Feasibility of double sleeve lobectomy after neoadjuvant chemotherapy in patients with non-small-cell lung cancer

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Abstract

OBJECTIVES: This study intends to appraise the feasibility of double sleeve lobectomy after neoadjuvant chemotherapy in central non-small-cell lung cancer with bronchovascular aggression.

METHODS: This retrospective study included non-small-cell lung cancer patients who received double sleeve lobectomy from January 2014 to June 2020. Patients were divided into 2 groups: the neoadjuvant chemotherapy group and the non-neoadjuvant chemotherapy group. Demographic data and perioperative outcomes were compared between these 2 groups.

The first three authors contributed equally to this work.
**INTRODUCTION**

Lung cancer is the second most common malignancy worldwide, with non-small-cell lung cancer (NSCLC) accounting for over 85% of all cases [1, 2]. Surgical treatment is currently the primary treatment modality with proven curative potential for resectable NSCLC [3, 4]. Centrally located NSCLC harbours a more aggressive behaviour and tends to invade the main bronchus and pulmonary artery, the surgical treatment for which is therefore a challenge. For central NSCLC with bronchovascular invasion, pneumonectomy has been the standard therapeutic strategy for years. Over the past decades, with the advancement of the surgical techniques and the increase of surgeons’ experience, double sleeve (vascular and bronchial) lobectomy, which preserves more pulmonary parenchyma and does not sacrifice the oncological radicality, has been a reasonable alternative to pneumonectomy [5, 6]. However, due to technical difficulty, double sleeve lobectomy is a challenging procedure even in hands of experienced surgeons.

In addition, most cases of central NSCLC invading the pulmonary artery and bronchus simultaneously are locally advanced tumours at the time of diagnosis. For this population, neoadjuvant chemotherapy, which can reduce tumour staging and improve surgical prognosis, plays an important role in treatment [7, 8]. Nevertheless, vascular fragility and tissue adhesions caused by neoadjuvant chemotherapy may influence the healing of reconstructed structures and potentially increase the perioperative complication and morbidity risk after double sleeve lobectomy [9]. As a result, there is an increased concern about the feasibility of performing this challenging and complex double sleeve lobectomy after oncological treatment.

Therefore, this study intends to explore the feasibility of double sleeve lobectomy in patients receiving neoadjuvant chemotherapy by comparing the perioperative outcomes with those without neoadjuvant chemotherapy.

**RESULTS:** Of the 110 patients who received double sleeve lobectomy during this period, 35 patients (31.8%) received neoadjuvant chemotherapy. Compared with the non-neoadjuvant chemotherapy group, patients who received neoadjuvant chemotherapy were associated with younger age \( (p = 0.026) \), smaller pathologic tumour size \( (p = 0.005) \), higher forced expiratory volume in 1 s \( (p = 0.007) \), higher forced expiratory volume in 1 s of predicted value \( (p = 0.005) \) and higher clinical stage \( (p < 0.001) \). In the neoadjuvant chemotherapy group, 18 patients (51.4%) attained a partial response and 17 patients (48.6%) achieved stable disease. The postoperative hospital stays \( (p = 0.042) \) and chest tube drainage duration \( (p = 0.030) \) were longer in the neoadjuvant chemotherapy group and other perioperative performances were similar between these 2 groups. No statistically significant difference was reported in postoperative complications and mortality between these 2 groups.

**CONCLUSIONS:** The intraoperative performance and postoperative outcomes of double sleeve lobectomy following neoadjuvant chemotherapy were similar to direct surgery, indicating that double sleeve lobectomy after neoadjuvant chemotherapy is feasible and safe in central lung cancer involving both the pulmonary artery and bronchus.

**Keywords:** Neoadjuvant chemotherapy • Double sleeve lobectomy • Non-small-cell lung cancer

**ABBREVIATIONS**

| Abbreviation | Description                  |
|--------------|------------------------------|
| BMI          | Body mass index              |
| CI           | Confidence interval          |
| FEV1         | Forced expiratory volume in 1 s |
| IQR          | Interquartile range          |
| NSCLC        | Non-small-cell lung cancer   |
| OR           | Odds ratio                   |

**PATIENTS AND METHODS**

**Ethical statement**

Our Institutional Review Board approved this retrospective study protocol (no: L20-333) and waived the requirement for informed consent of all patients.

**Data availability statement**

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

**Study population**

This study included consecutive central NSCLC patients who underwent double sleeve lobectomy from January 2014 to June 2020. Patients with incomplete information on clinical characteristics and treatment, tumours other than NSCLC and carinal reconstruction were excluded. At our institution, patients who received double sleeve lobectomy must meet the following criteria: (i) histologically confirmed lung cancer; (ii) tumours simultaneously involved the pulmonary artery and bronchus validated by computed tomography or bronchoscopy; (iii) no distant metastasis was observed; (iv) patients had normal liver, kidney and cardiovascular function; (v) preoperative forced expiratory volume in 1 s \( (FEV1) >1.5 \) and there is no evidence of either undue dyspnoea on exertion or interstitial lung disease; and (vi) double sleeve lobectomy is expected to achieve a radical resection after comprehensive evaluation of the surgeon. Patients who met the following criteria were eligible for neoadjuvant chemotherapy: (i) stage IIIA disease, such as T3 invading chest wall, T4 invading mediastinal structure, trachea or T1–3/N2 lesions, and (ii) patients can tolerate the side effects of chemotherapy drugs.

Relevant clinical data were manually extracted from patients medical and surgical records, including demographic variables and perioperative data. Charlson Comorbidity Index was used to evaluate preoperative comorbidities [10]. Postoperative complications were stratified by Clavien-Dindo classification [11]. Prolonged air leakage was defined as a persistent air leak for \( >5 \) days after surgery. Perioperative mortality was defined as death within 30 days of the operation.
Neoadjuvant chemotherapy

The neoadjuvant chemotherapy protocols were chosen based on international guidelines recommendations [12]. The regimens of neoadjuvant chemotherapy were based on platinum drugs but combined with a variable second drug (gemcitabine, paclitaxel, pemetrexed, docetaxel or vinorelbine). Four weeks after neoadjuvant chemotherapy, the patients were restaged with computed tomography or PET. The efficacy of neoadjuvant chemotherapy was reported by the response evaluation criteria in solid tumours [13].

Surgical techniques

In this study, all patients routinely had a multiple disciplinary team discussion before double sleeve lobectomy. Surgical techniques have been described in detail in our previous publications [14].

Statistical analysis

All statistical analyses were performed with SPSS 22.0 (SPSS Inc., Armonk, NY, USA). Continuous variables were described as mean and standard deviation or median and interquartile range (IQR), which were compared by the Student’s t-test or the Mann–Whitney U-test. The normality of continuous variables was assessed by Q–Q plots. Categorical variables were reported as frequencies (percentages), which were assessed with Fisher’s exact test or chi-squared test. Univariable and multivariable logistic regression analyses were performed to adjust the possible confounders. Multivariable logistic regression analyses were constructed using a forward selection (likelihood ratio) test, starting with all relevant clinicopathological variables and variables with P < 0.10 in univariable analyses. Statistical significance was reported at P < 0.05.

RESULTS

Clinicopathological characteristics of patients

Finally, 110 central NSCLC patients who received double sleeve lobectomy were enrolled in this study (Fig. 1), of them 35 patients (31.8%) received neoadjuvant chemotherapy. The 2 groups were coincident in time. There were 99 men (90.0%) and 11 women (10.0%) in the entire cohort, with a median age of 63 years (range, 36–79 years) (Table 1). The percentage of current or former smokers was 37.3 and the stage IIIB was both the most common clinical and pathological stage. Patients received neoadjuvant chemotherapy were associated with better pulmonary functions [higher FEV1 (2.42 ± 0.52 vs 2.16 ± 0.42, P = 0.007)], higher FEV1 of predicted value [87.90 (IQR, 81.20–95.30) vs 78.80 (IQR, 68.90–89.10), P = 0.005] and higher clinical stage (stage IIIB: 100% vs 57.3%, P < 0.001). In contrast, older age [64 (IQR, 59–68) vs 61 (IQR, 53–65) years, P = 0.026] and larger pathological tumour size [4.0 (IQR, 3.0–5.0) vs 3.2 (IQR, 2.2–4.5) cm, P = 0.005] were found in the non-neoadjuvant chemotherapy group. Subgroup analyses of tumour location in patients receiving neoadjuvant chemotherapy are presented in Supplementary Material, Table S3. Thirty patients (85.7%) had tumours on the left side, and 31 patients (88.6%) had tumours on the upper lobe. Patients with tumours on the left side were associated with older age (61.17 ± 7.21 vs 50.80 ± 8.44 years, P = 0.048) and lower FEV1 (2.34 ± 0.45 vs 2.88 ± 0.701, P = 0.029). There was no statistically significant difference in clinicopathological characteristics and perioperative outcomes between patients with tumours on the upper lobe and the middle/lower lobe.

Clinical efficacy of neoadjuvant chemotherapy

A total of 29 patients (82.9%) underwent 2 cycles of neoadjuvant chemotherapy, 4 patients (11.4%) underwent 3 cycles, 1 patient (2.9%) underwent 4 cycles and 1 patient (2.9%) underwent 5 cycles (Supplementary Material, Table S1). No significant difference was found in the postoperative complications (pneumonia, P = 0.070; prolonged air leak, P = 0.805; cardiac arrhythmia, P = 0.869) among different chemotherapy schemes (Supplementary Material, Table S2). There were 18 patients (51.4%) who attained partial response and 17 patients (48.6%) who achieved stable disease according to the response evaluation criteria in solid tumour criterion (Fig. 2). The mean time from the end of neoadjuvant chemotherapy to double sleeve lobectomy was 34.6 ± 2.8 days. Restaging was according to the eighth edition of the American Joint Committee on Cancer (AJCC) staging system after double sleeve lobectomy. The final pathological stage showed a downstage in 19 (54.3%) patients (11 downstaged to N0 and 8 downstaged to N1).

Perioperative outcomes

Perioperative outcome data are summarized in Table 2. Of 110 included patients, 59 patients (53.6%) received video-assisted thoracoscopic surgery procedure, while 51 patients (46.4%) received thoracotomy procedures. No patients required conversions to thoracotomy. The operation time [221 (IQR, 191–275) vs 235 (IQR, 208–290) min, P = 0.167], the intraoperative blood loss [221.53 ± 297.83 vs 192.86 ± 178.35 ml, P = 0.600], the intraoperative transfusion (4.0% vs 8.6%, P = 0.325) and the perioperative transfusion (21.3% vs 29.4%, P = 0.359) had no significant difference between the neoadjuvant chemotherapy and neoadjuvant chemotherapy groups. No statistically significant difference was reported in the number of resected lymph nodes.
Table 1: Patient and cancer characteristics between patients with and without neoadjuvant chemotherapy

| Variable                              | All patients (n = 110) | Non-neoadjuvant chemotherapy group (n = 75) | Neoadjuvant chemotherapy group (n = 35) | P-Value* |
|---------------------------------------|------------------------|---------------------------------------------|----------------------------------------|----------|
| Age, years, median (IQR)              | 63 (57.8–67.3)         | 64 (59–68)                                  | 61 (53–65)                             | **0.026**|
| Sex, n (%)                            | 99 (90.0)              | 70 (93.3)                                   | 29 (82.9)                              | 0.101    |
| BMI (kg/m²), n (%)                    | 70 (63.6)              | 46 (61.3)                                   | 24 (68.6)                              | 0.462    |
| Smoking history, n (%)                | 69 (62.7)              | 49 (65.3)                                   | 20 (57.1)                              | 0.408    |
| Pulmonary function                    |                        |                                             |                                        |          |
| FEV1 (l), mean ± SD                   | 2.24 ± 0.47            | 2.16 ± 0.42                                 | 2.42 ± 0.52                            | **0.007**|
| FEV1% (of predicted), median (IQR)   | 83.55 (70.70–91.10)    | 78.80 (68.90–89.10)                         | 87.90 (81.20–95.30)                    | **0.005**|
| CCI, n (%)                            |                        |                                             |                                        | 0.629    |
| 0                                     | 5 (4.5)                | 2 (2.7)                                     | 3 (8.6)                                |          |
| 1                                     | 24 (21.8)              | 17 (22.7)                                   | 7 (20.0)                               |          |
| 2                                     | 47 (42.7)              | 32 (42.7)                                   | 15 (42.9)                              |          |
| 3                                     | 26 (23.6)              | 17 (22.7)                                   | 9 (25.7)                               |          |
| 4                                     | 7 (6.4)                | 6 (8.0)                                     | 1 (2.9)                                |          |
| 5                                     | 1 (0.9)                | 1 (1.3)                                     | 0 (0)                                  |          |
| Squamous histology, n (%)             | 74 (67.3)              | 53 (70.7)                                   | 21 (60.0)                              | 0.267    |
| Tumour location, n (%)                |                        |                                             |                                        | 0.278    |
| Left upper lobe                       | 94 (85.5)              | 66 (88.0)                                   | 28 (80.0)                              |          |
| Left lower lobe                       | 4 (3.6)                | 2 (2.7)                                     | 2 (5.7)                                |          |
| Right upper lobe                      | 10 (9.1)               | 7 (9.3)                                     | 3 (8.6)                                |          |
| Right middle lobe                     | 1 (0.9)                | 0 (0)                                       | 1 (2.9)                                |          |
| Right lower lobe                      | 1 (0.9)                | 0 (0)                                       | 1 (2.9)                                |          |
| Pathologic tumour size (cm), median (IQR) | 3.8 (3.0–5.0)       | 4.0 (3.0–5.0)                               | 3.2 (2.2–4.5)                          | **0.005**|
| Clinical T stage, n (%)               |                        |                                             |                                        | 0.002    |
| 2a                                    | 60 (54.5)              | 35 (46.7)                                   | 7 (20.0)                               |          |
| 2b                                    | 23 (20.9)              | 20 (26.7)                                   | 12 (34.3)                              |          |
| 3                                     | 21 (19.1)              | 16 (21.3)                                   | 6 (17.1)                               |          |
| 4                                     | 6 (5.5)                | 4 (5.3)                                     | 10 (28.6)                              |          |
| Clinical stage, n (%)                 |                        |                                             |                                        | **<0.001**|
| 1B                                    | 16 (14.5)              | 11 (14.7)                                   | 0 (0)                                  |          |
| 1A                                    | 5 (4.5)                | 4 (5.3)                                     | 0 (0)                                  |          |
| 1B                                    | 23 (20.9)              | 17 (22.7)                                   | 0 (0)                                  |          |
| 1A                                    | 48 (43.6)              | 34 (45.3)                                   | 25 (71.4)                              |          |
| 1B                                    | 18 (16.4)              | 9 (12.0)                                    | 10 (28.6)                              |          |
| pT stage, n (%)                       |                        |                                             |                                        | 0.061    |
| 2a                                    | 67 (60.9)              | 41 (54.7)                                   | 26 (74.3)                              |          |
| 2b                                    | 20 (18.2)              | 16 (21.3)                                   | 4 (11.4)                               |          |
| 3                                     | 14 (12.7)              | 13 (17.3)                                   | 1 (2.9)                                |          |
| 4                                     | 9 (8.2)                | 5 (6.7)                                     | 4 (11.4)                               |          |
| pN stage, n (%)                       |                        |                                             |                                        | 0.615    |
| 0                                     | 45 (40.9)              | 30 (40.0)                                   | 15 (42.9)                              |          |
| 1                                     | 35 (31.8)              | 26 (34.7)                                   | 9 (25.7)                               |          |
| 2                                     | 30 (27.3)              | 19 (25.3)                                   | 11 (31.4)                              |          |
| Pathological stage, n (%)             |                        |                                             |                                        | 0.657    |
| 1B                                    | 24 (21.8)              | 16 (21.3)                                   | 8 (22.9)                               |          |
| 1A                                    | 7 (6.4)                | 4 (5.3)                                     | 3 (8.6)                                |          |
| 1B                                    | 36 (32.7)              | 26 (34.7)                                   | 10 (28.6)                              |          |
| 1A                                    | 40 (36.4)              | 28 (37.3)                                   | 12 (34.3)                              |          |
| 1B                                    | 3 (2.7)                | 1 (1.3)                                     | 2 (5.7)                                |          |

*P-value between patients with and without neoadjuvant chemotherapy. P < 0.05, indicating a significant difference.
BMI: body mass index; CCI: Charlson Comorbidity Index; FEV1: forced expiratory volume in 1 s; IQR: interquartile range; SD: standard deviation.
[12 (IQR, 9–16) vs 13 (IQR, 9–16), P = 0.602] and station of resected lymph nodes [6 (IQR, 5–7) vs 6 (IQR, 5–7), P = 0.327] between these 2 groups. The neoadjuvant chemotherapy group was associated with longer postoperative hospital stay [7 (IQR, 5–9) vs 6 (IQR, 5–7) days, P = 0.047] and chest tube drainage duration [6 (IQR, 5–8) vs 5 (IQR, 4–7) days, P = 0.030]. Other

**Table 2**: Perioperative outcomes comparisons between patients with and without neoadjuvant chemotherapy before double sleeve lobectomy

| Perioperative outcomes | All patients (n = 110) | Non-neoadjuvant chemotherapy group (n = 75) | Neoadjuvant chemotherapy group (n = 35) | P-Value* |
|------------------------|------------------------|---------------------------------------------|----------------------------------------|----------|
| Surgical approach, n (%) | 0.255                  |                                             |                                        |          |
| Thoracotomy             | 51 (46.4)              | 32 (42.7)                                   | 19 (54.3)                              |          |
| Thoracoscopy            | 59 (53.6)              | 43 (53.3)                                   | 16 (45.7)                              |          |
| Operation time (min), median (IQR) | 228.5 (195.8–278.8) | 221 (191–275)                               | 235 (208–290)                          | 0.167    |
| Blood loss (ml), mean ± SD | 212.4 ± 265.2 | 221.53 ± 297.83                             | 192.86 ± 178.35                        | 0.600    |
| Intraoperative transfusion, n (%) | 0.325                 | 6 (5.5)                                     | 3 (4.0)                                |          |
| Perioperative transfusion, n (%) | 0.359                 | 26 (23.9)                                   | 16 (21.3)                              |          |
| Lymph nodes, median (IQR) | 0.327                  | 6 (5–7)                                     | 6 (5–7)                                |          |
| Total stations          | 12 (9–16)              | 12 (9–16)                                   | 13 (9–16)                              | 0.602    |
| Total numbers           | 11 (11.0)              | 7 (9.3)                                     | 4 (11.4)                               | 0.733    |
| Intrapericardial dissection, n (%) | 0.172                 | 39 (35.5)                                   | 26 (34.7)                              |          |
| Flap use                | 29 (26.4)              | 21 (28.0)                                   | 8 (22.9)                               |          |
| Pleural                 | 6 (5.5)                | 3 (4.0)                                     | 3 (8.6)                                |          |
| Pneumonia               | 2 (1.8)                | 2 (2.7)                                     | 0 (0)                                  |          |
| Prolonged air leak      | 8 (7.3)                | 4 (5.3)                                     | 5 (14.3)                               | 0.111    |
| Cardiac arrhythmia      | 2 (1.8)                | 2 (2.7)                                     | 0 (0)                                  | 0.252    |
| Pulmonary embolism      | 1 (0.9)                | 1 (1.3)                                     | 0 (0)                                  | 1.000    |
| Chylothorax             | 0 (0)                  | 0 (0)                                       | 0 (0)                                  |          |
| Postoperative stay (days), median (IQR) | 0.042                 | 6 (5–8)                                     | 6 (5–7)                                |          |
| Drainage (days), median (IQR) | 0.030                | 5 (4–7)                                     | 6 (5–8)                                |          |
| 24 h drainage volume (ml), median (IQR) | 0.471                  | 300 (200–450)                               | 320 (200–450)                          |          |
| ICU stay (days), median (IQR) | 0.792                 | 1 (1–2)                                     | 1 (1–2)                                |          |
| Clavien–Dindo grades, n (%) | 0.792                  | 75 (68.2)                                   | 50 (66.7)                              |          |
| 0                      | 5 (4.5)                | 3 (4.0)                                     | 2 (5.7)                                |          |
| 1                      | 24 (21.8)              | 19 (25.3)                                   | 8 (22.9)                               |          |
| 3                      | 4 (3.6)                | 1 (1.3)                                     | 0 (0)                                  |          |
| 4                      | 2 (1.8)                | 2 (2.7)                                     | 0 (0)                                  |          |
| Complications, n (%)    | 27 (24.5)              | 17 (22.7)                                   | 10 (28.6)                              | 0.503    |
| Pneumonia               | 14 (12.7)              | 8 (10.7)                                    | 6 (17.1)                               | 0.342    |
| Prolonged air leak      | 9 (8.2)                | 4 (5.3)                                     | 5 (14.3)                               | 0.111    |
| Pulmonary embolism      | 2 (1.8)                | 2 (2.7)                                     | 0 (0)                                  | 1.000    |
| Mortality within 30 days, n (%) | 1.000                | 0 (0)                                       | 0 (0)                                  |          |
| Mortality within 90 days, n (%) | 1.000                | 1 (0.9)                                     | 0 (0)                                  | 0.000    |

*P-value between patients with and without neoadjuvant chemotherapy. P < 0.05, indicating a significant difference.

ICU: intensive care unit; IQR: interquartile range; SD: standard deviation.
perioperative outcomes, including flap use, 24 h drainage volume and intensive care unit stay, were similar in these 2 groups. The overall rate of complication was 24.5% (n = 27/110) (Table 2). The primary complication in both groups was pneumonia (12.7%), followed by prolonged air leakage 8.2%. The Clavien–Dindo classification was similar between these 2 groups (grade ≥3: 4% vs 0%, P = 0.792). Severe complications did not develop in the neoadjuvant chemotherapy group. In the non-neoadjuvant chemotherapy group, 2 patients (2.7%) presented with pulmonary embolism and received thrombolytic therapy, 1 of whom died of haemoptysis on postoperative day 47. In addition, 1 patient (1.3%) experienced chylothorax and underwent thoracic duct ligation. Body mass index (BMI) [odds ratio (OR) = 2.741, 95% confidence interval (CI): 1.082–6.940, P = 0.033] and tumour side (OR = 0.222, 95% CI: 0.061–0.804, P = 0.222) were shown to be associated with postoperative complications (Table 3). There was no statistically significant difference in mortality within 30/90 days between the 2 groups.

DISCUSSION

Double sleeve lobectomy is an effective treatment strategy for central NSCLC patients concurrently invading the pulmonary artery and bronchus. Recently, abundant evidence indicates that neoadjuvant chemotherapy is a beneficial choice for locally advanced NSCLC, which is increasingly administrated in central NSCLC with bronchovascular invasion [7, 15]. However, it will inevitably aggravate the adhesion in the thoracic cavity, which increases the difficulty of double sleeve lobectomy. Therefore, the feasibility of double sleeve lobectomy after neoadjuvant chemotherapy remains a clinical concern. Our results revealed that double sleeve lobectomy is feasible and safe for patients received neoadjuvant chemotherapy, avoiding terrible related complications and having similar perioperative outcomes compared to those without neoadjuvant chemotherapy.

The safety of sleeve lobectomy even in patients after neoadjuvant therapy has been proved by several studies [16, 17]. Gomez-Caro et al. [16] reported that the final pathological stage in the induction chemoradiotherapy group displayed a downstage with pN0 or pN1 in 21 (80%) patients. The clinical response rate was 51.4% to neoadjuvant chemotherapy of 35 patients in our study, and 19 (54.3%) of them had mediastinal downstaging (11 N0 and 8 N1). Theoretically, the difficulty of performing double sleeve lobectomy after neoadjuvant chemotherapy is greater than without neoadjuvant chemotherapy because of tissue adhesions and vascular fragility. However, there was no statistically significant difference regarding operative time and intraoperative blood loss between the 2 groups in our study (P = 0.167 and P = 0.600), and operative time and intraoperative blood loss were also similar with other studies [18, 19]. We speculated that it might be due to the higher proportion of patients in the neoadjuvant chemotherapy group who underwent thoracotomy, which reduced the operation time to some extent. With the accumulation of our experience in double sleeve lobectomy, we believe that adequate tissue separation along the pulmonary arteries, veins and bronchus is essential to reduce the intraoperative blood loss and difficulty of the surgery.

In our study, the rate of postoperative complications in our study was 28.6% (10/35) and 22.7% (17/75) in the neoadjuvant chemotherapy group and the non-neoadjuvant chemotherapy group, which was slightly higher than that reported by our previous study (4/21, 19%) [5]. This discrepancy may be related to excessive vascular fragility and intraoperative tissue adhesion after neoadjuvant chemotherapy. It is not conducive to tissue separation and contributes to more trauma during manipulation [9]. In the neoadjuvant chemotherapy group of our study, pneumonia was the most common complication (6/35, 17.1%), followed by

| Table 3: Logistic regression analysis for postoperative complication in the entire cohort |

| Factor considered               | Univariable OR (95% CI) | P-Value | Multivariable OR (95% CI) | P-Value |
|---------------------------------|-------------------------|---------|---------------------------|---------|
| Age                             | 0.960 (0.906–1.017)     | 0.168   | 2.741 (1.082–6.940)       | 0.033   |
| Sex (male/female)               | 1.520 (0.308–7.514)     | 0.607   |                           |         |
| BMI (normal/overweight)         | 2.361 (0.973–5.726)     | 0.057   |                           |         |
| Smoking (ever)                  | 0.797 (0.319–1.988)     | 0.626   |                           |         |
| FEV1                            | 1.846 (0.733–4.649)     | 0.193   |                           |         |
| Charlson Comorbidity Index >2   | 0.923 (0.358–2.381)     | 0.868   |                           |         |
| Neoadjuvant chemotherapy (yes)  | 1.365 (0.549–3.394)     | 0.504   |                           |         |
| Side (left)                     | 0.273 (0.080–0.933)     | 0.038   | 0.222 (0.061–0.804)       | 0.022   |
| Location (upper lobe)           | 0.633 (0.109–3.664)     | 0.610   |                           |         |
| Tumour size                     | 1.073 (0.843–1.368)     | 0.566   |                           |         |
| Clinical T stage                |                         |         |                           |         |
| 2a                              | Reference               |         |                           |         |
| 2b                              | 1.663 (0.559–4.944)     | 0.360   |                           |         |
| 3                               | 1.983 (0.608–6.470)     | 0.256   |                           |         |
| 4                               | 1.159 (0.261–5.148)     | 0.846   |                           |         |
| Clinical N stage                |                         |         |                           |         |
| 0                               | Reference               |         |                           |         |
| 1                               | 1.333 (0.361–4.918)     | 0.666   |                           |         |
| 2                               | 0.704 (0.233–2.133)     | 0.355   |                           |         |

BMI: body mass index; CI: confidence interval; FEV1: forced expiratory volume in 1 s; OR: odds ratio. 
P < 0.05, indicating a significant difference.
prolonged air leakage (5/35, 14.3%). This indicates that patients who received neoadjuvant chemotherapy can successfully undergo double sleeve lobectomy, but we should pay more attention to postoperative management, especially with regard to anti-infection, and nutrition.

Published literature has demonstrated that postoperative complication risk was found to be significantly associated with a low BMI [20, 21]. In our study, we have drawn the conclusion that overweight patients were more likely at an increased risk of developing postoperative complications compared with patients with normal BMI. The possible reasons for this might include the following 2 reasons. First, overweight patients had poor respiratory compliance and decreased lung volume. Second, the operation time of overweight patients is relatively longer, which may have an influence on postoperative complications [22]. Based on our experience, the most important factor in preventing these patients from developing postoperative complications is thorough and appropriate postoperative care starting on the day of surgery, including increased physical therapy, respiratory therapy and aggressive prophylactic anticoagulant drug therapy [23].

Besides, patients with tumour on the left were associated with a protective effect on postoperative complications according to our results (OR = 0.222, 95% CI: 0.061–0.804, P = 0.222). Our findings are consistent with those reported in other studies, which have shown that increased postoperative complications and mortality for patients with tumour on the right who receive surgery [24]. Several potential reasons could lead to the differences between right and left side NSCLC. First, the pulmonary artery, vein and main bronchus are arranged differently between the left and right lung and the anatomical structures of the right lung are more complex, which means more difficult to operate for patients with tumour on the right. Second, the right lung contributes more to overall lung function than the left lung. Therefore, surgery of the right lung may result in greater loss of alveolar volume and reduction of respiratory function. In general, patients with tumour on the right may require more intensive care due to the high risk of postoperative complications.

In addition, radiation is a very important option as induction therapy before surgery. Neoadjuvant radiation can improve overall survival by decreasing local tumour recurrences. Evidence suggests that neoadjuvant radiation is more likely to play a role in stage III disease, given the good local control in patients with stage I and II resected tumours [25]. However, in our early clinical practice, we found that neoadjuvant radiation alone has not been shown to improve resectability or survival and may further increase the risk of pulmonary and airway complications, which has been confirmed by other studies [26]. Therefore, neoadjuvant radiation is not routinely performed in our institution during the study period. In addition, 2 randomized trials have shown that neoadjuvant chemoradiotherapy did not improve OS compared with neoadjuvant chemotherapy alone, even when pathological complete remission rates were higher [27, 28].

Limitations

We acknowledge that our study has several limitations. First, there was inevitably included bias in data collection because of the retrospective and single-centre data of this study. The preference and experience of the surgeons might also contribute to the bias, and our present conclusions need to be further validated by prospective multicentre studies in the future. Second, our study population only included the Chinese, and therefore, our findings may not be generalizable to other populations. Further international research is required to confirm our results. Finally, the potential long-term prognosis of double sleeve lobectomy after neoadjuvant chemotherapy for patients is still unclear due to the relatively short follow-up time after surgery. Therefore, the influence of double sleeve lobectomy after neoadjuvant chemotherapy on the long-term prognosis remains to be further explored.

CONCLUSION

In conclusion, our current study suggests that double sleeve lobectomy after neoadjuvant chemotherapy is associated with similar perioperative performances with direct double sleeve lobectomy. Therefore, double sleeve lobectomy after neoadjuvant chemotherapy can be safely performed in central NSCLC simultaneously aggressing the pulmonary artery and bronchus.

SUPPLEMENTARY MATERIAL

Supplementary material is available at ICVTS online.

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Author contributions

Yi Bao: Conceptualization; Data curation; Formal analysis; Writing—original draft. Chao Jiang: Formal analysis; Writing—original draft. Zhiwei Wan: Data curation; Methodology; Writing—original draft. Yang Wang: Formal analysis; Investigation; Methodology. Yifan Zhong: Investigation; Methodology; Validation. Jiajun Deng: Methodology; Software; Supervision. Yunlang She: Supervision; Visualization. Lei Jiang: Methodology; Supervision; Validation; Visualization. Xuefei Hu: Methodology; Software. Yuming Zhu: Investigation; Visualization. Chang Chen: Funding acquisition; Validation; Writing—review & editing. Chang Chen: Funding acquisition; Resources; Writing—review & editing.

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