Simultaneous bilateral thoracoscopic lobectomy for synchronous bilateral multiple primary lung cancer—single center experience

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Background: The aim of this study was to investigate the feasibility and safety of simultaneous bilateral thoracoscopic lobectomy and compare perioperative and late outcomes between simultaneous and staged bilateral thoracoscopic lobectomy.

Methods: Between January 2013 and December 2017, the medical records of patients who underwent bilateral thoracoscopic lobectomy for synchronous bilateral multiple primary lung cancer (SPLC) were reviewed retrospectively. Univariate analysis was used to examine the factors associated with morbidity. Survival was estimated with the Kaplan-Meier method.

Results: In the simultaneous resection group (n=41) and the staged groups (n=66), 11 and 16 patients underwent postoperative complication, respectively, whereas no significant differences existed between two groups (P=0.850). Univariate analysis showed that preoperative comorbidities (P=0.009), FEV₁ <2 L (P=0.001), FEV₁% <80% (P=0.036), and the number of pulmonary segments resected ≥9 (P=0.014) were the risk factors to increased simultaneous resection postoperative complication. In addition, simultaneous resection could significantly reduce total cost compared to staged resection (10,854.6±1,998.8 vs. 16,241.4±2,972.8 USD, P<0.001). In long-time outcomes, the patients with simultaneous resection showed better disease-free survival (DFS) than patients with staged resection at 5 years (67.7% vs. 45.9%, P=0.039).

In subgroup analysis, simultaneous resection also had a significantly better survival than staged resection in patients with bilateral pure solid lesions or the biggest tumor size >3 cm.

Conclusions: Bilateral thoracoscopic lobectomy could be a feasible option for SPLC based on appropriate patient selection and careful perioperative management. Meanwhile, simultaneous resection has significantly advantaged in reducing the cost, preventing tumor progression compare to staged resection.

Keywords: Bilateral lobectomy; thoracoscopic; bilateral multiple primary lung cancers (bilateral MPLC); simultaneous resection

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Introduction

As a result of advances in diagnostic techniques, such as high-resolution computer tomography (CT), the detection rate of multiple primary lung cancers (MPLC) increased gradually. At the same time, more synchronous bilateral multiple primary lung cancers (SPLC) were found, based on the diagnostic criteria proposed by Martini and Melamed in 1975. In a survey of members of the interdisciplinary International Association, the majority of respondents recommended surgical resection for multifocal lung cancer (1). Studies had also reported that the 5-year survival rate after treatment for patients with SPLC ranged from 34% to 75.8%, which was better than that of patients with a tumor classified as stage IIIB or IV (2-6).

In theory, simultaneous bilateral resection should be the ideal treatment for patients with SPLC. However, due to the higher risk of postoperative complications and limited experience, staged bilateral resection was widely practiced in most hospitals, especially for bilateral lobectomy. At present, video-assisted thoracic surgery (VATS) is widely used in highly complex surgeries, due to advantages including reduced postoperative complication and pain, a shorter recovery period, and preservation of respiratory function (7,8). A series of studies have also documented that bilateral thoroscopic surgical treatment can be performed with low morbidity for bilateral multiple primary lung cancer (9-12).

In this report, our goal was to identify feasible candidates for simultaneous bilateral thoracoscopic lobectomy for SPLC. The perioperative and long-term outcomes between simultaneous and staged resection were compared to select the appropriate surgical procedure.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/jtd-20-3325).

Methods

Patients

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review board of Shanghai Pulmonary Hospital (No. k-19-005-1) and informed consent was taken from all the patients. According to the criteria proposed by Martini and Melamed, and the modified criteria from the American College of Chest Physicians (ACCP) guidelines (13,14), we identified patients with MPLC in our hospital between January 2013 and December 2017. The exclusion criteria were as follows: metachronous MPLC, unilateral MPLC, thoracotomy, lateral or bilateral sub-lobectomy. Patients lost follow-up were also excluded from further analyses. Ultimately, we retrospectively reviewed the records of 107 patients who underwent bilateral thoracoscopic lobectomy for SPLC. Of those patients, 41 underwent simultaneous resection, and 66 patients underwent staged resection (Figure 1).

Preoperative examination and policy

All patients underwent preoperative systematic evaluation including CT scans, flexible bronchoscopy, pulmonary function test, positron emission tomography CT (PET-CT) scans, and bone and brain magnetic resonance imaging (MRI) to exclude distant metastasis. Mediastinoscopy for mediastinal lymph node or endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) was only performed for patients with lymph node >10 mm on CT to exclude mediastinal lymphatic metastases. The number of segment resections were calculated as described by Zeiher and colleagues (15). The lower lobes were divided into 3 lung segments each, the right upper lobe was divided into 2 segments, the right middle lobe into 3 segments, the right middle lobe into 2 segments, and the left upper lobe into 4 segments.

The operative policy for SPLCs was determined at a multi-disciplinary meeting that included specialists from our hospital in oncology, respiratory, surgery, and radiology. Surgical procedures were mainly selected based on tumor size, location, radiologic characteristics, pulmonary function, and intraoperative frozen biopsy. Lobectomy with systemic lymph node dissection was recommended for pure-solid lesions of more than 2 cm, due to its highly invasive nature. In contrast, mixed ground glass opacity (GGO) lesions that were of large size or centrally located, were not appropriate candidates for sub-lobar resection. In addition, patients with clinical N2 disease or a predicted postoperative FEV1 of less than 1 L were excluded from surgery.

Surgical technique

All patients were placed in the full lateral decubitus position and received general anesthesia with double-lumen endotracheal tube intubation. The incision was usually performed at the fourth or fifth intercostal space so that the needle holder could be placed parallel to the hilum. The method of thoracoscopic lobectomy began with ligation of the lobe vein, followed by either the bronchus or artery. For
simultaneous resection, the procedure started at the side whose pulmonary function loss were less after resection. Then the patient position was changed to perform the relatively complicated lobectomy. For staged resection, tumors in advanced stages were removed first. The time of the second operation was based on each patient's recovery condition and high-resolution CT after surgery. All cases were followed by systemic mediastinal lymph node dissection. Pathological staging was based on the most advanced stage of all lesions according to the 8th edition of the TNM staging system for lung cancer. An intravenous analgesia pump and postoperative ward analgesia program, and preventive antiemetic were routinely applied in the post anesthesia recovery room.

**Follow-up**

Follow-up data were obtained from telephone calls, or direct outpatient examinations. Patients were recommended to repeat CT and pulmonary function test at the 1, 3, 6, 12 months during the first 2 years after operations. During each follow up session, information regarding patients' survival, cancer recurrence or metastasis, and cause of death was collected. In present study, the endpoint of follow-up was March 2019. Mortality was defined as 30-day mortality or in-hospital mortality. Overall survival (OS) and disease-free survival (DFS) rates were defined, respectively, as the time from the first operation to the last follow-up, or as the time from the first operation to death or recurrence.

**Statistical analysis**

Categorical variables were expressed as numbers and percentages. Continuous variables were expressed as the mean value ± standard deviation. Student’s t-test or the Wilcoxon rank-sum test was used to compare continuous variables. Univariate analyses were used to identify the clinical factors that predict postoperative complications. A multivariate analysis was performed by a logistic regression analysis using SPSS Statistics 21 (IBM, United States). Pearson Chi-Square, Fisher's exact tests, or Continuity Correction was used to compare categorical variables. OS and DFS were estimated by the Kaplan-Meier estimation using the log-rank test. All statistical tests were two-sided, with a significance level set at 0.05, utilizing the Statistical Package for the Social Sciences (SPSS) software (version 23, IBM, Armonk, NY, USA).

**Results**

**Patients characteristics**

Characteristics of the patients are summarized in Table 1. The mean age was 55.93±9.44 years in the simultaneous
### Table 1 Overall characteristics of the patients who underwent bilateral VATS lobectomy for synchronous bilateral multiple primary lung cancer

| Characteristics                              | Simultaneous bilateral VATS lobectomy (n=41) | Staged bilateral VATS lobectomy (n=66) | P value |
|----------------------------------------------|---------------------------------------------|---------------------------------------|---------|
| Age, years                                   | 55.93±9.44 [33–70]                          | 59.30±7.91 [39–76]                   | 0.49    |
| Gender                                       |                                             |                                       | 0.16    |
| Male                                         | 16 (39%)                                    | 35 (53%)                              |         |
| Female                                       | 25 (61%)                                    | 31 (47%)                              |         |
| Smoking                                      |                                             |                                       | 0.09    |
| Never                                        | 37 (90%)                                    | 51 (77%)                              |         |
| Current                                      | 4 (10%)                                     | 15 (23%)                              |         |
| Number of tumors                             |                                             |                                       | 0.71    |
| 2                                            | 24 (59%)                                    | 41 (62%)                              |         |
| ≥3                                           | 17 (41%)                                    | 25 (38%)                              |         |
| Size of the largest tumor, mm                |                                             |                                       | 0.42    |
| ≤3                                            | 25 (61%)                                    | 35 (53%)                              |         |
| >3                                            | 16 (39%)                                    | 31 (47%)                              |         |
| CT features of the bilateral largest tumor   |                                             |                                       | 0.01    |
| Bilateral pure solid                         | 23 (56%)                                    | 14 (21%)                              |         |
| Non-bilateral pure solid                    | 18 (44%)                                    | 52 (79%)                              |         |
| Preoperative comorbidities                   |                                             |                                       | 0.50    |
| No                                           | 32 (78%)                                    | 55 (83%)                              |         |
| Hypertension                                 | 4 (10%)                                     | 4 (6%)                                |         |
| Diabetes mellitus                            | 3 (7%)                                      | 3 (5%)                                |         |
| Cardiopathy                                  | 2 (5%)                                      | 4 (6%)                                |         |
| Pulmonary function at first operation        |                                             |                                       | 0.12    |
| FVC (mean, L)                                | 3.12±0.76                                   | 2.87±0.84                             |         |
| FEV₁ (mean, L)                               | 2.57±0.48                                   | 2.46±0.50                             | 0.25    |
| FEV₁ %                                       | 87.95±9.98                                  | 85.60±8.07                            | 0.18    |
| Surgery type                                 |                                             |                                       | 0.94    |
| RUL + LUL                                    | 11 (27%)                                    | 15 (23%)                              |         |
| RUL + LUL + RS6                              | 1 (2%)                                      | 2 (3%)                                |         |
| RUL + LUL + LS7/8                            | 1 (2%)                                      | 4 (6%)                                |         |
| RUL + LLL                                    | 7 (18%)                                     | 9 (14%)                               |         |
| RML + LUL                                    | 13 (32%)                                    | 18 (27%)                              |         |
| RML + LLL                                    | 2 (5%)                                      | 5 (7%)                                |         |
| RML + LLL + LS4/5                            | 1 (2%)                                      | 0 (0%)                                |         |
| RLL + LUL                                    | 2 (5%)                                      | 4 (6%)                                |         |
| RLL + LLL                                    | 2 (5%)                                      | 6 (9%)                                |         |
| RLL + LLL + LS3                              | 1 (2%)                                      | 3 (5%)                                |         |

VATS, video-assisted thoracic surgery; FVC, forced vital capacity; FEV₁, the forced expiratory volume in 1 s; FEV₁ %, percent of the predicted FEV₁; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; RS6, the right superior segment; LS4/5, left lingular segment; LS7/8, left anterior medial basal segment; LS3, left anterior segment.
group and 59.30±7.91 years in the staged group (P=0.49). There was no significant difference between the two groups in terms of gender, smoking status, tumor numbers, preoperative comorbidities, pulmonary function at first operation, and surgery type. However, the distributions of CT features of the bilateral largest tumor were different between the two groups (P=0.01). The time of the second operation was based on each patient’s recovery condition and high-resolution CT after surgery. In our study, the median interval between the first and second lobectomies was 7 months, with a range of 2 to 22 months.

**Pathologic characteristics**

As shown in Table 2, there were no significant differences in histology between the simultaneous group and the staged group. In the simultaneous group, the histologic classification was identical in 29 of 41 (71%) patients (24 patients with Ad-Ad and 5 patients with Sq-Sq). In patients with different histologic types, Ad-Sq was the most common finding (n=6). Postoperative TNM staging was classified according to the most advanced lung cancer in bilaterally resected tumors. In the simultaneous group, 23 patients were staged at IA, 8 at IB, 2 at IIA, 5 at IIB, and 3 at IIIA. In the staged group, 28 patients were staged at IA, 15 at IB, 6 at IIA, 12 at IIB, and 5 at IIIA.

| Characteristics               | Simultaneous bilateral lobectomy resection (n=41) | Staged bilateral lobectomy resection (n=66) | P value |
|-------------------------------|--------------------------------------------------|--------------------------------------------|---------|
| Pathology                     |                                                   |                                            |         |
| Identical histology           | 29 (71%)                                         | 41 (62%)                                   | 0.36    |
| Ad-Ad                         | 24 (57%)                                         | 33 (50%)                                   |         |
| Sq-Sq                         | 5 (12%)                                          | 8 (12%)                                    |         |
| Different histology           | 12 (29%)                                         | 25 (37%)                                   |         |
| Ad-Sq                         | 6 (14.5%)                                        | 10 (15%)                                   |         |
| Others                        | 6 (14.5%)                                        | 15 (22%)                                   |         |
| Pathologic stage              |                                                   |                                            | 0.74    |
| IA                            | 23 (56%)                                         | 28 (29%)                                   |         |
| IB                            | 8 (20%)                                          | 15 (35%)                                   |         |
| IIA                           | 2 (5%)                                           | 6 (11%)                                    |         |
| IIB                           | 5 (12%)                                          | 12 (16%)                                   |         |
| IIIA                          | 3 (7%)                                           | 5 (9%)                                     |         |
| Pathology T stage             |                                                   |                                            | 0.55    |
| T1                            | 25 (61%)                                         | 35 (53%)                                   |         |
| T2                            | 15 (37%)                                         | 26 (39%)                                   |         |
| T3                            | 1 (2%)                                           | 5 (8%)                                     |         |
| Pathology N stage             |                                                   |                                            | 0.93    |
| N0                            | 34 (83%)                                         | 53 (80%)                                   |         |
| N1                            | 4 (10%)                                          | 8 (12%)                                    |         |
| N2                            | 3 (7%)                                           | 5 (8%)                                     |         |

Ad, adenocarcinoma; Sq, squamous carcinoma.
in the staged group (P<0.001). The total cost was significantly less with simultaneous resection than with staged resection (10,854.6±1,998.8 USD vs. 16,241.4±2,972.8 USD, P<0.001). The total hospital stay time was less for the simultaneous resection group than for the staged resection group (12.8±9.1 vs. 16.5±4.3 d, P=0.005). There was no difference in the intraoperative total blood loss between the two groups (176.1±123.4 vs. 182.4±131.1 mL, P=0.805).

Complications and 30-day mortality
There were no perioperative deaths in the simultaneous resection group, but one patient who underwent staged resection died due to pulmonary embolism on the fourth day after surgery. Postoperative complications did not differ significantly between the two groups (11 in the simultaneous group vs. 16 in the staged group, P=0.850). Complications included pulmonary embolus (no patients in the simultaneous group vs. 1 in the staged group), prolonged air leakage over 5 days (3 patients vs. 5 patients), arrhythmia (2 patients vs. 3 patients), atelectasis (1 patient vs. 2 patients), pulmonary infection (2 patients vs. 3 patients), and postoperative bleeding (3 patients vs. 2 patients).

Based on univariate analysis, the factors related to increased postoperative morbidities after simultaneous bilateral VATS lobectomy were preoperative comorbidities (P=0.009), FEV₁ less than 2 L (P=0.001), FEV₁% less than 80% (P=0.036), and the number of segments resected greater than or equal to 9 (P=0.014). Being male (P=0.045) and the number of segments resected greater than or equal to 9 (P=0.004) had a trend toward significance, leading to complications after staged bilateral VATS lobectomy (Table 4).

Survival for simultaneous resection and staged resection
The median follow-up time was 41 months. In our study, the median interval between the first and second lobectomies was 7 months, with a range of 2 to 22 months. During follow-up, 7 patients had the contralateral tumors progressing after the first surgery in the staged resection group, of which 2 patients had distant metastasis detected at 8 months and 11 months by PET-CT postoperatively. Recurrence was observed in 9 patients in the simultaneous resection group, and 25 patients in the staged resection group. The DFS of patients with simultaneous resection was 67.7% at 5 years, but for patients with staged resection was 45.9% at 5 years. There was significant difference in DFS between the two groups (Figure 2A, P=0.039). The 5-year survival rate was 59.7% in the simultaneous group, whereas the rate was 39.4% in the staged resection group. There was no significant difference in OS between the simultaneous resection and staged resection groups in this cohort study (Figure 2B, P=0.087). However, subgroup analysis revealed...

| Parameter                          | Simultaneous bilateral lobectomy resection (n=41) | Staged bilateral lobectomy resection (n=66) | P value |
|------------------------------------|-------------------------------------------------|--------------------------------------------|---------|
| Total operative time, mean ± SD, min | 196.8±53.3                                      | 252.7±43.1                                 | <0.001  |
| Total hospital stays, mean ± SD, d | 12.8±9.1                                         | 16.5±4.3                                   | 0.005   |
| Total cost, mean ± SD, $           | 10,854.6±1,998.8                                 | 16,241.4±2,972.8                          | <0.001  |
| Total blood loss, mean ± SD, mL    | 176.1±123.4                                      | 182.4±131.1                               | 0.805   |
| 30-day mortality, n (%)            | 0 (0.0)                                          | 1 (1.5)                                   |         |
| Complications, n (%)               | 11 (26.8)                                        | 16 (24.2)                                 | 0.850   |
| Prolong air leak >7 d              | 3 (7.3)                                          | 5 (7.6)                                   |         |
| Atrial fibrillation                | 2 (4.9)                                          | 3 (4.5)                                   |         |
| Pulmonary infection                | 2 (4.9)                                          | 3 (4.5)                                   |         |
| Postoperative bleeding             | 1 (2.4)                                          | 2 (3.0)                                   |         |
| Pulmonary embolus                  | 0 (0)                                            | 1 (1.5)                                   |         |
| Atelectasis                        | 3 (7.3)                                          | 2 (3.0)                                   |         |
that simultaneous resection had a significantly better OS than staged resection when bilateral tumors were pure solid \((\text{Figure 2C}, \ P=0.024)\), or when the biggest tumor size was more than 3 cm \((\text{Figure 2D}, \ P=0.009)\). Multivariable regression analysis revealed that age \(\geq 60\) \((P=0.025)\), lymph node involvement \((P=0.011)\), tumor size >3 cm \((P=0.006)\), and bilateral pure solid lesions \((P=0.007)\) were associated with poor prognosis after bilateral VATS lobectomy \((\text{Table 5})\).

**Discussion**

According to the diagnostic criteria of Martini and Melamed, the incidence of MPLC ranges from 0.2% to 20% as reported in previous studies \((16,17)\). The synchronous type account for 60% of MPLC, while there are fewer of the metachronous type \((6,18)\). A remarkable proportion of these SPLC were pure solid, larger, centrally located lesions that were often unresectable by sublobectomy. Therefore, lobectomy was required in these scenarios. However, the feasibility and surgical timing of bilateral lobectomy has been controversial in the management of SPLC. In this study, we retrospectively analyzed 107 patients who received bilateral lobectomy in our hospital.

Staged bilateral resection is a widely accepted procedure, especially for bilateral lobectomy. This is because staged resection has been considered to be less invasive and has low morbidity and mortality. Morbidity occurred in 24.2% of our patients with staged bilateral VATS lobectomy, similar to the 28% reported by Shah and colleagues, although their study included both bilateral and unilateral thoracoscopic approaches \((9)\). Our result is also better than the 38% reported by Hattori _et al._ for staged bilateral lobectomy with thoracotomy \((19)\). The use of thoracoscopy may be one of the explanations for the good results in our study. In addition, as one of the largest centers for thoracoscopic surgery, our hospital has accumulated rich experience in thoracoscopic lobectomy.

However, the second operation was usually performed about 2 to 4 months after the first one, even if postoperative recovery went smoothly. If not, the treatment term was prolonged, which may have led to considerable physical strain and increased the risk of cancer progression. Ramer-Quinn also found that the release of inflammatory cytokines and the destruction of the immune system may increase the risk of secondary surgery \((20)\). During follow-up, there were two patients that distant metastasis was detected at 8 and 11 months by PET-CT postoperatively. Chemotherapy and stereotactic body radiotherapy were recommended instead of a second stage lobectomy. Therefore, staged resection also had limitations, especially for more malignant tumors.

Simultaneous bilateral thoracotomy was not routinely preferred, mainly because of the potential for a greater one-time loss of pulmonary function, increased physical trauma, and higher mortality and morbidity. However, simultaneous bilateral resection should be recommended from an oncological viewpoint, since it is considered an effective strategy for preventing cancer progression. Simultaneous resection also reduces the risk and cost of secondary surgery. Recently, thoracoscopic surgery has been widely accepted as a less invasive technique for the treatment of non-small cell lung cancer (NSCLC), especially with regard to the effect

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**Table 4** Results of a univariate analysis for predictors of postoperative complications after simultaneous and staged bilateral VATS lobectomy

| Characteristics | Simultaneous bilateral lobectomy resection | Staged bilateral lobectomy resection |
|-----------------|------------------------------------------|-------------------------------------|
|                 | Complications (n=11) | Non-complications (n=30) | P value | Complications (n=16) | Non-complications (n=50) | P value |
| Gender (male vs. female) | 5/6 | 11/19 | 0.881 | 5/11 | 30/20 | 0.045 |
| Age (<60 vs. \(\geq 60\) years) | 8/3 | 17/13 | 0.575 | 6/10 | 23/27 | 0.551 |
| Smoking (yes vs. no) | 2/9 | 2/28 | 0.289 | 2/14 | 13/37 | 0.436 |
| Preoperative comorbidities (yes vs. no) | 6/5 | 3/27 | 0.009 | 4/12 | 7/43 | 0.521 |
| FEV1 (<2 vs. \(\geq 2\) L) | 6/5 | 1/29 | 0.001 | 2/14 | 11/39 | 0.638 |
| FEV1% (<80% vs. \(\geq 80\)% | 5/6 | 3/27 | 0.036 | 4/12 | 10/40 | 0.941 |
| Number of segments (\(\geq 9\) vs. <9) | 5/6 | 2/28 | 0.014 | 9/7 | 8/42 | 0.004 |

VATS, video-assisted thoracic surgery; FEV1, the forced expiratory volume in 1 s; FEV1%, percent of the predicted FEV1.
on postoperative respiratory function. Subsequently, a series of studies demonstrated the safety and feasibility of bilateral thoracoscopic resection (6,12,21,22). However, most of them were sub-lobectomy, and bilateral lobectomy has only been reported in a small number of cases. In 2007, Mun et al. reported on 19 patients who underwent single-stage bilateral resection, including 14 bilateral VATS resections. The conclusion was that simultaneous bilateral resection of synchronous bilateral multiple lung cancer (SBMLC) achieved satisfactory results in select patients (10). In 2017, Iida et al. reported on successful single-stage VATS right upper lobectomy and left lower lobectomy for SBMLC.

They thought that bilateral thoracoscopic lobectomy for SBMLC has advantages for select patients (11). In our study, there were 41 patients who underwent simultaneous bilateral VATS lobectomy. There were no deaths in the perioperative period, and only 9 patients had postoperative complications. There was no significant difference in postoperative complications compared with previous reports of simultaneous bilateral sub-lobectomy (6,10,23).

In addition to reducing the risk of tumor progression caused by staging surgery, simultaneous surgery had other advantages. From our results, we found that simultaneous bilateral VATS lobectomy requires a mean of 3 hours to
Table 5 Univariate and multivariate Cox regression analysis of overall survival after bilateral VATS lobectomy for SPLC

| Characteristics                                      | Univariable analysis |        |        | Multivariate analysis |        |        |
|------------------------------------------------------|----------------------|--------|--------|-----------------------|--------|--------|
|                                                      | HR                   | 95% CI | P value | HR                    | 95% CI | P value |
| Sex (male vs. female)                                | 0.630                | 0.370–1.073 | 0.890   | 2.015                | 1.094–3.710 | 0.025   |
| Age (≥60 vs. <60 years)                              | 2.620                | 1.471–4.666 | 0.001   | 2.015                | 1.094–3.710 | 0.025   |
| Smoking (yes vs. no)                                 | 2.234                | 1.148–4.346 | 0.018   | 1.292                | 0.601–2.778 | 0.512   |
| Preoperative comorbidities (yes vs. no)              | 1.618                | 0.772–3.388 | 0.202   |                      |        |        |
| Number of segments resected (≥9 vs. <9)              | 1.997                | 1.106–3.606 | 0.022   | 1.882                | 0.931–3.803 | 0.078   |
| N stage (N1-2 vs. N0)                                | 4.716                | 2.399–9.270 | <0.001  | 4.092                | 1.824–9.180 | 0.011   |
| Bilateral CT features (solid vs. non-solid)          | 2.144                | 1.203–3.822 | 0.010   | 2.462                | 1.260–4.332 | 0.007   |
| Pathology (identical vs. different)                  | 0.841                | 0.484–1.462 | 0.542   |                      |        |        |
| Surgery time (simultaneous vs. staged)               | 1.635                | 0.920–2.903 | 0.094   |                      |        |        |
| Size of the largest tumor (>3 vs. ≤3 cm)             | 2.779                | 1.577–4.896 | <0.001  | 2.376                | 1.277–4.418 | 0.006   |
| Number of tumors (≥3 vs. <2)                         | 1.875                | 1.068–3.291 | 0.029   | 1.002                | 0.481–2.086 | 0.996   |

VATS, video-assisted thoracic surgery; SPLC, synchronous bilateral multiple primary lung cancer.

Complete surgery, whereas a staged operation requires an additional 1 hour of total operative time to complete surgery. Meanwhile, simultaneous bilateral thoroscopic resection could decrease the length of the hospital stay and could benefit patients by reducing the surgical pressure of the staged or open operation. The shorter postoperative chest tube duration could also reduce postoperative pain, which may improve the postoperative quality of life for patients. In addition, simultaneous resection could significantly reduce the cost of treatment and result in more rapid treatment of bilateral disease, which may be particularly beneficial for poorer families, if permitted by the preoperative conditions of the patients.

For postoperative complications, univariate analysis showed that a preoperative FEV1 of less than 2 L and a FEV1% lower than 80% trended toward significance, leading to complications for simultaneous resection. A previous study reported that the recommended value of FEV1 for safe resection was more than 2 L for pneumonectomy and more than 1.5 L for lobectomy (24). Later guidelines added that for lobectomy and pneumonectomy, FEV1 and DLCO should be more than 80% of the predicted value (25). Therefore, for those patients with FEV1 less than 80% or FEV1 less than 2 L, simultaneous bilateral lobectomy was not recommended. In our study, exercise tolerance or lung volumes. Therefore, the data for DLCO were limited. In addition, it was extremely important to estimate the number of pulmonary segments that can be safely removed. This could also be used to predict postoperative pulmonary function as described by Zeiher (15). Our results showed that the number of pulmonary segments resected greater than or equal to 9 was a significant predictor of the risk of complications for simultaneous resection and staged resection. Right lower lobectomy with left lobectomy was the least common surgical type in the simultaneous resection. The right lower lobe is the largest lobe and accounts for about 25% of total pulmonary function. Therefore, right lower lobectomy with left lobectomy causes a considerable decline in pulmonary function. Simultaneous bilateral lobectomy should be considered carefully for those patients.

There was no significant difference in OS between the simultaneous resection and staged resection groups. However, a significant difference in DFS was found between the two groups. We performed a subgroup analysis based on the size and morphology of tumors. Our study revealed that the prognosis for simultaneous bilateral lobectomy was better than for staged bilateral resection for those patients with a tumor size more than 3 cm and bilateral pure solid lesions. A possible reason is that lesions of increased size and bilateral pure solid could have an increased probability of micro-metastases. Simultaneous resection could
remove tumors in time to prevent tumor progression. So, after comprehensive assessment of each patient’s physical condition, simultaneous bilateral lobectomy was recommended for those patients.

Inevitably, this study has some primary limitations. Frist, it is a retrospective study which has selection bias. The adjuvant chemotherapy data were not collected. In this pilot study stage, the selection of simultaneous surgeries was mostly relied on surgeons’ judgement. In addition, bilateral thoracoscopic lobectomy is more difficult than bilateral thoracoscopic sub-lobectomy, requiring more experience surgeon to successfully complete it. Last, the patients enrolled in this study is small size. Therefore, prospective study with a large number of patients is needed to further validate our results.

Conclusions

Simultaneous or staged bilateral thoracoscopic lobectomy could be a feasible option in SPLC with careful perioperative management and appropriate patient selection. Simultaneous resection has significant advantages compared to staged resection, including better DFS and reductions in cost, total operative time and hospital stays. At the same time, simultaneous resection had a significantly better OS than staged resection for those patients with bilateral pure solid nodules or tumor size >3 cm. Simultaneous bilateral VATS lobectomy was considered as an alternative method for the treatment of SPLC.

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Conclusions

Simultaneous or staged bilateral thoracoscopic lobectomy could be a feasible option in SPLC with careful perioperative management and appropriate patient selection. Simultaneous resection has significant advantages compared to staged resection, including better DFS and reductions in cost, total operative time and hospital stays. At the same time, simultaneous resection had a significantly better OS than staged resection for those patients with bilateral pure solid nodules or tumor size >3 cm. Simultaneous bilateral VATS lobectomy was considered as an alternative method for the treatment of SPLC.

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