ORIGINAL ARTICLE

Simultaneous bilateral pulmonary resection via single-utility port VATS for multiple pulmonary nodules: A single-center experience of 16 cases

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Abstract

Background: The detection rate of bilateral multiple pulmonary nodules (BMPNs) is increasing due to widespread use of chest computed tomography (CT) screening. However, there is no consensus on the treatment options for BMPNs and whether simultaneous bilateral pulmonary resection is safe remains controversial. The purpose of this study was to evaluate the feasibility and safety of simultaneous bilateral pulmonary resection for BMPNs.

Methods: A total of 16 consecutive patients with BMPNs who underwent simultaneous bilateral pulmonary resection in Beijing Hospital from June 2013 to July 2020 were enrolled in this study. Clinical characteristics, imaging and pathological features, and perioperative outcomes were retrospectively reviewed.

Results: There were 10 males and six females included in the study with a mean age of 61.9 (range: 39–78) years. A total of 35 nodules were resected in 16 patients including 12 patients with bilateral primary lung cancer, three patients with primary lung cancer on one side and a benign nodule on the contralateral side, and one patient with bilateral benign nodules. All patients underwent bilateral pulmonary resection via single-utility port video-assisted thoracoscopic surgery (VATS). Nine, four, two, and one patients underwent lobectomy with contralateral segmentectomy or wedge resection, segmentectomy with contralateral wedge resection, bilateral segmentectomy and bilateral wedge resection, respectively. All operations were accomplished successfully without intraoperative blood transfusion, conversion to thoracotomy, major complication and postoperative 90-day death. The mean operation time was 220.1 ± 65.6 minutes, median thoracic drainage duration was four days (range: 2–8 days), mean pleural drainage was 1387.5 ± 694.7 mL, and median postoperative hospital stay was seven days (range: 5–18 days). There were three cases (18.8%) of minor complications, including one case of pulmonary air leakage, one case of atrial fibrillation, and one case of poor healing of surgical site. A total of 50% (8/16) of the patients had severe postoperative pain and required additional analgesia.

Conclusions: For selected patients, simultaneous bilateral pulmonary resection via single-utility port VATS is a safe and feasible minimally invasive procedure for BMPNs. Adequate postoperative analgesia via a multimodal analgesia strategy should be used to prevent postoperative pain.

Key points

Significant findings of the study: The incidence of major complication after minimally invasive bilateral pulmonary resection is low for patients with good pulmonary function, but there is a relatively high incidence of minor complications and pain at the surgical site. Adequate postoperative analgesia via multimodal analgesia strategy should be used to prevent postoperative pain.

What this study adds: For the treatment of bilateral multiple pulmonary nodules, simultaneous bilateral pulmonary resection via single-utility port video-assisted thoracoscopic surgery is safe and feasible for selected patients.

Introduction

Due to the widespread use of chest computed tomography (CT) screening and advancement of diagnostic technology, the detection rate of bilateral multiple pulmonary nodules (BMPNs) is increasing, among which synchronous multiple primary lung cancers (SMPLCs) accounts for a large proportion.[1] Although there is no consensus on the treatment options for BMPNs, minimally invasive surgery has been demonstrated to be one of the best methods for the diagnosis and treatment of BMPNs, and patients with confirmed SMPLCs could therefore benefit from surgical treatment.[2–4]

For BMPNs that need to be removed, most centers currently perform two-stage bilateral pulmonary resection with intervals of weeks to months, and believe that perioperative risk of one-stage surgery is significantly increased. Currently, the data of one-stage surgical strategy is limited, and safety and effectiveness of simultaneous bilateral pulmonary resection are still controversial.[5–10] In this retrospective cohort study, we report our single-center experience of simultaneous bilateral pulmonary resection for BMPNs and summarize its perioperative safety.

Methods

Patients

From June 2013 to July 2020, 16 patients underwent simultaneous bilateral pulmonary resection for BMPNs at Beijing Hospital. Clinical data, imaging and histological features, surgical methods and perioperative outcomes of these patients were retrospectively reviewed.

Preoperative chest CT, abdominal ultrasound, cranial magnetic resonance image (MRI) or CT, and whole body bone scan were performed in all patients to determine the nature of the lesions, evaluate tumor stage and exclude metastasis. Positron emission tomography (PET) was performed when necessary. Arterial blood gas, pulmonary function and echocardiography were performed to assess surgical tolerance. Patients with critical pulmonary function impairment underwent a cardiopulmonary exercise test to determine whether they could tolerate the operation.

For pathologically confirmed lung cancer, tumor stage was determined according to eighth edition of American Joint Committee on Cancer/Union for International Cancer Control TNM (Tumor, Node, Metastasis) staging system.[11] Multiple primary lung cancers were diagnosed based on Martini-Melamed criteria[12] and each lesion was staged independently.

Surgical techniques

All patients underwent combined intravenous and inhalation general anesthesia with double-lumen endotracheal intubation or single-lumen tube using bronchial blocker to maintain single-lung ventilation. All patients underwent simultaneous bilateral video-assisted thoracoscopic surgery (VATS) using single-utility port technique as previously reported.[13] Our surgical strategy was to complete the operation on the major lesion side first and then rotate the patient to the opposite side to complete the contralateral operation. The patient was placed in a lateral decubitus position throughout the operation. A 1 cm incision was made in the seventh or eighth intercostal space along the midaxillary line as the observation port, and a 3 cm incision in the fourth or fifth intercostal space along the anterior axillary line was made as the operation port.

Depending on preoperative pulmonary function, location, size, and pathology of the pulmonary lesions, lobectomy, segmentectomy or wedge resection on each side was performed. Systemic lymph node dissection was performed if the pulmonary lesion was diagnosed as malignant by intraoperative rapid frozen pathology. At the end of the operation a pleural drainage tube was placed in each pleural cavity, respectively. The patient received a chest radiograph on the second day after surgery, and bilateral

pleural drainage tubes could be removed if there was no active bleeding or air leakage.

Postoperative complications and pain assessment

Complications and postoperative 90-day mortality were recorded based on the definitions of General Thoracic Surgery Database of the Society of Thoracic Surgeons.[14] Postoperative pain assessment adopted the visual analogue scale (VAS). Postoperative pain score and use of analgesics were recorded.

Follow-up

For patients with pathologically confirmed malignant tumors, chest CT, abdominal ultrasound and blood tumor markers were reviewed every three months in the first two years after surgery, every six months in the next three years, and then every year after five years of surgery. Cranial MRI and whole body bone scan were reviewed annually or when there were corresponding symptoms.

Statistical analysis

Statistical analyses were performed using SPSS version 22.0 software. Continuous variables are presented as mean values ± standard deviation or median and range. Categorical variables are presented as numbers and percentages.

Results

Clinical characteristics

A total of 16 patients who underwent simultaneous bilateral pulmonary resection were enrolled in this study. There were 10 males and six females, with a mean age of 61.9 years (range: 39–78) years. Eight patients had comorbidities including hypertension ($n = 7$), diabetes mellitus ($n = 2$), coronary heart disease ($n = 1$), cerebral infarction combined with atrial fibrillation ($n = 1$), and other malignancies ($n = 2$). Nine patients had a smoking history and mean smoking index was 36.7 (range: 0.1–90) pack-years. Six patients had normal pulmonary function, six patients had ventilatory dysfunction, three patients had ventilatory dysfunction with diffusion dysfunction, and one patient

Table 1 Clinical characteristics and imaging features of 16 patients

No.	Age (years)	Gender	Smoking index	Comorbidity	Tumor marker	Nodule number (R/L)	Nodule location (R/L)	Maximum diameter (mm) (R/L)	Imaging manifestation (R/L)
1	78	M	0.1	HTN	Cyfra21-1, elevated	1/1	RU/LU	20/40	SN/SN
2	61	M	40	N	Normal	1/1	RU/LU	19/54	SN/SN
3	68	F	N	HTN/DM/CHD/AF/CI	Normal	1/1	RU/LU	20/13	pGGO/SN
4	64	F	90	HTN	Normal	1/1	RU/LU	13/29	mGGO/pGGO
5	65	M	40	HTN	Normal	2/1	RU, RM/LL	37, 14/15	SN,SN/SN
6	46	M	30	N	CEA, elevated	1/1	RU/LL	10/8	pGGO/mGGO
7	62	M	10	N	Normal	1/1	RM/LU	5/13	SN/SN
8	74	M	30	N	Cyfra21-1, elevated	1/1	RU/LU	31/26	SN/SN
9	63	F	N	HTN/Breast cancer	Normal	1/1	RL/LU	6/13	pGGO/mGGO
10	65	F	N	N	Normal	1/1	RU/LL	10/9	mGGO/mGGO
11	63	M	75	N	Normal	1/1	RU/LL	11/12	pGGO/mGGO
12	64	M	N	HTN	Normal	1/1	RU/LU	19/15	mGGO/mGGO
13	56	F	N	HTN	Normal	1/1	RU/LL	15/12	pGGO/SN
14	57	M	15	N	Cyfra21-1, elevated	1/2	RL/LL, LL	63/12	SN/SN, SN
15	66	M	N	N	Cyfra21-1, elevated	1/2	RM/LU, LL	34/12, 5	mGGO/ mGGO, mGGO
16	39	F	N	Thyroid cancer, total thyroidectomy	CA199, elevated	1/1	RM/LU	7/9	pGGO/pGGO

AF, atrial fibrillation; CHD, coronary heart disease; CI, cerebral infarction; DM, diabetes mellitus; F, female; HTN, hypertension; L, left; LL, left lower lobe; LU, left upper lobe; M, male; mGGO, mixed ground-glass opacity; N, no; pGGO, pure ground-glass opacity; R, right; RL, right lower lobe; RM, right middle lobe; RU, right upper lobe; SN, solid nodule; Y, yes.

Table 2 Pulmonary function and surgical details of 16 patients

	Pulmonary function					Operation information					
NO.	FEV1 (L)	FEV1 % Pred (%)	MVV (L)	MVV % Pred (%)	DLCO % pred (%)	Resection range (R/L)	Surgical approach (R/L)	Operation time (minutes)	Thoracic drainage duration (days)	Pleural drainage (mL)	Postoperative hospital stay (days)
1	2.09	85	68.49	89	56	W/S	V/V	230	2	600	10
2	2.22	67.1	66.62	54.5	84.4	W/L + S	V/V	285	8	2950	10
3	2.06	83	84.81	116	150	W/S	V/V	202	4	1480	7
4	2.01	77	74.75	91	137	L/S	V/V	230	6	2380	7
5	1.84	65	51.81	51	80	L + W/W	V/V	315	7	1550	18
6	4.16	106.9	124.7	90	86.2	S/W	V/V	235	5	2130	6
7	2.56	95	83.62	86	98	W/W	V/V	65	3	290	5
8	2.19	87	56.86	68	82	L/S	V/V	315	4	1870	13
9	1.87	88	64.58	76	83	W/L	V/V	155	4	1100	10
10	1.81	101.8	54.34	69	80.8	S/W	V/V	170	3	820	5
11	2.1	71.3	81.94	73	77.6	S/S	V/V	255	4	1450	6
12	2.89	97.6	74.44	66.1	75.4	S/S	V/V	210	4	1380	7
13	2.53	105.3	85.79	91.9	111.8	S/L	V/V	215	3	870	6
14	2.27	74.8	48.43	42.2	80.5	L/W	V/V	160	2	700	6
15	2.99	107.6	89.61	83.4	115	L/S + W	V/V	190	4	1250	5
16	3.27	105.5	98.11	88.5	77.3	L/S	V/V	290	3	1380	9

DLCO, carbon monoxide diffusing capacity; FEV1, forced expiratory volume in one second; L, lobectomy; MVV, maximal voluntary ventilation; S, segmentectomy; V, video-assisted thoracoscopic surgery; W, wedge resection.
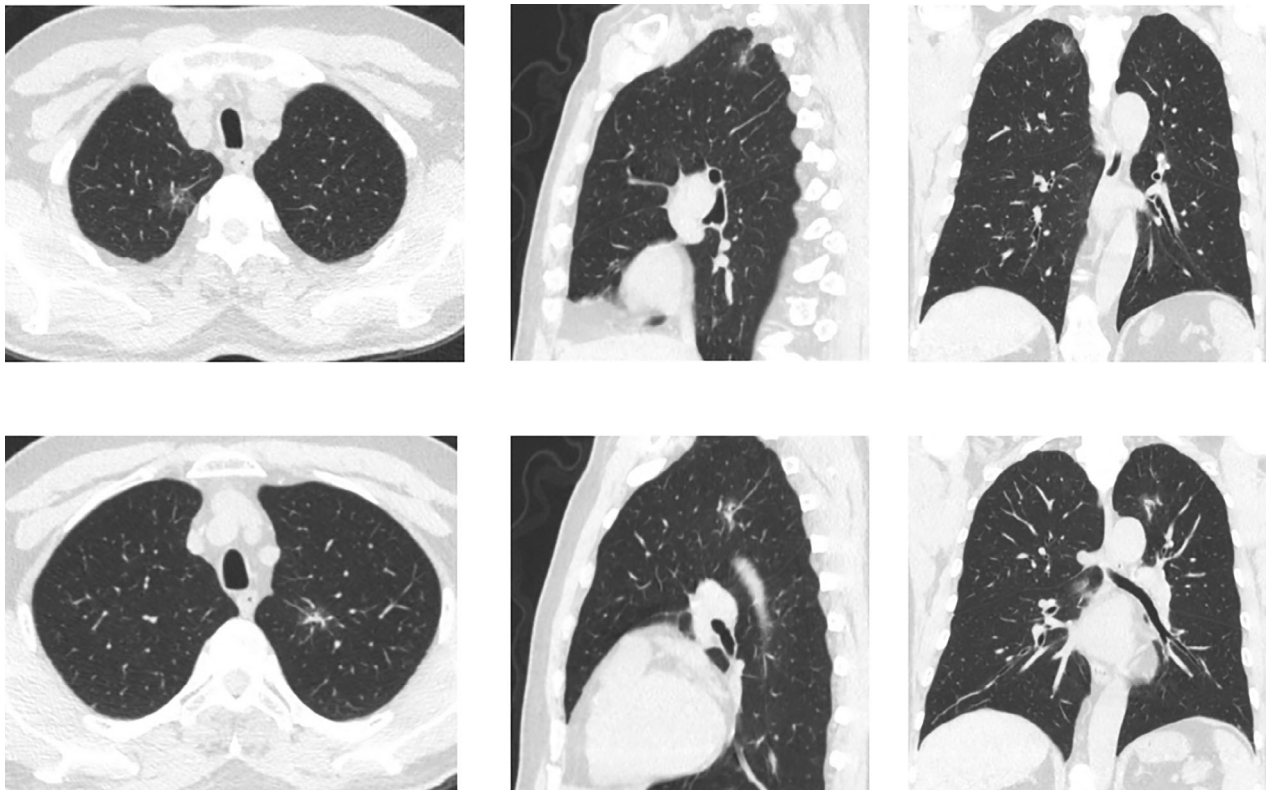

Figure 1 Case 12: A 64-year-old male in which preoperative chest CT showed a mixed ground-glass opacity (GGO) in the apical segment of the right upper lobe (19 × 19 mm) and a mixed GGO in the apicoposterior segment of the left upper lobe (15 × 9 mm). The patient underwent right apical segmentectomy and left apicoposterior segmentectomy via single-utility port video-assisted thoracoscopic surgery (VATS). Pathologically, GGO in the right upper lobe was lepidic predominant adenocarcinoma and GGO in the left upper lobe was acinar pattern of adenocarcinoma.

had mild diffusion dysfunction. The clinical characteristics and preoperative pulmonary function are shown in Tables 1 and 2.

Imaging and pathological features

A total of 35 nodules were resected in 16 patients including 18 nodules in the left lung and 17 nodules in the right lung. Pathologically, 11 patients had bilateral invasive carcinoma, three patients had invasive carcinoma on one side and a benign nodule on the other, one patient had bilateral carcinoma in situ, and one patient had bilateral benign nodules. Among all the resected nodules, there were eight pure ground-glass opacities (GGO), 11 mixed GGO and 16 solid nodules. Images of typical cases are shown in Figs 1 and 2. Seven of eight pure GGO were malignant lesions including one adenocarcinoma in situ, three lepidic predominant adenocarcinoma (LPA), one acinar pattern of
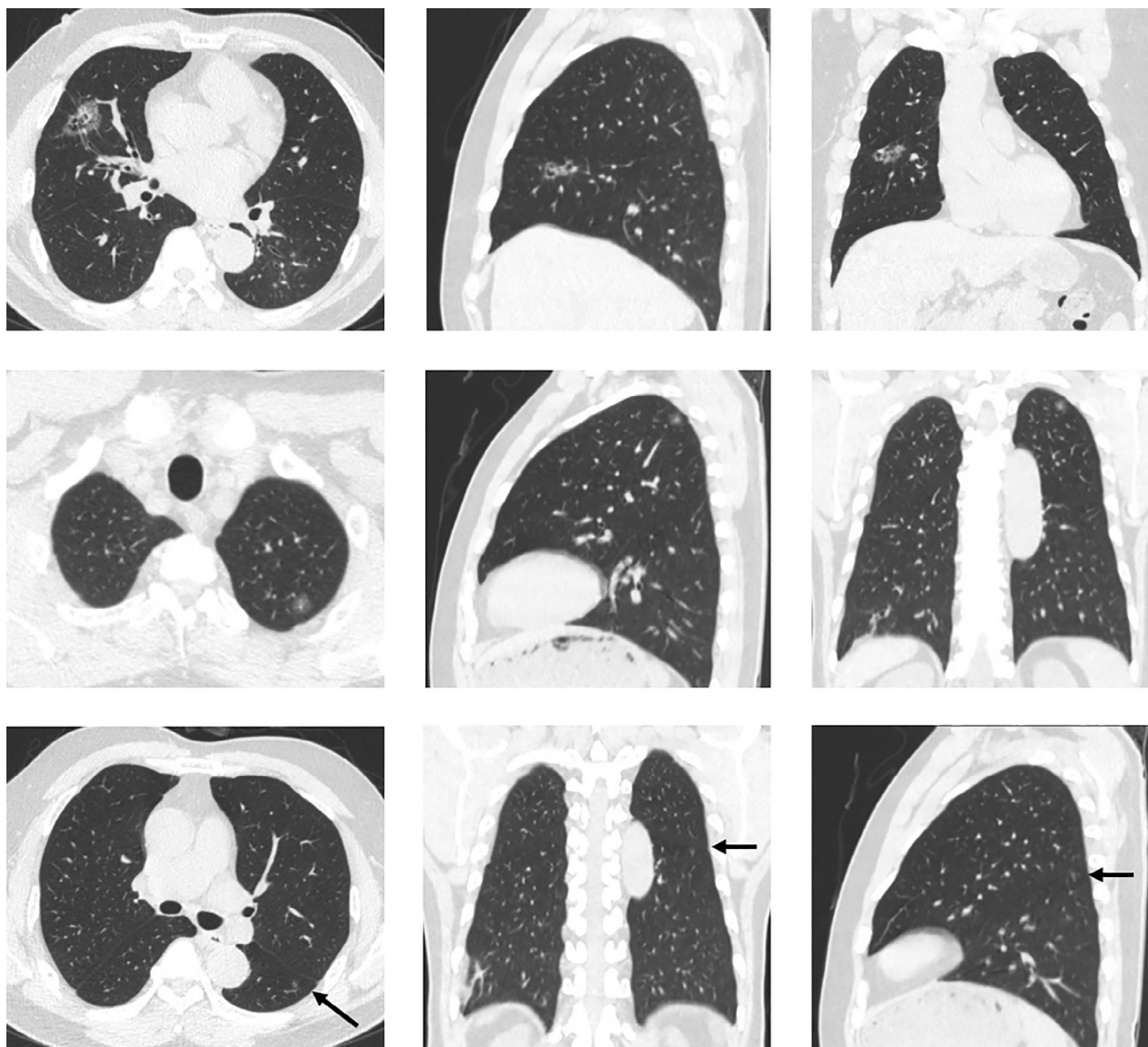

Figure 2 Case 15: A 66-year-old male in which preoperative chest CT scan showed a mixed ground-glass opacity (GGO) in the right middle lobe (34 × 20 mm), a mixed GGO in the apicoposterior segment of the left upper lobe (12 × 8 mm), and a mixed GGO in the dorsal segment of the left lower lobe (5 × 3 mm [arrow]). The patient underwent right middle lobectomy, wedge resection of the left upper lobe and left dorsal segmentectomy via single-utility port video-assisted thoracoscopic surgery (VATS). Pathologically, GGO in the right middle lobe indicated a papillary pattern of adenocarcinoma, GGO in the left upper lobe minimally invasive adenocarcinoma, and GGO in the left lower lobe atypical adenomatous hyperplasia.

adenocarcinoma (APA), two LPA combined with APA, and the other pure GGO was benign. All 11 mixed GGO were malignant or precancerous lesions, including seven invasive adenocarcinomas, two minimally invasive adenocarcinomas, one adenocarcinoma in situ and one atypical adenomatous hyperplasia. A total of 10 of 16 solid nodules were invasive carcinoma and the other six were benign. The imaging and pathological features are shown in Tables 1 and 3.

Perioperative outcomes

A total of 15 patients underwent bilateral pulmonary resection via single-utility port VATS approach, and one patient underwent bilateral pulmonary resection via single-utility port VATS approach on the right side and

traditional three-ports VATS approach on the left side. Nine, four, two, and one patients underwent lobectomy with contralateral segmentectomy or wedge resection, segmentectomy with contralateral wedge resection, bilateral segmentectomy and bilateral wedge resection, respectively.

All operations were accomplished successfully without intraoperative blood transfusion, conversion to thoracotomy, major complication and postoperative 90-day death. The mean operation time was 220.1 ± 65.6 minutes, median thoracic drainage duration was four days (range: 2–8 days), and mean pleural drainage was 1387.5 ± 694.7 mL. There were three cases (3/16, 18.8%) of minor complications, including one case of pulmonary air leakage, one case of atrial fibrillation, and one case of poor healing of surgical site, respectively. Eight (8/16, 50%) patients had severe postoperative pain with a pain score above seven

Table 3 Postoperative outcomes and pathological results of 16 patients

No.	Postoperative complications	Postoperative pain score and additional analgesics	Pathology (R/L)	VPI (R/L)	LVI (R/L)	pTNM stage (R/L)	*EGFR* mutation
1	N	9/Y	ADC/ADC	N/N	N/N	T1bN0M0, IA2/T2aN0M0, IB	Exon 21 (L858R)
2	Pulmonary air leakage	3/N	LPA/70%LCNEC+30%ADC	N/Y	N/Y	T1bN0M0, IA2/T3N0M0, IIB	Exon 21 (L858R)
3	Atrial fibrillation	3/N	LPA/85%LPA + 10%PPA + 5%MPA	Y/N	N/N	T2aN0M0, IB/T1bN0M0, IA2	Exon 19 deletion
4	N	7/Y	60%APA + 30%LPA + 10% MPA/LPA	N/N	N/N	T1aN0M0, IA1/T1cN0M0, IA3	Exon 21 (L858R)
5	Poor healing of surgical site	9/Y	70%APA + 20%PPA + 10%SPA, Benign/benign	N/N	N/N	T1bN0M0, IA2/–	Exon 21 (L858R)
6	N	10/Y	AIS/AIS	N/N	N/N	TisN0M0/TisN0M0	Negative
7	N	3/N	Benign/hamartoma	N/N	N/N	—	None
8	N	8/Y	ASC/ASC	N/N	Y/N	T2aN0M0, IB/T1cN0M0, IA3	Negative
9	N	8/Y	Benign/60%PPA + 30%LPA + 10%APA	N/N	N/N	–/T1bN0M0, IA2	Negative
10	N	8/Y	MIA/80%APA + 20%LPA	N/N	N/N	T1aN0M0, IA1/T1aN0M0, IA1	Negative
11	N	3/N	APA/70%LPA + 30%APA	N/N	N/N	T1aN0M0, IA1/T1bN0M0, IA2	Negative
12	N	3/N	LPA/APA	N/N	N/N	T1bN0M0, IA2/T1bN0M0, IA2	Exon 19 deletion
13	N	8/Y	LPA/60%PPA + 40%APA	N/Y	N/N	T1bN0M0, IA2/T2aN0M0, IB	Exon 19 deletion
14	N	2/N	SCC/Benign, benign	N/N	Y/N	T3N0M0, IIB/–	None
15	N	2/N	60%PPA + 30%LPA + 10%APA/ MIA, AAH	N/N	N/N	T1bN0M0, IA2/T1AN0M0, IA1	Exon 19 deletion
16	N	2/N	80%LPA + 20%APA/80%LPA + 20%APA	N/N	N/N	T1aN0M0, IA1/T1aN0M0, IA1	Negative

AAH, atypical adenomatous hyperplasia; ADC, adenocarcinoma; AIS, adenocarcinoma in situ; APA, acinar pattern of adenocarcinoma; ASC, adenosquamous carcinoma; Be, benign; Ha, hamartoma; LCNEC, large cell neuroendocrine carcinoma; LPA, lepidic predominant adenocarcinoma; LVI, lymphovascular invasion; MIA, minimally invasive adenocarcinoma; MPA, micropalillary pattern of adenocarcinoma; N, no; PPA, papillary pattern of adenocarcinoma; pTNM, pathological tumor node metastasis; SCC, squamous cell carcinoma; SPA, solid pattern of adenocarcinoma; VPI, visceral pleural invasion; Y, yes.

and required additional oral or intravenous analgesia. All patients were discharged successfully and median postoperative hospital stay was seven days (range: 5–18 days). The surgical details and perioperative outcomes are shown in Tables 2 and 3.

Discussion

Lung cancer is the leading cause of cancer-related mortality worldwide and early detection of lung cancer is important. Guidelines of National Comprehensive Cancer Network suggests using low-dose computed tomography of the chest to screen selected patients who are at a high risk of lung cancer.[15,16] With the popularity of lung cancer screening, the detection rate of multiple pulmonary nodules has increased over recent years, especially pulmonary nodules with components of GGO.[17,18] In our study, 87.5% (7/8) pure GGO and all mixed GGO were pathologically confirmed as malignant or precancerous lesions. It is worth noting that for solid nodules, although 10 of 16 solid nodules were pathologically confirmed as invasive carcinoma, benign lesions accounted for nearly 40% (6/16). Therefore, the differentiation of benign and malignant pulmonary nodules is particularly important. The following features increased the risk of pulmonary nodule malignancy:[15] a pure nonsolid nodule larger than 10 mm, a subsolid nodule with solid components larger than 5 mm, atypical subsolid nodules with spiculated contours, bubbly appearance, or reticulation, pure nonsolid nodules or part-solid nodules with solid components smaller than 5 mm that show interval change in size or attenuation, and solid lesions with characteristics that are suspicious for invasive carcinoma.

In our study, 75% (12/16) patients were pathologically confirmed as synchronous bilateral primary lung cancer. The diagnostic criteria of multiple primary lung cancers reported by Martini and Melamed[12] in 1975 is still the most widely used definition of synchronous multiple primary lung cancers (SMPLCs). Although there is no consensus on the treatment of bilateral SMPLCs (bSMPLCs), some studies[19–21] have shown that radical resection of bilateral lesions may be the optimal treatment choice and could provide a good long-term prognosis. The surgical method used in most studies is to remove the pulmonary nodule on one side and perform a second operation on the other side over a period of time, namely two-stage surgical strategy, aiming to reduce perioperative risk and achieve a better postoperative recovery. It should be noted that this may increase hospitalization costs, risk of tumor progression and patient stress during the intervening period. Although one-stage surgical strategy for bSMPLCs could prevent patients from undergoing a second operation, reduce surgical trauma and hospitalization costs, minimize the risk of tumor progression during two operations and

may provide better prognosis, there are still concerns about its perioperative safety. Several studies[6–10,20] have suggested simultaneous bilateral pulmonary resection by video-assisted thoracoscopic surgery (VATS) is safe and feasible; however, most of those studies were retrospective of small sample size. Atrial fibrillation, pneumonia, persistent air leakage and transient respiratory insufficiency are common postoperative complications. In our study, single-utility port technique was used to minimize surgical trauma, and three (18.8%) patients had minor complications including air leakage, atrial fibrillation and poor healing of the surgical site with no occurrence of major complication.

For bSMPLCs, there is still no consensus on resection range of bilateral lung. In studies[6–9] reporting one-stage bilateral pulmonary resection, lobectomy with contralateral sublobectomy or bilateral sublobectomy are the most common used surgical strategy. A meta-analysis[22] published in 2019 suggested that overall survival of MPLC patients who underwent sublobar resection (segmentectomy or wedge resection for at least one lesion) was comparable with those who underwent standard resection approach (lobectomy or pneumonectomy for all lesions) (hazard ratio = 1.07, 95% CI: 0.67–1.71, P = 0.784). Further analysis found no difference in subgroups of synchronous and metachronous, different population region and dominant sex type. This meta-analysis revealed that sublobar resection is acceptable for patients with SMPLCs at an early stage because of the equivalent prognosis to lobectomy and better pulmonary function preservation. In our study, 56% (9/16) of patients underwent lobectomy on one side with contralateral sublolar resection and no patients underwent bilateral lobectomy. Out of all 27 malignant lesions, anatomic lung resections which included nine lobectomies and 13 segmentectomies were performed in 22 lesions, and wedge resections were performed in five lesions.

It should be noted that pain at the surgical site was an important problem affecting postoperative quality of life, and 50% of patients needed extra analgesia during hospitalization in our study. Postoperative pain can lead to respiratory complications, poor quality of life, longer hospital stays and chronic post-thoracotomy pain syndrome. In addition to postoperative acute pain, chronic post-surgical pain (CPSP) occurred three and six months after thoracotomy with an incidence of 57% and 47%, respectively.[23,24] Predictive factors for CPSP included age <60 years old, female gender, pre-existing hypertension, prolonged duration of post-operative chest tube drainage (≥4 days), and method of postoperative pain management.[25] To alleviate pain, multimodal anesthesia which combines systemic and regional anesthesia may be a more effective method. The multimodal analgesia strategy currently used in our center includes intraoperative intercostal nerve block and paravertebral nerve block,

postoperative patient-controlled intravenous analgesia and continuous paravertebral nerve block, and additional oral or intravenous analgesics during hospitalization if necessary. Other methods to reduce postoperative pain include minimizing intraoperative damage to the intercostal nerve and soft tissue of chest wall, reducing the number of incisions and thoracic drainage tubes, indwelling smaller and softer thoracic drainage tubes, and removing thoracic drainage tubes as soon as possible after surgery.

It should be emphasized that this was a retrospective cohort study with inevitable selection bias with a small sample size; therefore, the number of enrolled patients should be expanded to observe the safety and efficacy of this surgical strategy. Furthermore, due to the limitation of follow-up time, our study only reported the short-term results of postoperative outcomes, and the follow-up time should be extended to observe the long-term results of simultaneous bilateral pulmonary resection for bSMPLCs.

In conclusion, our study suggests that simultaneous bilateral pulmonary resection via single-utility port VATS is safe and feasible for the treatment of BMPNs in selected patients with good pulmonary function. Although the incidence of postoperative major complication was low in this study, there was a relatively high incidence of minor complications and pain at the surgical site. Adequate postoperative analgesia via multimodal analgesia strategy should be used to prevent postoperative pain.

Acknowledgments

Disclosure

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