Pivotal role of video-assisted thoracoscopic surgery in improving survival outcome of stage I non-small cell lung cancer in day surgery patients

Lisha Jiang1 | Tiantian Lei1 | Kun Zhou2 | Hongsheng Ma1 | Guowei Che2

1Day Surgery Center, Sichuan University West China Hospital, Chengdu, China
2Department of Thoracic Surgery, Sichuan University West China Hospital, Chengdu, China

Correspondence
Guowei Che, Department of Thoracic Surgery, Sichuan University West China Hospital, Chengdu 610041, China.
Email: cheguowei_hx@aliyun.com

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INTRODUCTION

Lung cancer is the leading cause of cancer-related death worldwide, and also has high morbidity rates.1 Due to growing health awareness, the medical examination is universal. The implementation of lung cancer screening for high-risk patients and low dose chest computed tomography (LDCT) diagnosis of lung cancer is increasing globally, especially for non-small cell lung cancer (NSCLC), which accounts for approximately 85% of all types of lung cancer.4 It should be noted that because SARS-CoV-2 associated infectious disease occurred at the end of 2019, it was declared a global health emergency and declared the COVID-19 epidemic globally on February 12, 2020.5 Meanwhile, thoracic computed tomography (CT) has been widely used during the pandemic to facilitate COVID-19 diagnosis, prevention, and control. Hence, many pulmonary nodules are detected by CT scan, including solid and subsolid nodules, according to...
the density. The subsolid nodule has two subgroups: pure ground-glass (pGGNs) and mixed ground-glass nodules (mGGNs). Some studies have revealed that subsolid nodules are correlated with adenocarcinoma. Despite fewer than 5% of all pulmonary nodules turning out to be lung cancer, it is still a significant number based on our population. Luckily, most of these patients experience localized disease and are categorized as stage I according to the eighth edition of lung cancer stage classification. Since lobectomy has been recommended as the best approach for stage I NSCLC patients based on a randomized controlled trial performed in 1995 standard lobectomy with systemic lymph node dissection has become the recommended surgical treatment for clinical stage I NSCLC. It has been revealed that the 5-year survival and complication rates for traditional lobectomy and video-assisted thoracoscopic surgery (VATS) in stage I NSCLC patients are comparable. However, China is facing a dilemma between increasing healthcare demands and inefficient use of healthcare resources, with only 4.3 beds available for every 1000 inhabitants according to the Organization for Economic Co-operation and Development (OECD), which causes long waiting times for surgery and an overwhelming medical burden.

New medical service management, such as day surgery, has significantly alleviated the pressure on healthcare by integrating and utilizing medical resources. It has multidimensional benefits for patients, hospitals, and the national economy, to which policymakers pay great attention. In this context, VATS as a day surgery case enables prompt surgical treatment, while providing the same quality of medical care. This study aimed to assess the safety of stage I NSCLC patients who underwent VATS at day surgery center. It effectively alleviated the social problems of long waiting times for surgery and an overwhelming medical burden.

METHODS

This was a single-center retrospective study. All patients underwent wedge resection, segmentectomy, or lobectomy with systematic lymph node dissection for pulmonary nodules of highly suspected primary lung cancer, with curative intent. The specific surgical treatment was dependent on the results of the intraoperative frozen biopsy. A flowchart of the study selection process is presented in Figure 1.

Patient selection

We retrospectively analyzed the clinical characteristics and thoracic CT features at a single West China Medical Center, and a University Teaching Hospital from June 1, 2019, to December 31, 2020. All patients with pulmonary nodules indicated for VATS in the day surgery center fulfilled all inclusion criteria. This study was reviewed by the Biomedical Ethics Committee of West China Hospital, Sichuan University No. 2020 (341).

Patients eligible for inclusion had to meet all the inclusion criteria as follows: (i) Age above 16 years but younger than 70 years, (ii) thoracic CT scan revealed solid or subsolid nodules (pGGN and mGGN), with a maximum diameter ≤ 3 cm, (iii) American Society of Anesthesiologists (ASA) physical status grade I or II, and (iv) willingness to accept VATS in day surgery center, which means admission, surgery, and discharge within 24 h.

Patients who met any of the following exclusion criteria were not included in the study: (i) significantly impaired cardiopulmonary function, (ii) pulmonary nodules located in the bronchus, causing obstructive pneumonia, (iii) menstrual period, coagulation mechanism disorder, and bleeding tendency, (iv) complications of chronic obstructive pulmonary disease and asthma, (v) complicated cardiovascular and cerebrovascular diseases, (vi) multiple pulmonary nodules with intrapulmonary metastasis or distant metastasis, (vii) post radiotherapy, chemotherapy, immunotherapy, or targeted therapy, and (viii) thickened pleura of any reason, and suspected severe adhesion of the thoracic cavity.

Preoperative auxiliary examination and preparation

After the primary evaluation by thoracic surgeons in the outpatient department, patients completed preoperative auxiliary examinations before hospital admission. These tests included ECG, pulmonary function test, head, chest, and abdominal contrast-enhanced CT. Laboratory tests including complete blood count (CBC), liver function, kidney function, serum electrolyte, blood sugar, and pretransfusion tests. Anesthetic clinical evaluation was performed before surgery. Significantly, the benefit for day surgery in VATS patients is that the cost of preoperational tests and examination is covered by medical insurance within 30 days before surgery. Preoperative health education and guidance were provided to the patients and their families, including general education, the introduction to the day surgery ward environment, surgery type introduction, and respiratory rehabilitation training.

Surgical treatment

VATS was performed at the day surgery center of the West China Hospital. It included wedge resection, segmentectomy, or lobectomy with systematic lymph node dissection, which was chosen according to the pulmonary nodule size, location, and pathological results of intraoperative freezing. Aortic nodes (AP zone), inferior mediastinal nodes (subcarinal zone and lower zone), and 10 hilar nodes were dissected in left lung cancer. Superior mediastinal nodes (upper zone), part of inferior mediastinal nodes (seven subcarinal and eight paracardophagal), and 10 hilar nodes were dissected in right lung cancer. Patients underwent general anesthesia with endotracheal intubation and were placed in the decubitus position.

Perioperative pain management and multimodal analgesia

We adopted a multimodal pain management scheme for postoperative pain management. We used parecoxib sodium for injection half an hour before surgery and 6 h after the first injection. In addition, we prescribed a compound tablet of oxycodone and acetaminophen after discharge, and each tablet contained 5 mg oxycodone hydrochloride and 325 mg acetaminophen. All patients were given one tablet orally at night before the surgery. Nonsteroidal anti-inflammatory
analgesics were injected intravenously according to the patient’s condition before incision, and the intercostal nerve block was performed at the incision site. Fentanyl transdermal patches (4.2 mg/patch) were applied for postoperative pain. We used a numerical rating scale (NRS) for pain evaluation. Meanwhile, we educated patients that the proper use of NRS due to pain is relatively subjective. In NRS, a straight line is divided into 10 segments, and the numbers 0–10 are used to replace the words to indicate the degree of pain. Zero points mean no pain, 1–3 points mean mild pain (pain does not affect sleep), 4–6 points mean moderate pain, 7–9 points mean severe pain (inability to fall asleep or waking up painfully during sleep), and 10 points, intolerable severe pain. During hospitalization, we used intravenous injection or intramuscular injection of analgesic drugs according to the NRS score and patient cooperation. We also prescribed a 1-week dose of acetaminophen oxycodone tablets or nonsteroidal anti-inflammatory drugs for postoperative pain. Additionally, a fentanyl transdermal patch could be applied again if the NRS score was higher than 5. We suggested that patients visit a pain clinic if they were diagnosed with neuropathic pain.

Discharge criteria

The discharge or transfer to the next phase of recovery decision was based on the post-anesthetic Discharge scoring system (PADSS), which was obtained by surgeon 1 or half an hour before discharge. Patients were discharged after PADSS scores ≥9, with stable hemodynamics, limited surgical complications, adequate analgesia without nausea and vomiting, and ability to walk, eat, and urinate. PADSS scores <9 were transferred to the inpatient department or community hospital depending on the clinical assessment.

Perioperative pulmonary rehabilitation

Preoperative pulmonary rehabilitation (PR) has been studied in-depth, and was proposed as an intervention to decrease postoperative pulmonary complications (PPCs). Our previous study revealed that 1 week with systematic and highly intensive preoperative PR training before lobectomy significantly increased 6-min walking distance (6-MWD), peak expiratory flow (PEF), and quality of life (QOL) scores, and facilitated patients’ enhanced recovery, while decreasing the incidence of PPCs, especially in patients older than 70 years. However, in this study, we excluded patients older than 70 years. All patients received a 1-week preoperative rehabilitation regimen that included inspiratory muscle training (IMT) and aerobic endurance training. Abdominal breathing training of IMT plays an essential role in expelling phlegm and recruitment maneuvers, avoiding pneumonia. Surgeons guide and educate patients on IMT exercises for long-term benefits. IMT mainly involves abdominal breathing and inspiration exercises. Patients need to exercise twice a day for 20 min by nasal inhalation to the maximum lung capacity, holding their breath for 2–3 s, then exhaling slowly through the mouth to strengthen abdominal and diaphragm muscles. A respiratory training device (Voldyne 2500, Sherwood Medical Supplies) was used for inspiratory muscle exercise. Physiotherapists taught and trained patients to complete the daily endurance exercise in the rehabilitation training center before surgery. Surgeons usually supervise patients during their hospital stays. Nurses assist surgeons and physiotherapists in making preoperative PR programs run smoothly, educating patients on how to use breath-training devices properly, airway clearance techniques, and daily exercise in the ward.

Postoperative PR is crucially important. IMT and aerobic endurance training are essential after surgery. The physiotherapist provides patients with one-on-one PR training guidance that is slightly different between corresponding preoperative PR items, based on different goals and purposes. In general, postoperative patients’ physical status recovered after a one-month PR regimen.
Catheter management
A single chest tube drainage was placed after VATS to observe the volume of fluid drained and air. We used an 18F Foley catheter as a chest tube inserted through a portal wound in the third or fourth intercostal mid-axillary line, which then descended toward the dorsal region. Gas and fluid can be drained from the 18F Foley catheter, and pain is reduced due to the absence of extra incision(s) and sutures in fixing the chest tube. Chest radiography was performed at least 4 h after discharge from the post-anesthesia care unit (PACU). Patients were planned for chest tube removal before discharge from the day surgery center if they met all of the criteria shown in Table 1. Patients were advised to empty their bladders before entering the operating room. In general, an indwelling urinary catheter was not placed unless an emergency occurred during surgery, such as intraoperative heavy bleeding or some other reason which necessitated surgery for over 2 h. An indwelling urinary catheter was used when patients experienced difficulty in urinating after surgery.

Follow-up protocol and contingency plan
Traditional telephone follow-up was performed on at least three occasions: postoperative days 2, 7 and 30. Furthermore, the focus of each follow-up was different. On postoperative day 2, postoperative pain, nausea, and emesis persisted, and the patients were worried and anxious since the postoperative rehabilitation and rest had changed from hospital to home. We reassured the patients by providing professional and scientific guidance. On postoperative days 7 and 30, we mainly enquired about complications and recovery. After the surgeon’s evaluation, the sutures could be removed 2 weeks later, but there may have been a delay due to the incision’s condition or the chest tube. Patients underwent chest radiography 30 days after surgery and had postoperative pathology to diagnose the result before attending the thoracic surgery clinic for evaluation and further treatment planning.

The patients could contact us or give feedback via a 24/7 follow-up line if they had symptoms such as fever, shortness of breath, palpitation, and tachycardia, or signs such as sweating, subcutaneous emphysema, local incision redness, swelling, and malodorous secretion. We provided patient guidance over the telephone. Moreover, we initiated a contingency plan if they had a life-threatening emergency according to the feedback and guided them to access medical services immediately.

Statistical analysis
All databases were constructed using Excel for Mac, version 16.47.1 (21032301), Microsoft Corporation. We used Prism 8 for macOS, version 8.4.0 (455), and GraphPad software to conduct statistical analysis and create figures.

RESULTS

Patient demographics and tumor characteristics
In this study, 209 patients were included and analyzed from June 1, 2019, to December 31, 2020. All patients were in ASA II status and scheduled for VATS (wedge resection, segmentectomy, lobectomy, or combined, with systematic lymph node dissection) under general anesthesia at the day surgery center. The median age of the surgical patients was 43 (range, 19–67) years. The number of female patients was significantly higher than that of male patients (163 [78.0%] vs. 46 [22.0%]). The average operation duration was 71.7 ± 21.0 min, range 37–205 min. The average intraoperative blood loss was 43.6 ± 14.1 ml, range 5–1800 ml. Of the 209 patients, 114 had right lung nodules, and 95 had left lung nodules (54.5% vs. 45.5%). The longest diameter of the pulmonary nodule was less than 1 cm in 137 (65.6%) patients, more than 1 cm and less than 2 cm in 70 (33.5%) patients, and was between 2 and 3 cm in only two (1.0%) patients. A total of 108 (51.7%) patients underwent segmentectomy, 87 (41.6%) underwent lobectomy, and 14 (6.7%) underwent wedge resection with systematic lymph node dissection. Among the 87 patients who underwent lobectomy, 18 underwent left lobectomy (10 inferior lobe and 8 superior lobe) and 51 underwent right lobectomy (40 superior lobe, 18 middle lobes, and 11 inferior lobe). According to the AJCC/UICC eighth edition of lung cancer stage grouping, stage IA, IA1, IA2, and IA3 were 195 (93.9%), 122 (58.4%), 50 (23.9%), and one (0.5%), respectively. A total of 36 (17.2%) patients were stage 0. Adenocarcinoma dominated the postoperative pathological diagnosis. Of these, 138 (66.0%) were adenocarcinoma and 57 (27.3%) were minimally invasive adenocarcinomas. A total of 14 (6.7%) had benign, atypical epithelium hyperplasia, and granulomatous inflammation in 10 (4.8%) and four (1.9%) patients, respectively. A total of 201 (96.17%) patients were discharged without a chest tube in situ, and eight (3.83%) patients with chest tubes were transferred to the community hospital or thoracic surgery department for further treatment. Patient demographics, surgical treatment details, and tumor characteristics are summarized in Table 2.

| Item no. | Entry content |
|----------|---------------|
| 1 | There was no air leakage during the coughing when patients in any position |
| 2 | The drainage fluid was pale bloody, and volume no sustained increase |
| 3 | Anteroposterior-lateral X-ray of the chest showed no obvious pleural gas, effusion (less than 450 ml/24 h) and atelectasis |
| 4 | No signs of pleural hemorrhage or chylothorax |
| 5 | The patient did not have severe subcutaneous emphysema |
| 6 | Patients were willing to remove chest tube after fully comprehend risks |
| 7 | Easy and convenient to access medical care after discharged |
Short-term follow-up outcome

Intraoperative and postoperative complications were also recorded. Patients were discharged on postoperative day 1, and follow-up was started on days 2, 7, and 30 postoperatively by telephone for surgical complications. Our day surgery center runs for 24 h and has a 24/7 telephone line. The telephone follow-up response rate was 100%. The peak timing of postoperative complications of VATS patients in the day surgery center occurs within the first 2 weeks after surgery, but the symptoms decrease over time. The most common chief complaints were cough, incisional pain, and

### TABLE 2  Patient demographics, surgical treatment details and tumor characteristics

| Variables                        | Classification            | Number of cases | Percentage (%) |
|----------------------------------|---------------------------|-----------------|----------------|
| Age (years)                      | Median age                | 43              | /              |
|                                  | Range                     | 19–67           | /              |
| Sex                              | Male                      | 46              | 22.0           |
|                                  | Female                    | 163             | 78.0           |
| ASA classification               | ASA I                     | 0               | 0.0            |
|                                  | ASA II                    | 209             | 100            |
| Operation time (min)             | Average time              | 71.7 ± 21.0     | /              |
|                                  | Range                     | 37–205          | /              |
| Blood loss (ml)                  | Average volume            | 43.6 ± 14.1     | /              |
|                                  | Range                     | 5–1800          | /              |
| Location of the tumor            | Left lung                 | 95              | 45.5           |
|                                  | Right lung                | 114             | 54.5           |
| Longest diameter of the tumor (cm)| T ≤ 1 cm                  | 137             | 65.6           |
|                                  | 1 cm < T ≤ 2 cm           | 70              | 33.5           |
|                                  | 2 cm < T ≤ 3 cm           | 2               | 1.0            |
| T (primary tumor)                | T0                        | 14              | 6.7            |
|                                  | Tis                       | 22              | 10.5           |
|                                  | T1ami                     | 35              | 16.7           |
|                                  | T1a ≤ 1 cm                | 87              | 41.6           |
|                                  | T1b > 1–2 cm               | 50              | 23.9           |
|                                  | T1c > 2–3 cm               | 1               | 0.5            |
| AJCC/UICC stage (2017)           | Stage 0                   | 36              | 17.2           |
|                                  | Stage I A1                | 122             | 58.4           |
|                                  | Stage I A2                | 50              | 23.9           |
|                                  | Stage I A3                | 1               | 0.5            |
| Surgical treatment               | Lobectomy                 | 87              | 41.6           |
|                                  | Segmentectomy*            | 108             | 51.7           |
|                                  | Wedge resection*          | 14              | 6.7            |
| Discharged with a chest tube     | Yes                       | 8               | 96.17          |
|                                  | No                        | 201             | 3.83           |
| Postoperative pathological diagnosis | MIA                      | 57              | 27.3           |
|                                  | Adenocarcinoma            | 138             | 66.0           |
|                                  | Epithelium atypical hyperplasia | 10          | 4.8            |
|                                  | Granulomatous inflammation | 4               | 1.9            |

Abbreviations: AJCC, American Joint Committee on Cancer; UICC, Union Internationale Contre le Cancer; MIA, minimally invasive adenocarcinoma.

*Systemic lymph node dissection.
shortness of breath. No severe complications or life-threatening emergencies were observed. The detailed follow-up data of postoperative symptoms are shown in Figures 2 and 3. Nine out of 209 patients were transferred to a community hospital or inpatient department with a chest tube. One patient had a major intraoperative blood loss of 1800 ml because of variation in the blood vessel. The patient’s vital signs were stable after active rescue during the operation. After the operation, the patient was transferred to the thoracic surgery department for further treatment, where vital signs and laboratory findings were stable without any pharmacological support. Eight patients experienced air leaks but did not qualify for the removal criteria; two out of eight patients refused chest tube insertion before surgery. Complication details of the nine cases of transferred patients are shown in Table 3. All patients were treated promptly and recovered well, and no life-threatening emergencies occurred.

DISCUSSION

With the increase in the incidence of cancer-related mortality of lung cancer in China and globally, the demand for surgical treatment for lung cancer has also increased. Surgery offers the best chance of cure for patients with NSCLC, especially for patients with stage I NSCLC. The eighth edition of lung cancer grouping subdivides stage I lung cancer into four subgroups (stage IA1, IA2, IA3, and IB) and reveals the survival benefits and cost-effectiveness of timely surgical treatment for stage I or early-stage NSCLC. Hence, VATS in a day surgery center is an ideal management and innovation for stage I NSCLC patients in the context of soaring medical demand in China, where the patient is admitted, operated, and discharged within 24 h, or on the same calendar day.

With the development of minimally invasive surgical techniques and anesthesia, minimally invasive surgery is widely used such as thoracoscopic lobectomy for early-stage lung cancer, laparoscopic radical resection for colon cancer, and laparoscopic radical resection in renal cancer. VATS is a case in point, and it is an alternative to traditional thoracotomy in the treatment of thoracic diseases, and is the best choice for the diagnosis and treatment of pulmonary nodules. Its advantages are a shorter operation time, less bleeding, smaller incision, and shorter recovery time. VATS is the most common surgery for the thoracic surgery department performed at the day surgery center in recent years. Successful results from a randomized clinical trial were reported in 1994, and lobectomy is considered the gold standard of treatment for NSCLC. However, a number of studies have revealed that lobectomy can substitute sublobar resection for early stage or small peripheral stage I NSCLCs, including wedge resection and segmentectomy, as outcomes are comparable to those after lobectomy. In our study, 108 cases of segmentectomy were performed because the primary tumors were less than 2 cm and were located in the peripheral lung. Moreover, the patients’ ages were relatively young. We maximized the preservation of lung tissue and function based on radical surgical resection. Wedge resection was performed for benign intraoperative frozen biopsies. Fourteen out of 209 patients underwent wedge resection in this study, and the final diagnosis by paraffin biopsy confirmed that it was benign.

Chest tube drainage assists in determining if there is any bleeding, air leakage or lymphatic leakage. Our previous study revealed that a Foley catheter used as chest tube drainage is feasible and safe compared to a 28-F chest tube, for patients undergoing VATS lobectomy. Evidence also revealed that chest tube times and length of hospital stay could be shortened by preoperative PR. Postoperative morbidity

| Case | Age | Gender | Complication | Discharge decision | Outcome |
|------|-----|--------|--------------|--------------------|---------|
| 1    | 50  | Female | Air leak, pleural effusion | Transfer to community hospital | Recovered |
| 2    | 45  | Male   | Air leak, subcutaneous emphysema | Transfer to community hospital | Recovered |
| 3    | 51  | Female | Air leak | Transfer to community hospital | Recovered |
| 4    | 42  | Female | Air leak, cough | Transfer to community hospital | Recovered |
| 5    | 47  | Female | Air leak | Transfer to community hospital | Recovered |
| 6    | 60  | Female | Air leak, chest tightness, wound exudation | Transfer to community hospital | Recovered |
| 7    | 44  | Male   | Air leak, postoperative hemorrhage | Transfer to community hospital | Recovered |
| 8    | 51  | Female | Air leak, postoperative hemorrhage | Transfer to community hospital | Recovered |
| 9    | 35  | Female | Intraoperative hemorrhage | Transfer to inpatient department | Recovered |
and costs also decreased.\textsuperscript{17,31} Although patients in the day surgery center were planned for discharge within 24 h, we removed the chest tube according to patients’ recovery and willingness for a better quality of life. This minimizes patient and domestic medical care costs in a cost-effective manner.

The medical quality of VATS day surgery is the same as that of the inpatient department in optimizing the medical process and improving medical services. Patients need to complete auxiliary examinations at the outpatient department before surgery, and in our study crucial surgical treatment was performed at the West China Hospital and patients’ recovered at home or at community hospitals. The day surgery program is also in line with China’s hierarchical diagnosis and treatment policy and the Healthy China 2030 policy. However, approximately 30.8\% of patients in this study were unwilling to undergo VATS at the day surgery center because of the short length of hospital stay, relatively more minor medical care, inexperienced home caregiving, and the uncertainty in recognizing and dealing with emergencies. Based on our 11-year day surgery management experience, a well-established contingency protocol can effectively solve emergencies after discharge. So far, there have been no day surgery–related deaths. Thus, future efforts should aim to improve the acceptance of day surgery.

This was a single-center, retrospective study with a relatively small sample size. Some bias may exist. First, all surgeries were performed by the same chief surgeon and his medical team, and all patients underwent a follow-up after 1 month. Only short-term complications and outcomes were observed and analyzed for safety analysis of day surgery mode VATS, and long-term survival outcomes need to be monitored and further investigated. Second, this study showed a higher proportion of patients with lung cancer. However, it does not reveal the actual incidence of lung cancer in West China. All patients were carefully evaluated for surgery, and thoracic surgeons and radiologists should discuss patients who are highly suspected of having lung cancer. Most benign cases underwent regular follow-up examinations at the outpatient clinic. Third, 14 benign cases were included in this study as the subject was stage I NSCLCs. Thus, we presented the data clearly in the results and analyzed the data in the discussion, which may give readers more information and inspiration.

In conclusion, the day surgery mode of VATS for stage I NSCLC is safe and feasible, and patients can be discharged without a chest tube within 24 h after full preparation and critical medical evaluation. One month follow-up for postoperative complications is crucial for the safety of patients and medical quality. VATS as day surgery makes surgical treatment ideal in time for stage I NSCLC patients providing the same quality of medical care.

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CONFLICT OF INTEREST
The authors confirm that there are no conflicts of interest.

ORCID
Lisha Jiang https://orcid.org/0000-0002-5602-3792
Tiantian Lei https://orcid.org/0000-0001-9884-185X
Kun Zhou https://orcid.org/0000-0002-2016-3398
Hongsheng Ma https://orcid.org/0000-0003-1967-4964
Guowei Che https://orcid.org/0000-0002-5779-8274

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