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ORIGINAL ARTICLE

Surgical outcomes of segmental bronchial sleeve resection in central non-small cell lung cancer

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Abstract

Background: The purpose of this study was to present the clinical and surgical results in patients who underwent segmental bronchial sleeve reconstruction.

Methods: The clinical and pathological data of 16 patients with central non-small cell lung cancer (NSCLC) who underwent segmental bronchial sleeve resection from April 2015 to May 2019 were retrospectively analyzed.

Results: According to the type of segmental bronchial reconstruction, procedures were divided into four types: right upper S6 sleeve lobectomy in three cases (type A); left lower lingular sleeve lobectomy in 10 cases (type B); left upper S6 sleeve lobectomy in two cases (type C); and left lower propriolateral superior sleeve lobectomy in one case (type D). A total of three patients (18.75%) experienced anastomotic complications, including two with anastomotic stenosis and one with anastomotic fistula. All patients achieved R0 resection. Apart from one patient who died of acute lung infection after surgery, the rest were successfully discharged. The average follow-up time was 28 months, and the overall survival rates of patients at one, two, and three years were 80.0%, 53.3%, and 40.0%, respectively.

Conclusions: Segmental bronchial sleeve resection is complex in technique and may have an increased risk of complications compared to a standard sleeve resection, but it is an effective and safe procedure, especially for selected patients with central lung cancer.

Introduction

At present, the incidence and mortality of lung cancer are first worldwide.[1] The mortality rate of lung cancer in China ranks first among men and women, and the incidence rate ranks first among men, and second among women.[2] For resectable lung cancer, the most effective method is still surgical resection and pneumonectomy, or sleeve bronchectomy is considered to be a safe and effective method for central lung cancer.[3] In recent years, with the widespread application of bronchial sleeve resection, many studies[4–8] have shown that compared with pneumonectomy, bronchial sleeve resection can preserve more lung parenchyma for patients, give a better quality of life, and significantly reduce the incidence of postoperative complications and mortality. There are nearly 30 types of bronchial sleeve reconstruction reported in the literature, but few reports of segmental bronchial sleeve resection. Herein, we collected retrospectively the clinical data of 16 patients undergoing segmental bronchial sleeve resection, and then focused on the procedure and its clinical outcomes.

Methods

Clinical data of patients

The clinical and pathological data of 16 patients with non-small cell lung cancer (NSCLC) who underwent segmental bronchial sleeve resection from April 2015 to May 2019 were retrospectively analyzed. There were 12 males and four females, with ages ranging from 48 to 68 years, and an average age of 60.21 $\pm$ 5.48 years. There were 11 patients with left lower lung tumor (68.8%), three patients with right upper lung tumor, and two patients with left upper lung tumor. There were two patients who underwent chemotherapy before surgery, six with underlying diseases before surgery, 10 with a history of smoking, three patients with a history of tumor

disease, including two patients with a history of thyroid cancer, and one patient with a history of gastric cancer. This retrospective study was approved by the Ethics Committee of Huazhong University of Science and Technology, Tongji Medical College and patient consent was waived based on the nature of this study. Table 1 lists the baseline characteristics.

Preoperative examination and evaluation methods

All patients underwent routine blood, blood biochemical, and coagulation tests to evaluate their general hematological status prior to surgery, ECG (electrocardiogram), echocardiography, blood gas analysis, and pulmonary function assessment of patients' surgical tolerance, and fiberoptic bronchoscopy to evaluate trachea and bronchial conditions. A chest enhanced computed tomography (CT) scan, head CT or MRI, neck ultrasound, abdominal ultrasound, and whole body bone scans were performed, and if necessary, a whole body PET-CT examination to assess distant metastasis. For patients where mediastinal lymph node metastasis was suspected prior to surgery, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was used.

Operative technique

All 16 operations were performed by the same surgeon. Irrespective of whether the procedure was a right or left thoracotomy, it was performed from the fifth intercostal posterolateral incision. Lymph nodes two, three, four, seven, eight, and nine for right thoracotomies, lymph nodes five, six, seven, eight, and nine for left thoracotomies, and noted lymph nodes 10, 11, 12, and 13 during thoracotomies on both sides were dissected for staging and a better exposure. After entering the thorax, the tumor invasion of the bronchi and surrounding large blood vessels was carefully evaluated, and freed according to standard lobectomy. First, the artery and vein of the lung lobe or segment were freed, then the artery, vein and lymph nodes around the bronchi were removed so that the bronchus was fully free of the target segment and main bronchus. When freeing the bronchus, we tried to avoid damaging the nutritional blood vessels around the bronchi to prevent poor healing of the anastomosis, and then the affected segment bronchus and part of the main bronchus was removed. The bronchial stump was sent for intraoperative frozen section analysis for pathology to confirm the bronchial margins were negative. In order to avoid the inconsistency between the size of the segmental bronchus and main bronchus, the segmental-bronchus was sutured continuously with a single layer of 5–0 proline after plastic surgery of the main bronchus. The anastomosis started from the posterior bronchial wall, and then the anterior wall was anastomosed with a 5–0 proline single-layer continuous suture. In order to avoid excessive anastomotic tension, in addition to fully freeing the bronchi and the main bronchus, the lower lung ligament was routinely fully freed and the pericardium opened around the pulmonary veins. After the anastomosis had been completed, intraoperative fiberoptic bronchoscopy was used to observe whether there was bleeding from the anastomosis and whether it had been effective. At the end of the suture, whether there was air leakage was checked by submerging the lung in saline solution and reventilating it under an airway pressure of 15 mmHg. If there was a leak, it could be successfully repaired. In order to further prevent anastomotic fistulas, our center is accustomed to using pedicled pericardial or thoracic surgical repair membrane to surround the anastomosis during left side

Table 1 Clinical characteristics of patients

No.	Gender	Age, years	Tumor location	Smoking history	Comorbidity	Tumor history	Neoadjuvant treatment	Tumor size (cm)	cN stage	cTNM stage*
1	Female	58	RUL	NO	NO	NO	NO	3.5	N0	IIA
2	Male	52	LLL	YES	NO	NO	NO	4.0	N2	IIIA
3	Male	53	LLL	YES	Hypertension	NO	NO	5.2	N0	IIB
4	Male	48	LLL	YES	NO	NO	NO	4.2	N1	IIB
5	Female	67	LLL	NO	Diabetes	YES	NO	3.8	N1	IIB
6	Male	62	LLL	NO	NO	NO	NO	4.5	N2	IIIA
7	Male	62	LLL	YES	Hypertension	NO	NO	5.8	N0	IIB
8	Female	60	LLL	NO	NO	NO	NO	4.3	N1	IIB
9	Male	61	RUL	YES	Diabetes	YES	Chemotherapy	4.8	N2	IIIA
10	Male	68	LUL	YES	NO	NO	NO	3.8	N0	IIA
11	Male	65	LUL	NO	Hypertension	NO	NO	3.5	N1	IIB
12	Male	58	LLL	YES	NO	NO	NO	4.1	N2	IIIA
13	Male	66	LLL	YES	Hypertension	NO	Chemotherapy	6.2	N1	IIIA
14	Male	64	LLL	YES	NO	NO	NO	3.5	N0	IIA
15	Female	56	RUL	NO	NO	YES	NO	4.6	N2	IIIB
16	Male	55	LLL	YES	NO	NO	NO	5.5	N0	IIB

LLL, left lower lobe; LUL, left upper lobe; RUL, right upper lobe. *The IASLC eighth edition of TNM classification.

Table 2 Perioperative and long-term results of patients

No.	Operation time (minutes)	Intraoperative blood loss (mL)	Type	pTNM stage*	Postoperative complications	Postoperative hospital stay duration (days)	Adjuvant treatment	Recurrence status	Survival months	Cause of death
1	215	150	AD	IIB	NO	7	Chemotherapy	NO	44	Alive
2	230	100	SCC	IIIA	NO	6	Both	Local	20	Recurrence
3	220	50	SCC	IIB	NO	10	NO	NO	38	Alive
4	210	100	AD	IIB	NO	8	Radiotherapy	NO	42	Alive
5	200	250	SCC	IIIA	Arrhythmia	12	Chemotherapy	Distant	11	Recurrence
6	320	180	SCC	IIIA	NO	7	Both	Local	34	Alive
7	240	40	SCC	IIIA	NO	9	Radiotherapy	NO	37	Heart disease
8	231	100	SCC	IIIA	Arrhythmia	11	Chemotherapy	Local	21	Recurrence
9	245	300	SCC	IIIB	Pneumonia	Death	-	-	-	-
10	275	280	AD	IIB	NO	6	NO	Local	34	Alive
11	210	150	SCC	IIB	Stricture	14	Chemotherapy	NO	43	Pneumonia
12	190	300	AD	IIIA	NO	7	Radiotherapy	Local	18	Recurrence
13	230	400	SCC	IIIA	BPF	24	Chemotherapy	Distant	11	Recurrence
14	180	50	SCC	IIB	NO	7	Chemotherapy	NO	40	Alive
15	300	200	AD	IIIB	NO	9	Both	Distant	8	Recurrence
16	246	350	SCC	IIIA	Stricture	10	Chemotherapy	Local	15	Pneumonia

AD, adenocarcinoma; SCC, squamous cell carcinoma. *The IASLC eighth edition of TNM classification was used; BPF: bronchopleural fistula; Both: chemotherapy + radiotherapy.

surgery; on the right side, the anastomosis is wrapped with a pedic vein or a thoracic surgical repair membrane which is a kind of surgical repair material made from bovine pericardium.

Statistical analysis

Statistical analysis was performed using SPSS 23.0 software. Continuous variables were presented as mean values±standard deviation, and categorical variables were presented as numbers and percentages. Comparison of clinical data between the two types of patients was performed using the X^2 test. Fisher's exact probability test was used when $n < 40$. *P*-values<0.05 were considered to indicate statistical significance.

Results

Perioperative results

Surgery was successful in all patients. The average operation time was 239.6 ± 38.6 minutes (180–320 minutes). The average intraoperative blood loss was 252.4 ± 101.8 mL (40–400 mL), and average postoperative hospital stay was 11.7 ± 5.8 days (6–24 days). A total of six patients (37.5%) had complications after operation, two had arrhythmia, one had pulmonary infection, two had anastomotic stenosis, and one had an anastomotic fistula. Apart from one patient who died as a result of acute lung infection after surgery, the rest of the patients improved after symptomatic supportive treatment and were discharged smoothly. The perioperative results are shown in Table 2.

Type of procedure and postoperative results

According to the different types of segmental bronchial reconstruction, procedures were divided into four types (Fig. 1): type A: right upper S6 sleeve lobectomy in three cases; type B: left lower lingular sleeve lobectomy in 10 cases; type C: left upper S6 sleeve lobectomy in two cases; type D: left lower propriolateral superior sleeve lobectomy in one case. Among the patients in type A, there was one case of a right upper lung

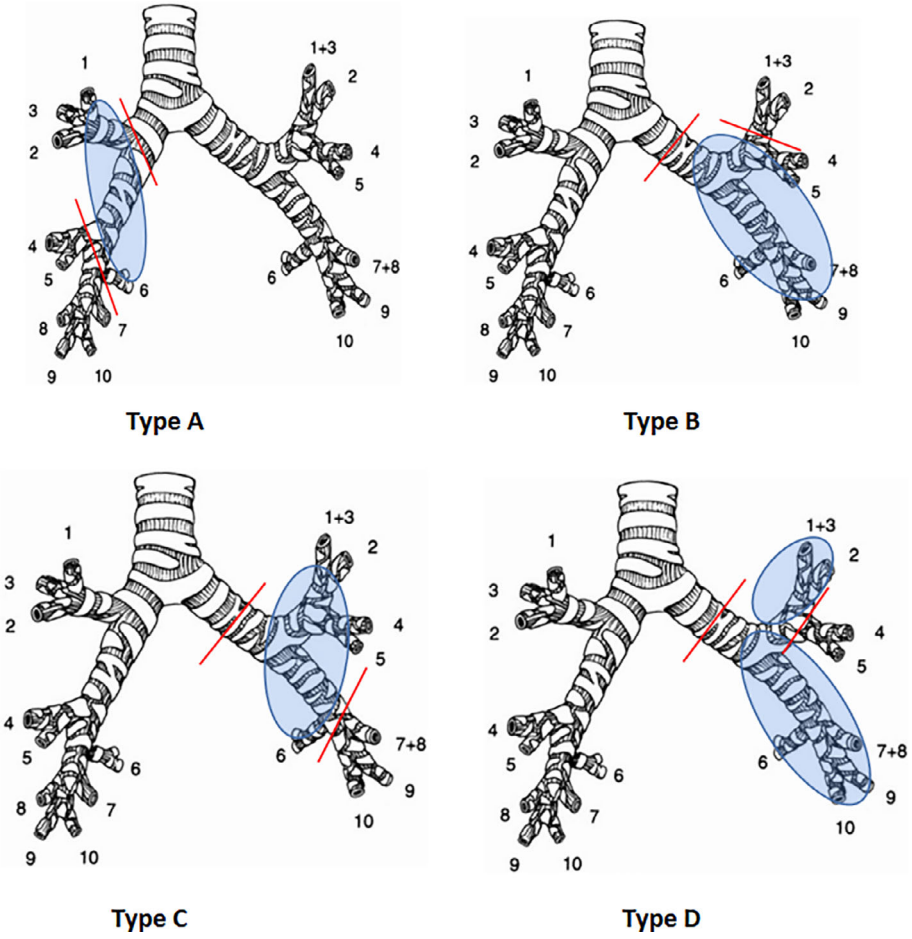

Figure 1 Four types of segmental bronchial reconstruction.

tumor which invaded the right upper lobe bronchus opening and the right lower dorsal pulmonary artery, and two cases of right upper lung tumor which directly invaded the right lower lung superior segment (S6). Among the patients in type B, there were five cases of left lower lung tumor which directly invaded the left tongue lobe (S4 + S5), three cases of left lower lung tumor which invaded the lower lobe bronchus opening and involved the left tongue lobe artery, and two cases of left lower lung tumor which invaded the left lingual bronchial root. In type C, there were two cases of left upper lung tumor which directly invaded the left lower lung superior segment (S6). Patients in type D had a left lower lung tumor with hilar lymph nodes invading the left propriolateral superior lobe artery. Postoperative stump was negative in all patients. Postoperative pathology: there were 11 cases of squamous cell carcinoma and five cases of adenocarcinoma. Postoperative pathological staging: there were six cases who were stage IIB, eight cases who were stage IIIA, and two cases who were stage IIIB. The type of procedure and postoperative pathological results are shown in Table 2.

Postoperative recovery

Comparing the pulmonary function and arterial blood gas examination results of the patients before and one month postoperatively, it was found that the patients' FEV1, FEV1%, DLCO%, and PaO2 did not significantly decrease postoperatively, and the PaO2 and FEV1% indicators increased, but there was no significant increase. This shows that for patients with central lung cancer, segmental bronchial sleeve resection can largely preserve the lung parenchyma and improve the quality of life of patients. See Table 3 for details.

Postoperative follow-up

Patients who were discharged smoothly after surgery were followed up, either in the outpatient clinic or by telephone. Fiberoptic bronchoscopy, pulmonary function, and arterial blood gas analysis were reviewed one month after surgery to evaluate the anastomosis and postoperative pulmonary function recovery. Chest CT, tumor markers, and abdominal B-ultrasounds were reviewed every three months in the first year after surgery; the above indicators were reviewed every six months in the second year after surgery; the above indicators were reviewed annually thereafter. During the follow-up period, if the patient was determined to have lung symptoms, a bronchoscopy was performed together with other necessary procedures at any time. The follow-up time was calculated from the postoperative day and followed up to October 2019. The average follow-up time was 28 months (8–44 months). The overall survival rates of patients at one, two, and three years were 80.0%, 53.3%, and 40.0%, respectively. To date, six patients have survived.

Table 3 Comparison of pulmonary function and blood oxygen pre- and postoperatively

Variables	Preoperative	One month postoperative
FEV1	2.5 ± 0.8	2.3 ± 0.7
FEV1%	73.2 ± 9.3	75.8 ± 8.7
DLCO%	82.6 ± 7.8	81.5 ± 8.2
PaO_2 (kPa)	10.2 ± 1.6	12.4 ± 1.8

DLCO, diffusing capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in one second.

Discussion

Compared with lobectomy or sleeve lobectomy, patients with pneumonectomy had higher mortality and complications. During the 1980s and 1990s, the perioperative 30-day mortality rate for patients with pneumonectomy reported in the literature was approximately 6%–7%.[9–11] In recent years, with the increasing number of pneumonectomy studies, foreign scholars have found that the mortality rate of pneumonectomy is about 4.6%–9.2%,[4,7,12] but the mortality rates following lobectomy and sleeve lobectomy are 0.8% and 1.6%–2.0%, respectively.[5,6] Therefore, for resectable central non-small cell lung cancer (NSCLC), we should consider choosing sleeve lobectomy in order to avoid pneumonectomy.

However, the application of sleeve lobectomy is limited to the tumor invasion site and area. If the tumor involves multiple lobes or multilobed bronchus, simple sleeve lobectomy becomes difficult to complete. Therefore, expanded sleeve resection is warranted. A number of studies have reported[13–15] that for locally advanced lung cancer, expanded sleeve resection is safe and feasible, and it can provide a better long-term prognosis compared with pneumonectomy. Segmental bronchial sleeve resection is a type of extended sleeve resection, but there are few reports on its feasibility and safety.[16] In this study, for patients with tumors involving multiple lung lobes or multilobed bronchus, but not involving the segmental bronchus, we performed segmental main bronchial sleeve resection, and the postoperative mortality and complication rate did not increase compared with extended sleeve lobectomy.[13,14] Extended sleeve lobectomy is an atypical bronchoplasty with resection of more than one lobe, which includes two lobe sleeve resection and single lobe or multiple lobes + single segment or multiple segments sleeve resection. All procedures in our study involved sleeve resection of the lung segment, and we called this procedure "segmental bronchial sleeve resection".

Compared with sleeve lobectomy, extended sleeve lobectomy may increase the risk of postoperative complications. It has been previously reported [15] that the incidence of postoperative pulmonary infection, postoperative delayed air leakage, and postoperative anastomotic fistula after extended sleeve

lobectomy were 14%, 13%, and 8%, respectively, and the total complication rate was 43%. In this study, the incidence of postoperative complications was 37.5%. Apart from one patient who died of postoperative acute lung infection, only one patient had an anastomotic fistula, two patients had arrhythmia, and two patients had an anastomosis, with no other complications. The reason is that good postoperative management is very important. A fiberoptic bronchoscopy is routinely performed at the end of the operation at our center in order to observe whether the anastomosis is bleeding and determine the condition of anastomosis. At the same time, the hemostasis and sputum at the distal end of the anastomosis can be sucked away. We determine whether fiberoptic bronchoscopy is needed according to a patient's cough and sputum after surgery, as a small amount of sputum can cause anastomotic occlusion to form atelectasis, pneumonia, and even respiratory failure, because anastomotic edema is increased in the first two days after surgery.

For central lung cancer, the complete resection of the tumor is the guarantee of postoperative efficacy. Some researchers[17] believe that the bronchial stump needs to be at least 1 cm away from the tumor to meet the requirements of expanded bronchial sleeve resection. In our procedure, we leave an approximately 12 mm tumor-free margin. More importantly, before deciding to perform an expanded bronchial sleeve resection, we should fully consider the patient's quality of life, the risk of postoperative recurrence, and the occurrence of postoperative complications. Therefore, the preoperative evaluation of the patient is very important. In this study, the pulmonary function and arterial blood gas in patients were compared and analyzed before and after surgery, and we found that patients who tolerated segmental bronchial sleeve resection have good postoperative pulmonary function recovery, and subsequently a better quality of life. In terms of postoperative survival, the average follow-up time was 28 months (8–44 months), and the overall survival rates for patients one, two, and three were 80.0%, 53.3%, and 40.0% respectively. This result is similar to previous research.[18] Therefore, segmental bronchial sleeve resection is safe and feasible in selected patients with central NSCLC.

In recent years, with the application of neoadjuvant therapy, particularly neoadjuvant immunotherapy, the survival rate of patients with unresectable NSCLC has improved. However, the benefit of this strategy in patients with resectable NSCLC remains unknown. Previous studies[19–21] have shown that neoadjuvant therapy may cause hilar inflammation and fibrosis, which will increase surgical difficulties. For patients with resectable NSCLC who need sleeve resection, it may be better to perform surgical treatment followed by adjuvant treatment.

In conclusion, segmental bronchial sleeve resection expands the surgical indications for lung cancer, avoids pneumonectomy, and improves the quality of life of patients, especially for those with central NSCLC. Although its technology is more complicated, it is still a safe and feasible surgical procedure.

Disclosure

The authors report no conflicts of interest.

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