# Pain, Quality of Life, and Clinical Outcomes after **Robotic Lobectomy**

Valerie Lacroix<sup>1</sup> Thierry Pieters<sup>3</sup>

Philippe Noirhomme<sup>1</sup>

Zahra Mosala Nezhad<sup>1</sup> David Kahn<sup>2</sup> Arnaud Steyaert<sup>2</sup> Alain Poncelet<sup>1</sup>

Address for correspondence Valerie Lacroix, Department of

Luc, Avenue Hippocrate 10, Bruxelles 1200, Belgium

Cardiovascular and Thoracic Surgery, Cliniques Universitaires Saint

<sup>1</sup>Department of Cardiovascular and Thoracic Surgery, IREC, Cliniques Universitaires Saint Luc, Bruxelles, Belgium

<sup>2</sup> Department of Cardiac Anesthesia, Cliniques Universitaires Saint Luc, Bruxelles, Belaium

<sup>3</sup>Division of Pulmonary Medicine, Cliniques Universitaires Saint Luc, Bruxelles, Belgium

Thorac Cardiovasc Surg

Abstract

Background To evaluate pulmonary function, pain, and quality of life at midterm after

(e-mail: valerie.lacroix@uclouvain.be).

robotic lobectomy performed in a single institution. Methods Sixty-five consecutive patients underwent robotic thoracic surgery over 32 months using a complete four-arm portal technique. Sixty-one patients underwent lobectomies predominantly for stage I non-small cell lung cancer. Pulmonary function tests were repeated at midterm follow-up. Pain and quality of life were evaluated during the follow-up on a subgroup of 39 patients, excluding the learning period.

Results At a mean of 7-month follow-up, there was no significant difference in preoperative and midterm postoperative pulmonary function. A total of 62.5% of the patients reported a variable intensity of discomfort or pain at the surgical site, with a mean pain intensity score of  $2.1 \pm 1.4$ . Mean pain interference score were weak  $(1.8 \pm 1.9)$ , with patients with moderate pain reporting significantly higher pain interference scores than those with mild pain (p = 0.0025). Only one patient suffered from neuropathic-like pain. Quality of life was globally favorable and related to the pain level, with a significant interference on the physical component.

Conclusion Robotic lobectomy does not appear to have an impact on midterm

pulmonary function. Persistent postoperative pain is mild, nonneuropathic-like, with

weak interference on daily activities. Quality of life is satisfactory but related to the pain

# **Keywords**

- robotic surgery
- lobectomy
- NSCLC
- quality of life

pain

pulmonary function level.

# Introduction

Robotic pulmonary resection is gaining acceptance as a routine minimally invasive technique in thoracic surgery, and its indications are increasing. High-specification systems offering three-dimensional visualization, optimal magnification, and wristed instruments have produced outcomes comparable to video-assisted thoracoscopic surgery (VATS).<sup>1,2</sup> Although teaching pathways for safe robotic surgery are described,<sup>3</sup> robotic lobectomy still follows a learning curve<sup>4</sup> regardless of whether

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the surgeon has classical open surgery or VATS experience, with even expert VATS surgeons encountering technical difficulties when starting robotic surgery.

Here we describe our single-center experience of introducing robotic lobectomy into a unit with primarily open thoracic surgery experience. We particularly focused on the results of functional tests as well as the surgery-related pain and quality of life (QoL) at midterm follow-up. We also report our clinical and oncological outcomes as well as our technical progression over time.

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# **Materials and Methods**

#### **Study Cohort**

This is a retrospective cohort of 65 consecutive patients scheduled for robot-assisted thoracic oncologic surgery at our center between December 2012 and August 2015. Of them, 61 patients had lobectomies.

Preoperative staging included positron emission tomography-computed tomography (PET-CT), chest CT, and pulmonary function tests. Diagnosis was confirmed by bronchoscopy biopsy, brushing, or transthoracic needle biopsy. Fine needle aspiration endoscopic bronchial ultrasound or/and mediastinoscopy was performed in cases with radiologically detected enlarged lymph nodes and/or positive lymph nodes on PET-CT scans.

The inclusion criteria for robotic lobectomy were adequate cardiopulmonary functional reserve, absence of a centrally located lesion or chest wall invasion, and no previous thoracic surgery or neoadjuvant treatment. Advanced age and single-N2 station lymph node involvement were not contraindications to robotic lobectomy.

## **Surgical Techniques**

A single surgeon performed all lobectomies using the da Vinci robotic system (Intuitive Surgical, Inc., Mountain View, California, United States). A complete four-arm portal technique was used. Between December 2012 and January 2014  $(n = 22, \text{ considered our learning period}^4)$ , we used the surgical technique described by Melfi et al<sup>5</sup> with a 30-degree angle-down camera (**Fig. 1**). The four ports were placed in the seventh intercostal space in the midaxillary and posterior axillary lines, the fifth intercostal space in the anterior axillary line, and the auscultatory area. After January 2014, we altered the robotic port insertion approach for the remaining 39 lobectomies, instead opting for insertion of the four ports in the same intercostal space (over the top of the eighth rib) and a 0-degree camera<sup>6</sup> to obtain single intercostal space access. Robotic arm 3 (most posterior) was a 5-mm port, robotic arms 1 and 2 were 8-mm ports, and the camera was a 12-mm port. Each arm was then placed 9 to 10 cm apart beginning at the paravertebral space (3 cm from the spine). Carbon dioxide was insufflated to a pressure of 8 mm Hg. A 12-mm access port was then placed above the 10th rib between the camera and the anterior robotic arm, this incision later being enlarged (to a maximum of 5 cm) for lobe retrieval. Preoperative analgesia provided by a paravertebral block in the seventh, eighth, and ninth intercostal spaces was performed with 20 mL levobupivacaine (Chirocaïne, Abbvie) 0.25%.

All patients underwent complete mediastinal lymph node dissection. With respect to operative technique and tumor resection, the first 46 lobectomies were performed by approaching the central vessels and dividing the bronchovascular structures and then the fissural parenchyma (**-Fig. 1**). Later on, due to favorable results<sup>7</sup> and evidence of reduced postoperative risk of prolonged air leak, the fissure was first completely opened prior to moving to the bronchovascular structures (n = 15). A single chest drain was routinely placed.

Postoperative management was in the thoracic surgery unit. Drainage tubes were removed when the output dropped below 250 mL and there was no air leak for 24 hours. We followed a standardized analgesia protocol consisting of patient-controlled intravenous morphine with acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs; if not contraindicated). The analgesia target was a patientreported pain level of less than 3 on a numerical rating scale ranging from 0 to 10 at rest and on movement prior to switching to oral treatment with acetaminophen and tramadol (Tradonal, Meda Pharma, Bad Homburg, Germany) as required before discharge. Adjuvant therapy was administered if needed.

# **Postoperative Care and Follow-Up**

Patient demographics and operative data were collected prospectively in our institutional thoracic database and analyzed. Total operative time, defined as the time from first incision until closure of the last incision, was recorded.



**Fig. 1** Flow chart presenting the progress with time of the robotic approach technique and surgical dissection technique. The number of patients related to each technique is mentioned.

Operative mortality was defined as death within 30 days after the operation from any cause or before discharge.<sup>8</sup>

A multidisciplinary lung cancer team followed patients up every 3 months for the first 2 years and every 6 months thereafter for 3 years. Postoperative follow-up included clinical and radiological examination with alternating chest X-rays and chest CT scans. The mean follow-up time was  $11 \pm 9$  months.

In addition to standard data accrual in the database, we sought to prospectively study postoperative pulmonary function and use specific surveys to examine pain and QoL. The hospital ethical review board (IRB 00001530) approved the study, and all patients provided written consent. The postoperative pulmonary function tests were complete in 44 patients (72%). To study a homogeneous patient group following the same surgical approach and eliminate bias caused by the initial learning period, we excluded the first tertile from our postoperative evaluation of postoperative QoL and pain. Therefore, this subgroup consisted of 39 patients, of which complete data were available for 87% (n = 34). The mean time for evaluation since surgery was 7.3  $\pm$  4.4 months.

# **Pulmonary Function Tests**

Pulmonary function tests were performed using a Morgan TLC spirometer (Morgan Medical, Rainham, UK; MDas v.4.01 software) with determination of forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), secondary calculation of the FEV1/FVC ratio, and diffusing capacity for carbon monoxide divided by the alveolar volume. All measurements were obtained preoperatively (baseline) and are expressed in percentages with respect to a reference value (**~Table 1**). FEV1 and FVC were repeated during follow-up visits.

#### **Quality of Life and Pain Evaluation**

Health-related QoL was assessed using the Medical Outcomes Study 36-item Short Form (SF-36), a widely used 36-item scale constructed to survey health status and QoL. This questionnaire was selected because it is commonly used and considered one of the most appropriate by European thoracic surgeons.<sup>9</sup> Our team has also previously used this tool for assessing outcomes from chest wall resection surgery.<sup>10</sup>

The SF-36 assesses eight health concepts: physical functioning, role limitation caused by physical problems, bodily pain, general health perception, energy and vitality, social functioning, role limitation caused by emotional problems, and mental health. These individual dimensions are then grouped into two summary scores: a physical component scale (PCS) and an emotional component scale (MCS, mental component scale). Each score ranges from 0 to 100, a higher score indicating better QoL.<sup>11,12</sup>

Pain was evaluated with the French version of the Brief Pain Inventory (BPI) questionnaire. The BPI is a validated and widely used instrument in postoperative pain research, including after thoracic surgery.<sup>13</sup> Patients were asked to locate their pain, to rate its intensity over the course of the previous week ("at its worst," "at its least," "on average," and "right now"), to describe the relief they felt from current pain medication, and the degree to which their pain interfered with various aspects of daily life (general activity, walking,

Table	1 Patient	demographics,	clinical,	and	oncological
charact	teristics				

Characteristics	Lobectomies (n = 61)			
Age (y), mean (range)	68 (41–85)			
Male, n (%)	34 (66%)			
Comorbidities (%)				
Pulmonary disease	29 (48%)			
BMI >24	35 (57%)			
Hypertension	32 (52%)			
Diabetes mellitus	14 (23%)			
Coronary artery disease	8 (13%)			
Cerebrovascular disease	9 (15%)			
Renal disease	9 (15%)			
Pulmonary function				
% FEV1, mean	91 ± 19			
% DLCO/AV, mean	83 ± 18			
VEMS/FVC $<$ 70%, n	17 (28%)			
DLCO < 80%, n	19 (31%)			
Diagnosis (%)				
NSCLC				
Adenocarcinoma	46 (75%)			
Squamous carcinoma	7 (11%) <sup>a</sup>			
Neuroendocrine tumor	6 (9%)			
Metastasis	3 (5%)			
Tumor size (mm), median (range)	21 (10–63)			
Clinical stage for NSCLC ( $n = 52$ )				
Stage I ( $n = 45$ )	IA 34 (65%)			
	IB 11 (21%)			
Stage II ( $n = 6$ )	IIA 2 (4%)			
	IIB 4 (8%)			
Stage III ( $n = 1$ )	IIIA 1 (2%)			

Abbreviations: BMI, body mass index; DLCO/AV, diffusion capacity of lung for carbon monoxide divided by the alveolar volume; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NSCLC, non-small cell lung cancer.

<sup>a</sup>One patient had two tumors in the same lobe with both types of NSCLC.

work, mood, enjoyment of life, relationships with others, and sleep). Each item was scored on a 0 to 10 numerical scale, and individual scores were averaged to obtain a mean intensity score and a mean interference score.<sup>13–15</sup>

Patients with pain were also asked to complete the first seven items of the DN4 questionnaire, a screening tool for neuropathic pain. Each positive item receives a score of 1 and each negative item a score of 0. The total score is the sum of each item's individual scores.<sup>16</sup> In this seven-item version, a total score equal or greater than 3 indicated a high probability of neuropathic pain.<sup>17</sup>

### **Statistical Analysis**

All statistical analyses were performed in SPSS v22.0 (IBM Inc., Chicago, Illinois, United States). Categorical variables were reported as absolute numbers and percentages. Continuous variables were expressed as mean  $\pm$  standard deviation. Differences between study groups were assessed using the independent sample Student's paired *t*-test for normally distributed continuous variables. Normality was tested with the Shapiro–Wilk test. One-way analysis of variance was used to compare QoL and pain score means. A *p*-value  $\leq$  0.05 was considered statistically significant.

# Results

## Surgery-Related Experiences and Outcomes

Sixty-one patients (mean age 68; range, 41–85) underwent lobectomies. Preoperative patient characteristics are detailed in **-Table 1**. The predominant indication for lobectomy was non-small cell lung cancer (NSCLC, 86%), with other indications including neuroendocrine tumors and unilobar metastatic lesions requiring lobectomy (**-Table 1**). Patients with NSCLC were predominantly stage I (86%; see **-Table 1**). The median tumor size was 21 mm (range, 10–63 mm). The majority of procedures were right-sided (60%) and upper lobectomies (55%) (**-Table 2**). The median operating time decreased over time (median, 236 minute for the first tertile and 154 minute for the last tertile). Early in our experience (during the first 11 operations), there were three conversions for uncontrolled bleeding (n = 2) and completion of bronchial suture (n = 1). No patient required reoperation.

There was one in-hospital death on the 10th postoperative day due to invasive aspergillosis in an immunocompromised patient. Two patients had atrial fibrillation with subsequent stroke (one temporary visual impairment and one upper leg

Table 2 Operation details

Variables	Total lobectomies ( $n = 61$ )
Lobes	
RUL	21 (34%)
RML	5 (8%)
RLL	11 (18%)
LUL	13 (21%)
LLL	11 (18%)
Wedge resection <sup>a</sup>	2 (3%)
Operative time (min) (incision to closure, median)	185
First tertile	263
Second tertile	178
Third tertile	154
Conversion	3 (5%)

Abbreviations: LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

<sup>a</sup>These patients had both lobectomies and wedge resection on another lobe.

Table 3 Postoperative minor complications and outcomes

Variables	Total lobectomies (n = 61)
Pneumonia	4 (7%)
Arrhythmia	5 (8%)
Bleeding <sup>a</sup>	1 (2%)
Chest drain duration (d), median	4
Prolonged air leak (>5 d)	11 (18%)
Hospital stay (d), median	6

<sup>a</sup>Bleeding did not require reoperation.

weakness, both of which resolved within 6 months). Minor morbidities are presented in **-Table 3**. The median chest drain duration was 4 days, and there was no vocal cord palsy, chylothorax, myocardial infarction, or acute renal failure. The median length of hospital stay was 6 days.

One tumor (measuring 63 mm) was microscopically incompletely resected at the bronchus (R1 margin). The mean number of lymph node stations removed was 4. The mean number of resected mediastinal lymph nodes was  $14 \pm 7$ . Sixteen patients (26%) were upstaged on histopathological assessment, of which six patients (10%) had lymph node-related upstaging (**-Table 4**).

Two patients died over the follow-up period: one from gastrointestinal bleeding at 8 months and another from metastatic progressive disease at 22 months. There were metastatic recurrences in three patients, all three with pathological stage IIIA NSCLC over a mean follow-up interval of 11 months.

# **Pre- and Postoperative Pulmonary Function**

There were no significant differences in FEV1, FVC, and FEV1/ FVC pre- and postoperatively with a mean interval of 7 months (**-Table 5** and **-Fig. 2**).

# Postoperative Pain and Quality of Life

The mean acute postoperative pain scores at rest and during movement were  $2.3 \pm 1.9$  and  $5.4 \pm 1.7$  on postoperative day 1 and  $1.7 \pm 1.3$  and  $4.9 \pm 1.8$  on postoperative day 2 (**Fig. 3A**). At a mean of 7-month follow-up, 20 patients

Table 4 Pathological staging

Pathological stage for NSCLC ( $n = 52$ )			
Stage I (n = 39)	IA 26 (50%) IB 13 (25%)		
Stage II ( $n = 7$ )	IIA 1 (2%) IIB 6 (11.5%)		
Stage III ( $n = 6$ )	IIIA 6 (11.5%)		
Lymph node upstaging (n, %)	6 (10%)		
N0 to N1	3		
N0 to N2	2		
N1 to N2	1		

Abbreviations: N, lymph node; NSCLC, non-small cell lung cancer.

Functional tests	Preoperative mean value $\pm$ SD	Postoperative mean value $\pm$ SD	p-Value
FEV1 (L)	$2.4\pm0.7$	2.3 ± 0.6	0.31
FVC (L)	$3.3\pm0.9$	3.2 ± 0.8	0.13
FEV1/FVC	73.4 ± 10.9	71.2 ± 9.5	0.63

 Table 5
 Pre- and postoperative (at a mean 7-month interval) pulmonary function

Abbreviations: FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

(62.5%) reported a variable intensity of discomfort or pain at the surgical site, with a mean BPI score of  $2.1 \pm 1.4$ . Twelve patients (37.5%) reported mild pain and eight patients (25.0%) reported moderate pain (**~Fig. 3B**). The mean pain interference score was  $1.8 \pm 1.9$ , with patients with moderate pain reporting significantly higher pain interference scores ( $2.7 \pm 2.2$ ) than those with mild pain ( $1.1 \pm 1.5$ ) (p = 0.0025) (**~Fig. 3C**). According to the DN4 questionnaire, only 1/20 patients (5%) suffered from likely neuropathic pain. The majority of patients were not taking pain medication (n = 11; 55%), and those that did took nonopioid analgesics such as acetaminophen (n = 6; 30%) or NSAIDs (n = 2; 10%). Only one patient took tramadol.

The mean PCS and MCS were  $64.3 \pm 17.6$  and  $62.6 \pm 19.6$ , respectively. PCS scores were significantly lower in patients with moderate pain ( $51.6 \pm 14.2$ ) than those with mild pain ( $69.4 \pm 17.7$ ) or without pain ( $67.8 \pm 16.1$ ) (p = 0.05). The trend was similar for MCS score ( $53.8 \pm 17.9$  vs.  $67.1 \pm 19.5$  vs.  $63.8 \pm 20.4$ ), but this was not statistically significant (p = 0.33) (**¬Table 6** and **¬Fig. 4**).

# Discussion

Robotic thoracic surgery for cancer, mostly by lobectomy, is rapidly gaining acceptance from the global surgical commu-

3,5 3 2,5 2,5 1,5 1,5 0,5 0 FEV1 FVC Preoperative Postoperative

**Fig. 2** Graphic representation of the pulmonary function test of the patients before and at a mean interval of 7 months postoperatively. FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity, in liters.

nity and for variety of reasons. Postoperative comfort and QoL seem better with robotic surgery compared with rib- and nerve-sparing open surgery.<sup>6</sup> Pain reduction techniques and modalities are of particular importance for patients who have a tendency for analgesia dependency, lower pain thresholds, and cancers. In this study, we intended to particularly focus on the parameters of pulmonary function, pain, and QoL following robotic lobectomy. During this early experience, we adapted our strategy in terms of surgical approach and dissection technique to minimize adverse surgical outcomes. We used a single intercostal space (seventh) for the insertion of all robotic arms to minimize potential diffuse secondary neuropathic pain. Persistent postoperative pain has already been well studied for thoracotomy and VATS, and it has been showed to negatively impacts QoL, mainly physical QoL.<sup>18</sup> In a recent meta-analysis, the incidence of pain was 57 and 47%, respectively, 3 and 6 months after thoracotomy, with average pain scores of 3.0  $\pm$  2 and 3.7  $\pm$  2.<sup>19</sup> The incidence of persistent postthoracotomy pain is as high as 68% in some recent prospective studies,<sup>18</sup> with an average pain score of less than 4 for the majority of patients. There are conflicting reports on



**Fig. 3** A graphic representation of the pain assessment. (A) Mean pain scores for all patients in relation to postoperative time (day 1, day 2, and for a mean 7-month follow-up). (B) The pie distribution of the cohort at a mean 7-month follow-up with their reported pain intensity in percentage. (C) BPI interference score regarding the pain intensity at a mean 7-month follow-up.

	Total (n = 32)	No pain ( <i>n</i> = 12)	Mild pain ( $n = 12$ )	Moderate pain ( $n = 8$ )
BPI pain score (mean $\pm$ SD)	1.3 ± 1.4	$0\pm 0$	$1.2\pm0.6$	$3.5\pm0.8$
BPI interference score (mean $\pm$ SD)	1.8 ± 1.9	$0 \pm 0$	1.1 ± 1.5	2.7 ± 2.2
PCS (mean $\pm$ SD)	64.3 ± 17.6	67.8 ± 16.6	69.4 ± 17.6	51.6 ± 14.2
MCS (mean $\pm$ SD)	62.6 ± 19.6	$63.8\pm20.4$	67.1 ± 19.5	53.8 ± 17.9

Table 6 Postoperative (at a mean 7-month interval) pain scores, interference scores, and quality of life with respect to pain

Abbreviations: BPI, Brief Pain Inventory; MCS, emotional component scale; PCS, physical component scale; SD, standard deviation.

the long-term pain outcomes after VATS,<sup>15,20-24</sup> but persistent pain seems to develop less often than after thoracotomy. In a recent prospective study,<sup>21</sup> only 11% of patients reported moderate or higher pain scores 3 months after VATS. There was, however, no significant difference between VATS and thoracotomy groups in the incidence and pain scores during the 6-month follow-up (29 and 21% chronic pain, respectively). At 8-month follow-up, 10 and 12% of patients reported pain scores exceeding 4, respectively. Pain after robotic procedure has been described by Cerfolio et al,<sup>6</sup> with a significant lower 3-week postoperative pain score than a rib- and nerve-sparing thoracotomy procedure (2.5 vs. 4.4). In our study, the mean BPI score at the 7-month follow-up was 1.3  $\pm$  1.4. Although 62.5% of patients reported some pain at follow-up, most (37.5%) rated their pain as mild, which means a pain score below 3. A further 25% of patients reported moderate pain (pain score between 3 and 6). Pain only modestly interfered with their daily activities. These values appear favorable and similar to those reported for other thoracic minimally invasive approaches. Only one patient had neuropathic pain, as assessed by the DN4 questionnaire. This is surprising, since a recent meta-analysis reported that 66% of chronic pain after thoracic surgery was probably neuropathic in origin,<sup>25</sup> and DN4 questionnaire scores have been shown to be well correlated with a clinical diagnosis of neuropathic pain in postthoracotomy pain patients.<sup>26</sup>

With respect to QoL, Cerfolio and colleagues<sup>6</sup> first studied QoL in thoracic robotic surgery patients. They used a shorter





modification of the SF-36 questionnaire and observed a significantly higher average mental QoL score 3 weeks postoperatively and a trend toward increased physical QoL compared with open surgery, although by postoperative month 4 there were no significant differences in mental or physical QoL between groups. In one prospective study of QoL over the first postoperative year after lung resection using thoracoscopy or thoracotomy techniques,<sup>15</sup> the PCS and pain scores were similar for both procedures with a score of 46 after 8 months. The MCS was higher in the thoracotomy group, with a score of 47 at 8 months. These differences may be explained by patients' expectations being higher than the experienced pain. In comparison, here we observed an MCS of 62 and a PCS of 64 in postoperative robotic lobectomy patients, which compares to mean PCS and MCS values of 40 and 44, respectively, for chest wall resections.<sup>10</sup> These midterm QoL results after robotic surgery appear to be favorable.

Pre- and postoperative pulmonary function tests remained unchanged and satisfactory, even in patients with relatively poor pulmonary function and other comorbidities. These results seem particularly favorable, since recent studies<sup>27</sup> have shown a significant drop of 20% in the values of FEV1 and FVC 6 months postoperatively for patients undergoing open lobectomy for stage I NSCLC. For VATS lobectomy,<sup>28</sup> the drop in postoperative FEV1 has been evaluated to be 13.6 and 8.5% at 3 and 12 months, respectively. The drop in postoperative FVC has been evaluated to be 14.1 and 6.3% at 3 and 12 months, respectively.

Our study is limited by its retrospective design and its evaluation of an early and evolving experience, including a change in surgical technique during the study period. This had an impact on the cohort and completeness of follow-up, especially for patients in the first tertile. The cohort is relatively small; however, the NSCLC subgroup was acceptable for an early study.

In conclusion, here we describe our early experience with robotic surgery. Even though the procedure evolved over time and was subject to technical improvements, our clinical, pathological, and QoL outcomes were favorable with no procedure-related deaths, acceptable and manageable postoperative pain and QoL, and maintenance of pulmonary function.

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