

Comparison of single-stage and two-stage bilateral video-assisted thoracic surgery

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Abstract

Objective: Single-stage sequential bilateral video-assisted thoracoscopic surgery (VATS) is a controversial procedure. In the present study, we retrospectively compared the outcomes of single-stage and two-stage VATS.

Methods: This study involved patients who underwent single-stage sequential bilateral VATS (SS-VATS group) or two-stage VATS at a 3-month interval (TS-VATS group) for treatment of nonsmall cell lung cancer from 2010 to 2018. The major outcome was the comparison of intraoperative changes.

Results: The inspiratory peak pressure was higher, the incidences of intraoperative hypoxia and unstable hemodynamics were higher, the surgical time was longer, and the durations of the intensive care unit stay and postoperative hospitalization were longer in the SS-VATS group than in the TS-VATS group. However, the chest tube duration, incidence of postoperative mechanical ventilation, and clinical complications were not different between the two groups.

Conclusions: Compared with two-stage VATS, single-stage sequential bilateral VATS can be performed for successful treatment of bilateral pulmonary lesions with a shorter total time and higher cost-effectiveness in terms of anesthesia and hospitalization but with a higher incidence of intraoperative adverse effects and a longer hospital stay.

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Keywords

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Introduction

Diagnostic techniques have been improving in association with the diversifying and widening spectrum of diseases. With these diagnostic improvements, the performance of overlapping surgery is increasing. In overlapping surgery, the start of one surgical procedure overlaps with the end of another, and both procedures are performed by the same surgeon.¹ Overlapping surgery has been advocated because it can improve the operation efficiency, allows for reasonable arrangement of specialist surgeons, and may increase patient safety.^{2,3}

With the exception of a prolonged operation time, overlapping surgery does not increase complications or mortality for patients undergoing orthopedic procedures.⁴ However, whether this is also true for patients with bilateral pulmonary lesions is unclear. In most clinical scenarios, two-stage thoracic surgeries are often chosen to avoid complications that result operation.5,6 prolonged from а Nevertheless, single-stage bilateral thoracic surgery has recently been advocated to resolve primary spontaneous pneumothorax with avoidance of subsequent anesthetic procedures, operative procedures, and a duration of hospitalization.^{7,8} longer However, most such support has arisen from small-sample studies of patients with bilateral pneumothorax with limited statisgeneralizability.7-10 power and tical Furthermore, few investigations of singlestage sequential thoracic surgery for bilatpulmonary eral masses have been

performed, and all such studies have lacked comparisons with two-stage bilateral thoracic surgery.^{11–13} In addition, the decision to perform single-stage sequential bilateral thoracic surgery is usually made from a surgical point of view and seldom from a comprehensive evaluation.

Using a single-center registry of a large sample of operations, we performed a retrospective study to compare the effects of single-stage and two-stage bilateral thoracic surgery on patients' intraoperative changes and postoperative recovery.

Methods

This retrospective observational study was approved by the Research Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University on 12 September 2018 (Ethics Committee 2018 No. K-21). The requirement for patient consent was waived because this was a retrospective observational study.

Patients' data were collected from their medical records from 1 January 2010 to 30 August 2018. The inclusion criteria were an age of >18 years and the performance of either single-stage sequential bilateral video-assisted thoracoscopic surgery (VATS) (SS-VATS group) or two-stage VATS at a 3-month interval (TS-VATS group) for treatment of bilateral non-small cell lung cancer. Two-stage VATS included both first-stage and second-stage VATS. The exclusion criteria were thoracotomy, bullectomy, lung volume reduction surgery, mediastinal tumor resection, mediastinoscopy, thoracentesis, tracheal resection, esophageal surgery, an American Society of Anesthesiologists physical status of \geq IV, surgeries involving other organs besides the lung, two-stage surgery with a \geq 4-month interval, and operations performed in another institute. The patients chose to undergo either SS-VATS or TS-VATS after they had received an explanation of these surgical procedures by the surgeon and a preoperative evaluation had been completed by the anesthesiologist. All patients' preoperative characteristics, variables of intraoperative hemodynamics and ventilation (at 15 minutes after pleural opening), and postoperative recovery data were collected.

Anesthesia procedure

All patients underwent general anesthesia by endotracheal intubation. Anesthesia proceeded with target-controlled infusion of propofol and remifentanil, intravenous dexmedetomidine, and inhalation of sevoflurane titrated to maintain a bispectral index of 40% to 60%. Intermittent intravenous cisatracurium was used to maintain muscle relaxation. One-lung ventilation was implemented with a tidal volume of 6 mL/kg, positive end-expiratory pressure of 5 cmH₂O, and respiratory rate of 15 breaths/minute.

An intraoperative oxygen saturation (SpO_2) of <94% was taken as evidence of hypoxemia. The fraction of inspired oxygen was increased to maintain an SpO_2 of $\geq94\%$. An unstable hemodynamic event was defined as a mean arterial pressure of <60 mmHg for 10 minutes; in such cases, dopamine or norepinephrine was administered to maintain the mean arterial pressure at >60 mmHg. Patients were transferred to the post-anesthesia care unit to undergo extubation or remain intubated after the

operation. Finally, they were sent to the intensive care unit (ICU) or general ward.

Surgical procedures

All thoracic procedures complied with the guidelines of the American Association for Thoracic Surgery.¹⁴ In the SS-VATS group, the patients underwent three-port VATS as described by McKenna.¹⁵ The patient was flipped over to the opposite side to undergo the contralateral surgery after completion of the unilateral operation. The approach was the same as the first surgery. The surgical procedure in the TS-VATS group was the same as that in the SS-VATS group, and the patients then underwent the second-stage operation 3 months later. Generally, if the tumor diameter was <1.0cm and microinvasion or carcinoma in situ was considered, wedge resection was performed; if the tumor diameter was 1.1 to 2.0 cm, lobectomy or segmental resection with the scope of lymph node dissection was performed; and if the tumor diameter was >2.0 cm, lobectomy with the scope of lymph node dissection was performed.^{16,17} If more than one tumor was distributed among multiple lobes, the two combined procedures were performed according to the above principles.

A blood cell analysis was performed preoperatively and 1 day postoperatively. The postoperative clinical complications included thoracentesis for treatment of pleural effusion or pneumothorax, dyspnea, air leakage in the chest tube, arrhythmia, reoperation, and death.

Statistical analyses

Statistical analyses were performed with IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean \pm standard deviation or as median (lower quartile, upper quartile).

Dichotomous variables are presented as number (%). If the missing variable was <10%, the mean or median was used to replace it: otherwise, the whole variable was deleted. All continuous variables were analyzed by one-way analysis of variance to evaluate the homogeneity of variance and by the one-sample Kolmogorov-Smirnov test to evaluate the normality of the data. Between-group differences were analyzed with an independent-samples t-test for continuous variables with homogeneity of variance and a normal distribution. Categorical variables were analyzed with the chi-square test, the Mann-Whitney U-test, or the Kruskal-Wallis H-test. The changes in the preoperative and postoperative leukocyte, neutrophil, and hemoglobin values in each group were analyzed by a paired-samples t-test and analysis of covariance. Stepwise binary logistic regression was used to analyze the risk factors for intraoperative unstable hemodynamics in a

multivariate model. A *P* value of <0.05 was considered statistically significant.

Results

The SS-VATS group comprised 54 patients, and the TS-VATS group comprised 42 patients. A study flow chart is shown in Figure 1.

Preoperative characteristics

The patients' preoperative characteristics were not different between the two groups with the exception of a higher proportion of patients with an American Society of Anesthesiologists physical status of III in the TS-VATS than SS-VATS group (P = 0.034). The cardiopulmonary function parameters, total types of the first and second procedures, surgical location, tumor size, tumor pathology, and TNM stage were not significantly different between the groups. The main pathological



Figure 1. Flow chart of patient selection. ASA, American Society of Anesthesiologists.

diagnosis was adenocarcinoma, and the main pathological stages were T1 and N0–N1. No patients had metastasis (Table 1).

Intraoperative variables

The peak respiratory pressure was higher and the SpO₂ was lower in the SS-VATS than TS-VATS group (22.37 vs. 15.05 vs. 16.38 cmH₂O, P < 0.001 and 97.30% vs. 98.95% vs. 98.64%, P < 0.001, respectively), but the end-expiratory carbon dioxide partial pressure was higher in the second stage in the TS-VATS group (33.87 vs. 35.33 vs. 39.12 mmHg, P = 0.002). The incidences of intraoperative hypoxia and unstable hemodynamics were higher in the SS-VATS than TS-VATS group (17% vs. 5% vs. 2%, P = 0.027 and 44% vs. 24% vs. 23%, P = 0.041, respectively). The surgical time was longer and the blood loss was higher in the SS-VATS than TS-VATS group (203 vs. 130 vs. 85 minutes, P < 0.001 and 50 vs. 45 vs. 10 mL. P < 0.001, respectively) (Table 2).

Later recovery in the ward

The median ICU stay and postoperative hospitalization were longer in the SS-VATS than TS-VATS group (1 vs. 0 vs. 0 days, P < 0.001 and 6 vs. 6 vs. 4 days, P = 0.016, respectively). However, the chest tube duration, requirement for postoperative mechanical ventilation, and incidence of postoperative clinical complications were similar between the groups. The cost of anesthesia was higher in the SS-VATS group than in each stage in the TS-VATS group (8303 vs. 7685 vs. 6983 CNY, P = 0.001) (Table 3).

Risk factors for intraoperative unstable hemodynamics

The binary logistic regression analysis showed that the percent predicted forced vital capacity, the surgical time, and the preoperative neutrophil ratio were risk factors for intraoperative unstable hemodynamics (Table 4).

Changes in blood assay

The postoperative leukocyte count and neutrophil ratio were higher than their preoperative counterparts (P < 0.01), and the postoperative leukocyte count was lower in the TS-VATS than SS-VATS group (11.35 vs. 12.08 vs. 14.12×10^9 , P = 0.004) (Figure 2).

Discussion

In this study, we evaluated the perioperative variables of patients who underwent single-stage and two-stage VATS for the treatment of bilateral non-small cell lung cancer. The single-stage bilateral VATS group had a higher peak respiratory pressure, higher incidence of intraoperative hypoxia, higher incidence of unstable hemodynamics, longer surgical time, and greater blood loss. Additionally, patients who underwent single-stage bilateral VATS had a higher postoperative leukocyte count and required longer postoperative ICU and hospital stays. However, the postoperative mechanical ventilation rate, complication rate, and chest tube duration were similar between the two groups.

Single-stage bilateral thoracotomy for spontaneous pneumothorax was first introduced in 1957¹⁸ and has been suggested for prophylactic treatment of contralateral pneumothorax.^{6,19} Theoretically, singlestage bilateral pulmonary resection also decreases the risk of disease progression, especially in patients with bilateral malignant tumors; shortens the patients' total hospitalization time; and decreases postoperative complications.^{11–13,20} Our study indicated that the incidence of unstable hemodynamics may increase in patients undergoing single-stage sequential bilateral

	SS-VATS group	TS-VATS group	
Variable	(n = 54)	(n = 42)	P value
Age, years	56.15±10.28	$\textbf{58.90} \pm \textbf{10.52}$	0.200
Sex			0.456
Male	28 (52)	25 (59)	0.506
Female	26 (48)	17 (39)	0.335
Body mass index, kg/m ²	22.48 ± 3.14	22.32 ± 2.72	0.799
ASA physical status			0.313
	45 (83)	32 (76)	0.579
II	9 (17)	7 (17)	1.000
III	0 (0)	3 (7)	0.034
Comorbidity			0.255
Cardiovascular disease	14 (26)	5 (12)	0.089
Diabetes	5 (9)	I (2)	0.169
Neurological disease	0 (0)	I (2)	0.257
Pulmonary disease	2 (4)	I (2)	0.713
Thyropathy	0 (0)	2 (5)	0.107
Revised cardiac risk index			0.510
l point	48 (89)	39 (93)	0.767
2 points	6 (11)	3 (7)	0.346
LVEF, %	69.44 ± 10.27	69.19±4.96	0.886
Pulmonary function parameters	n = 52	n = 40	
FVC % predicted	101.41±13.18	$\textbf{98.71} \pm \textbf{23.68}$	0.489
FEV ₁ % predicted	$\textbf{92.85} \pm \textbf{14.50}$	89.55 ± 25.24	0.432
FEV ₁ /FVC%	$\textbf{91.53} \pm \textbf{7.13}$	$\textbf{89.79} \pm \textbf{10.89}$	0.358
MVV, L/minute	$\textbf{98.57} \pm \textbf{21.84}$	$\textbf{99.28} \pm \textbf{22.95}$	0.882
Type of first procedure			<0.001
Wedge resection	44 (82)	12 (28)	<0.001
Lobectomy	6 (11)	23 (55)	<0.001
Segmentectomy	4 (7)	3 (7)	1.000
Two combined procedures	0 (0)	4 (10)	0.007
Total types of first and second procedures			0.133
Wedge resection	57 (53)	33 (39)	0.144
Lobectomy	35 (32)	39 (47)	0.091
Segmentectomy	12 (11)	7 (8)	0.491
Two combined procedures	4 (4)	5 (6)	0.527
Surgical site in the right lung			0.615
Upper lobe	30 (56)	26 (61)	0.644
Middle lobe	6 (11)	4 (10)	0.827
Lower lobe	17 (31)	10 (24)	0.345
Two lobes	I (2)	2 (5)	0.257
Surgical site in the left lung			0.585
Upper lobe	39 (72)	29 (69)	0.801
Lower lobe	15 (28)	10 (24)	0.579
Two lobes	0 (0)	3 (7)	0.034
Tumor size on computed tomography, mm			
Left lung	12 (8, 22)	9 (6, 16)	0.155
Right lung	12 (6, 19)	15 (7, 20)	0.281

Table 1. Patients' preoperative characteristics.

(continued)

Table 1. Continued.

	SS-VATS group	TS-VATS group	
Variable	(n = 54)	(n = 42)	P value
Final pathology			
First procedure			0.419
Squamous carcinoma	I (2)	2 (5)	0.257
Adenocarcinoma	53 (98)	40 (95)	0.829
Second procedure			0.454
Squamous carcinoma	2 (4)	3 (7)	0.564
Adenocarcinoma	52 (96)	39 (93)	0.827
T stage			0.675
TI stage	49 (91)	37 (88)	0.823
T2 stage	5 (9)	5 (12)	0.513
N stage			0.272
N0–N1 stage	47 (87)	33 (79)	0.535
N2–N3 stage	7 (13)	9 (21)	0.170
Preoperative chemotherapy	I (2)	3 (7)	0.200

Data are presented as mean \pm standard deviation, n (%), or median (lower quartile, upper quartile).

SS-VATS, single-stage sequential bilateral video-assisted thoracoscopic surgery; TS-VATS, two-stage video-assisted thoracoscopic surgery at a 3-month interval; ASA, American Society of Anesthesiologists; LVEF, left ventricular ejection fraction; FVC% predicted, percent predicted forced vital capacity; FEV₁% predicted, percent predicted forced expiratory volume in the first second; MVV, maximal voluntary ventilation.

TS-VATS group SS-VATS group First stage Second stage Variables (n = 54)(n = 42)(n = 42)P value Ventilation variables Tidal volume, L $\textbf{0.33} \pm \textbf{0.06}$ 0.34 ± 0.05 0.32 ± 0.06 0.438 Peak, cmH₂O $\textbf{22.37} \pm \textbf{5.45}$ 15.05 ± 8.33** $16.38 \pm 9.14^{**}$ < 0.001 $98.95 \pm 1.51 ^{**}$ SpO₂, % 97.30 ± 2.75 98.64 ± 1.50** < 0.001 P_{ET}CO₂, mmHg $\textbf{33.87} \pm \textbf{5.51}$ $\textbf{35.33} \pm \textbf{7.84}$ 39.12±8.01***,# 0.002 FiO₂, % 74.91 ± 12.94 $70.17 \pm 6.45^{*}$ $\textbf{73.31} \pm \textbf{13.23}$ 0.134 Vital signs during operation $\mathbf{69.50} \pm \mathbf{9.90}$ 0.095 HR, beats/minute 72.43 ± 6.77 69.10±8.16 79.56 ± 7.40 78.57 ± 5.73 $76.52 \pm 5.10^{*}$ 0.064 MAP, mmHg Intraoperative hypoxia 0.027 No 45 (83) 40 (95) 41 (98) Yes 9 (17) 2 (5) I (2) Unstable hemodynamics 0.041 No 30 (56) 32 (76) 32 (76%) Yes 24 (44) 10 (24) 10 (24) 85 (60, 121) <0.001 Surgical time, minutes 203 (150, 260) 130 (105, 173) Blood loss, mL 50 (20, 100) 45 (19, 50) 10 (5, 23) < 0.001

 Table 2. Comparison of intraoperative ventilation and hemodynamics.

Data are presented as mean \pm standard deviation, n (%), or median (lower quartile, upper quartile).

*P < 0.05, **P < 0.01 when compared with SS-VATS group.

 $^{\#}P < 0.05$ when second stage compared with first stage in the TS-VATS group.

SS-VATS, single-stage sequential bilateral video-assisted thoracoscopic surgery; TS-VATS, two-stage video-assisted thoracoscopic surgery at a 3-month interval; Peak, peak respiratory pressure; SpO_2 , oxygen saturation; $P_{ET}CO_2$, end-expiratory carbon dioxide partial pressure; FiO_2 , fraction of inspired oxygen; HR, heart rate; MAP, mean arterial pressure.

		TS-VATS group		
Variables	SS-VATS group (n = 54)	First stage (n = 42)	Second stage (n = 42)	P value
ICU stay, days	I (0, 2)	0 (0, 1)	0 (0, 1)	<0.001
Chest tube duration, days	2 (2, 4)	2 (2, 3)	2 (0, 3)	0.066
Postoperative hospitalization, days	6 (4, 10)	6 (5, 8)	4 (3, 6)	0.016
Postoperative mechanical ventilation				0.201
No	49 (91)	41 (98)	41 (98)	0.843
Yes	5 (9)	I (2)	I (2)	0.023
Postoperative clinical complications				0.517
No complications	44 (81)	32 (76)	37 (89)	0.592
Thoracentesis	2 (4)	7 (17)	0 (0)	<0.001
Dyspnea	5 (9)	2 (5)	3 (7)	0.565
Air leakage in chest tube	I (2)	I (2)	l (2)	1.000
Arrhythmia	2 (4)	0 (0)	l (2)	0.368
Reoperation	0 (0)	0 (0)	0 (0)	
Death	0 (0)	0 (0)	0 (0)	
Anesthesia cost, CNY	8303 ± 1563	7685 ± 1599	$\textbf{6983} \pm \textbf{1941}$	0.001
Total hospitalization cost, CNY	106,698 \pm 52,634	91,395 \pm 38,976	$\textbf{84,591} \pm \textbf{57,426}$	0.091

Table 3. Later recovery in the ward.

Data are presented as median (lower quartile, upper quartile), n (%), or mean \pm standard deviation. SS-VATS, single-stage sequential bilateral video-assisted thoracoscopic surgery; TS-VATS, two-stage video-assisted thoracoscopic surgery at a 3-month interval; ICU, intensive care unit.

Complications	Variables	P value	OR (95% CI)
Intraoperative unstable	Sex	0.011	0.121 (0.024-0.610)
hemodynamics	FVC% predicted	0.017	1.077 (1.014–1.145)
	Surgical time	0.010	1.038 (1.009–1.069)
	Anesthesia time	0.028	0.972 (0.948-0.997)
	Preoperative neutrophil ratio	0.045	4.377 (1.030–18.599)

Table 4. Risk factors for intraoperative unstable hemodynamics.

OR, odds ratio; CI, confidence interval; FVC% predicted, percent predicted forced vital capacity.

VATS if these patients have a lower percent predicted forced vital capacity, longer surgical time, or higher preoperative neutrophil count. Therefore, the preoperative evaluation should be rigorous for patients who are scheduled for single-stage sequential bilateral thoracic surgery. Patients with normal pulmonary function and no obvious preoperative infection can undergo singlestage bilateral VATS, and the surgical time should not be too long so that the hemodynamics can remain stable.

Notably, during single-stage bilateral VATS, the peak inspiratory pressure was higher and hypoxemia occurred in 17% of patients. The aftereffects of lung collapse and lung injury caused by surgical traction and resection in the first-side lung surgery may account for the higher respiratory pressure and higher incidence of



Figure 2. Changes in blood assay. *P < 0.05, **P < 0.01 for TS-VATS vs. SS-VATS group postoperatively. $^{\Delta D}P < 0.01$ for postoperative vs. preoperative values SS-VATS, single-stage sequential bilateral video-assisted thoracoscopic surgery; TS-VATS, two-stage videoassisted thoracoscopic surgery at a 3-month interval.

intraoperative hypoxemia, which were in parallel with the second-side lung surgery. Moreover, the longer surgical time and the need to flip the patient's position may had led to unstable hemodynamics, which in turn increased the use of vasoactive drugs and may have even increased blood loss. Synchronous subxiphoid uniportal VATS for bilateral pulmonary lesions may decrease the incidence of unstable hemodynamics and decrease the time in the flipped position.²¹ Although the chest tube duration and the incidence of postoperative clinical complications were similar in the two groups, the durations of the ICU stay and postoperative hospitalization were longer in the single-stage VATS group. These findings may indicate that although singlestage and two-stage bilateral VATS are not different in terms of postoperative complications, single-stage VATS requires a longer recovery. Therefore, single-stage VATS is feasible, but the intraoperative management may be challenging and patients often need different postoperative monitoring; 9% of patients in the present study also needed postoperative mechanical ventilation. This is not consistent with the findings reported by Matsubara et al.,²⁰ who advocated the safety of single-stage bilateral pulmonary metastasectomy based on a study sample of 19 patients. However, such a small sample does not provide convincing results.

Regardless of whether single-stage or two-stage VATS is performed, the total types of the first and second procedures were the same, while the first procedure performed was not similar. More wedge resections were performed among patients who underwent single-stage VATS, while more lobectomies were performed among those

who underwent two-stage VATS. Singlestage VATS often begins with wedge resection because the surgeon must ensure that the patients have enough residual lung tissue to tolerate one-lung ventilation during the operation of the other side. However, lobectomy and two combined procedures were more frequently performed among patients who underwent two-stage VATS because the patients could recover their pulmonary function after a few months.^{13,22} Several published articles comparing different procedures have reported conflicting results, making it difficult to achieve a consensus on which procedure is the best for small pulmonary nodules.^{23,24} Our study showed no difference in tumor size, pathologic classification, preoperative chemotherapy, or surgical site in our study. This indicates that the specific location of the tumor (such as whether the tumor straddles two lung lobes and whether it is close to the main bronchus) and the experience of the surgeons may be factors that influence the choice of different thoracic procedures.

This study had several limitations. First, this was a retrospective single-institute investigation involving data collected during an 8-year period, introducing inevitable bias. However, cases of bilateral lung tumors are relatively scarce, and a singleinstitute investigation can reduce differences in therapy protocols. Second, the types of thoracic procedures were included rather than a specific type. The main reason for this was to simulate the real clinical scenario. We also focused only on bilateral nonsmall cell lung cancer. Third, our study lacked oncological long-term results. The survival status at the 1-year follow-up may be affected by many factors, such as patients' compliance with follow-up treatment. assisted therapy, and others. Therefore, we only evaluated the impact of these two surgical methods mainly in terms of postoperative hospitalization.

Conclusions

Single-stage sequential bilateral VATS can be performed to successfully treat bilateral pulmonary lesions with a shorter total time and higher cost-effectiveness than two-stage VATS. However, surgeons should be cautious of intraoperative hypoxia, a higher peak respiratory pressure, a longer surgical time, unstable hemodynamics, a longer duration of ICU stay, and longer hospitalization. The preoperative evaluation should be rigorous for patients who are scheduled for single-stage sequential bilateral thoracic surgery.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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