Original Article Effects of uniportal thoracoscopic pulmonary segmentectomy and lobectomy on patients with early-stage non-small-cell lung cancer and risk factors of postoperative complications

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Abstract: Objective: To determine the effects of uniportal thoracoscopic pulmonary segmentectomy and lobectomy on patients with early-stage non-small-cell lung cancer (ES-NSCLC) and risk factors of postoperative complications. Methods: The clinical data of 97 patients with early lung cancer treated in Mingguang People's Hospital between October 2019 and December 2021 were retrospectively analyzed. A total of 45 patients who underwent pulmonary segmentectomy were assigned to the observation group. The remaining 52 patients who underwent lobectomy were assigned to the control group. The perioperative indexes of the two groups were compared, including operation time, intraoperative blood loss, intraoperative lymph node dissection, postoperative indwelling time of drainage tube and postoperative drainage volume. The treatment cost and hospitalization time of the two groups were compared. The changes of inflammatory indexes including C-reactive protein (CRP), interleukin (IL)-1β, IL-6, and tumour necrosis factor (TNF)-α before and after treatment were compared between the two groups. The changes of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were compared between the two groups. The incidence of postoperative complications in the two groups was counted. Logistic regression was conducted for analyzing the risk factors of postoperative complications. Results: The two groups were similar in operation time, intraoperative blood loss, and number of intraoperative lymph node dissected (all P>0.05). The observation group experienced a significantly shorter postoperative indwelling time of drainage tube and less postoperative drainage volume than the control group after surgery (P<0.05). The observation group presented significantly lower CRP, IL-1β, IL-6, and TNF- α levels than the control group (P<0.001). The observation group presented significantly higher FEV1 and FVC levels than the control group at 3 months after operation (P<0.001). The treatment cost of the two groups was not greatly different (P>0.05), but the observation group experienced a significantly shorter hospitalization time than the control group (P<0.001). The two groups were similar in the incidence of complications (P>0.05). According to multivariate logistics regression analysis, age, operation time, and number of lymph nodes dissected were independent risk factors for postoperative complications (P<0.05). Conclusion: To sum up, for patients with early LC, pulmonary segmentectomy is significantly more effective than lobectomy in terms of pulmonary function and inflammatory response, and age, operation time and number of lymph node dissected during operation are independent risk factors affecting postoperative complications.

Keywords: Uniportal thoracoscopy, pulmonary segmentectomy, lobectomy, early-stage non-small-cell lung cancer, complications, risk factors

Introduction

Lung cancer is a frequently-seen malignancy in China and even in the whole world. In 2020, over 19 million new cancer cases were diagnosed worldwide. Lung cancer and breast cancer are the top two, with the highest incidence worldwide [1]. LC, prostate cancer, and colorectal cancer are the most frequently seen among men [2]. The main histopathological type of lung cancer is non-small cell lung cancer (NSCLC). This is the most frequently seen lung cancer in China and even in the world, occupying over 85% of all lung cancer cases [3]. Early lung cancer usually lacks typical symptoms, like cough and hemoptysis. Early treatment rate is comparatively low, and it is often in the middle/ late stage when related symptoms appear [4]. Over the past few years, with the improvement of people's awareness of physical examination and the wide application of low-dose spiral CT in physical examination, the detection rate of pulmonary nodules is increasing, and some pulmonary nodules show signs of early lung cancer [5].

Surgical treatment is the preferred selection for early LC. Traditional surgical treatment includes thoracotomy for lung lesion resection. Resection of the diseased lung lobe under direct vision after thoracotomy can reduce the difficulty of operation and shorten the operation time [6]. Compared with thoracoscopic surgerv. thoracotomy causes a larger incision. bringing more trauma to chest wall and more complications [7]. Video-assisted thoracoscopic surgery (VATS) is a major breakthrough in the development of minimally invasive thoracic surgery, with the main advantage of significant reduction of trauma, from both the reduction of chest wall incision and the reduction of pulmonary contusion. As a result, it greatly shortens the time of thoracotomy and chest closure and reduces the injury of chest wall and intercostal muscles, ribs, and intercostal nerves, Postoperative recovery is rapid and the hospital stay is greatly shortened [8, 9].

The frequently used surgical treatment for lung cancer is thoracoscopic lobectomy plus systematic lymph node dissection. In recent ten years, with the popularization of low-dose spiral CT in small and medium-sized medical institutions, more and more early pulmonary nodules have been screened out [10]. Some scholars have concluded that pulmonary segmentectomy can be applied to NSCLC patients whose mass diameter is less than 2 cm [11]. In the last century, a randomized controlled trial by the North American Lung Cancer Research Group [12] and a retrospective analysis by Sienel et al. [13] showed that pulmonary segmentectomy caused a higher local recurrence rate and mortality than lobectomy, but with the increase of surgeons' proficiency and experience in thoracoscopic surgery, more and more studies came to the opposite conclusion.

This study was designed to analyze the effects of uniportal thoracoscopic pulmonary segmentectomy and lobectomy on patients with earlystage non-small-cell lung cancer (ES-NSCLC) and risk factors of postoperative complication to provide reference for the selection of clinical therapeutic regimen.

Materials and methods

Clinical data

The clinical data of 97 patients with early lung cancer treated in Mingguang People's Hospital between October 2019 and December 2021 were retrospectively analyzed. A total of 45 patients who underwent pulmonary segmentectomy were assigned to the observation group. The remaining 52 patients who underwent lobectomy were assigned to the control group. This study was done with permission from the Medical Ethics Committee of Mingguang People's Hospital.

Inclusion and exclusion criteria

Inclusive criteria: Patients whose chest HRCT (32 rows) showed that the tumour diameter was 2 cm or less, with solid component less than 50%, and whose disease was diagnosed as NSCLC by intraoperative rapid freezing and postoperative pathology [14]; patients without distant metastasis of the tumour, and without invasion of large blood vessels and chest wall; patients whose tumour was single lesion; patients whose distance between the resected lung tissue margin and the lesion margin was more than 2 cm, and whose rapid pathological findings during operation showed that the lesion margin was negative; and patients with detailed clinical data.

Exclusion criteria: Patients with active pulmonary tuberculosis before hospitalization; patients who had received thoracotomy; patients whose surgical method was changed during operation, such as pulmonary segmentectomy to wedge resection; patients whose heart, brain, liver, or kidney functions were significantly abnormal or complicated with malignant tumours.

Therapeutic regimen

Uniportal thoracoscopic lobectomy: After intravenous inhalation combined with general anesthesia, the patient was put in a lateral position, and a small incision of 4 cm was made between the 4th-5th ribs of the anterior axillary line or the midline axillary line. The skin and subcutaneous tissue were separated layer by layer till reaching chest cavity. After placement of the incision protective sleeve, the patient was placed under the thoracoscope for exploration. Surgical treatment was performed according to the location of the lesion determined before surgery. If the lesion was located on the periphery of the lung lobe, wedge lobectomy was performed before the pathological nature was determined. The resected lesions were sent for inspection immediately. If the pathological results were confirmed as LC, lobectomy combined with mediastinal lymph node dissection was performed. The pulmonary artery, pulmonary vein and bronchus of the patient were dissociated. The affected lung was severed with a disposable incision obturator, and the lymph nodes were cleaned after the affected lung was isolated.

Uniportal thoracoscopic pulmonary segmentectomy: After intravenous inhalation combined with general anesthesia, the patient was put in a lateral position, and a small incision of 3 cm was made between the 4th-5th ribs in the anterior axillary line or the midline axillary line. After placement of the incision protective sleeve, thoracoscopic exploration was carried on. The hilum and mediastinal lymph nodes of the patient were sampled and biopsied. The biopsied lymph nodes in groups 7, 8, and 9 were in the lower lobe of the lung, and the biopsied lymph nodes in groups 5 and 6 were in the upper lobe of the left lung. The biopsied lymph nodes in groups 2, 3, and 4 were in the upper lobe of the right lung. Those with negative biopsy results were provided a pulmonary segmentectomy. Those with better results were provided with lobectomies. During pulmonary segmentectomy, the small structures of the segmental hilum should be identified according to the preoperative pulmonary CT three-dimensional reconstruction technique, and the intersegmental plane should be judged by the expansion and collapse method after severing the small structures of the target segment. A 26 # thoracic drainage tube was placed at the operation hole after operation.

Enzyme-linked immune-sorbent assay (ELISA)

Before the operation and at 3 days after the operation, 5 ml fasting peripheral venous blood

was acquired from each patient. This was followed by conventional centrifugation to obtain supernatant which was saved at -80°C for testing. Serum C-reactive protein (CRP, PC198), interleukin (IL)-1 β (PI305), IL-6 (PI330), and tumour necrosis factor (TNF)- α (PT518) were quantified via an enzyme-linked immunospot analyzer. All kits were from Shanghai Beyotime Biotechnology.

Pulmonary function test

The forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) of patients were measured by Maibang M&B pulmonary function instrument before operation, and at one month after operation and three months after operation.

Outcome measures

Primary outcome measures: The perioperative indexes of the two groups were compared, including operation time, intraoperative blood loss, intraoperative lymph node dissection, postoperative indwelling time of drainage tube and postoperative drainage volume. The changes of inflammatory indexes including CRP, IL-6, and TNF- α before and after treatment were compared between the two groups. The changes of FEV1 and FVC were compared between the two groups.

Secondary outcome measures: Clinical data of two groups were compared. The incidence of postoperative complications in the two groups was counted. Logistic regression was conducted for analyzing the risk factors of postoperative complications. The treatment cost and hospitalization time of the two groups were compared.

Statistical analyses

SPSS 20.0 software was adopted for processing data, and the Shapiro-Wilk method was used for normality test first. The measured data in normal distribution (mean \pm SD) were compared by the t test. Their inter-group comparison was conducted by the independent-samples T test, and their intro-group comparison by the paired t test. Counted data were expressed by (%), and were compared by χ^2 test. Logistic regression analysis was conducted for analyzing the risk factors affecting the complications Effects of uniportal thoracoscopic pulmonary segmentectomy and lobectomy on ES-NSCLC

Factor	Observation group (n=45)	Control group (n=52)	χ^2 value	P value	
Gender			1.434	0.231	
Male	28	25			
Female	17	25			
Age (years)			0.141	0.706	
≥55	19	20			
<55	26	32			
BMI (kg/m²)			1.263	0.261	
≥25	15	12			
<25	30	40			
Affected side			1.176	0.278	
Left lung	24	22			
Right lung	21	30			
Clinical stages			0.436	0.803	
Phase la	20	20			
Phase Ib	15	18			
Phase IIa	10	14			
History of smoking			1.434	0.231	
Yes	28	25			
No	17	25			
History of diabetes mellitus			0.131	0.716	
Yes	10	10			
No	35	42			
History of hypertension			1.263	0.261	
Yes	15	12			
No	30	40			

 Table 1. Comparison of baseline data

Note: BMI: Body Mass Index.

on patients. P<0.05 suggested a significant difference.

Results

Comparison of baseline data

According to inter-group comparison of clinical data, the two groups were similar in clinical data (P>0.05, **Table 1**).

Comparison of perioperative indexes

The perioperative indexes of the two groups were compared. Results showed the two groups were similar in operation time, intraoperative blood loss, and number of intraoperative lymph node dissected (all P>0.05, **Figure 1A-C**), but the observation group experienced a significantly shorter postoperative indwelling time of drainage tube and less postoperative drainage volume than the control group after surgery (all P<0.05, **Figure 1D**, **1E**).

The changes of inflammatory indexes before and after operation

The changes of CRP, IL-1 β , IL-6, and TNF- α in the two groups before and after treatment were compared. Results showed that before surgery, the levels in the two groups were similar (all P>0.05). After surgery, serum CRP, IL-1 β , IL-6, and TNF- α levels in both groups increased significantly (all P<0.0001). There were significantly lower levels in the observation group than those in the control group (all P<0.001, **Figure 2**).

The changes of pulmonary function before and after surgery

The changes of FEV1 and FVC were compared between the two groups before and after therapy. According to the results, before surgery, the two groups were similar in FEV1 and FVC levels (both P>0.05). At 3 months after operation, FEV1 and FVC in the observation group did not



Figure 1. Comparison of perioperative indexes. A. Comparison of operation time between the two groups. B. Comparison of intraoperative blood loss between the two groups. C. Comparison of intraoperative lymph node dissection between the two groups. D. Comparison of postoperative indwelling time of drainage tube between the two groups. E. Comparison of postoperative drainage volume between the two groups. Note: ^{ns}P>0.05, ^{***}P<0.001.

change greatly (both P>0.05), and FEV1 and FVC in the control group decreased significantly (both P<0.001). At 3 months after operation, the observation group presented significantly higher FEV1 and FVC levels than the control group (both P<0.001, **Figure 3**).

Inter-group comparison of treatment cost and hospitalization time

According to inter-group comparison of treatment cost and hospitalization time, the two groups were similar in terms of treatment cost (P>0.05, **Figure 4A**), but the observation group experienced a significantly shorter hospitalization time than the control group (P<0.001, **Figure 4B**).

Postoperative complications of patients

Statistics of the incidence of postoperative complications of the two groups revealed no significant difference between them (P>0.05, Table 2).

Analysis of risk factors of postoperative complications

Patients with complications were assigned to the occurrence group (n=22), and those without complications to the non-occurrence group (n=75). According to univariate analysis, age, operation time, number of intraoperative lymph node dissected, and hospitalization time were the risk factors for postoperative complications (**Table 3**, P<0.01). According to multivariate logistic regression analysis, age, operation time and number of intraoperative lymph node dissected were independent risk factors for postoperative complications (**Table 4**, all P<0.05).

Discussion

LC, with a high morbidity and mortality worldwide, is treated by surgical resection [15]. It was treated by thoracotomy. With the development of minimally invasive surgery, thoracotomy is gradually replaced by VATS [16]. For patients with early LC, anatomical lobectomy is the first choice. With continual development of medical technology and the in-depth practice of pulmonary segmentectomy in the medical community, there are disputes between the lobectomy and pulmonary segmentectomy in the treatment of lung cancer [17].

This study compared the improvement effects of lobectomy and pulmonary segmentectomy on pulmonary function and disease condition of patients with early LC. According to the results, the observation group experienced a significantly shorter postoperative indwelling time of drainage tube, postoperative hospital-



Figure 2. Changes of inflammatory indexes in patients before and after surgery. A. Comparison of CRP changes in the two groups before and after surgery. B. Comparison of IL-1 β changes in the two groups before and after surgery. C. Comparison of IL-6 changes in the two groups before and after surgery. D. Comparison of TNF- α changes in the two groups before and after surgery. Notes: ***P<0.001, ****P<0.0001. CRP: C-reactive protein; IL: Interleukin; TNF: Tumour necrosis factor.



Figure 3. Changes of pulmonary function in patients before and after surgery. A. Comparison of FEV1 changes between the two groups before surgery and at 3 months after surgery. B. Comparison of FVC changes between the two groups before surgery and at 3 months after surgery. Note: ***P<0.001. FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity.



Figure 4. Comparison of treatment cost and hospitalization time. A. Comparison of treatment cost between the two groups. B. Comparison of hospitalization time between the two groups. Note: nsP>0.05, ***P<0.001.

ization time and less postoperative drainage volume than the control group, but the two groups were similar in operation time, intraoperative blood loss, number of intraoperative lymph node dissected and treatment cost. In the minimally invasive treatment of early LC, pulmonary segmentectomy causes fewer traumas to patients, and exposure of the visual field during the operation reduces the repeated pulling of the lung lobes, making the normal lung lobes less damaged [18]. Differing from the lobectomy group, the pulmonary segmentectomy group retained healthy lung tissue to a greater extent while resecting the lesion. This protected the patient's pulmonary function, promoted postoperative recovery, and significantly shortend the patient's hospitalization time [19]. Similar to our study, Li et al. [20] have found insignificantly less intraoperative blood loss in the pulmonary segmentectomy group than that in the lobectomy group. They have

found more lymph nodes dissected, longer postoperative indwelling time of thoracic drainage tube, more thoracic drainage volume and longer postoperative hospitalization time in the lobectomy group than those in the pulmonary segmentectomy group. This was comparable to our results. In their research, the pulmonary segmentectomy group experienced significantly longer operation time than the lobectomy group. This was inconsistent with our research. We think it has something to do with the skill of the surgeon. This study compared the effects of two groups in terms of pulmonary function. The results showed that the FEV1 and FVC levels of patients in the observation group did not change significantly at 3 months after surgery, but those of patients in the control group were significantly lower at 3 months after surgery compared with those before treatment. The FEV1 and FVC levels in the observation group were significantly higher than those in the

control group. This is because uniportal thoracoscopic pulmonary segmentectomy has little influence on postoperative pulmonary function of patients with LC. The reason may be that this surgical method can preserve lung tissue to the maximum extent, maintain thoracic integrity, and repair respiratory function of patients utmost feasibility. This helps to preserve more pulmonary function and is more conducive to postoperative recovery of patients, gaining significant clinical treatment advantages [21, 22].

Both operations are traumatic. Traumatic operation will cause local or whole inflammatory reaction. This is one of the primary factors causing postoperative infection and recurrence [23]. This study detected CRP, IL-1 β , IL-6, and TNF- α in the two groups after treatment. Results showed after surgery, the observation group presented significantly lower CRP, IL-1 β , IL-6, and TNF- α levels than the control group.

Group	Observation group (n=45)	Control group (n=52)	χ^2 value	P value
Pneumonia	3	3		
Bronchopleural fistula	1	2		
Lung leakage	2	1		
Incision infection	2	1		
Myocardial infarction	1	0		
Hoarseness	4	3		
Total incidence rate	12 (26.65%)	10 (19.20%)	0.760	0.383

Table 2. Statistics of postoperative complications

Table 3. Univariate analysis of	postoperative	complications
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Factor	Occurrence group (n=22)	No-occurrence group (n=75)	χ²/t value	P value
Gender	0 1 ()		0.968	0.325
Male	10	43		
Female	12	32		
Age (years)			9.263	0.002
≥55	15	24		
<55	7	51		
BMI (kg/m ²)			2.421	0.119
≥25	9	18		
<25	13	57		
Affected side			1.554	0.212
Left lung	13	33		
Right lung	9	42		
Clinical stages			0.663	0.717
Phase la	10	30		
Phase Ib	8	25		
Phase Ila	4	20		
History of smoking			0.247	0.619
Yes	11	42		
No	11	33		
History of diabetes mellitus			2.181	0.139
Yes	7	13		
No	15	62		
History of hypertension			0.369	0.543
Yes	5	22		
No	17	53		
Operation time (min)	176.04±15.04	148.96±17.99	6.426	<0.001
Intraoperative blood loss (mL)	57.00±5.47	59.29±6.45	1.513	0.133
Number of intraoperative lymph node dissected (one)	11.68±1.46	8.88±2.01	6.067	<0.001
Postoperative indwelling time of drainage tube (d)	4.13±1.12	4.14±1.07	0.039	0.968
Postoperative drainage volume (mL)	247.68±47.15	262.72±42.79	1.416	0.160
Hospitalization time (d)	8.77±0.97	7.48±1.42	3.979	0.001

This indicated that both lobectomy and pulmonary segmentectomy could greatly affect serum inflammatory factors. From the changes of inflammatory factors, pulmonary segmentectomy had less impact on the inflammatory reaction in patients than lobectomy. Compared with lobectomy, pulmonary segmentectomy could maximize the retention of normal lung tissue

Fastar	0	SE	χ²	Р	OR	95% CI	
Factor	β		value	value	value	Lower limit	Upper limit
Age	2.408	0.979	6.052	0.014	11.108	1.632	75.63
Operation time	0.116	0.032	13.163	<0.001	1.123	1.055	1.195
Number of intraoperative lymph nodes dissected	1.045	0.289	13.102	<0.001	2.844	1.615	5.009
Hospitalization time (d)	0.736	0.480	2.348	0.125	2.088	0.814	5.355

Table 4. Multivariate analysis

and reduce the number of inflammatory factors in tissues [24, 25].

Over the past few years, the wide application of minimally invasive surgery has greatly reduced the surgical trauma. This has allowed elderly patients with stage I lung cancer who are in poor physical condition participate with the surgical opportunity. This is beneficial to the prognosis [26]. VATS has been widely used in clinical practice because of its advantages of minimal invasion and guick recovery, and it is effective in treating stage I LC. With the clinical application, it has been found that the incidence of postoperative complications is high, affecting the surgical effect and postoperative recovery [27]. This study counted the complications of patients after treatment. According to results, age, operation time and number of intraoperative lymph nodes dissected were independent risk factors for postoperative complications. Early research found that advanced age is not the contraindication of thoracoscopic surgery, but with the increase of age, various physiological functions and important organ functions will decline, and the reserve capacity will decline. The elderly patients may be complicated with basic diseases, facing a higher risk of complications [28]. With the prolongation of operation time, the risk of operation will increase, the wound will be exposed for a long time, and the chance of incision contamination will increase. This can cause rise to infection, aggravating the disease condition and compromising the prognosis [29]. Lymph node dissection can effectively prevent postoperative recurrence, but the recurrent laryngeal nerve will be exposed, and bronchial blood supply will be blocked when lymph node dissection is performed during operation. The more lymph nodes dissected, the longer the operation time will be, and the amount of blood loss will increase, leading to more postoperative complications [30].

This study has confirmed by analysis that pulmonary segmentectomy is superior to lobectomy in the treatment of early LC. This study had some limitations. This study was a retrospective single-center study. The representativeness of the results is low. We didn't follow the patients lenghtily. More studies are needed to demonstrate whether the two surgical procedures impact the long-term survival of patients. We hope to carry out more experiments in the follow-up research to improve the research conclusions.

To sum up, for patients with early LC, pulmonary segmentectomy is significantly more effective than lobectomy in terms of pulmonary function and inflammatory response, and age, operation time and number of lymph node dissected during operation are independent risk factors affecting postoperative complications.

Disclosure of conflict of interest

None.

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