postoperative stay and pain in postoperative day 1(POD1)) or categorical variables (conversion rates) were retrieved to estimate the comparitiveoutcomes. A subgroup analysis stratified by study type (propensity-matched analysis& randomized-controlled trial versus non-propensity matched analysis) was performed.

Result A total of 19 studies with 3809 patients were included in this meta-analysis. U-VATS was performed on 1747 patients, whereas the other 2062 patients underwent M-VATS. This meta-analysis showed that there was no significant difference in operative time (U-VATS: 146.48±55.07min versus M-VATS: 171.70±79.40min, P=0.81), blood loss (74.49±109.03mL versus 95.48±133.67mL, P=0.18), resected lymph nodes (17.28±9.46 versus 18.31±10.17, P=0.62), conversion rate (6.18% versus 4.34%, P=0.14), drainage duration (3.90±2.94 days versus 4.44±3.12 days, p=0.09), length of postoperative stay (6.16±4.40 days versus 6.45±4.80 days, P=0.22), and pain in POD1 (3.94±1.68 versus 3.59±2.76, p=0.07). Subgroup analysis showed the value of PSM&RCT group consistency with overall value.

Conclusion This up-to-date meta-analysis shows that the perioperative outcomes of U-VATS and M-VATS anatomical pulmonary resection are equivalent. In addition to minimizing the incisions, thoracic surgeons should pay more emphasize on providing high-quality and personalized surgical care for patients, to improve the survival ultimately.

Background

Since the first pneumonectomy was performed for a patient with non-small cell lung cancer (NSCLC) in 1933, surgery is one of the main treatment methods for NSCLC.[1] The past decades have witnessed continuous evolution and progress of surgical techniques, such as the utilization of segmentectomy and the development of video-assisted thoracoscopic surgery (VATS). Compared with the traditional thoracotomy, VATS has significant advantages, such as reduced postoperative pain, less intraoperative blood loss, and better quality of life, which have been widely recognized by prospective randomized controlled trials.[2–4] Conventionally, the traditional VATS, known as multiportal VATS (M-VATS) was commonly performed through 3 or 4 small incisions in the thoracic wall. In recent years, uniportal VATS (U-VATS) has become a new technique in thoracic surgery. Uniportal minimally invasive surgery has developed rapidly since Dr. Rocco first reported in 2004, expanding from the minor thoracic procedures such as wedge resection to complex operations such as lobectomy, segmentectomy, and even bronchial or pulmonary angioplasty.[5]

There have already been numerous articles on the feasibility of U-VATS approach in the treatment of lung neoplasm. Quite a few studies showed no difference between the approaches in the key intra- and postoperative outcome. [6–10]Besides, some articles have demonstrated several potential advantages of the uniportal VATS technique, such as lower mortality, shorter hospital stay, and reduced postoperative pain, [11–13] however, the results of these studies were highly heterogeneous. For instance, Lin et al indicated that U-VATS significantly increased operation time compared to M-VATS approach,[14] while Bourdages-Pageau et al held the idea that operation time was significantly decreased in U-VATS group.[15] One study reported shorter average hospital stay with uniportal VATS [16], while another showed it was longer.[10] Comparative clinical outcomes of U-VATS versus M-VATS still remain uncertain.

Here in, we conducted a comprehensive meta-analysis of prospective and retrospective comparative studies, to compare the outcomes of U-VATS and M-VATS anatomical pulmonary resection (lobectomy or segmentectomy) for NSCLC.

Materials And Methods

Study Selection

A literature review was conducted by 2 independent investigators (Y.R. Yan and Q.Y. Huang) through PubMed and Web of Science online data sources (up to Octobor 31st, 2019), using the following search terms:

((uniport*) OR (single port) OR (single-port) OR (single incision)) AND ((Lung Neoplasms [MeSH Major Topic]) OR (pulmonary neoplasms) OR (lung cancer) OR (none small cell lung cancer) or (NSCLC)) AND ((VATS [MeSH Major Topic]) OR (video-assisted thoracoscopic surgery) OR (thoracoscop*) or (video assist*))

Additionally, reference lists of the identified papers were scanned for relevant articles to obtain further studies.

Studies that comply with the following criteria were included in this meta-analysis: (1)An unmatched or propensity score matched comparison between U-VATS and M-VATS; (2) Included at least one of the following outcomes was reported: operative time, resected lymph nodes, drainage duration, blood loss, length of postoperative stay (LOS), and pain in postoperative day 1 (POD 1); (3) Focused on NSCLC; (4) Published full text article; (5) Written in English.

Data Extraction And Assessment Of Methodological Quality

Two independent investigators (Y.R. Yan and Q.Y. Huang) extracted data from all included studies by Microsoft Office Excel 2010 (Microsoft, Redmond, WA). In the case of conflicts, disagreements were adjudicated by a third impartial reviewer (Y. Zhang) and resolved by combined agreement. Baseline variables retrieved included the following: study name, first author, location, publication year, study period, study design, surgical procedure, and tumor stage. The following results were retrieved as comparative outcomes: operation time, blood loss, number of resected lymph nodes, conversion rate, drainage duration, length of postoperative stay and pain in POD1. Two independent investigators (Y.R. Yan and Q.Y. Huang) assessed the methodological quality of the pertinent studies according to the Newcastle Ottawa Scale (NOS), a scale of 0 to 9. Studies scored 6 or more were included in this article.

Data analysis

This meta-analysis retrieved and analyzed data according to the preferred reporting items for systemic reviews and meta-analysis (PRISMA) statement.[16] Meta-analysis was performed using R Studio Version 3.6.1 Meta packages (version 4.9-7). The effective values of continuous variables (operation time, blood loss, number of resected lymph nodes, drainage duration, length of postoperative stay, and pain in POD1) were estimated by standard mean differences or weighted mean difference (SMD or WMD) with 95% confidence intervals (CI), while those of categorical variables (conversion rate) were estimated by odds ratio (OR) with 95% confidence intervals. We performed a subgroup analysis stratified by study type (randomized controlled trials (RCTs) & propensity matched (PSM) studies versus non-propensity matched (non-PSM) studies) in operation time, blood loss, number of resected lymph nodes, drainage duration, and length of postoperative stay. Statistical heterogeneity was evaluated by Cochrane Chi-square test, with I^2 values of 25%, 50% and 75% representing low, moderate, and high heterogeneity. A random-effect model was used if $I^2 > 25\%$, otherwise, a fixed-effect model was adopted. Funnel plots were used to graphically assess publication bias. Meanwhile, Egger's test and Begg's test were used to quantify the publication bias. A statistical difference was taken as two-sided P value < 0.05.

Results

Study selection and risk of bias assessment

A total of 347 studies were identified from PubMed and 288 studies were searched from Web of Science online database by the previously mentioned electronic search strategy up to October 31, 2019. Upon a manual search and inspection of the reference lists of other systematic reviews and meta-analyses identified 36 additional relevant studies. After exclusion of duplicates, irrelevant studies or unoriginal studies, there were 106 studies remained and assessed for eligibility by screening the full text. Finally, 19 full-text studies reporting comparative clinical outcomes of U-VATS versus M-VATS met the inclusion criteria and were suitable for meta-analysis. The PRISMA flow chart describing the process of study selection is shown in Fig. 1.

The studies selected for this meta-analysis were conducted in 6 countries which were published before 31st October, 2019. Among these 19 studies, four of them were prospective studies; one of them was RCT; and seven of them were PSM studies. This analysis included 3809 patients, of which 1747 patients underwent U-VATS and 2062 patients underweTnt M-VATS. The quality of the included studies was assessed by the NOS scale and scores ranged from 6 to 8. Table 1 summarized basic characteristics and demographics of the included studies.

Operative Outcomes

In this meta-analysis, the comparison of perioperative outcomes between U-VATS and M-VATS was estimated by intraoperative outcomes (operation time, blood loss, number of resected lymph nodes, and conversion rate) and postoperative outcomes (drainage duration, length of postoperative stay, and pain in POD1). Table 2 summarized the overall comparative outcomes of uniportal and multiportal group.

Table 1
Basic characteristics and demographics of the included studies

First Author	Country	Year of Publication	Study year	Retrospective/ Prospective	Study Type	Patients	Lobe	Seg	TNM[8th] Stage	NOS score
Bourdages-Pageau[15]	Canada	2019	2014–2017	Retrospective	PSM	722	247/247	0/0	T1N0M0	8
Chang [17]	China Taiwan	2016	2012–2014	Retrospective	No	121	26/55	3/2	T1-2N0M0	7
Chung [7]	South Korea	2015	2013–2014	Retrospective	No	150	90/60	0/0	T1-2N0M0	7
Dai [18]	China	2016	2013–2015	Retrospective	PSM	143	63/63	0/0	T1-3N2M0	7
French [19]	Canada	2016	2014–2015	Retrospective	PSM	100	40/42	10/8	T1N0M0	7
Han [20]	South Korea	2016	2006–2015	Retrospective	No	439	167/212	0/0/	Stage I or II	7
Heo [21]	South Korea	2017	2012–2015	Retrospective	PSM	104	32/32	0/0	T1-2N0-2M0	7
Hirai [22]	Japan	2019	2012–2019	Prospective	No	212	142/70	0/0	T1N0M0	7
Li[23]	China	2019	2015–2017	Retrospective	PSM	492	215/232	31/14	NG	8
Lin [14]	China	2016	2013–2014	Retrospective	No	67	21/46	0/0	NG	7
Liu [9]	China Taiwan	2016	2005–2014	Retrospective	No	442	100/342	49/47	NG	7
Liu [24]	China	2019	2015–2016	Prospective	No	328	166/162	0/0	T1N0M0	8
McElnay [8]	UK	2014	2012–2013	Retrospective	No	110	15/95	0/0	NG	7
Mu [10]	China	2015	2014–2015	Prospective	PSM	405	28/21	8/8	Stage I-III	8
Perna [25]	Spain	2016	2015–2016	Prospective	RCT	131	51/55	0/0	T1-2N0M0	8
Shen [26]	China	2016	2013–2014	Retrospective	PSM	396	100/100	0/0	T1-3N0M0	7
Song [27]	South Korea	2017	2011–2016	Retrospective	PSM	73	26/26	0/0	Stage I-III	7
Zhao [28]	China	2019	2013–2015	Retrospective	No	129	73/56	0/0	Stage I	7
Zhu [29]	China	2015	2014 Aug-2014 Oct	Retrospective	No	82	33/49	0/0	Stage I or II	7

NOS score = Score of Newcastle Ottawa Scale

RCT = randomized controlled trial

PSM = propensity matched

Lobe = Lobectomy

NG = Not given

Seg = Segmentectomy

TNM[8th] = 8th edition of TNM classification of lung cancer

Table 2
Summary of the perioperative outcomes between U-VATS and M-VATS in this meta-analysis

	Comparative outcomes	Number of studies	Study group		SMD/WMD/OR	95%CI	P value	Heterogeneity (I^2,P)	Meta-analysis model
			Uniportal	Multiportal					
Intraoperative Outcomes	Operation time	18	1732	1967	-0.04	-0.33 ~ 0.26	0.81	I^2 = 94%, p < 0.01	Random
	Blood loss	14	1374	1590	-0.14	-0.35 ~ 0.06	0.18	I^2 = 86%, P < 0.01	Random
	Number of resected lymph nodes	15	1391	1618	0.03	-0.08 ~ 0.13	0.62	I^2 = 45%, p = 0.03	Random
	Conversion rate	13	1375	1358	1.27	0.83 ~ 1.94	0.14	I^2 = 13%, P = 0.32	Fixed
Postoperative Outcomes	Drainage duration	18	1322	1411	-0.13	-0.27 ~ 0.02	0.09	I^2 = 68%, p < 0.01	Random
	Length of postoperative stay	10	931	898	-0.11	-0.28 ~ 0.07	0.22	I^2 = 64%, p < 0.01	Random
	Pain in POD1	5	234	313	-0.78	-1.61 ~ 0.05	0.07	I^2 = 97%, p < 0.01	Random

Operation Time

A total of 18 studies including 3699 patients provided comparative data on operative duration. The overall operation time was 146.48 ± 55.07 min and 171.70 ± 79.40 min in U-VATS and M-VATS group, respectively. The present meta-analysis revealed that the overall operation time has no significant difference between U-VATS group and M-VATS group (SMD=-0.04, 95%CI = (-0.33, 0.26), P = 0.81, Fig. 2a). Random-effect model was used due to the high heterogeneity (I^2 = 94%, P < 0.01). Subgroup analysis of PSM&RCT studies further confirmed the comparable operation time between two approaches ((SMD = 0, 95%CI = (-0.21, 0.22)) was consistent with the overall value.

Blood Loss

Blood Loss was reported in 14 studies with a combination of 2964 patients. The overall blood loss was 74.49 ± 109.03 mL and 95.48 ± 133.67 mL in U-VATS and M-VATS group, respectively. The present meta-analysis indicated that the overall blood loss has no significant difference between U-VATS group and M-VATS group (SMD=-0.14, 95%CI = (-0.35, 0.06), P = 0.18, Fig. 2b). Random-effect model was used due to the high heterogeneity (I^2 = 86%, P < 0.01). According to subgroup analysis, blood loss in PSM&RCT group (SMD=-0.22, 95%CI = (-0.54, 0.10)) has no significant difference with that in non-PSM group.

Number Of Resected Lymph Nodes

Totally, 15 studies including 3009 patients reported the comparative outcomes of number of resected lymph nodes, which were 17.28 ± 9.46 and 18.31 ± 10.17 in U-VATS and M-VATS groups, respectively. The meta-analysis result of number of resected lymph nodes showed that there was no significant difference between U-VATS and M-VATS group (SMD = 0.03,95%CI=(-0.08,0.13), P = 0.62, Fig. 2c). Number of resected lymph nodes in PSM&RCT group (SMD = 0.03, 95%CI = (-0.08, 0.14)) has no significant difference in non-PSM group. Random-effect model was used due to the moderate heterogeneity (I^2 = 25%,P = 0.20).

Conversion Rate

In all, there were 13 studies including 2733 patients reporting conversion rate, which was defined as the rate of conversion to thoracotomy or need extra incisions. In U-VATS group, the total conversion rate was 6.18%, while the total value was 4.34% in M-VATS group. The meta-analysis result of conversion rate showed that there was no significant difference between U-VATS and M-VATS group (OR = 1.27, 95%CI= (0.83, 1.94), Fig. 2d). Fixed-effect model was used due to the low heterogeneity (I^2 = 13%, P = 0.32).

Drainage Duration

Drainage duration was defined as the period of time from the operation date to the extubation date. A total of 18 studies with a combination of 2743 patients provided comparative data on length of drainage. The overall duration of drainage was 3.90 ± 2.94 days and 4.44 ± 3.12 days in U-VATS and M-VATS group, respectively. The present meta-analysis indicated that the overall operation time has no significant difference between U-VATS group and M-VATS group (SMD=-0.13, 95%CI = (-0.27, 0.02), P = 0.09, Fig. 3a). And the value of drainage duration in PSM&RCT group (SMD=-0.12, 95%CI = (-0.30, 0.07)) showed consistence with the overall value. Random-effect model was used due to the high heterogeneity (I^2 = 68%, P < 0.01).

Length Of Postoperative Stay

There were totally 10 studies including 1829 patients reporting length of postoperative stay. The overall postoperative hospital stay was 6.16 ± 4.40 days in U-VATS group and 6.45 ± 4.80 days in M-VATS group. The present meta-analysis indicated that the length of postoperative stay has no significant difference between U-VATS and M-VATS group (SMD=-0.11, 95%CI= (-0.28, 0.07), P = 0.22, Fig. 3b). According to subgroup analysis, length of postoperative stay in PSM&RCT group was (SMD=-0.01, 95%CI = (-0.18, 0.16)). By the virtue of moderate heterogeneity (I^2 = 64%, P < 0.01), random-effect model was applied to this analysis.

Pain in POD1

A total of 5 studies including 547 patients provided comparative outcomes on pain scoring in postoperative day 1 (POD1). All these five included studies utilized the visual analogue scale (VAS) to evaluate pain in POD1, and the overall value of VAS was 3.94 ± 1.68 and 3.59 ± 2.76 in U-VATS and M-VATS group, respectively. Since all these studies utilized the same method to assess pain in POD1, the effective valuables of pain in POD 1 were estimated by WMD. The present meta-analysis indicated that the value of pain in POD1 has no significant difference between U-VATS and M-VATS group (WMD=-0.78, 95%CI= (-1.61, 0.05), P = 0.07, Fig. 3c). Random-effect model was applied due to the high heterogeneity (I^2 = 97%, p < 0.01).

Publication Bias

Funnel plots were utilized to graphically describe the publication bias of included studies in operation time, blood loss, number of resected lymph nodes, conversion rate, drainage duration, and length of postoperative stay. All funnel plots (See in Supplementary materials) showed a good symmetric distribution. Then Egger's test and Begg's test were used to quantize the publication bias, which demonstrated that there was no significant bias in each outcome.

Discussion

This meta-analysis included 19 comparative studies reporting perioperative outcomes between U-VATS and M-VATS in 3809 patients with lung cancer undergoing anatomical pulmonary resection. Compared with previous studies, this meta-analysis, which included the latest researches, has been the largest one on the comparative clinical outcomes between U-VATS and M-VATS approaches for NSCLC so far. Our meta-analysis showed that there was no significant difference between U-VATS and M-VATS with regard to operative time, blood loss, number of resected lymph nodes, conversion rate, drainage duration, length of postoperative stay and pain in POD1.

Recently, several meta-analyses had so far compared the perioperative outcomes of U-VATS and M-VATS for lung cancer.[30–32]Some of the previous meta-analyses demonstrated U-VATS technique had several potential advantages over M-VATS approach. Yang X.Y. et al reported that patients in U-VATS group had a significant reduction with regard to blood loss (SMD = − 0.27, 95% CI= (− 0.46, − 0.08)) and length of stay (SMD = − 0.30, 95% CI= (− 0.41, − 0.19)), pain in POD1 (SMD = − 2.42, 95% CI= (− 4.40, − 0.44)) compared with patients undergoing M-VATS approach.[31] Yang Z. et al reported that U-VATS approach significantly shortened hospital stay ((WMD=-0.50, 95% CI= (-0.87, -0.13)) against M-VATS approach.[32] By contrast, even though we found that there was a reduction in blood loss and length of

postoperative stay, our meta-analysis demonstrated that there was, however, no significant difference between U-VATS and M-VATS approach on these results, which showed that U-VATS approach has limited advantage over M-VATS in perioperative management.

Both Yang Z. et al and Yang X.Y. et al showed that the U-VATS achieved a significant reduction in the length of stay. This present analysis adopted length of postoperative stay as the parameter, and demonstrated no significant difference between U-VATS and M-VATS approach. Length of hospital stay includes length of postoperative stay and length of waiting for surgery. The latter depended on preoperative workup process, and could vary a lot according to protocols and criteria in different medical centers and treatment groups. Thus, the utility of length of postoperative stay could avoid potential biases and heterogeneity, and is much more objective o reflecting the postoperative recovery.

There have been few studies reporting the long-term outcomes of U-VATS so far. Han et al demonstrated that there was no significant difference between single-incision group, two-incision group, and three-incision group in both recurrence free survival and overall survival.[20] It is noteworthy that there is a study reporting a significant worse long-term survival in the U-VATS group compared with M-VATS group by Borro et al in 2016. According to this research, Borro found that U-VATS led to a significant lower survival rate in tumor size (T2) and tumor stage (stage I) for patients with NSCLC by stratifying analysis. Besides that, Borro indicated that U-VATS approach was correlated with a higher risk (HR = 1.78) of death.[33] Due to the lack of studies with regard to long-term outcomes, unfortunately, we are unable to make a meta-analysis of the long-term results. As surgical oncologists, the major impetus is always focused on optimal oncologic results,[34] and a procedure should never be performed by sacrificing the long-term survival. Although it is arbitrary to conclude that U-VATS result in poorer long-term outcomes based on only one study, thoracic surgeons should be cautious to avid uptake of this novel technique without well selecting the appropriate patients with lung cancer. Further studies of the survival of U-VATS are warranted.

VATS techniques are among the major progresses in the history thoracic surgery beyond all doubt. Innovation of surgical approach is of great importance, but minimizing the size and number of incisions is only one part of minimally invasive surgery (MIS). We believe that the utilization of MIS should lead to preserving normal organs, prolonging survival, and improving quality of life[35]. For instance, with the help of precise intraoperative frozen section diagnosis of pre-invasive lung adenocarcinoma, we are able to perform sublobar resection for these patients, to spare pulmonary function without impairing the survival.[36]

There are some limitations in this meta-analysis. Firstly, only four included studies are prospective in design, and the majority is retrospective which is of lower quality and inevitably introduce potential biases to the results.. U-VATS emerges as a novel surgical technique, so investigators have a propensity to publish positive outcomes to demonstrate the superiority or, at least, feasibility of U-VATS. Besides, due to the limited operating space and the narrow surgical field, U-VATS is usually performed in experienced hands [7, 18, 19, 21, 24] Consequently, the equivalent results between two approaches reported in this meta-analysis should be quite conservative. Secondly, our meta-analysis showed a high heterogeneity in the comparative outcomes (except conversion rates and number of resected lymph nodes). We made a subgroup analysis between PSM&RCT studies and non-PSM studies, and found that the result of PSM studies was consistent with that of all included studies.

Conclusions

To conclude, our results indicate that there is no significant difference in perioperative outcomes between U-VATS and M-VATS approaches in the treatment of NSCLC, which means that U-VATS, up to now, still cannot bring extra benefits over M-VATS on the perioperative recovery of patients. In addition, the differences in long-term outcomes of these two approaches are still unclear. Hence, U-VATS should be prudently chosen in the treatment of NSCLC.

Abbreviations

NSCLC	Non-small cell lung cancer
U-VATS	Uniportal video-assisted thoracoscopic surgery
M-VATS	Multiportal video-assisted thoracoscopic surgery
POD1	Postoperative day 1
FEV1	Forced expiratory volume in one second
NOS	Newcastle Ottawa Scale
PRISMA	Preferred reporting items for systemic reviews and meta-analysis
PSM	Propensity-matched
RCT	Randomized controlled trial
SMD	Standard mean difference
WMD	Weighted mean difference
OR	Odds ratio
VAS	Visual analogue scale

Declarations

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

We declared that no conflicts of interest or financial ties to disclose.

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Author contribution statement

YY and QH designed and collected the data for the review. YY, QH, YZ and HH assisted with the data extraction and analysis. YZ was involved as the third reviewer to solve disagreement when necessary. YY drafted the article. HC provided general advice and assisted with the writing of the review. All authors read and approved the final manuscript

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Figures

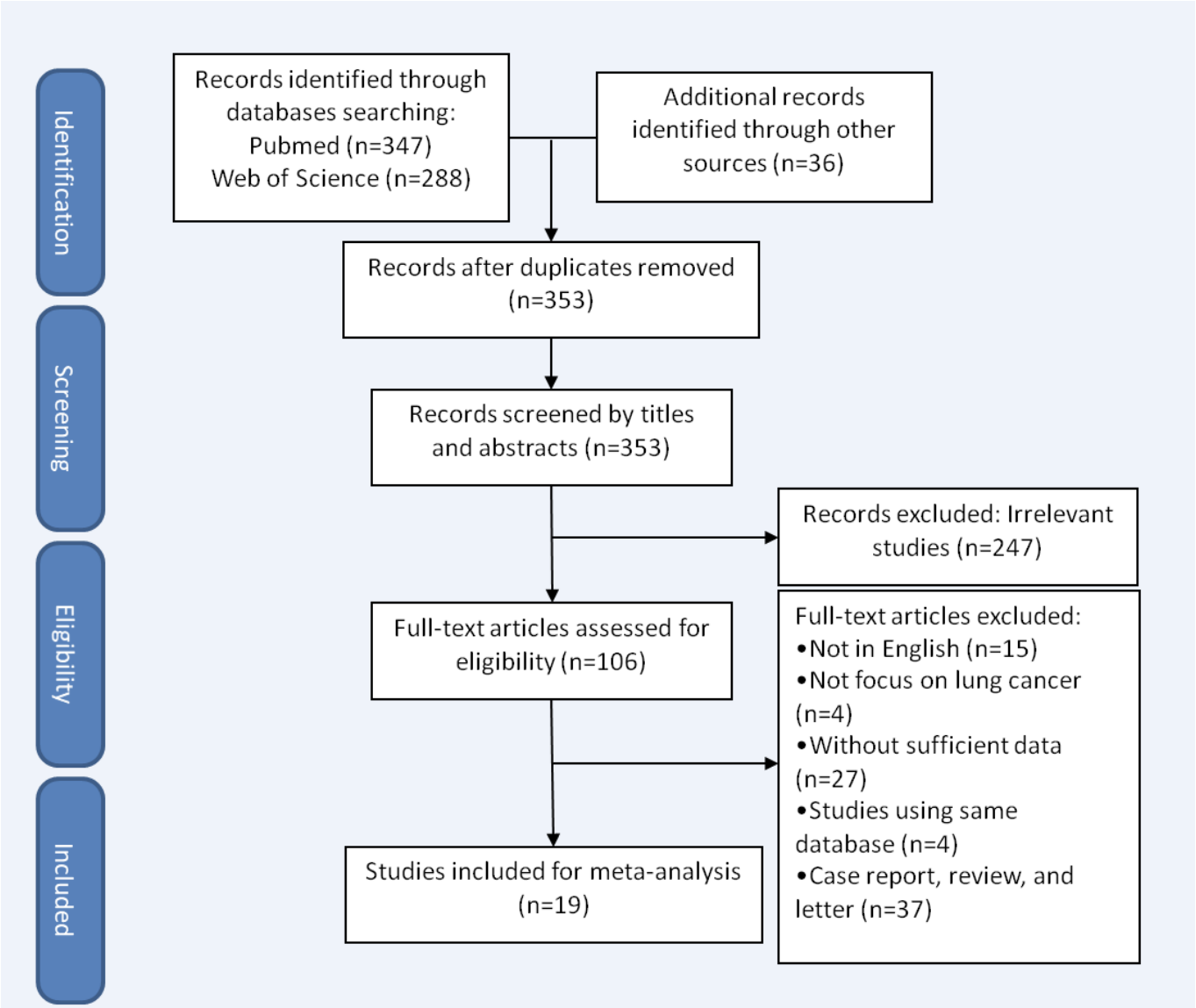


Figure 1

Flow chart detailing the search strategy and process of study selection

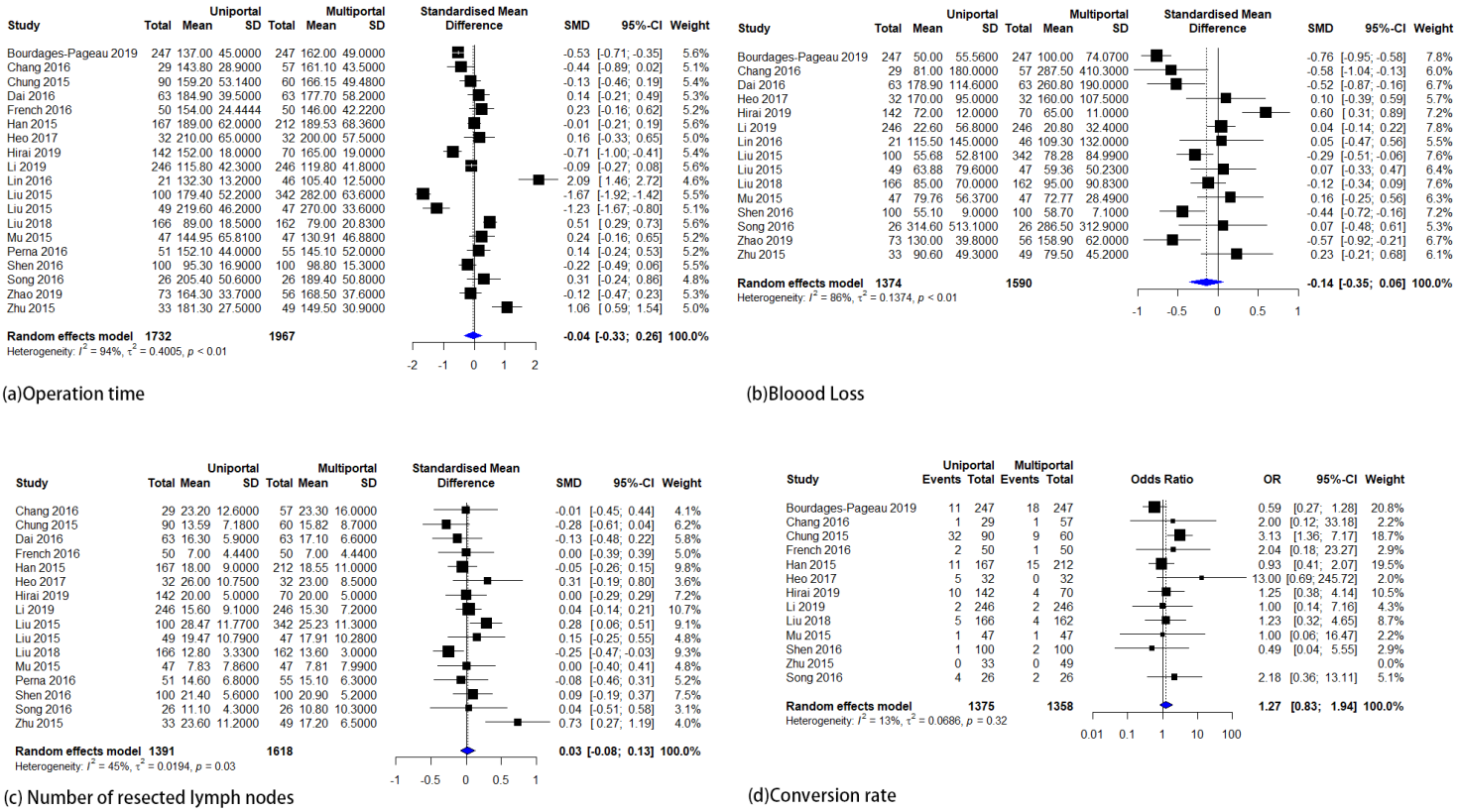
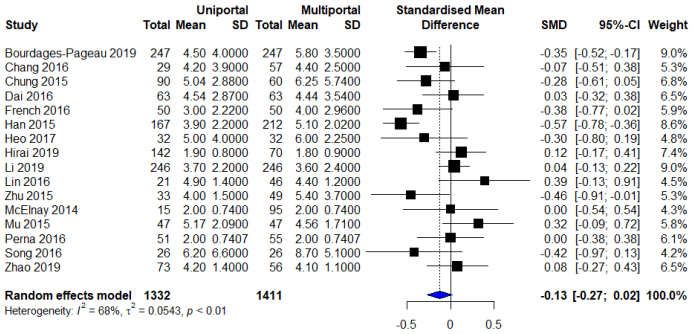
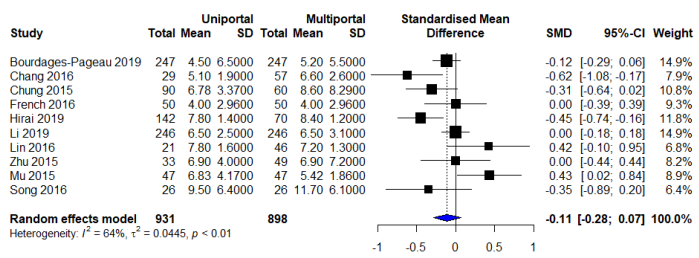


Figure 2

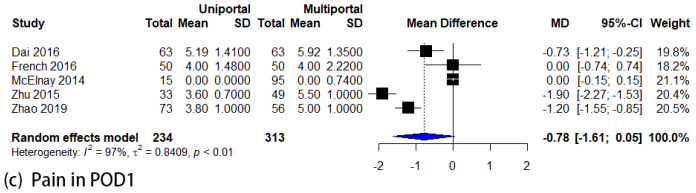
Forest plot of intraoperative outcomes for U-VATS and M-VATS groups. (a) Forest plot of operation time. (b) Forest plot of blood loss. (c) Forest plot of number of resected lymph nodes. (d) Forest plot of conversion rate.



(a) Drainage duration



(b) Length of postoperative stay



(c) Pain in POD1

Figure 3

Forest plot of postoperative outcomes for U-VATS and M-VATS groups. (a) Forest plot of drainage duration. (b) Forest plot of length of postoperative stay. (c) Forest plot of pain in POD1.

Supplementary Files

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- Supplementarymaterials.docx
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