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ORIGINAL RESEARCH

Comparison of Double Sleeve Lobectomy by Uniportal Video-Assisted Thoracic Surgery (VATS) and Thoracotomy for NSCLC Treatment

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Background: With the development of the surgical technique and experience of surgeons, uniportal VATS has been used in double sleeve lobectomy to treat non-small cell lung cancer (NSCLC). This retrospective study aims to evaluate the efficacy and safety of uniportal VATS in NSCLC treatment.

Methods: We reviewed 42 NSCLC patients who underwent double sleeve lobectomy in Shanghai Pulmonary Hospital from June 2015 to November 2017. 21 patients received double sleeve lobectomy through uniportal VATS and 21 through conventional thoracotomy with large incision.

Results: The characteristics of patients were similar between the two groups. The operation time was longer in the uniportal VATS group (p=0.021) and the drainage on postoperation day 1 was significantly less in the uniportal VATS group (p=0.004). Patients reported a lower postoperative pain level in the uniportal VATS group than in the thoracotomy group (p=0.002). No statistically significant difference showed in other aspects.

Conclusion: Uniportal VATS double sleeve lobectomy for NSCLC treatment is safe and effective. Lower postoperative pain level was found in the uniportal VATS group. Its complication rate and postoperation survival were similar to the conventional thoracotomy approach with large incision. But a large randomized clinical trial is still necessary for further investigation.

Keywords: sleeve lobectomy, uniportal video-assisted thoracic surgery, VATS, thoracotomy

Introduction

Lung cancer is one of the commonest cancers with high mortality in the world.[1] Nowadays, a variety of methods have been applied to lung cancer treatment, such as operation,[2,3] chemotherapy, target therapy[4] and immunotherapy.[5] But complete resection is still a critical treatment with curative intent for early stage lung cancer. For central lung cancer, pneumonectomy was a common procedure in the past. In recent years there were several studies finding that sleeve lobectomy could be an alternative to pneumonectomy.[6–8] With the development of the technique and surgeons' experience, video-assisted thoracic surgery (VATS) sleeve lobectomy and even VATS double sleeve lobectomy have been reported.[9–11] Thus, it is essential to investigate whether VATS double sleeve lobectomy, especially uniportal VATS, can provide a similar or even better outcome compared to the thoracotomy method.

We did a retrospective study to explore the safety and efficacy of uniportal VATS double sleeve lobectomy for non-small cell lung cancer (NSCLC) and compare the outcome with the operation performed through thoracotomy.

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Methods

Patients

We reviewed 42 patients who received double sleeve lobectomy through conventional thoracotomy or uniportal VATS with curative intent for lung cancer from June 2015 to November 2017 in our hospital. Bronchoscopy was routinely performed before surgery in order to make sure of the possibility for bronchial sleeve resection. Preoperative classification was determined after an enhanced chest CT scan, ultrasound bronchoscopy, brain MRI and bone imaging of the patients. Postoperative pathological classification was according to the IASLC Eighth Edition of the TNM Classification for Lung Cancer.[12] The study was approved by Shanghai Pulmonary Hospital, Tongji University, in accordance with the guidelines of the Helsinki Declaration of 1975, revised in 1983. All participants provided written informed consent.

Procedure

All patients underwent standard general anesthesia and double-lumen endotracheal intubation. The patients' position was lateral decubitus. For patients who had uniportal VATS, we made a 4 cm incision at the anterior axillary line in the fourth intercostal space to insert the surgical instrument. The tourniquet technique[13] was applied to occlude the proximal and distal pulmonary artery. Scissors were used to divide and trim the bronchus and the artery. The corresponding lobe was resected simultaneously. Hilar and mediastinal lymph node resection was conducted during the operation. The resected bronchial stump was sent for frozen pathological examination to identify whether the margin was free of cancer. If it was negative, the bronchus anastomosis would be performed. We performed a suture with 3–0 prolene for cartilaginous and membranous portions. When the bronchial anastomosis was completed, the artery was anastomosed continuously with 5–0 prolene. The resected lobe was removed through the port. Saline was used to wash the chest and the lung was inflated to identify any potential air leak. A 28 Fr chest tube was put into the chest.

For the thoracotomy group, we performed a conventional posterolateral thoracotomy large incision of about 20 cm at the fourth or fifth intercostal space and the muscle was incised. The involved bronchus was resected and sent for frozen pathological examination. Related lobe and mediastinum lymph nodes were also removed. We performed bronchus anastomosis with 3–0 prolene for continuous suturing or 4–0 vicryl for interrupted suturing. Pulmonary arterial anastomosis was also performed by continuous suturing with 5–0 prolene. Saline was used to wash the chest and the lung was inflated to identify any potential air leak. A 28 Fr chest tube was put into the chest.

After operation, patients would be sent back to the wards after they were stable in the intensive care unit. We used the numeric rating scale (NRS) to measure the pain level of the patients, in which 0 represented "no pain" and 10 represented "the worst pain". The highest score was used to represent the postoperative pain level. Postoperative complications were defined as symptoms that occurred within 30 days after surgery.

Follow-up was conducted every 3 months, and the patients underwent the CT scan or chest radiography. The follow-up was to June 2018.

Statistical Analysis

Statistical analysis was obtained by SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Measurement data shown as the mean (SD) were analyzed by *t*-test, or shown as the median (P_{25}–P_{75}) were analyzed by the Wilcoxon rank sum test. Enumeration data expressed as the number (proportion) were analyzed by the chi-square test. For survival analysis, we used the Kaplan–Meier method and compared by the log rank test. The Cox model was applied for multivariable analysis in survival data and the result would be shown as the hazard ratio (HR) and corresponding 95% confidence interval (95% CI). Statistical significance was considered as p value less than 0.05.

Results

Of the 42 patients, 21 had double sleeve lobectomy through thoracotomy and 21 through uniportal VATS. Characteristics of patients in the two groups are shown in Table 1. The proportion of patients with a smoking history showed no statistical significance. There were two patients in both groups having neoadjuvant chemotherapy before operation and no patient had a history of thoracic surgery. No significant difference between the two groups was found in preoperative pulmonary function and arterial blood gas analysis. Tumor characteristics of the patients were also collected and are shown in Table 1. The diameter of the tumor showed no statistical difference between the two groups. Either the uniportal VATS group or the thoracotomy group had more patients with

Table 1 Characteristics of Patients

	Uniportal VATS (n=21)	Thoracotomy (n=21)	*p* Value
Age (years)	62 (59–68)	61 (56–64)	0.134
Sex			1.000
Male	19 (90.5%)	19 (90.5%)	
Female	2 (9.5%)	2 (9.5%)	
Smoking			0.057
Yes	16 (76.2%)	10 (47.6%)	
No	5 (23.8%)	11 (52.4%)	
BMI (kg/m^2)	22.75 (3.09)	22.68 (2.38)	0.903
Albumin (g/L)	37.71 (2.61)	40.14 (3.84)	0.021*
Hb (g/L)	127.43 (14.37)	133.19 (12.71)	0.176
FEV1 (L)	2.20 (0.51)	2.52 (0.51)	0.057
$PaCO_2$(mmHg)	39.11 (2.18)	39.14 (3.05)	0.968
PaO_2(mmHg)	87.38 (8.22)	87.95 (12.18)	0.860
SaO_2(%)	97.12 (0.74)	97.20 (1.02)	0.797
Diameter (cm)	3.73 (1.38)	4.18 (2.92)	0.525
Lesion			0.694
Left upper lobe	18 (85.7%)	16 (76.2%)	
Right upper lobe	3 (14.3%)	5 (23.8%)	
Pathology			0.798
Squamous cell carcinoma	14 (66.7%)	16 (76.2%)	
Adenocarcinoma	4 (19.0%)	4 (19.0%)	
Large cell carcinoma	2 (9.5%)	0 (0.0%)	
Sarcoid carcinoma	1 (4.8%)	1 (4.8%)	
TNM stage			0.642
1a	1 (4.8%)	1 (4.8%)	
1b	7 (33.3%)	6 (28.6%)	
2a	1 (4.8%)	0 (0.0%)	
2b	3 (14.3%)	6 (28.6%)	
3a	7 (33.3%)	8 (38.1%)	
3b	2 (9.5%)	0 (0.0%)	

Notes: Data are presented as mean (SD), median (P_{25}–P_{75}) or n (%). *$p<0.05$.
Abbreviations: VATS, video-assisted thoracic surgery; BMI, body mass index; Hb, hemoglobin; FEV1, forced expiratory volume in 1 second.

lesions located at the left upper lobe. But the tumor location between the two groups showed no statistical difference. The distribution of histologic types and postoperative pathological staging between the two groups had no significant difference. The postoperative nodal stage is extracted in Table 2 separately.

All patients had the angioplastic procedure of vascular sleeve resection. There was no patient in the uniportal VATS group converting to thoracotomy during operation. The

Table 2 Nodal Status of Patients

	Uniportal VATS (n=21)	Thoracotomy (n=21)	*p* Value
N0	10 (47.6%)	8 (38.1%)	0.231
N1	2 (9.5%)	7 (33.3%)	
N2	9 (42.9%)	6 (28.6%)	

median operation time was 4 h in uniportal VATS and 3 h in thoracotomy, and statistical difference was found between the two groups (p=0.021). No significant difference in perioperative blood loss between the two operation methods was found in our study (Table 3). The number of lymph node stations and lymph nodes harvested during operation are listed in Table 3 and showed no statistical difference. No positive margin was reported in both groups. Drainage on postoperation day 1 was significantly more in thoracotomy than in uniportal VATS (p=0.004). However, the length of postoperative hospital stay had no statistical difference. Also, no patients in both groups were readmitted because of operation-related problems after they were discharged. The complications reported in our study were fever, subcutaneous emphysema, infection and arrhythmia. No life-threatening complications were reported. Three patients in uniportal VATS and one patient in thoracotomy suffered postoperative complications but the difference was not statistically significant. There was no operation-related death reported. Postoperative pain data were also collected and analyzed (Figure 1). Ppostoperative pain scores were significantly higher in the thoracotomy group than in the uniportal VATS group (p=0.002).

All patients in the thoracotomy group completed the follow-up, but three patients (14.3%) in the uniportal VATS group were lost. The estimated median disease free survival in uniportal VATS was 36 months in our study. In univariate analysis, no statistically significant difference was detected in disease free survival (Figure 2) and overall survival (Figure 3). No variable showed a statistically positive or negative effect on DFS of the patients (Table 4).

Discussion

Since sleeve lobectomy was performed for bronchogenic carcinoma in 1954,[8] it had been considered as an alternative method for pneumonectomy. Sleeve lobectomy could maximally remove the tumor and maximally preserve normal lung tissue.[7] Several studies had demonstrated that sleeve lobectomy might provide a better outcome than pneumonectomy.[6,14–16] VATS had shown

Table 3 Operation Data

	Uniportal VATS (n=21)	Thoracotomy (n=21)	*p* Value
Operation time (h)	4 (3–5)	3 (2–4)	0.021*
Operative blood loss (mL)	200 (100–200)	100 (100–400)	0.658
Lymph node station	5 (5–6)	6 (5–7)	0.111
Lymph node number	9 (8–13)	10 (7–14)	0.870
Positive lymph nodes	1 (0–4)	1 (0–2)	0.712
Drainage on POD1 (mL)	250 (150–300)	400 (300–450)	0.004*
Postoperative hospital stay (days)	6 (4–7)	6 (5–8)	0.380
Complications	3 (14.3%)	1 (4.8%)	0.599
Fever	2 (9.5%)	0 (0.0%)	0.469
Subcutaneous emphysema and pulmonary infection	1 (4.8%)	0 (0.0%)	1.000
Cardiac arrhythmia	0 (0.0%)	1 (4.8%)	1.000

Notes: Data are presented as median (P_{25}–P_{75}) or n (%). *p<0.05.
Abbreviation: POD1, postoperation day 1.

its similar, even better, outcome when compared to thoracotomy.[17–21] VATS had a lower level of acute phase reaction and slighter suppression of the patient immune reaction.[22] Recently, sleeve lobectomy with or without angioplastic procedure has been reported to be performed by VATS,[9,23–25] even uniportal VATS.[10,11,26,27]

In our study, the operation time was longer in uniportal VATS. Considering that uniportal VATS double sleeve lobectomy is a more complicated procedure, the requirement of longer time should be acceptable. Operative blood loss ranged from study to study. Mahtabifard et al reported that median operative blood loss was 250 mL.[28] Xu et al showed the average operative blood loss was 207±96 mL.[29] Another study in a Chinese population reported that as 390 ±206 mL.[30] A multicenter study showed that the median operative blood loss was 224 mL.[25] We found the median operative blood loss was 200 mL and it showed no significant difference when compared to thoracotomy. This consequence corresponded to a previous study.[31] This result indicated that the VATS approach might have smaller damage to the lungs of the patients.

Before operation, patients always had some days for diagnosis and preoperative examination. Thus, compared to total hospitalization, the postoperative hospital stay might be a more sensitive variable to show safety of the operation indirectly. So, we collected postoperative hospital stay as our data for analysis. It showed no statistical difference between the two groups. But one study found that the VATS approach had an obviously shorter postoperative hospital stay.[31] In another study, the median postoperative hospital stay was 10 days,[29] which was similar to that found by Huang et al.[25]

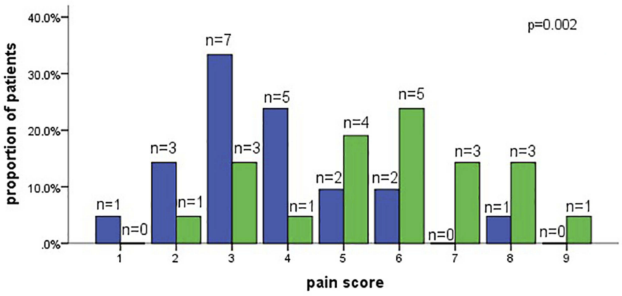

Figure 1 Patients' reported pain scores after surgery.

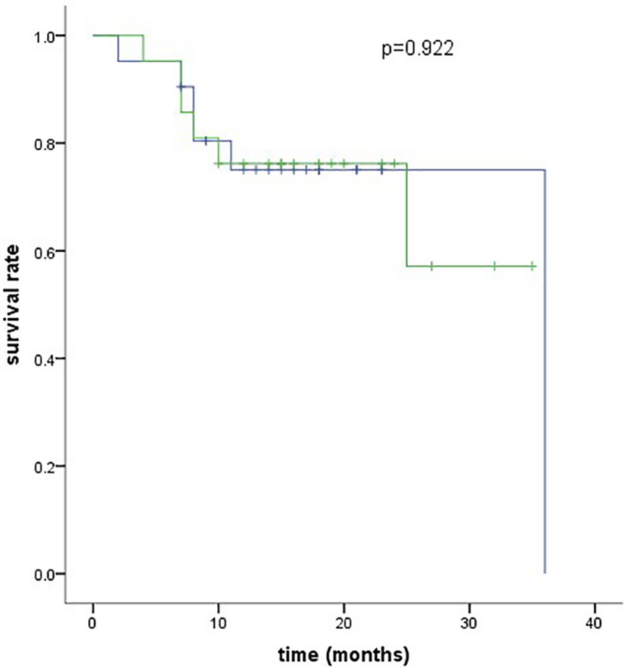

Figure 2 Kaplan–Meier curve for disease free survival.

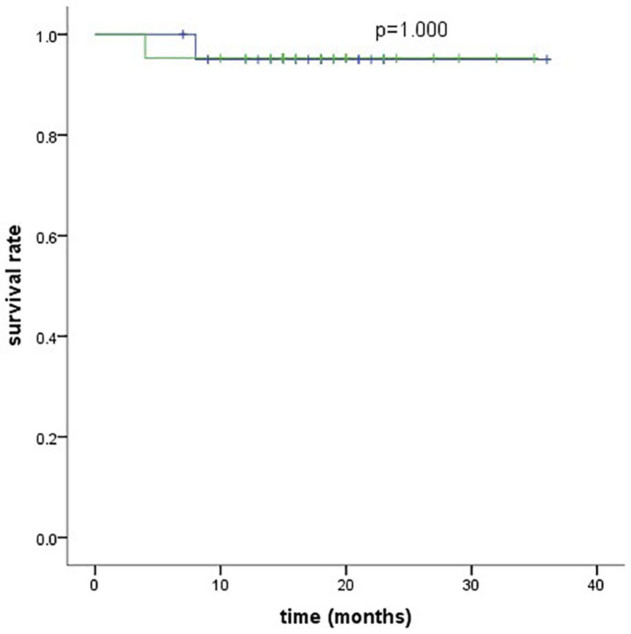

Figure 3 Kaplan–Meier curve for overall survival.

Because of safety, complete resection and technological issues, conversion to thoracotomy might be required. Hilar lymphadenopathy and bleeding were the commonest reason for conversion followed by fusion of fissure and lymph node metastasis.[32] We found that the total lymph node station and total lymph nodes which were resected in the uniportal VATS operation were similar to those in thoracotomy. This result was also confirmed by Zhou et al.[31] The result might suggest that uniportal VATS was effective for patients who needed lymphadenectomy.

Pneumonia, pulmonary embolism, atelectasis, prolonged air leak, empyema, etc. might occur as major complications after sleeve lobectomy.[8] Some of them are severe and life-threatening, such as bronchovascular fistula, bronchopleural fistula and bronchial stenosis. According to our study, only three patients in the uniportal VATS group had postoperative complications and no patient suffered from those severe complications or died within 30 days after operation. Compared to thoracotomy, uniportal VATS had relatively more complications but no significant difference occurred. Zhou et al described that only one patient of 10 in the VATS group had atrial fibrillation as a complication.[31] Huang et al reported that only one patient who had had six cycles of neoadjuvant chemotherapy was diagnosed with pneumonia after operation.[25] Some studies reported that major postoperative complications could not occur.[29,30] But Mahtabifard et al reported that two patients went through severe complications after surgery.[28] This discrepancy may relate to individual difference of the patients and surgeons' experience, not just the VATS approach itself.

Intense postoperative pain will make patients debilitated and have a negative impact on patients' recovery. Thus, postoperative pain should also be considered as an

Table 4 Multivariable Analysis for Disease Free Survival (DFS)

Variable	HR	95% CI	*p* Value
Approach			
Thoracotomy	Reference	–	–
Uniportal VATS	0.573	0.126–2.608	0.471
Sex			
Male	Reference	–	–
Female	6.734	0.177–256.310	0.304
Age (years)			
<62	Reference	–	–
≥62	1.017	0.286–3.621	0.979
Smoking			
Never	Reference	–	–
Current	1.462	0.149–14.321	0.744
Location of the lesion			
LUL	Reference	–	–
RUL	1.125	0.143–8.849	0.911
Diameter (cm)			
<4	Reference	–	–
≥4	6.809	0.520–89.090	0.144
Preoperative chemotherapy			
Have	Reference	–	–
Never	4.16	0.594–38.708	0.159
Pathology			
Squamous cell carcinoma	Reference	–	–
Adenocarcinoma	2.546	0.715–9.068	0.149
Large cell carcinoma	1.88	0.213–16.621	0.57
Sarcoid carcinoma	0	–	0.988
TNM stage			
I	Reference	–	–
II	5.814	0.646–52.343	0.116
III	6.136	0.726–51.135	0.094
N stage			
N0	Reference	–	–
N1	2.836	0.471–17.080	0.255
N2	4.594	0.925–22.826	0.062

important factor when evaluating an operation method. Present studies have confirmed less postoperative pain in multiportal VATS. A study containing 3900 patients found that patients who underwent VATS were less likely to use opioids after surgery.[33] A randomized trial found that more patients reported moderate-to-severe pain (NRS≥3) in thoracotomy than VATS. Also, patients in VATS tended to have a significantly shorter duration of epidural analgesia after the surgery. Meanwhile, during the whole follow-up, the EuroQol 5 Dimensions (EQ5D) scores reported by patients were significantly better in the VATS group.[18] In our study, we obtained the result that the pain scores were significantly lower in patients who had double sleeve lobectomy through uniportal VATS. This corresponded to the previous studies. Theoretically, uniportal VATS with only one port can be considered as a less invasive approach than multiportal VATS. In general opinion, it should be a less painful approach. But in a present study, McElnay et al found the dosage of morphine used in the first 24 h after operation and patients reported pain scores were comparable between the uniportal and multiportal groups.[34] This suggests further studies are indispensable to investigate whether uniportal VATS has a different pain level.

Survival is another important aspect to evaluate the efficacy of operations. Several studies have reported long-term survival data for thoracotomy sleeve lobectomy. Chunwei et al reported that the overall survival rate at 5 and 10 years was 48.9% and 38.8% respectively.[35] Takeda et al showed the 5-year overall survival rate was 54.3%, while the rate in the work of Ludwig et al was just 39%.[14,16] A meta-analysis reported the overall 5-year survival rate was 50.3% and the median overall survival was 60 months.[6] Long-term outcome of VATS sleeve lobectomy was limited. It was reported in a retrospective study that the overall 1-, 2-, 3-, and 4-year survival rate was 100%, 89%, 63%, and 40% respectively. Also, they suggested the overall median survival was similar between VATS and the thoracotomy approach.[31] According to our study, the survival between uniportal VATS and thoracotomy showed no statistical difference. This indicated that we could use the less invasive method to achieve a similar goal of survival. For prognosis, nodal status is also considered as a reliable factor. The survival rate varied between different pathological nodal stages.[35] However, it did not occur in our present study. This might be due to our relatively small sample size and short follow-up.

It had been reported that bronchoplastic surgery was still a safety operation method for patients who had had induction therapy.[36] However, Takeda et al showed that three patients who received induction therapy before sleeve lobectomy finally died because of empyema or respiratory failure.[14] Huang et al reported that a patient receiving six cycles of neoadjuvant chemotherapy suffered pneumonia after thoracoscopic double sleeve lobectomy.[25] In our study, severe complications had not been found. But one patient who had had chemotherapy before surgery had a fever after surgery. This might suggest that uniportal VATS double sleeve lobectomy could be safe to apply for patients with neoadjuvant chemotherapy, but these patients would need more attention after surgery.

Our study compares double sleeve lobectomy through uniportal VATS and thoracotomy which is relatively limited currently. But some limitations exist in our study. First, the number of samples in our study is small. Second, this is a retrospective study, which means its non-randomization and unknown confounding variables might affect the study result.

Conclusion

We can preliminarily infer that uniportal VATS double sleeve lobectomy is a safe and effective operation method for NSCLC patients. This operative technique shows a comparable occurrence of complications and survival as the conventional thoracotomy approach with large incision does. At the same time, it brings patients a lower level of postoperative pain. But considering the limitations that exist in our study, large randomized trials should be conducted in the future.

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Disclosure

The authors report no conflicts of interest in this work.

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