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ORIGINAL ARTICLE

Comparative study on efficacy of thoracoscopic anatomic segmentectomy and lobectomy in treating pulmonary ground-glass nodules

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Summary

Purpose: *To compare the efficacy and safety of thoracoscopic anatomic segmentectomy and lobectomy in the treatment of pulmonary ground-glass nodules (GGNs).*

Methods: *The clinical data of patients with pulmonary GGNs who were treated with thoracoscopic anatomic segmentectomy (n=58, Segmentectomy group) or thoracoscopic lobectomy (n=58, Lobectomy group) were collected and retrospectively analyzed. Next, the operative time, intraoperative blood loss, number of lymph nodes dissected, indwelling time of postoperative thoracic drainage tube, thoracic drainage volume, length of postoperative hospital stay, perioperative complications and preoperative and postoperative changes in pulmonary function were compared between the two groups of patients. Additionally, patients were followed up and their survival status was recorded.*

Results: *The operative time was obviously longer in the Segmentectomy group than in the Lobectomy group. The intraoperative blood loss was smaller in the Segmentectomy group than in the Lobectomy group, showing no statistically significant difference. The number of lymph nodes dissected, the indwelling time of postoperative thoracic drainage tube, the thoracic drainage volume and the length of postoperative hospital stay were significantly increased in the Lobectomy group compared with those in the Segmentectomy group. The numerical rating scale (NRS) score of patients in the Segmentectomy group was similar to that in the Lobectomy group at 1, 3 and 7 d after surgery. The Karnofsky performance status (KPS) score was dramatically higher in the Segmentectomy group than in the Lobectomy group 1 year after surgery. Compared with that before surgery, the pulmonary function of patients was prominently weakened in both groups after surgery. At 3 and 12 months after surgery, the pulmonary function indexes forced vital capacity (FVC), the percentage of forced expiratory volume in one second (FEV_1%) and maximal voluntary ventilation (MVV) were remarkably better in the Segmentectomy group than in the Lobectomy group. The disease-free survival (DFS) rate was 89.7% (52/58) in the Segmentectomy group and 93.4% (54/58) in the Lobectomy group.*

Conclusion: *Thoracoscopic anatomic segmentectomy for the treatment of pulmonary GGNs is able to achieve similar short-term and long-term outcomes to those of lobectomy. Besides, it has advantages such as short duration of postoperative thoracic drainage, less drainage volume, short length of hospital stay, better postoperative recovery of pulmonary function and higher quality of life, without increase in the incidence rate of postoperative complications.*

Key words: *pulmonary ground-glass nodule, thoracoscopy, anatomic segmentectomy, lobectomy*

Introduction

In the wake of the development of imaging technology and the popularization of high-resolution computed tomography (CT) examination, more people with early lung cancer manifested as ground-glass nodules (GGNs) are screened out. According to reports, 80% of GGNs are manifestations

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of early lung cancer [1]. GGNs can be classified into pure GGNs (pGGNs) and mixed GGNs (mGGNs). MGGNs are more likely to be malignant, so early surgery is recommended [2,3]. Thoracoscopic lobectomy is a standard approach for the treatment of early lung cancer, in which, however, more healthy lung tissues will be removed. In thoracoscopic anatomic segmentectomy, more healthy lung tissues can be preserved to maintain pulmonary function as much as possible. For this reason, the application of segmentectomy has been started in treating partial selective peripheral non-small cell lung cancer (NSCLC) and solitary pulmonary nodules (SPNs). In addition, segmentectomy is increasingly applied in the surgical treatment of GGNs since it can reduce postoperative complications, shorten the length of hospital stay and improve postoperative quality of life [4-6].

In this study, the data of 58 patients receiving anatomic segmentectomy (Segmentectomy group) and 58 patients undergoing lobectomy (Lobectomy group) under thoracoscope in our department were retrospectively analyzed, and the clinical efficacy and safety of the two surgical methods for pulmonary GGNs were evaluated, hoping to provide a reference for clinical decisions.

Methods

General data

The data of 116 asymptomatic patients with pulmonary GGNs treated with thoracoscopic operation in the hospital from January 2014 to January 2016 were retrospectively analyzed. Besides, a single peripheral GGN was detected in these patients through CT examination in physical examination. In addition, the GGN diameter was ≤2 cm. Moreover, these patients received no treatment before surgery and met the indications for thoracoscopic operation. Before surgery, blood routine indicators, urine routine indicators, hepatic and renal function indicators, coagulation function indicators and hematologic tumor indexes (carcinoembryonic antigen, neuron-specific enolase and squamous cell carcinoma antigen) were examined, and they were all within the normal range. Based on head MRI, bone ECT scan, color Doppler ultrasound of bilateral adrenals, liver, gallbladder, the pancreas and spleen or PET/CT examination, no distant metastases were found. At 0.5 h before surgery, CT-guided puncture positioning was conducted, and a hook-wire was used for making. Half of the 116 patients underwent thoracoscopic anatomic segmentectomy, and another half had thoracoscopic lobectomy. There were 66 males and 50 females aged 35-76 years old, with an average of 54.16±9.70 years. There were no statistically significant differences in baseline data between the two

Table 1. Baseline demographic and clinical characteristics of the studied patients

Parameters	*Segmentectomy group (n=58)* *n (%)*	*Lobectomy group (n=58)* *n (%)*	*p value*
Age, years	53.57±9.43	54.94±9.82	0.445
Gender			0.574
Male	31 (53.4)	35 (60.3)	
Female	27 (46.6)	23 (39.7)	
Nodule location			0.887
Left upper lobe	17 (29.3)	16 (27.6)	
Left lower lobe	9 (15.5)	10 (17.2)	
Right upper lobe	19 (32.8)	17 (29.3)	
Right middle lobe	7 (12.1)	8 (13.8)	
Right lower lobe	6 (10.3)	7 (12.1)	
Nodule diameter (cm)	1.64±0.51	1.77±0.69	0.251
Imaging Features			0.337
pGGN	19 (32.8)	24 (41.4)	
mGGN	39 (67.2)	34 (58.6)	
Smoking history	32 (55.2)	36 (62.1)	0.088
Systemic disease			
Hypertension	7 (12.1)	11 (19.0)	0.305
Diabetes mellitus	5 (8.6)	6 (10.3)	0.751
Coronary heart disease	2 (3.4)	1 (1.7)	0.559
Cerebrovascular disease	4 (5.9)	1 (1.7)	0.170
Arrhythmia	3 (5.2)	2 (3.4)	0.648

pGGN: Pure groud-glass nodule; mGGN: Mixed groud-glass nodule.

groups of patients (Table 1, p>0.05). This study was approved by the Ethics Committee of Heping Hospital Affiliated to Changzhi Medical College. All patients enrolled were informed and signed the informed consent in accordance with the *Declaration of Helsinki.*

Surgical methods

General anesthesia through endotracheal intubation combined with intravenous anesthesia was used in all patients. The patients were placed lying on the unaffected side, with unaffected-lung ventilation during surgery. Then, the three-hole minimally invasive surgery was conducted, with a 1 cm incision made at the 7th or 8th intercostal space on the midaxillary line as the observation hole through which a 30° thoracoscope was inserted, a 2-4 cm incision made at the 4th or 5th intercostal space between the anterior axillary line and the midclavicular line as the main operation hole, and a 0.5-1 cm incision made at the 7th intercostal space on the posterior axillary line as the secondary operation hole. Incision protective sleeves were routinely used during surgery.

Some patients definitely diagnosed with benign GGNs before surgery (for example, patients with bullae and pulmonary cysts) had widely distributed lesions that could not completely removed by pulmonary wedge resection. Besides, for some patients with deeper lesions, pulmonary wedge resection could lead to ventilation-perfusion mismatch and postoperative hemoptysis due to the damage to or distortion of inappropriate blood vessels and bronchioles of residual lung tissues. Hence, segmentectomy or lobectomy were carried out straightway. For patients with suspected malignant lesions based on preoperative examinations, pulmonary wedge resection was performed first. After malignant nodules were confirmed according to intraoperative pathological diagnosis, and segmentectomy was considered feasible after exploration, No. 10, 11 and 13 lymph nodes were sampled first, and intraoperative quick-frozen pathological sections were then sent for examination. Next, segmentectomy was implemented if the lymph nodes were negative, otherwise lobectomy was conducted.

In lymph node dissection, No. 5, 6, 7, 8, 9, 10, 11 and 12 lymph nodes on the left and No. 2R, 4R, 7, 8, 9, 10, 11 and 12 lymph nodes on the right were dissected.

Observation indexes

The operative time, intraoperative blood loss, number of lymph nodes dissected, indwelling time of thoracic drainage tube (indications for extubation: 24 h thoracic drainage volume <100 mL, no bubble spillage after coughing, and good lung recruitment in accordance with chest frontal and lateral images in re-examination), thoracic drainage volume and length of postoperative hospital stay of patients were observed and recorded. The pain degree of patients was scored using numerical rating scale (NRS) at 1, 3 and 7 d after surgery and expressed as 0, 1, 2, 3, 4, 5 ,6, 7, 8, 9 or 10 (0: painlessness, 1-3: mild pain, 4-6: moderate pain, and 7-10: severe pain). Participants marked one of the numbers according to their own pain. The perioperative complications of patients in the two groups were recorded, and the quality of life was evaluated using the Karnofsky performance status (KPS) score.

The forced vital capacity (FVC), the percentage of forced expiratory volume in one second (FEV_1%) and maximal voluntary ventilation (MVV) of patients were tested by the same medical staff using a HYPAIR pulmonary function tester before surgery and at 3 and 12 months after surgery, respectively. All patients were followed up, and the recurrence rate of GGNs and the survival of patients were recorded.

Statistics

SPSS 22.0 (IBM, Armonk, NY, USA) was utilized for statistical analyses. Measurement data were expressed as mean ± standard deviation, and t-test was employed for the comparison between two groups. Enumeration data were expressed as ratio (%), and x^2 test was used for comparison among groups. P<0.05 suggested that the difference was statistically significant.

Results

Surgical conditions of patients in the two groups

The surgery in both groups was done under thoracoscope, and it went well, without conversion to thoracotomy or secondary operation. In the Segmentectomy group, there were 5 cases of resection of the apico-posterior segment of the left upper lobe, 3 cases of resection of the posterior segment, 6 cases of resection of the apico-anterior and -posterior segments (intrinsic segments), 3 cases of resection of the lingual segment, 6 cases of resection of the dorsal segment of the left lower lobe, 3 cases of resection of the basal segment, 7 cases of resection of apical segment of the right upper lobe, 8 cases of resection of the anterior segment, 4 cases of resection of the posterior segment, 10 cases of resection of the dorsal segment of the right lower lobe, and 3 cases of resection of the basal segment. In the Lobectomy group, there were 16 cases of resection of the left upper lobe, 10 cases of resection of the left lower lobe, 17 cases of resection of the right upper lobe, 8 cases of resection of the right middle lobe, and 7 cases of resection of the right lower lobe. The tumor location and surgical methods showed no statistical differences between the two groups of patients (p>0.05).

Comparisons of perioperative indicators between the two groups of patients

The operative time was obviously longer in the Segmentectomy group than in the Lobectomy group [(140.58±24.39) min *vs.* (118.62±23.40) min, p<0.001]. The intraoperative blood loss was smaller in the Segmentectomy group than in the Lobectomy group [(102.85±79.11) mL *vs.* (107.41±72.42) mL, p=0.747], but the difference was not statistically significant. The number of lymph nodes dissected [(22.8±5.8) *vs.* (19.2±5.3), p<0.001], the indwelling time of postoperative thoracic drainage tube [(5.7±1.8) d *vs.* (4.8±1.9) d, p=0.010], the thoracic drainage volume [(854.93±303.86) mL *vs.* (767.64±223.51) mL, p=0.041] and the length of postoperative hospital stay [(7.4±3.1) d *vs.* (6.1±2.5) d, p=0.014] were significantly increased in the Lobectomy group compared with those in the Segmentectomy group. The postoperative complications of patients in the two groups mainly included incision infection, pulmonary infection, atelectasis, chylothorax, pulmonary air leak and arrhythmia, which were attenuated after symptomatic treatment. The incidence rate of postoperative complications had no statistically significant difference between the two groups (p>0.05) (Table 2).

Postoperative pathological conditions of patients in the two groups

Based on the postoperative pathological findings, there were 21 and 24 cases of invasive adenocarcinoma, 17 and 11 cases of microinvasive adenocarcinoma (MIA), 6 and 9 cases of adenocarcinoma *in situ* (AIS), 6 and 4 cases of atypical adenomatous hyperplasia (AAH), 1 and 4 cases of squamous cell carcinoma, and 2 and 3 cases of neuroendocrine carcinoma in the Segmentectomy and the Lobectomy group, respectively. Besides, 1 case of small cell carcinoma and 2 cases of benign lesions were found in the Lobectomy group. In the Segmentectomy group, 5 cases of benign lesions (including 2 cases of hamartoma and 3 cases of sclerosing hemangioma) were detected.

Table 2. Comparison of perioperative parameters and complications of the studied patients in the two groups

Parameters	*Segmentectomy group (n=58)*	*Lobectomy group (n=58)*	*p value*
Operation time (min)	140.58±24.39	118.62±23.40	0.001
Blood loss (ml)	102.85±79.11	107.41±72.42	0.747
Number of lymph node dissection	19.2±5.3	22.8±5.8	0.001
Postoperative thoracic drainage indwelling time (day)	4.8±1.9	5.7±1.8	0.010
Thoracic drainage volume (ml)	767.64±223.51	854.93±303.86	0.041
Hospital stay time (day)	6.1±2.5	7.4±3.1	0.014
Complication, n (%)			
Incision infection	1 (1.7)	2 (3.4)	0.559
Pulmonary infection	2 3.4)	4 (6.9)	0.402
Atelectasis	2 (3.4)	0 (0)	0.154
Chylothorax	0 (0)	1 (1.7)	0.315
Pulmonary air leakage	3 (5.2)	2 (3.4)	0.648
Arrhythmia	4 (6.9)	3 (5.2)	0.697

Table 3. Comparison of postoperative pathological results of the studied patients in the two groups

Parameters	*Segmentectomy group (n=58) n (%)*	*Lobectomy group (n=58) n (%)*	*p value*
NSCLC			0.556
Invasive adenocarcinoma	21 (36.2)	24 (41.4)	
Microinvasive adenocarcinoma	17 (29.3)	11 (19.0)	
Adenocarcinoma in situ	6 (10.3)	9 (15.5)	
Atypical adenomatous hyperplasia	6 (10.3)	4 (6.9)	
Squamous cell carcinoma	1 (1.7)	4 (6.9)	
Neuroendocrine carcinoma	2 (3.4)	3 (5.2)	
SCLC	0 (0)	1 (1.7)	
Benign lesion			
Hamartoma	2 (3.4)	1 (1.7)	
Sclerosing hemangioma	3 (5.2)	1 (1.7)	

NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer.

There was no statistically significant difference in the classification of postoperative pathological results between the two groups of patients (p=0.556) (Table 3).

Comparisons of postoperative pain score and quality of life score between the two groups of patients

The NRS score of patients in the Segmentectomy group was similar to that in the Lobectomy group at 1, 3 and 7 d after surgery [(7.29±1.17) *vs.* (7.53±1.29), (5.03±1.23) *vs.* (5.31±1.16), (2.28±1.22) *vs.* (2.10±1.10)], which displayed no statistically significant difference (p=0.296, p=0.210, p=0.406) (Figure 1). The KPS score was dramatically higher in the Segmentectomy group than that in the Lobectomy group at 1 year after surgery [(91.7±8.9) points *vs.* (82.6±9.4) points, p<0.001].

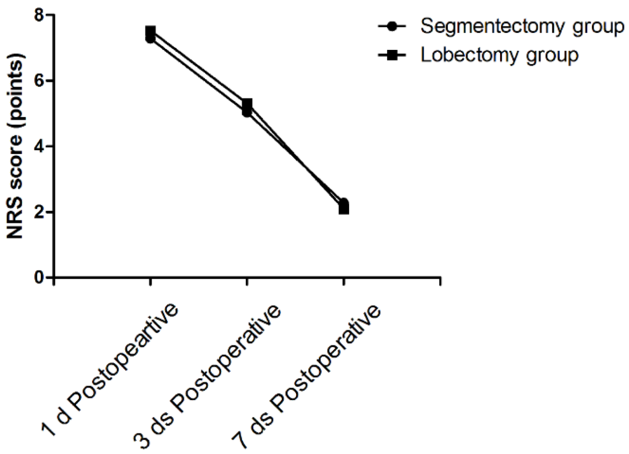

Figure 1. Comparison of postoperative NRS score of the studied patients in the two groups. The differences between 1 postoperative day, 3 postoperative days and 7 postoperative days NRS score of patients in the Segmentectomy group and the Lobectomy group had no statistically significant difference (p=0.296, p=0.210, p=0.406).

Comparisons of pulmonary function indicators

The pulmonary function indicators FVC, FEV_1% and MVV showed no statistically significant differences between the two groups before surgery (p=0.522, p=0.868, p=0.658). After surgery, these indicators declined in both groups compared with those before surgery (p<0.05), and they were superior in the Segmentectomy group to those in the Lobectomy group at 3 and 12 months after surgery (p<0.05) (Table 4).

Follow-up results of survival status of patients

After surgery, all 116 patients were followed up for 6-36 months through outpatient clinic visits and telephone interviews until March 2020. The median follow-up time was 25 months. During follow-up, there were no disease recurrence, metastasis or death.

Discussion

GGNs refer to image structures of cloud-like increases in lung tissue density on the head CT images, which do not cover the bronchi and pulmonary vessels. They are atypical manifestations able to be observed in the case of tumors, infections, interstitial fibrosis or local hemorrhage [7]. With the application of high-resolution CT in the clinic, the detection rate of early lung cancer with focal GGNs rises rapidly [8]. According to the classification of lung adenocarcinoma jointly issued by the International Association for Study of Lung Cancer, American Thoracic Society and European Respiratory Soci-

Table 4. Comparison of Preoperative and Postoperative pulmonary function indexes of patients in the two groups

Parameters	*Segmentectomy group (n=58) n (%)*	*Lobectomy group (n=58) n (%)*	*p value*
FVC (L)			
Preoperative	3.07±0.33	3.11±0.34	0.522
3 months Postoperative	2.78±0.41	2.51±0.43	0.001
12 months Postoperative	2.40±0.45	2.23±0.40	0.034
FEV_1(%)			
Preoperative	94.47±10.18	94.14±11.19	0.868
3 months Postoperative	84.28±8.84	79.93±9.38	0.012
12 months Postoperative	80.95±7.54	72.32±7.18	0.001
MVV (ml)			
Preoperative	95.87±10.22	95.05±9.69	0.658
3 months Postoperative	83.09±7.73	78.94±8.02	0.002
12 months Postoperative	77.81±6.16	71.47±6.50	0.001

FVC: Forced vital capacity; FEV: Forced Expiratory Volume; MVV: Maximum Ventilatory Volume.

ety, lung adenocarcinoma can be classified into pre-invasive lesions, MIA and invasive adenocarcinoma. The pre-invasive lesions are classified into AAH and AIS. Invasive adenocarcinoma includes lepidic predominant adenocarcinoma (LPA), alveolar adenocarcinoma, papillary adenocarcinoma, micropapillary adenocarcinoma and solid adenocarcinoma [9]. AIS and MIA have a better prognosis, and the specific survival rate can reach 100% after they are completely eliminated. A study manifested that about 80% of persistent GGNs are diagnosed as AAH, AIS, MIA or invasive adenocarcinoma [10].

The relation between GGNs and pathology has been extensively studied. GGNs, especially mGGNs, are more prone to be malignant, but the prognosis is good after surgical treatment [11,12]. Research denoted that 59% of persistently stable pGGNs are malignant, and mGGNs are often highly suggestive of lung adenocarcinoma [13]. Therefore, pulmonary GGNs should be actively treated, which is of great significance for the early diagnosis and treatment of lung cancer and the reduction of mortality. In recent years, partial lobectomy and selective lymphadenectomy are applied in treating early NSCLC [14,15]. The long-term survival rate has no difference between lymphadenectomy and lobectomy in the treatment of early lung cancer with a diameter of <2 cm [16]. Miller et al [17] compared lobectomy and sublobectomy (segmentectomy and wedge resection) in treating lung cancer with a diameter of ≤10 mm, and found that there are no statistical differences in survival and local recurrence. For pGGNs whose pathological type is AIS and MIA, sublobectomy (segmentectomy and wedge resection), rather than lobectomy, has been recommended as the surgical method [18]. VATS wedge resection has the advantages of simple technique, few complications and low mortality rate, mainly used for elderly patients with early-stage lung cancer complicated with cardiopulmonary insufficiency [19]. Systemic lymph node dissection offers no benefit on the survival of patients with early lung cancer. Studies have demonstrated that early NSCLC with GGNs ≥50% has no lymph node metastasis, so systemic lymph node resection is not essential. In this group, among mGGNs and pGGNs with lymphatic pathological changes, lymph node metastasis was discovered in 2 cases whose pathological type was invasive adenocarcinoma. The malignancy of mGGNs is associated with the proportion of solid components, and the increase in solid components suggests possible progression of malignant lesions. In the case of increased solid components of mGGNs or SPNs, selective or systemic lymph node resection should be considered [20,21]. Two multi-center randomized controlled clinical trials on the scope of resection for early lung cancer in the United States and Japan are ongoing. With the results of such two trials, the most objective conclusion will be made to standardize the standard surgical approaches for early-stage lung cancer. Hook-wire positioning of GGO under CT guidance has a high success rate and minor complications [22].

In this study, the efficacy and safety of thoracoscopic anatomic segmentectomy and lobectomy in the treatment of pulmonary GGNs were compared and the results revealed that the operative time ($p<0.001$), the number of lymph nodes dissected ($p<0.001$), the indwelling time of postoperative thoracic drainage tube ($p=0.010$), the thoracic drainage volume ($p=0.041$) and the length of postoperative hospital stay ($p=0.014$) were significantly raised in the Lobectomy group compared with those in the Segmentectomy group. In addition, there was no statistical difference in the incidence rate of complications between the two groups. Moreover, in contrast with the Lobectomy group, the Segmentectomy group exhibited notably higher pulmonary function indexes FVC, FEV_1% and MVV and considerably better postoperative quality of life ($p<0.05$). The biggest advantage of segmentectomy is that the range of lung resection is small, so that more lung tissues are preserved, and patients can have better pulmonary function and quality of life after surgery. However, segmentectomy requires more detailed dissection of hilar blood vessels and bronchial structures, so it is generally more difficult than ordinary lobectomy, and the time for dissection is longer than that of lobectomy.

This study is a single-center retrospective study with certain limitations. For instance, the sample size was small, and the follow-up period was short. Hence, prospective multi-center randomized controlled studies of large samples are further needed in the future to confirm the results of this study, so as to offer a reference for the selection of therapeutic schedules for pulmonary GGNs in clinic.

Conclusions

Thoracoscopic anatomic segmentectomy applied in the treatment of pulmonary GGNs achieves similar short-term and long-term outcomes to those of lobectomy. Besides, it has merits including short duration of postoperative thoracic drainage, less drainage volume, short length of hospital stay, better postoperative recovery of pulmonary function and higher quality of life, without increases in the incidence rate of postoperative complications.

Conflict of interests

The authors declare no conflict of interests.

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