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ORIGINAL ARTICLE

Short- and medium-term outcomes after uniportal and multiportal video-assisted thoracic surgery lobectomy in elderly patients with non-small cell lung cancer

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Summary

Purpose: *To investigate the short- and medium-term outcomes following treatment with uniportal video-assisted thoracic surgery lobectomy (uniportal VATS) in elderly patients with non-small cell lung cancer (NSCLC).*

Methods: *We conducted a retrospective analysis on the clinical and follow-up data of 74 elderly patients with NSCLC who underwent uniportal VATS between January 2015 and January 2020. One-to-one propensity score matching (PSM) was employed to select 71 elderly patients with NSCLC who underwent multiportal video-assisted thoracoscopic lobectomy (multiportal VATS) during the same period.*

Results: *The baseline characteristics of the two patient groups were comparable, with no statistically significant differences in postoperative complications, operation time, conversion to thoracotomy, or lymph node dissection. The amount of intraoperative blood loss and postoperative pain were lower in the uniportal VATS group than in the multiportal VATS group. The 3-year overall survival and disease-free survival of the two groups were similar.*

Conclusions: *Uniportal VATS achieved similar short- and medium-term outcomes as Multiportal VATS in elderly patients with NSCLC.*

Key words: *lobectomy, minimally invasive surgery, non-small cell lung cancer, uniportal video-assisted thoracic surgery, elderly*

Introduction

Lung cancer is the most common cancer and the leading cause of cancer death worldwide [1]. With advancements in medical technology, many modalities can be used to treat lung cancer. However, surgery remains the preferred treatment for early stage non-small cell lung cancer (NSCLC) [2]. In recent years, uniportal video-assisted thoracic surgery lobectomy (uniportal VATS) has been widely adopted in the field of thoracic surgery [3]. The continued aging of the population and the gradual increase in the prevalence of NSCLC have prompted growing interest in the surgical treatment of elderly patients with lung cancer [4]. Elderly patients exhibit poor cardiopulmonary function, low tolerance to postoperative pain, and poor postoperative recovery [4]. Furthermore, they are more likely than younger patients to experience postoperative complications in the cardiovascular and respiratory systems. Consequently, the risk associated with surgery is extremely high in elderly patients with NSCLC [4]. Compared with multiportal video-assisted thoracoscopic lobectomy (multiportal VATS), uniportal

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VATS causes less surgical trauma and less postoperative pain [5-14]. However, there have been no any English language report on the application of uniportal VATS in elderly patients (aged ≥ 70 years) with NSCLC. This study was designed to investigate the short- and medium-term outcomes of uniportal VATS for treating elderly patients with NSCLC

Methods

This study complied with the Declaration of Helsinki. This retrospective research was approved by the ethics review board of our institution. The need for informed consent from all patients was waived because of retrospective study, not prospective trial.

The data from patients aged ≥ 70 years who underwent uniportal or multiportal VATS at our institution between January 2015 and January 2020 were retrospectively analyzed. The inclusion criteria were as follows: (1) clinical stage I tumor; (2) primary NSCLC; (3) complete dataset. The exclusion criteria were: (1) NSCLC of the same stage in both lungs; (2) secondary lung cancer. Follow-ups by telephone and outpatient visits were initiated 1 month after surgery. The cutoff date for follow-up was June 1, 2020. To reduce the impact of confounding factors on the study results, SAS 9.3 software (SAS Institute, Inc., Cary, NC) was used. Propensity scores were calculated using surgical modality as the manipulated variable, while patients' gender, age, clinical stage, and smoking history were used as covariates. Patients in the two groups were ranked according to their propensity scores, and those with the closest propensity scores were matched in a 1:1 ratio. The caliper was set at 0.05. Analysis of the short-term efficacy and medium-term survival were performed in the two groups after matching. After exclusions, 172 patients were identified: 93 having uniportal VATS and 79 having multiportal VATS. Propensity score yielded two well-matched groups of 71 patients.

The surgical procedures were as follows. For uniportal VATS, a 3.0-cm incision was made in the 4th or 5th intercostal space between the ipsilateral anterior axillary line and midaxillary line. An incision protection sleeve was then placed on the incision, and a thoracoscope was inserted to examine the presence of pleural adhesions and tumor metastases. The lesion location and hilar anatomy were then determined. The specific surgical sequence was not identical in each lobectomy; instead, the anatomic structures, such as pulmonary veins, bronchial tubes, and pulmonary arteries were treated individually in all cases. Routine exploration and dissection of lymph node stations 2R, 4R, 7R, 8R, 9R, and 10R were performed

Table 1. Baseline characteristics of the two groups

Characteristics	*Uniportal VATS (n=71)*	*Multiportal VATS (n=71)*	*p value*
Age (y)	72 (70-75)	73 (70-76)	0.479
Gender			0.593
Male	46	49	
Female	25	22	
Charlson comorbidity index (CCI)			0.615
CCI ≤ 2	8	10	
CCI > 2	63	61	
Pulmonary function			
FVC (% predicted)	87 (79-91)	90 (80-92)	0.874
FEV1 (% predicted)	85 (81-93)	83 (78-90)	0.597
MVV (% predicted)	68 (57-75)	66 (54-72)	0.417
Clinical TNM stage			0.607
IA	26	29	
IB	45	42	
ASA score			0.595
I	64	62	
II	4	5	
III	3	4	
Smoking status			0.502
Yes	37	33	
No	34	38	
Tumor location			0.310
Left	34	28	
Right	37	43	

CCI: Charlson comorbidity index, ASA: American Society of Anesthesiologists, FEV1: Forced Expiratory Volume in the first second, MVV: maximal voluntary ventilation.

in the case of tumors in the right lung, while routine exploration and dissection of lymph node stations 6L, 7L, 8L, 9L, and 10L were performed in the left lung [5].The multiportal VATS procedures has been reported [15].

Statistics

All the statistical analyses were performed using SAS 9.3 software (SAS Institute, Inc., Cary, NC). Normally distributed variables were analyzed by Student *t*-test and presented as means and standard deviations. Non-normally distributed variables were analyzed by Mann–Whitney *U* test and presented as medians and ranges. Differences between semiquantitative results were analyzed by Mann–Whitney *U* tests. Differences between qualitative results were analyzed by chi-square or Fisher exact tests, as appropriate. Survival rates were analyzed by the Kaplan–Meier method, and differences between the two groups were analyzed by log-rank test. $P<0.05$ was considered to be statistically significant.

Results

The baseline characteristics of the two patient groups were comparable (Table 1). As for surgical outcomes, there were no statistically significant differences in postoperative complications, operation time or conversion to thoracotomy rate. At postoperative day 30, complications had occurred in 9 patients in the uniportal VATS group and in 11 patients in the multiportal VATS groups (Table 2). In the uniportal VATS group, complications included arrhythmia in one patient, pulmonary infection in 3 patients, atelectasis in one patient, respiratory failure in one patient, prolonged air leak in 2 patients, and heart failure in one patient. In the multiportal VATS group, complications included arrhythmia in 2 patients, prolonged air leak in 2 patients, pulmonary infection in 4 patients, atelectasis in one patient, respiratory failure in one patient, and heart failure in one patient (Table 2). Appropriate measures were taken to manage different complications: antiarrhythmic drugs for arrhythmia; antibiotics for pulmonary infection; bronchoscopic suctioning for atelectasis; mechanical ventilation for respiratory failure; and diuretic drugs for heart failure. All patients were discharged upon recovery.

The amount of intraoperative blood loss (Table 2) and pain scores 24, 48, and 72 h after surgery

Table 2. Surgical outcomes of the two groups

Characteristics	*Uniportal VATS (n=71)*	*Multiportal VATS (n=71)*	*p value*
Lobectomy			
Left upper lobe	21	13	0.116
Left lower lobe	13	15	0.673
Right upper lobe	15	21	0.247
Right middle lobe	5	7	0.546
Right lower lobe	17	15	0.688
Blood transfusion	0	0	-
Blood loss (ml)	100 (80-240)	120 (90-260)	0.045
Drainage duration (days)	4 (3-6)	5 (3-7)	0.247
Postoperative pain VAS score (h)			
24	4 (2–6)	5 (3–7)	0.030
48	3 (2–5)	4 (2–7)	0.044
72	2 (1–3)	3 (2–6)	0.046
Postoperative hospital stay (days)	9 (7-17)	10 (7-21)	0.354
Postoperative complications	9	11	0.629
Respiratory failure	1	1	
Atelectasis	1	1	
Prolonged air leak (>5 days)	2	2	
Pneumonia	3	4	
Arrythmia	1	2	
Heart failure	1	1	
Major complications	1	1	0.941
Minor complications	8	10	
Postoperative 30-day death	0	0	-

VAS: visual analogue scale.

were lower in the uniportal VATS group than in the multiportal VATS group (Table 2). The number of lymph node stations and lymph nodes dissected, as well as the number of mediastinal lymph node stations and mediastinal lymph nodes dissected, were not significantly different between the two groups (Table 3).

The median follow-up period of uniportal and multiportal VATS groups were 28 months and 30 months respectively (p=0.410). During the last follow-up, a total of 10 patients died in the uniportal VATS group, and a total of 14 patients died in the multiportal VATS group (Table 4, p=0.370). The three-year overall survival rates for the uniportal and multiportal VATS groups, were 74% and 76%, respectively (Figure 1, p=0.935). During the last follow-up, a total of 11 patients had cancer recurrence in the uniportal VATS group, and a total of 17 patients had cancer recurrence in the multiportal VATS group (Table 4, p=0.206). The three-year disease-free survival rates for the uniportal and multiportal VATS groups, were 69% and 67%, respectively (Figure 1, p=0.763).

Discussion

VATS has been widely used to diagnose and treat various thoracic diseases, such as diseases of the lung, mediastinum, pleural membrane, and esophagus [16-20]. Most conventional VATS procedures use portals. Rocco et al first reported uniportal pulmonary wedge resection in 2004 [21], and the indications for this procedure have since expanded to include many thoracic diseases, including those in the pleural membrane, mediastinum and lung [3]. In 2011, Gonzalez et al reported uniportal VATS, a technique that has been further promoted in recent years [22]. Currently, there is no definite age cutoff for elderly patients in clinical research involving these procedures. A review of the

Table 3. Pathological outcomes of the two groups

Outcomes	*Uniportal VATS (n=71)*	*Multiportal VATS (n=71)*	*p value*
Histological type			0.382
Adenocarcinoma	48	43	
Squamous cell carcinoma	23	28	
Number of harvested lymph nodes	18 (14-21)	19 (15-23)	0.478
Number of mediastinal lymph nodes dissected			
Pathological stage	7 (5-11)	8 (6-10)	0.404
IA			0.911
IB	15	16	
IIA	27	23	
IIB	10	12	1.000
IIIA	12	15	
Residual tumor	7	5	
R0			
R1	71	71	
R2	0	0	

Table 4. Follow-up outcomes of the two groups

	Uniportal VATS (n=71)	*Multiportal VATS (n=71)*	*p value*
Tumor recurrence during follow-up	11	17	0.206
Locoregional alone	4	3	
Distant alone	7	12	
Both locoregional and distant	1	2	
Port site	0	0	
Time to first cancer recurrence (months)	21 (10-30)	20 (5-42)	0.599
Mortality during follow-up period	10	14	0.370
Died of cancer	9	13	
Died of non-cancer causes	1	1	

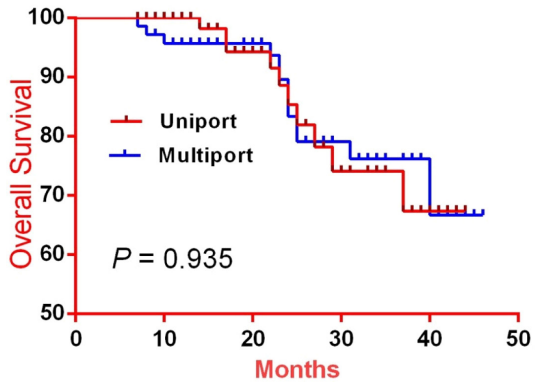

Figure 1. Comparison of overall survival rate between uniportal and multiportal VATS group. There was no significant difference between the two groups (p =0.935).

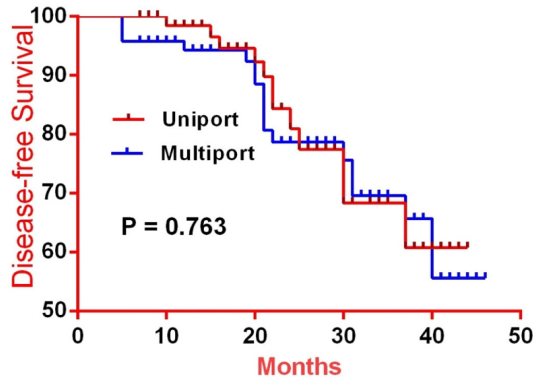

Figure 2. Comparison of disease-free survival rate between the uniportal and multiportal VATS group. There was no significant difference between the two groups (p =0.763).

relevant literature revealed four various age cutoffs used in elderly patients: 65 years old, 70 years old, 75 years old, and 80 years old [23-26]. Searches of domestic and foreign literature regarding VATS in the elderly showed that relatively more publications used ≥ 70 years old as the age cutoff. Thus, the age of elderly patients was set to ≥ 70 years old in the present study. We searched databases such as PubMed and EMBASE, but could not identify any English language report on the application of uniportal VATS in elderly patients (≥ 70 years) with NSCLC. The present study was the first to show that uniportal VATS is safe and effective for treating elderly patients with NSCLC, and that uniportal VATS causes less pain and confers less blood loss than multiportal VATS.

Uniportal VATS is a relatively new surgical modality, so conversion to thoracotomy is inevitable during its initial phase of adoption [9, 10, 27]. Common causes of conversion to thoracotomy include pleural adhesions, tumor invasion, massive intraoperative hemorrhage, and injury of vital structures. Chung et al conducted a retrospective analysis of 90 cases of uniportal VATS and found that conversion to thoracotomy occurred in 10 cases (11.1%) due to adhesions, tumor invasion, and tracheal injury [27]. Shen et al reported 100 cases of uniportal VATS and found that one patient (1%) had conversion to thoracotomy due to massive hemorrhage [9]. Yameen reported 55 patients who had undergone uniportal VATS, 5 of whom (9.1%) had conversion to thoracotomy due to pleural adhesions [10]. In the present study, one patient in each of the two groups had conversion to thoracotomy. The patient in the uniportal VATS group had pleural adhesions that occurred in the early stage of uniportal VATS, and the patient in the multiportal VATS group had massive intraoperative hemorrhage. The field of vision in uniportal VATS is closer to that in thoracotomy, which allows separation of the adhered pleural membranes. No subsequent conversion to thoracotomy due to adhesions was required. With advancements in surgical techniques, iatrogenic tissue injuries can be treated using uniportal VATS. Conversion to thoracotomy is required in cases of massive intraoperative hemorrhage to ensure the safety of the procedure.

The extent of lymph node dissection and the number of lymph nodes dissected are important parameters for assessing whether radical surgery is feasible as cancer treatment [2]. These parameters also serve as an important reference for accurate postoperative staging and prognosis [2]. The combination of lobectomy and systemic lymph node dissection is the standard surgical treatment for NSCLC [2]. The guidelines developed by the National Comprehensive Cancer Network (NCCN) recommend dissection of 3 or more mediastinal lymph node stations, and the total number of lymph nodes dissected should be at least 12 [28]. In the present study, the number of lymph nodes, lymph node stations, and N2 lymph nodes dissected in the uniportal VATS group did not differ from the equivalent numbers in the multiportal VATS group. In addition, the guidelines were met [28], indicating that uniportal VATS is safe and feasible for use in lymph node dissection.

Advancements and refinements in thoracoscopic technique have allowed minimally invasive thoracic surgery. Reduction of iatrogenic trauma and enhanced recovery after surgery (ERAS) have become the major directions for future development of thoracic surgery. The concept of ERAS necessitates collaboration across multiple disciplines, such as anesthesia, nursing, and surgery. It involves preoperative education, preoperative preparation, keeping patients warm, anesthetics with a shorter half-life, restrictive intraoperative

fluid replacement, and enabling mobility early after surgery [29]. ERAS involves cutting-edge techniques and concepts, with the core values of optimizing perioperative management and care measures, reducing complications and stress responses, and accelerating recovery. A study by Huang et al showed that adopting ERAS during the perioperative period of uniportal VATS can alleviate postoperative pain, shorten postoperative hospital stay and reduce the duration of chest tube placement [29]. In the present study, ERAS was implemented in the perioperative period. None of the patients in either group died within 30 days of surgery. In addition, postoperative complications after 30 days were mostly minor. One patient in each of the uniportal VATS and multiportal VATS groups had serious complications, which were cured after active treatment.

Long-term patient prognosis is the fundamental criterion for evaluating whether a novel approach to lung cancer surgery is superior to the conventional approach. Uniportal VATS was first reported in 2011 [22], while wide adoption in major medical centers began in 2014 [5-14]. According to our searches, most existing reports on uniportal VATS focus on short-term outcomes [5-14], and few have evaluated medium-term outcomes [13]. Zhao et al reported 3-year overall survival in patients with NSCLC aged ≥ 60 years [13], including 73 who underwent uniportal VATS and 56 who underwent multiportal VATS. The results showed that 3-year overall survival was not significantly different between the two groups [13]. This was consistent with the results of the present study, which showed that 3-year overall survival and disease-free survival were similar in the two groups.

Using the propensity score matching (PSM) method [30], a propensity score is calculated for each research subject. Individuals from the control group with the same or similar propensity scores as those in the treatment group are then selected and matched. The aim of PSM is to balance the covariates between the groups. Using this method, each propensity score is treated as an independent variable that is evenly distributed between the control and treatment groups. This method is used to achieve a similar effect to randomized controlled trials and minimize study bias. PSM is now widely used in retrospective studies and non-randomized clinical trial data [30].

Several limitations of this study must be considered. The present study was a retrospective analysis in which PSM could only balance the observable variables. The impact of potential unknown factors on the observation endpoints could not be corrected. Multi-center randomized controlled trials are needed in the future to elucidate the impact. Our institution first adopted UVATS in 2015, so long-term follow-up data are lacking, which was a limitation of the study. Thus, we eagerly await confirmation of the short- and medium-term effectiveness of the two surgical modalities in multi-center prospective randomized controlled trials.

Conclusion

Uniportal VATS is safe and effective for treating elderly patients with NSCLC with the advantage of less pain and less blood loss.

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Author contribution

Dian Zhong, Qing Lin and Zhiqiang Zhan contributed to study conception and design, Jinqiang Zhang, and Zhiqiang Zhan contributed to acquisition of data, Yujuan Liu and Zhiqiang Zhan contributed to analysis and interpretation of data, Dian Zhong, Qing Lin and Zhiqiang Zhan contributed to drafting of manuscript, Dian Zhong, Qing Lin and Zhiqiang Zhan contributed to critical revision.

Ethics approval and consent to participate

The study was approved by the ethics review board of our institution. Due to the retrospective study design and the anonymization of data, consent to participate was not necessary.

Conflict of interests

The authors declare no conflict of interests.

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