

Clinical analysis of the impact of sublobectomy on pulmonary function

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Abstract

The present study investigated and analyzed the clinical impact of sublobectomy on pulmonary functions.

Changes in pulmonary function before and after sublobectomy were compared to the changes after lobectomy.

Changes in the pulmonary function before and after sublobectomy and lobectomy did not exhibit remarkable differences in long-term effects. Surgery-related indexes of the sublobectomy group were significantly lower than those of the lobectomy group ($P < .05$). The indexes of pulmonary function both before and after surgery in the sublobectomy group were not associated with a significant decrease in the quality of survival based on pulmonary function as the main index ($P > .05$).

Compared with lobectomy, sublobectomy maximally retained the normal healthy pulmonary tissue, with similar local recurrence rate, 5-year recurrence-free survival rate, and 5-year survival rate. Sublobectomy decreased the impact on respiratory functions to the minimum. After the operation, the quality of survival with pulmonary functions as the main index did not decrease significantly. Therefore, sublobectomy could be an appropriate choice for elderly patients with poor cardiopulmonary function or with chronic diseases.

Abbreviations: FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, MVV = maximum spontaneous ventilation volume/s, NSCLC = non-small cell lung cancer.

Keywords: impact, pulmonary function, sublobectomy

1. Introduction

Lung cancer is a severe disease and a leading cause of mortality among patients with cancer.^[1] Non-small cell lung cancer (NSCLC) accounts for about 80% of all lung cancers, of which 75% are at an advanced stage at diagnosis, leading to an extremely low 5-year survival rate. According to the guidelines of the National Comprehensive Cancer Network^[2] and the American College of Chest Physicians,^[3] patients with stage I lung cancer suitable for surgery should receive anatomical lobectomy with mediastinal lymph node dissection or sampling. Nevertheless, with advances in imaging and diagnostic technologies, the number of patients detected at an early stage of lung cancer is increasing gradually each year, and the advantage of sublobectomy in the specific treatment of early lung cancer has been considered seriously.^[2,4–14]

Because of the smaller volume of lung being resected, sublobectomy has been suggested to be particularly suitable for patients with poor lung function and who could not tolerate lobectomy.^[2,4–14] In the case of elderly patients who are also

suffering from various chronic diseases (such as chronic bronchitis, emphysema, pulmonary heart disease, myocardial ischemia, and coronary heart disease), it is of great importance to achieve a proper balance among surgical efficacy, safety, postoperative complications, postoperative quality of life, and life expectancy considering the comorbidities. Indeed, some retrospective studies suggested that in elderly patients with lung cancer and poor cardiopulmonary functions who cannot tolerate lobectomy, sublobectomy (segment resection is preferred, followed by wedge resection as the second choice) could be an appropriate compromise.^[3,15–17]

Under the premise of complete removal of tumor lesions, preservation of maximum normal lung tissue in the patients should improve postoperative recovery, at least maintain the quality of life, and reduce the occurrence of complications. The reduction of surgical trauma is also an important issue in surgery, which has practical significance in patients with poor pulmonary functions. Most importantly, despite a study suggesting a higher recurrence rate after sublobectomy,^[18] studies have shown that survival after sublobectomy was similar to that after lobectomy.^[5,8,11,13] Therefore, advantages of sublobectomy in the treatment of early lung cancer have attained consideration from thoracic surgeons. Nevertheless, there is still a lack of data to support the use of sublobectomy for the treatment of lung cancer in elderly patients with comorbidities.

Therefore, the present study aimed to investigate the safety, efficacy, and feasibility of sublobectomy in the treatment of early NSCLCs and benign lung tumors and its impact on pulmonary functions and quality of life.

2. Materials and methods

2.1. Study design and patients

This study was approved by the Ethic Committee of our hospital (No. 20170001). Patients who underwent sublobectomy

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HY and YY contributed equally to this study.

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(pulmonary wedge resection or anatomical segmentectomy) were included in the sublobectomy group. A total of 87 cases at the department of thoracic surgery from February 2011 to October 2016 were included. Among them, 58 were diagnosed by physical examination, and 29 were diagnosed when they visited the hospital because of cough and chest pain. There were 53 males and 34 females, aged 67 to 85 years (average of 76 ± 7.3 years). Preoperative chest enhancement computed tomography (CT) showed tumors of 1.2–2.5 cm (average of 2.15 ± 0.35 cm). The mediastinal lymph nodes were not enlarged significantly. Chest-enhanced CT, abdominal-B ultrasound, head magnetic resonance imaging (MRI), whole-body enhanced CT or positron emission tomography/CT, and analysis of blood, urine, liver, and kidney functions, blood coagulation, blood gas, and tumor markers were performed before the operation. In addition, the respiratory function was assessed, and fiberoptic bronchoscopy was carried out. The tumor sites included 13 tumors (14.9%) in the back segment of the left lower lobe, 11 (12.6%) in the posterior segment of the right upper lobe, 15 (17.2%) in the basal segment of the left lower lobe, 14 (16.1%) in the tongue segment of the left upper lobe, 18 (20.68%) in the back segment of the left lower lobe, and 16 (18.39%) in the posterior segment of the left upper lobe. Comorbidities included 52 cases (59.77%) of coronary heart disease, 42 (48.27%) of myocardial ischemia, and 66 (75.86%) of chronic obstructive pulmonary disease. The criteria for sublobectomy instead of lobectomy were: elderly patients who exhibited poor pulmonary functions who could not tolerate lobectomy; patients with comorbidities who could not tolerate lobectomy; patients who did not receive chemotherapy and radiotherapy before the operation; and patients who did not present distant metastasis.

Patients who received lobectomy at our hospital during the same period were considered as the lobectomy (control) group. A total of 76 patients were included, of which, 44 were males and 32 were females, aged 56 to 76 years (average of 66 ± 4.2 years). All patients underwent chest-enhanced CT, which showed that the tumor size was 1.2 to 2.3 cm (average, 1.96 ± 0.34 cm), and that the mediastinal lymph nodes were without enlargement. The tumor sites included 14 tumors (18.42%) in the tongue segment of the left upper lobe, 12 (15.79%) in the posterior segment of the left upper lobe, 13 (17.10%) in the basal segment of the left lower lobe, 9 (11.84%) in the back segment of left lower lobe, 17 (22.37%) in the posterior segment of the right upper lobe, and 11 (14.47%) in the back segment of the right lower lobe. Preoperative examinations revealed similar results as in the sublobectomy group. All the patients were same as those in the sublobectomy group excluding those with poor pulmonary functions or exhibiting other serious diseases that cannot tolerate lobectomy. All patients did not receive chemotherapy or radiotherapy before surgery. All patients were without metastasis.

2.2. Methods

For the sublobectomy group, preoperative examination was essential to determine the possibility of sublobectomy and surgical methods and procedures. Preoperative pulmonary function training was performed for 5 to 7 days. In the case of patients who had been clearly diagnosed with benign tumors (such as pulmonary hamartoma, pulmonary cyst, pulmonary pseudotumor, or pulmonary tuberculosis) by preoperative examination, wedge resection was performed to ensure a surgical margin of >2 cm.^[19] In the case of patients with a wide range of benign lesions, pulmonary segment resection was performed

since pulmonary wedge resection could not completely resect the lesions. Furthermore, in patients highly suspected of malignant lesions, as assessed by preoperative examination, pulmonary wedge resection was performed initially followed by intraoperative rapid frozen pathology biopsy to clarify the nature of the lesion. If a malignant nodule was found, pulmonary segment resection could be performed. According to the different developments of intraoperative lung segment and leaf cleft, the sequences of the treatment of segmental arteries, veins, and bronchi were different. The anatomy and dissection should be in proximity to the hilum to detect the direction of vascular structure unambiguously, and then the segmental artery, vein, and bronchus could be treated. After determination of the level between pulmonary segments and the hilar, the low-pressure tidal volume inflated lung and boundaries of the pulmonary segment were evaluated by lung atrophy and inflatable boundaries; then, the separation was performed until there was no clear anatomical marker. Subsequently, sharp cutting and suturing were carried out.^[20,21] Ensuring a sufficient distance (≥ 2 cm) from the incision margin to the tumor could avoid positive margins, and extensive resection of lung tissue of the adjacent segment could be performed if necessary. Consecutively, a systematic lymph node dissection was performed, and the lymph nodes together with the surrounding adipose tissues were completely removed. Rapid frozen pathology was used to detect the mediastinal and hilar lymph nodes, and for patients with metastatic cancer cells, mediastinal lymphadenectomy was performed. Left lung tumors led to resection of the 5 to 10 groups of lymph nodes; right lung tumors led to resection of 2R, 4R, and 7 to 10 groups of lymph nodes.^[22] Routine nursing was administered after the operation. The indexes of pulmonary functions were reassessed 2 weeks postoperatively.

The patients in the lobectomy group underwent conventional lobectomy coupled with mediastinal lymphadenectomy.

2.3. Determination of the efficacy

As the quality of surgery was the most important, surgical-related indicators that could be observed initially included intraoperative blood loss, operation time, time of postoperative chest drainage tube, ratios of postoperative complications (including lung infection, recurrent laryngeal nerve injury, wound infection, and arrhythmia), and postoperative hospitalization stay. The quality of survival was assessed based on pulmonary functions as the main index between the 2 groups before and after the operation, which included tidal volume, forced expiratory volume in 1 second ($FEV_{1.0}$), the percentage of the first second forced expiratory volume in the forced vital capacity (FEV_1/FVC), peak expiratory flow, maximum spontaneous ventilation volume/s, $SpO_2\%$, arterial oxygen partial pressure (PaO_2), and arterial blood carbon dioxide partial pressure ($PaCO_2$).

2.4. Statistical analysis

SPSS 16.0 was used for statistical analysis (SPSS Inc, Chicago, IL). Continuous data were analyzed by *t* test and expressed as mean \pm standard variation. Categorical data were analyzed with the Fisher exact test and expressed as frequencies. $P < .05$ was considered statistically significant.

3. Results

All patients in the 2 groups underwent operation successfully and were discharged. The postoperative pathology in the sublobec-

Table 1
Comparison of the surgery-related indexes between the 2 groups.

Grouping	n	Intraoperative blood loss, mL	Operation time, min	Thoracic drainage time, days	Postoperative complication rate	Postoperative hospitalization stay, days
Sublobectomy	87	110±30	95±25.6	3.3±1.7	6.4%	6±1.7
Lobectomy	76	240±70	145±25	6.4±1.8	19.7%	12±2.8
t value	/	21.54	27.37	26.42	22.56	28.74
P	/	<.05	<.05	<.05	<.05	<.05

tomy group included 21 cases of adenocarcinoma, 57 of squamous cell carcinoma, 2 of tuberculoma, 2 of pulmonary hamartoma, 1 of lung cyst, and 1 of inflammatory pseudotumor. The 87 cases were followed-up for 6 to 36 months, with an average of 23±2.9 months, and 78 cases of lung cancer showed no recurrence and metastasis. The postoperative pathology in the lobectomy group included 27 cases of adenocarcinoma and 49 cases of squamous cell carcinoma; these 76 cases were also followed-up for 6 to 36 months, with an average of 20±2.6 months. All 76 cases with lung cancer were without recurrence and metastasis. Both groups underwent complete resection. The intraoperative and postoperative statuses of the subjects in the 2 groups were monitored; the surgery-related indexes of the sublobectomy group were found to be significantly lower than those of the lobectomy group ($P < .05$) (Table 1). The comparison of pulmonary function as the main indexes in the sublobectomy group before the operation and 2 weeks after the operation showed that the quality of survival did not decrease significantly ($P > .05$) (Table 2); this result was similar to that of the lobectomy group ($P < .05$) (Table 3).

4. Discussion

With the accelerated pace of life and gradual aging, the incidence of NSCLS shows an increasing trend.^[23] In addition, with emerging new imaging technology,^[24] we detect more early cancers in elderly patients who are suffering from a variety of chronic diseases and who cannot withstand lobectomy. Therefore, searching for a more suitable surgical method for such patients is a major concern for clinicians.

Presently, the surgical options for early lung cancer in the field of thoracic surgery are controversial. In 1995, the Lung Cancer Study Group (LCSG) led by Ginsberg et al^[18] completed the only 1 prospective multicenter randomized controlled study of early NSCLC treated with lobectomy and sublobectomy for tumors <3 cm. Although the results showed that the long-term survival rate of sublobectomy was similar to that of lobectomy, the local recurrence rate was higher than that of lobectomy.^[18] The local recurrence rate of pulmonary wedge resection was especially

high; nevertheless, sublobectomy was a compromise surgery for high-risk patients. Nevertheless, since its publication 20 years ago, the conclusions of this study^[18] has been challenged; some of its limitations are that the preoperative staging used chest x-ray at that time, and hence, the accuracy was poor and the inclusion criterion was defined as tumors <3 cm and “peripheral” was defined as tracheobronchoscopy, which are now known to be high-risk factors for local recurrence after sublobectomy.^[25] Therefore, after >20 years of research, studies showed that the effect of sublobectomy was similar to that of lobectomy.^[5,8,11,13]

In recent years, planned sublobectomy and mediastinal lymph node sampling have been gradually used in the treatment of NSCLC.^[26] In the present study, planned sublobectomy was chosen because of the compromise of poor cardiopulmonary functions. A comparative study has been performed to show the impact of the 2 surgical methods on pulmonary functions, showing that sublobectomy has more advantages than lobectomy. Analysis revealed that sublobectomy had significantly reduced surgical trauma, less impact on pulmonary functions, and the recovery was relatively rapid. After the operation, the quality of survival, assessed by the pulmonary functions as the main indexes, improved significantly. The follow-up after lung cancer surgery indicated no significant long-term difference between sublobectomy and lobectomy. The proportion of possible complications such as atelectasis, pneumonia and respiratory failure were reduced greatly. In addition, the rates of metastasis and recurrence did not increase after the operation. Notably, there were also some limitations of the single compromise sublobectomy. Surgical indications and margins should be strictly controlled to effectively eradicate the lung cancer.^[27-29] Scientific and accurate clinical staging is a critical prerequisite to determine the surgical treatment. Some evidence also suggests that the distance to the incision margin is the cause affecting the recurrence and metastasis after sublobectomy. In 2007, El-Sherif et al^[4] proposed the importance of retaining a sufficient margin in sublobectomy. Another study suggested that the recurrence and metastasis after sublobectomy were not solely associated with diameter and incision margin. In 2015, Kadota et al^[30] retrospectively studied the airway spread in lung cancer,

Table 2
Comparison of pulmonary functions in the sublobectomy group before and after operation.

Time	n	Tidal volume, mL	One-second forced expiratory volume, L	FVC _{1,0} %	Peak expiratory flow	MVV actual/predicted value	SaO ₂ %	PaO ₂ (kPa), mmHg	PaCO ₂ (kPa), mmHg
Preoperative	87	460±53	2.21±1.46	69±1.5	4.91±1.46	68±2.9	91±2.3%	81±2.1	41±2.1
Postoperative	87	410±45	2.07±0.18	62±2.7	4.67±0.82	60±1.2	90±1.9%	80±2.1	42±1.4
t value	/	6.13	4.71	5.62	4.68	3.79	2.95	3.11	5.23
P	/	>.05	>.05	>.05	>.05	>.05	>.05	>.05	>.05

FVC=forced vital capacity, MVV=maximum spontaneous ventilation volume/s.

Table 3**Comparison of pulmonary functions in the lobectomy group before and after operation.**

Time	n	Tidal volume, mL	One-second forced expiratory volume, L	FVC _{1.0} %	Peak expiratory flow	MVV actual/predicted value	SaO ₂ %	PaO ₂ (kPa), mmHg	PaCO ₂ (kPa), mmHg
Preoperative	76	475 ± 67	2.23 ± 0.23	71 ± 1.7	5.02 ± 1.72	73 ± 2.2	91 ± 2.3%	84 ± 1.3	39 ± 1.5
Postoperative	76	330 ± 30	2.16 ± 0.21	56 ± 2.4	3.46 ± 0.76	52 ± 1.6	81 ± 2.6%	78 ± 1.2	43 ± 1.1
t value	/	2.45	2.36	2.19	2.69	2.56	2.14	28	1.95
P	/	<.05	<.05	<.05	<.05	<.05	<.05	<.05	<.05

FVC=forced vital capacity, MVV=maximum spontaneous ventilation volume/s.

which revealed that in stage I lung cancer ≤ 2 cm, 38% patients showed airway spread, which was one of the risk factors for the recurrence of limited local resection. Importantly, in such cases, lymph nodes should be sampled, and incision margin should be obtained during the operation, using rapid frozen pathological examination. Subsequently, intraoperative staging should be performed to ensure radical resection of the surgery by combining with other auxiliary examinations such as imaging.^[2,10,14]

The elderly population is prone to lung cancer. Between 2005 and 2009, the proportion of patients >70 years' old was up to 71%, of which, one-third were >80 years' old. In the case of early NSCLC, surgical resection is the preferred treatment, and the standard surgical procedure is lobectomy, but elderly patients treated according to studies performed in younger patients give rise to various issues. Especially, poor cardiopulmonary function results in the loss of the opportunity for radical surgery in many patients. Even at the Mayo Clinic, the incidence of surgical complications in elderly patients who have received sublobectomy is as high as 48%, and the mortality is 6.3%.^[31] Among them, pulmonary failure accounts for >40% and cardiopulmonary failure accounts for >30%.

For elderly patients with high-risk of surgery, compromise sublobectomy including segmental and wedge resection may reduce the surgical risk to a limited extent. For elderly patients with limited life expectancy, the long-term effects of sublobectomy and lobectomy in early NSCLC are similar with increasing age.^[32] A retrospective analysis of 14,555 cases of stage I and stage II NSCLC from the SEER database revealed that because of the impact of pulmonary functions, the survival advantage of lobectomy was only limited to patients under 71 years of age as compared to sublobectomy, whereas that for population above 71 years' old, no significant difference was observed in the survival advantage between the 2 surgical procedures. Another retrospective study from Japan also showed similar results.^[9,33]

In summary, compared with lobectomy, compromise and planned sublobectomy preserve the normal healthy lung tissues maximally, and the impact on respiratory function is reduced to a minimum, as assessed by the local recurrence rate.^[6] The 5-year recurrence-free survival and 5-year survival rates are similar.^[12,34] The quality of survival with pulmonary functions as the major indexes improve significantly after the operation, and thus, it would be the optimal choice for elderly patients with poor cardiopulmonary function or combined with other chronic diseases.^[35] In addition, sublobectomy has several advantages; for example, it is technically simple, the operation time is reduced significantly, and surgical blood loss is reduced correspondingly. Moreover, there are few postoperative complications, recovery is rapid, hospitalization stay is shortened, and it is cost-effective. Nevertheless, further studies are necessary to obtain reliable

clinical evidences to supplement the short duration of the present study, the lack of long-term follow-up data, and relevant studies with large sample size.

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