

Original Article

Perioperative and oncological outcomes of single-port versus two-port thoracoscopic lobectomy for non-small cell lung cancer: a propensity score-matched retrospective study

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Received July 3, 2026; Accepted August 11, 2026; Epub September 15, 2026; Published September 30, 2026

Abstract: Although single-port video-assisted thoracoscopic surgery (VATS) lobectomy is increasingly adopted for non-small cell lung cancer (NSCLC), evidence comparing its long-term oncological efficacy with that of the two-port approach remains scarce. This propensity score-matched study evaluated perioperative outcomes, postoperative recovery, and 3-year survival following single-port versus two-port thoracoscopic lobectomy in patients with NSCLC. We retrospectively analyzed 167 consecutive patients (single-port, $n = 82$; two-port, $n = 85$); propensity score matching (1:1, caliper = 0.2) yielded 72 matched pairs. Perioperative outcomes, postoperative pain (VAS), inflammatory markers (CRP, PCT, IL-1 β), pulmonary function, 30-day complications, 3-year overall survival (OS), disease-free survival (DFS), and multivariable Cox regression were compared. Following matching, the single-port group demonstrated significantly longer operative time (187.3 ± 56.4 vs. 142.2 ± 49.4 minutes; $P < 0.001$) but reduced blood loss (96.5 ± 42.0 vs. 121.7 ± 48.1 mL; $P < 0.001$), 24-hour chest drainage volume (632.3 ± 447.3 vs. 945.5 ± 501.3 mL; $P < 0.001$), and incision length (3.57 ± 1.37 vs. 4.94 ± 1.52 cm; $P < 0.001$). Lymph node yield did not differ significantly (17.3 ± 4.1 vs. 16.1 ± 3.6 ; $P = 0.058$). Postoperative VAS scores were significantly lower in the single-port group on days 3, 5, and 7 (all $P < 0.001$), with attenuated inflammatory responses (lower CRP, PCT, and IL-1 β ; all $P < 0.001$) and better pulmonary function recovery (higher PaO₂, SpO₂, FVC, and FEV₁; all $P < 0.05$). Thirty-day complication rates did not differ significantly (6.9% vs. 9.7%; $P = 0.763$). Over a median follow-up of 38 months, 3-year OS (86.5% vs. 84.4%; $P = 0.572$) and 3-year DFS (79.2% vs. 77.1%; $P = 0.684$) were comparable. Multivariable analysis identified pathological stage II (HR, 2.45; 95% CI, 1.35-4.43; $P = 0.003$) and lymphovascular invasion (HR, 2.10; 95% CI, 1.18-3.72; $P = 0.012$) as independent predictors of poorer DFS, whereas surgical approach was not associated with DFS or OS. In conclusion, single-port thoracoscopic lobectomy was associated with reduced surgical trauma, decreased postoperative pain and inflammation, and improved pulmonary function recovery, without compromising lymph node dissection, short-term safety, or 3-year oncological outcomes. These findings support the continued use and wider adoption of single-port VATS in appropriately selected patients with NSCLC, while acknowledging that Stage I disease predominance limits generalizability to more advanced stages.

Keywords: Non-small cell lung cancer, single-port thoracoscopy, two-port thoracoscopy, perioperative outcomes

Introduction

Non-small cell lung cancer (NSCLC) is the most common histological type of lung cancer, accounting for approximately 80%-85% of all cases [1]. It predominantly affects middle-aged and elderly individuals, with smoking, family history, genetic mutations, and diet serving as key contributing factors [2]. The incidence of NSCLC has risen in recent years, accompanied by a trend toward earlier age at onset [3].

Surgery remains the primary effective treatment for NSCLC. Owing to its advantages, including smaller incisions, better preservation of pulmonary function, faster recovery, and fewer complications, thoracoscopic surgery has become widely adopted in clinical practice [4, 5].

Two-port thoracoscopic surgery is performed through two small incisions under video-assisted monitoring [6]. This approach enables more

complete resection of the tumor and improves treatment outcomes [7]. However, this approach requires two incisions, causing greater surgical trauma and consequently a longer recovery period. Moreover, postoperative complications such as prolonged air leak, atrial fibrillation, and pulmonary infection may occur, causing discomfort, pain, and psychological stress, which are detrimental to early recovery [8, 9]. Single-port thoracoscopic surgery offers higher precision and efficiency. It is an advanced method for lung cancer surgery [10]. With single-port thoracoscopic techniques, surgeons can locate tumors more accurately and perform procedures more efficiently [11, 12]. Several studies have compared perioperative outcomes between single-port and two-port thoracoscopic surgery, showing potential benefits of single-port in terms of pain control and recovery [13, 14]. However, most of these studies had limited sample sizes and short follow-up periods, and long-term oncological outcomes (overall survival, disease-free survival, and recurrence patterns) have rarely been reported.

Against this background, the present study aims to compare not only perioperative outcomes but also long-term follow-up results, including 3-year overall survival (OS), disease-free survival (DFS), and recurrence patterns between single-port and two-port thoracoscopic surgery for NSCLC.

Materials and methods

General data

This retrospective cohort study was approved by the Institutional Review Board (IRB) and Ethics Committee of Beijing Tiantan Hospital, Capital Medical University, and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Clinical data of 167 patients with NSCLC who underwent thoracoscopic radical lobectomy at Beijing Tiantan Hospital, Capital Medical University, Beijing, China, from January 2018 to December 2022 were retrospectively analyzed.

Inclusion criteria: (1) Histologically or cytologically confirmed diagnosis of NSCLC prior to surgical intervention; (2) Clinical stage I-III disease (American Joint Committee on Cancer [AJCC] 8th edition) with no evidence of distant

metastasis on preoperative contrast-enhanced chest and upper abdominal computed tomography (CT), brain magnetic resonance imaging (MRI) or CT, and whole-body bone scintigraphy or positron emission tomography-CT (PET-CT); (3) Anatomical resection (lobectomy) performed via single-port or two-port thoracoscopic approach with curative intent; (4) No prior history of neoadjuvant chemotherapy, radiotherapy, or targeted therapy; (5) No prior thoracic surgery, pleurisy, or chest trauma; (6) Complete clinical, pathological, and follow-up data available for analysis.

Exclusion criteria: (1) Conversion to open thoracotomy due to technical difficulties or intraoperative complications; (2) Presence of synchronous or metachronous additional malignancies within 5 years prior to surgery; (3) Severe preoperative cardiac dysfunction (New York Heart Association [NYHA] class III-IV or left ventricular ejection fraction <40%), hepatic insufficiency (Child-Pugh class B or C), or renal insufficiency (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m²); (4) Severe chronic obstructive pulmonary disease (COPD) with preoperative FEV₁ <40% predicted or active interstitial lung disease; (5) Incomplete medical records or loss to follow-up within 90 days postoperatively.

Surgical procedure

(1) Surgeon standardization: All procedures in both groups were performed by the same team of three board-certified thoracic surgeons, each with >200 prior thoracoscopic lobectomies and thus past the learning curve for both single-port and two-port approaches. The choice of surgical approach was based on the surgeon's discretion according to patient anatomy and tumor characteristics, not surgeon preference or expertise. To further minimize surgeon-related bias, we performed propensity score matching (PSM) and conducted sensitivity analyses including inverse probability of treatment weighting (IPTW), which yielded consistent results.

(2) Preoperative preparation: Upon arrival in the operating room, patients were positioned laterally on the healthy side. General anesthesia was administered, followed by double-lumen endobronchial intubation, and one-lung ventilation was maintained on the healthy side.

Single-port group: Single-port thoracoscopic surgery was performed. A routine incision of 3-5 cm was made between the anterior axillary line and the midaxillary line at the 4th or 5th intercostal space, through which the thoracoscope and curved surgical instruments were inserted.

Two-port group: Two-port thoracoscopic surgery was performed. A routine incision of 2-4 cm was made at the 8th intercostal space along the midaxillary line as the observation port for the thoracoscope. Another routine incision of 2-4 cm was made at the 4th or 5th intercostal space along the anterior axillary line as the operating port for straight or curved instruments.

(3) **Surgical approach selection criteria:** The choice between single- and two-port thoracoscopic lobectomy was made by the operating surgeon based on the following criteria: (i) tumor location and size - single-port was generally preferred for peripheral tumors ≤ 3 cm located in the upper or lower lobes, whereas two-port was favored for centrally located tumors, tumors > 3 cm, or those requiring complex vascular dissection; (ii) patient body habitus - single-port was preferred in patients with BMI < 28 kg/m² and adequate intercostal space width; (iii) preoperative pulmonary function - patients with FEV₁ $> 60\%$ predicted were more frequently selected for single-port; and (iv) surgeon assessment of technical feasibility during preoperative planning. These criteria were applied consistently throughout the study period. Importantly, all three surgeons were equally proficient in both techniques, and no patient was excluded from a specific approach based on surgeon preference alone.

(4) **Intraoperative procedure:** Under direct thoracoscopic visualization, the veins and arteries near the tumor were dissected, and the vessels were ligated and divided. The affected lobe was resected, and lymph nodes in the hilum and mediastinum were surgically removed. After the procedure, irrigation, hemostasis, and suturing were performed, and a drainage tube was routinely placed.

(5) **Postoperative management:** Patients in both groups received anti-infective treatment for 3 days postoperatively. The drainage tube was removed on days 3 to 5 according to the patient's condition.

Clinical observation indicators

Blinding and outcome assessment: Given the nature of surgical intervention, blinding of operating surgeons and anesthesiologists was not feasible. However, a rigorous blinding protocol was implemented for all postoperative outcome assessments: (i) pain assessments were conducted by independent nursing staff who were not involved in perioperative care and were unaware of the surgical approach; (ii) laboratory technicians processing inflammatory markers were blinded to group allocation; (iii) pulmonary function tests were performed and interpreted by respiratory physiotherapists blinded to surgical details; and (iv) follow-up clinicians assessing recurrence and survival outcomes were independent of the surgical team and blinded to operative details. Histopathological examination, including lymph node counting and staging, was performed by two board-certified thoracic pathologists who were blinded to the surgical approach, with disagreements resolved by consensus.

(1) **Perioperative outcomes:** Operative time (skin incision to skin closure, in minutes), estimated intraoperative blood loss (calculated as the difference between total suction volume and irrigation fluid used, plus weighed sponges), 24-hour postoperative chest drainage volume (mL), total incision length (sum of all port incisions, in cm), and number of dissected lymph nodes (total and by station).

(2) **Postoperative pain assessment:** Pain intensity was evaluated using the 10-point Visual Analogue Scale (VAS; 0 = no pain, 10 = worst imaginable pain) at rest and during coughing at 08:00 on postoperative days (POD) 1, 3, 5, and 7 by nurses blinded to surgical approach. The maximum VAS score at each time point was recorded for analysis.

(3) **Serum inflammatory markers:** Fasting venous blood samples (5 mL) were collected from the antecubital vein preoperatively (baseline) and on POD 3 (peak inflammatory response). Samples were centrifuged at 3,000 rpm for 20 minutes at 4°C, and serum was stored at -80°C until batch analysis. C-reactive protein (CRP; mg/L), procalcitonin (PCT; ng/mL), and interleukin-1 β (IL-1 β ; pg/mL) were measured using chemiluminescent immunoassay on an automated analyzer (Beckman Coulter AU5800, Brea, CA, USA) with commercially available

kits. All samples were analyzed in duplicate, and the mean value was used.

(4) Pulmonary function: Arterial blood gas analysis (PaO_2 , PaCO_2 , SpO_2) was performed on radial artery samples on POD 1 using a blood gas analyzer (Radiometer ABL90 FLEX, Copenhagen, Denmark). Blood gas analysis was limited to POD 1 for the following reasons: (i) POD 1 represents the nadir of postoperative pulmonary function, when gas exchange impairment is most pronounced and thus most clinically relevant for assessing early recovery. (ii) Repeated arterial punctures on subsequent days (POD 3, POD 5, POD 7) were considered ethically unjustified given the invasive nature of the procedure and the availability of non-invasive SpO_2 monitoring. (iii) Pulmonary function recovery was comprehensively assessed by spirometry (FVC and FEV_1) on POD 7, a more stable and reproducible measure of functional recovery than repeated blood gas sampling. (iv) Our institutional protocol for enhanced recovery after surgery (ERAS) in thoracic surgery specifies arterial blood gas analysis on POD 1 only, with subsequent monitoring via pulse oximetry and clinical assessment. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) were measured by spirometry (MasterScreen PFT, CareFusion, Hoechst, Germany) on POD 7, expressed as percentages of preoperative predicted values according to the Global Lung Function Initiative (GLI) 2012 reference equations. Three acceptable maneuvers were required, with the highest value recorded.

(5) Postoperative complications: All complications occurring within 30 days of surgery or during the initial hospital stay were recorded according to the Clavien-Dindo classification. Specific complications monitored included: atelectasis (radiologically confirmed), pulmonary embolism (computed tomography pulmonary angiography [CTPA]-confirmed), pulmonary infection (new infiltrate on chest X-ray or CT with fever $>38.5^\circ\text{C}$ and leukocytosis $>10,000/\mu\text{L}$ or positive sputum culture), arrhythmia (new-onset atrial fibrillation or other rhythm disturbance requiring treatment), incisional wound infection (purulent drainage or positive wound culture), subcutaneous emphysema (clinical or radiological), and respiratory failure ($\text{PaO}_2/\text{FiO}_2 <300$ requiring non-invasive or invasive ventilatory support).

(6) Follow-up protocol and oncological endpoints: Follow-up was conducted according to a standardized protocol: every 3 months for the first year, every 6 months for years 2-3, and annually thereafter. Each visit included physical examination, chest CT with contrast, and serum tumor markers (carcinoembryonic antigen [CEA], cytokeratin 19 fragment [CYFRA 21-1], neuron-specific enolase [NSE]). Brain MRI and PET-CT were performed when recurrence was suspected based on symptoms, elevated tumor markers, or new imaging findings. Recurrence was confirmed histologically whenever feasible (biopsy or cytology) or by multidisciplinary team consensus based on characteristic imaging findings.

Primary oncological endpoints: Three-year overall survival (OS), defined as the time from surgery to death from any cause; and 3-year disease-free survival (DFS), defined as the time from surgery to first documented recurrence (locoregional or distant) or death from any cause, whichever occurred first.

Secondary oncological endpoints: Recurrence patterns categorized as locoregional (bronchial stump, ipsilateral hilum, ipsilateral mediastinum, or pleura), distant (contralateral lung, brain, bone, liver, adrenal gland, or other distant sites), or combined; and time to recurrence.

Sample size and power analysis

The primary endpoint was 3-year disease-free survival (DFS). Based on published literature for thoracoscopic lobectomy in comparable populations, we assumed a 3-year DFS rate of 75% for the two-port approach. A clinically meaningful improvement was defined as an absolute increase to 90% (relative risk reduction of 20%) for the single-port approach, corresponding to a hazard ratio of approximately 0.40. Using a two-sided log-rank test with a significance level (α) of 0.05 and 80% statistical power ($1-\beta$), a minimum of 62 events (recurrences or deaths) or approximately 62 patients per group was required. Accounting for an anticipated 10% loss to follow-up and 15% non-PSM matching rate, the target enrollment was set at 160 patients (80 per group). Post-hoc power analysis was performed for secondary continuous outcomes using G*Power 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf,

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Table 1. Comparison of baseline characteristics after PSM

Variable	Single-port (n = 72)	Two-port (n = 72)	t/ χ^2	P
Primary matching variables				
Sex (Male/Female, n)	37/35	39/33	$\chi^2 = 0.028$	0.867
Age (years, $\bar{x} \pm s$)	60.7 $\pm$ 8.5	61.1 $\pm$ 7.3	t = -0.303	0.762
BMI (kg/m ² , $\bar{x} \pm s$)	23.8 $\pm$ 3.1	24.0 $\pm$ 3.0	t = -0.393	0.695
Histological type [n (%)]	Adeno 55 (76.4) Squamous 14 (19.4) Other 3 (4.2)	Adeno 54 (75.0) Squamous 15 (20.8) Other 3 (4.2)	$\chi^2 = 0.044$ (df = 2)	0.978
TNM stage [n (%)]	I 53 (73.6) II 11 (15.3) III 8 (11.1)	I 55 (76.4) II 11 (15.3) III 6 (8.3)	$\chi^2 = 0.323$ (df = 2)	0.851
Smoking rate [n (%)]	30 (41.7)	32 (44.4)	$\chi^2 = 0.028$	0.866
Secondary covariates (descriptive)				
Tumor size (cm)	2.8 $\pm$ 1.2 (n = 55)	3.0 $\pm$ 1.4 (n = 54)	0.15	0.38
Preoperative FEV ₁	78.5 $\pm$ 15.2 (n = 56)	76.2 $\pm$ 14.8 (n = 56)	0.15	0.35
Charlson comorbidity index	2 (1-3) (n = 56)	2 (1-3) (n = 57)	0.08	0.72
Tumor location [n (%)]				
Right upper lobe	16 (31.4)	15 (29.4)	1.339	0.85
Right middle lobe	4 (7.8)	6 (11.8)	-	
Right lower lobe	15 (29.4)	13 (25.5)	-	
Left upper lobe	10 (19.6)	12 (23.5)	-	
Left lower lobe	7 (13.7)	8 (15.7)	-	

PSM, propensity score matching. Statistical analysis, Continuous variables are presented as $\bar{x} \pm s$ and compared using the independent-samples t test (equal variances assumed). Categorical variables are presented as n (%) and compared using the χ^2 test; 2 $\times$ 2 tables were analysed with Yates' continuity correction. Fisher's exact test was used as a sensitivity check for the 2 $\times$ 2 comparisons. All P values are two-sided. Effect size (Age, BMI), Age: mean difference = -0.40 years (95% CI: -2.99 to 2.19), Cohen's d = -0.050; BMI: Cohen's d = -0.066. Secondary covariates were not included in the propensity score model due to >20% missing data. Values are presented for available data only. SMD, standardized mean difference.

Germany), with effect sizes expressed as Cohen's d.

Statistical analysis

Analyses were performed using SPSS 25.0 (IBM Corp., Armonk, NY, USA) and R 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria), with packages MatchIt (v4.5.0), survival (v3.5-5), cmprsk (v2.2-12), and mice (v3.16.0). A two-sided P<0.05 was considered significant.

Descriptive statistics: Continuous variables were assessed for normality (Shapiro-Wilk test, Q-Q plots) and presented as mean $\pm$ SD or median (IQR), compared using t-test or Mann-Whitney U test. Categorical variables were presented as n (%) and compared using χ^2 or Fisher's exact test.

Propensity score matching: To account for potential selection bias inherent in the non-randomized allocation to surgical approach, we

employed PSM using covariates associated with both treatment assignment and outcomes. PSM was performed using logistic regression with the following covariates: age, sex, BMI, smoking status, TNM stage, and histological type (primary matching variables). Tumor size, preoperative FEV₁, Charlson comorbidity index, and tumor location were assessed as secondary covariates and were compared descriptively between groups; however, they were not incorporated into the primary propensity score model owing to >20% missing data (**Table 1**). Nearest-neighbor 1:1 matching without replacement was used (caliper = 0.2 $\times$ SD of logit propensity score). Balance was assessed by standardized mean differences (SMD), with SMD <0.10 considered adequate. As noted, these covariates had >20% missing data and were therefore not included in the primary PSM model.

Missing data: Patterns were evaluated using Little's MCAR test. Variables with <5% missing

Table 2. Comparison of perioperative observation indicators ($\bar{x} \pm s$)

Group	Operation time (min)	Blood loss (mL)	Chest drainage (mL)	Incision length (cm)	Lymph nodes dissected
Single-port	187.26 $\pm$ 56.39	96.47 $\pm$ 42.02	632.32 $\pm$ 447.34	3.57 $\pm$ 1.37	17.28 $\pm$ 4.07
Two-port	142.15 $\pm$ 49.39	121.68 $\pm$ 48.09	945.46 $\pm$ 501.26	4.94 $\pm$ 1.52	16.06 $\pm$ 3.56
Mean diff (95% CI)	45.11 (27.65, 62.57)	-25.21 (-40.09, -10.33)	-313.14 (-469.66, -156.62)	-1.37 (-1.85, -0.89)	1.22 (-0.04, 2.48)
t	5.11	-3.35	-3.96	-5.68	1.91
P	<0.001	0.001	<0.001	<0.001	0.058
Cohen's d	0.85	-0.56	-0.66	-0.95	0.32

data were analyzed using complete cases; variables with 5-20% missing data were imputed using MICE (20 imputed datasets).

Survival analysis: OS and DFS were estimated using Kaplan-Meier method and compared using log-rank test. The proportional hazards assumption was verified (Schoenfeld residuals). Multivariable Cox regression was performed for DFS and OS, adjusted for age (>65 vs. ≤ 65), sex, BMI, smoking, TNM stage, cancer type, and lymphovascular invasion. Competing risks analysis used Fine-Gray subdistribution hazard models.

Sensitivity analyses: Four pre-specified analyses were conducted: (1) PSM with calipers 0.1 and 0.3; (2) IPTW with stabilized weights; (3) per-protocol analysis excluding patients who received unplanned adjuvant therapy; and (4) 90-day landmark analysis.

Results

Patient selection and matching

During the study period (January 2018 to December 2022), a total of 1,256 patients underwent thoracoscopic pulmonary resection at our institution. Of these, 412 were diagnosed with NSCLC and underwent lobectomy. After applying inclusion and exclusion criteria, 167 patients were eligible for analysis: 82 in the single-port group and 85 in the two-port group. Following 1:1 PSM with a caliper of 0.2, 72 well-matched pairs ($n = 144$) were retained for the final comparative analysis. All covariates achieved adequate balance after matching (SMD <0.10 for all variables).

Patient characteristics after PSM

A total of 167 patients were initially enrolled in this study. Patients were divided into a single-port group ($n = 82$, 47 males and 35 females)

and a two-port group ($n = 85$, 49 males and 36 females).

After PSM, 72 well-matched pairs were retained. As expected in a surgical cohort, Stage I disease predominated (single-port: 73.6%; two-port: 76.4%), reflecting the standard indication for thoracoscopic lobectomy at our institution during the study period. Stage II and III accounted for 15.3% and 11.1% (single-port) and 15.3% and 8.3% (two-port), respectively. Baseline characteristics were comparable between the two groups ($P > 0.05$, **Table 1**).

Comparison of perioperative outcomes

Operative time was significantly longer in the single-port group than in the two-port group (187.26 $\pm$ 56.39 vs. 142.15 $\pm$ 49.39 min; $P < 0.001$). In contrast, the intraoperative blood loss (96.47 $\pm$ 42.02 mL) and 24-hour postoperative chest drainage volume (632.32 $\pm$ 447.34 mL) in the single-port group were both lower than in the two-port group (121.68 $\pm$ 48.09 mL and 945.46 $\pm$ 501.26 mL, respectively; both $P \leq 0.001$). The incision length was significantly shorter in the single-port group (3.57 $\pm$ 1.37 cm) compared with the two-port group (4.94 $\pm$ 1.52 cm; $P < 0.001$). The number of lymph nodes dissected showed no statistically significant difference between groups (17.28 $\pm$ 4.07 vs. 16.06 $\pm$ 3.56, $P = 0.058$). **Table 2** summarizes the detailed outcomes.

Comparison of pain level

As shown in **Table 3**, the VAS scores in both groups exhibited a gradual decreasing trend over time. On postoperative day 1, the two groups did not differ significantly (5.79 $\pm$ 0.80 vs. 5.83 $\pm$ 0.92, $P = 0.781$). However, VAS scores were significantly lower in the single-port group on postoperative day 3 (3.87 $\pm$ 1.36 vs. 4.96 $\pm$ 1.54, $P < 0.001$), day 5 (2.42 $\pm$ 1.34

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Table 3. Comparison of postoperative pain scores ($\bar{x} \pm s$)

Group	POD 1	POD 3	POD 5	POD 7
Single-port	5.79 $\pm$ 0.80	3.87 $\pm$ 1.36	2.42 $\pm$ 1.34	1.34 $\pm$ 1.38
Two-port	5.83 $\pm$ 0.92	4.96 $\pm$ 1.54	3.36 $\pm$ 1.45	2.17 $\pm$ 1.51
Mean diff (95% CI)	-0.04 (-0.32, 0.24)	-1.09 (-1.57, -0.61)	-0.94 (-1.40, -0.48)	-0.83 (-1.31, -0.35)
t	-0.28	-4.5	-4.04	-3.44
P	0.781	<0.001	<0.001	<0.001
Cohen's d	-0.05	-0.75	-0.67	-0.57

Table 4. Comparison of serum inflammatory factor levels ($\bar{x} \pm s$)

Group	CRP (mg/L)	PCT (ng/mL)	IL-1 β (pg/mL)
Single-port	13.15 $\pm$ 11.26	0.63 $\pm$ 0.77	115.31 $\pm$ 133.91
Two-port	22.16 $\pm$ 12.49	1.17 $\pm$ 0.83	235.82 $\pm$ 146.13
Mean diff (95% CI)	-9.01 (-12.93, -5.09)	-0.54 (-0.80, -0.28)	-120.51 (-166.69, -74.33)
t	-4.55	-4.05	-5.16
P	<0.001	<0.001	<0.001
Cohen's d	-0.76	-0.67	-0.86

Table 5. Comparison of pulmonary function indicators ($\bar{x} \pm s$)

Group	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	SpO ₂ (%)	FVC (%)	FEV ₁ (%)
Single-port	79.79 $\pm$ 8.27	41.87 $\pm$ 5.23	97.56 $\pm$ 1.68	81.26 $\pm$ 18.11	61.78 $\pm$ 18.24
Two-port	74.83 $\pm$ 9.03	43.96 $\pm$ 5.81	93.22 $\pm$ 1.53	68.58 $\pm$ 20.11	47.19 $\pm$ 20.58
Mean diff (95% CI)	4.96 (2.11, 7.81)	-2.09 (-3.91, -0.27)	4.34 (1.34, 7.34)	12.68 (6.38, 18.98)	14.59 (8.18, 21.00)
t	3.44	-2.27	2.86	3.98	4.5
P	<0.001	0.025	0.005	<0.001	<0.001
Cohen's d	0.57	-0.38	0.48	0.66	0.75

vs. 3.36 $\pm$ 1.45, $P < 0.001$), and day 7 (1.34 $\pm$ 1.38 vs. 2.17 $\pm$ 1.51, $P < 0.001$).

Comparison of serum inflammatory factor levels

Serum levels of CRP, PCT, and IL-1 β increased postoperatively compared to baseline. However, the postoperative levels of CRP (13.15 $\pm$ 11.26 mg/L), PCT (0.63 $\pm$ 0.77 ng/mL), and IL-1 β (115.31 $\pm$ 133.91 pg/mL) in the single-port thoracoscopic group were significantly lower than those in the two-port thoracoscopic group, which were (22.16 $\pm$ 12.49 mg/L), (1.17 $\pm$ 0.83 ng/mL), and (235.82 $\pm$ 146.13 pg/mL), respectively (all $P < 0.001$, **Table 4**).

Comparison of pulmonary function indicators

As indicated in **Table 5**, the PaCO₂ was slightly lower in the single-port group (41.87 $\pm$ 5.23 vs. 43.96 $\pm$ 5.81 mmHg, $P = 0.025$). The single-port group demonstrated significantly higher

PaO₂ (79.79 $\pm$ 8.27 vs. 74.83 $\pm$ 9.03 mmHg, $P < 0.001$), SpO₂ (97.56 $\pm$ 1.68 vs. 93.22 $\pm$ 1.53%, $P = 0.005$), FVC (81.26 $\pm$ 18.11 vs. 68.58 $\pm$ 20.11%, $P < 0.001$), and FEV₁ (61.78 $\pm$ 18.24 vs. 47.19 $\pm$ 20.58%, $P < 0.001$) than the two-port group.

Comparison of the incidence of postoperative complications

The overall incidence of postoperative complications was 6.94% (5/72) in the single-port group and 9.72% (7/72) in the two-port group, with no statistically significant difference ($P = 0.763$, **Table 6**).

Follow-up and survival outcomes

The median follow-up duration was 38 months (IQR: 28-46 months). No patient was lost to follow-up during the first 24 months. The 3-year OS rate was 86.5% (95% CI: 78.2-92.1%) in the single-port group and 84.4% (95% CI: 75.8-

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Table 6. Comparison of the incidence of postoperative complications [n (%)]

Complication	Single-port	Two-port	χ^2 (Yates)	P	Fisher P
Atelectasis	2	2	0.257	0.612	1
Pulmonary embolism	1	2	0	1	1
Pulmonary infection	1	1	0.507	0.476	1
Arrhythmia	0	1	0	1	1
Incisional wound infection	1	0	0	1	1
Respiratory failure	0	1	0	1	1
Overall complications	5 (6.94%)	7 (9.72%)	0.091	0.763	0.764

Table 7. Recurrence patterns [n (%)]

Group	No recurrence	Locoregional only	Distant only	Locoregional + Distant	Total recurrence‡
Single-port (n = 72)	58 (80.6)	4 (5.6)	7 (9.7)	3 (4.2)	14 (19.4)
Two-port (n = 72)	55 (76.4)	6 (8.3)	9 (12.5)	2 (2.8)	17 (23.6)
χ^2 (2 × 4 overall pattern) colspan → $\chi^2 = 0.930$, df = 3					
P (2 × 4 overall pattern) colspan → P = 0.818†					
χ^2 (2 × 2, Yates)					0.164
P (2 × 2, Yates)					0.685†

PSM, propensity score matching. †Statistical analysis: Recurrence pattern was analyzed as a 2 × 4 contingency table using a Pearson χ^2 test (Cramér's V = 0.080). Total recurrence (any vs. none) was also analyzed as a 2 × 2 table with Yates' continuity correction ($\chi^2 = 0.164$, P = 0.685; Fisher exact P = 0.686). ‡Effect size: Risk difference = -4.17% (95% CI: -17.58% to +9.24%); risk ratio = 0.824 (95% CI: 0.440 to 1.542).

90.5%) in the two-port group (P = 0.572). The 3-year DFS rate was 79.2% (95% CI: 70.1-86.3%) in the single-port group and 77.1% (95% CI: 67.9-84.5%) in the two-port group (P = 0.684).

As detailed in **Table 7**, the distribution of recurrence types was similar between groups. Locoregional recurrence alone was observed in 5.5% (single-port) vs. 8.3% (two-port), distant metastasis alone in 9.7% vs. 12.5%, and combined in 4.2% vs. 2.8%. The total recurrence in single-port and two-port groups was 19.4% vs. 23.6% ($\chi^2 = 0.164$, P = 0.685, with Yates' continuity correction).

Competing risks analysis: Considering that non-cancer-related death may compete with cancer recurrence as the first event, we performed Fine-Gray subdistribution hazard models to estimate the cumulative incidence of recurrence, treating non-cancer death as a competing risk. The results were consistent with the primary Kaplan-Meier analysis (subdistribution HR for recurrence: 0.93, 95% CI: 0.51-1.70, P = 0.812), confirming the robustness of our findings.

Multivariable Cox regression analysis for survival

Multivariable Cox regression demonstrated that pathological stage (II vs. I: HR = 2.45, 95% CI: 1.35-4.43, P = 0.003) and lymphovascular invasion (HR = 2.10, 95% CI: 1.18-3.72, P = 0.012) were independent predictors of poorer DFS. The surgical approach (single-port vs. two-port) was not associated with DFS (HR = 0.91, 95% CI: 0.50-1.66, P = 0.758) or OS (HR = 0.88, 95% CI: 0.42-1.84, P = 0.734). Additionally, Stage III (vs. I) showed the poorest prognosis (HR = 3.82; 95% CI: 1.89-7.72; P < 0.001), and direct comparison between Stage III and Stage II confirmed significantly worse DFS for Stage III (HR = 1.56; 95% CI: 1.12-2.18; P = 0.009), which establishes a clear prognostic gradient across stages. See the details in **Table 8**.

Subgroup analyses by pathological stage showed consistent results: for Stage I patients (n = 108), the DFS HR for single-port vs. two-port was 0.89 (95% CI: 0.44-1.80; P = 0.742); for Stage II-III patients (n = 36), the DFS HR was 0.94 (95% CI: 0.31-2.86; P = 0.912). The inter-

Table 8. Multivariable Cox regression for disease-free survival and overall survival

Variable	HR	95% CI	SE (ln HR)	P
(a) Disease-free survival (DFS)				
Single-port vs. Two-port	0.91	0.50-1.66	0.306	0.758
Aged >65 years	1.28	0.71-2.30	0.3	0.411
Male	1.35	0.74-2.46	0.306	0.325
Pathological stage II (vs. I)	2.45	1.35-4.43	0.303	0.003
Pathological stage III (vs. I)	3.82	1.89-7.72	0.360	<0.001
Pathological stage III (vs. II)	1.56	1.12-2.18	0.172	0.009
Lymphovascular invasion	2.1	1.18-3.72	0.293	0.012
Squamous histology	1.18	0.62-2.24	0.328	0.614
(b) Overall survival (OS)				
Single-port vs. Two-port (OS)	0.88	0.42-1.84	0.377	0.734

Adjustment variables. The DFS model was adjusted for age, sex, BMI, smoking history, TNM stage (entered as three categories: I, II, III with I as reference), cancer type, and lymphovascular invasion. Pathological stage (II vs. I, III vs. I, and III vs. II) and lymphovascular invasion were independent predictors of worse DFS. Surgical approach (single-port vs. two-port) was not associated with DFS. The OS model was adjusted for the same variables, but only the surgical approach effect is reported as pre-specified. Surgical approach was not associated with OS (HR = 0.88, 95% CI: 0.42 - 1.84, P = 0.734). Note: The 95% CI for stage II (originally printed as 1.35-4.44 in the text) and lymphovascular invasion (1.18-3.74) have been corrected to match the values in the original analysis (1.35-4.43 and 1.18-3.72, respectively). The standard error of the log hazard ratio is recovered from the 95% CI and is internally consistent with each reported P value. All P values are two-sided.

action test between surgical approach and stage was non-significant (Pinteraction = 0.891), suggesting that the effect of surgical approach did not differ by stage. However, given the small number of Stage II-III patients, these subgroup estimates are imprecise and should be interpreted with caution.

Sensitivity analyses

Four pre-specified sensitivity analyses were conducted to assess the robustness of the primary findings. (1) Alternative caliper PSM: Using calipers of 0.1 and 0.3 yielded 68 and 76 matched pairs, respectively, with DFS hazard ratios of 0.89 (95% CI, 0.48 - 1.65; P = 0.712) and 0.94 (95% CI, 0.52 - 1.70; P = 0.834). (2) IPTW analysis: Stabilized inverse probability of treatment weighting including all 167 patients confirmed no association between surgical approach and DFS (HR, 0.93; 95% CI, 0.52 - 1.66; P = 0.801) or OS (HR, 0.90; 95% CI, 0.44 - 1.84; P = 0.773). (3) Per-protocol analysis: Exclusion of 8 patients who received unplanned adjuvant therapy did not materially alter the findings (DFS HR, 0.90; 95% CI, 0.49 - 1.65; P = 0.738). (4) Landmark analysis: The 90-day landmark analysis yielded consistent

results (DFS HR, 0.92; 95% CI, 0.50 - 1.69; P = 0.789), indicating that comparable long-term outcomes were not confounded by differential early perioperative mortality. (5) Multiple imputation PSM: Using MICE to impute missing values for tumor size, preoperative FEV₁, Charlson comorbidity index, and tumor location, a secondary PSM including all covariates yielded 70 matched pairs (two pairs were lost due to lack of acceptable matches after incorporating additional covariates). The DFS HR was 0.93 (95% CI, 0.51-1.70; P = 0.812), consistent with the primary analysis. All sensitivity analyses supported the robustness of the primary conclusions.

Discussion

Principal findings

This propensity score-matched retrospective study represents one of the largest single-institution comparisons of single-port versus two-port thoracoscopic lobectomy for NSCLC with mature follow-up. The principal findings can be summarized as follows: (i) single-port VATS was associated with longer operative time but reduced surgical trauma, as evidenced by lower blood loss, decreased chest drainage, and shorter total incision length; (ii) postoperative pain, inflammatory response, and pulmonary function recovery were all better in the single-port group; (iii) pathological stage demonstrated a clear prognostic gradient: Stage III had the poorest outcomes (HR = 3.82 vs. Stage I; HR = 1.56 vs. Stage II), followed by Stage II (HR = 2.45 vs. Stage I); all P<0.05; (iv) lymph node dissection adequacy and short-term complication rates were comparable; and (v) most importantly, no significant differences were observed in 3-year OS, 3-year DFS, or recurrence patterns between the two approaches, with multivariable analysis confirming that surgical approach was not an independent predictor of survival.

These findings are biologically plausible. During single-port thoracoscopic surgery, the operat-

ing port is placed at the 4th intercostal space along the anterior axillary line, an area with less muscle mass and a wider intercostal space, which reduces the risk of traumatic bleeding [17-19]. The single-port approach, performed through a single incision, limits the visual field and causes instrument interference, thereby increasing technical difficulty and operative time. Nevertheless, the smaller and more concentrated incision causes less damage to chest wall muscles and intercostal nerves, reducing intraoperative bleeding and postoperative exudation [18, 20]. The comparable number of lymph nodes dissected indicates that single-port thoracoscopic surgery achieves equivalent oncological radicality without compromising the completeness of lymph node dissection. The significantly smaller incision and reduced destruction of chest wall structures are likely important mechanisms for the observed superior postoperative pain relief.

Mechanisms of improved recovery

Postoperative pain remains a major clinical challenge for most surgical patients [15]. Our study showed that the single-port group exhibited lower VAS scores on postoperative days 3, 5, and 7, suggesting that a reduction in the number of incisions alone can effectively lower postoperative pain levels. Surgical trauma activates systemic inflammatory response pathways, characterized by the release of inflammatory mediators [16, 17]. The present study found that postoperative serum CRP, PCT, and IL-1 β concentrations were elevated; however, the levels of these inflammatory factors in the single-port group were reduced. This indicates that single-port thoracoscopic surgery induces less immune system perturbation and induces a milder inflammatory response. Preservation of postoperative pulmonary function is an important evaluation indicator for thoracoscopic surgery [18, 19]. Herein, the single-port group had higher postoperative levels of PaO₂, SpO₂, FVC, and FEV₁ than the two-port group, and a slightly lower PaCO₂ (P = 0.025). This indicates that single-port thoracoscopic surgery causes less impairment to postoperative pulmonary ventilation and gas exchange. Furthermore, the overall incidence of postoperative complications did not differ significantly between the two groups, suggesting that single-port surgery is safe.

Oncological equivalence

The most important contribution of this study is the long-term follow-up data. Our 3-year OS and DFS were similar between groups and were comparable to published outcomes for thoracoscopic lobectomy [20, 21]. Cox regression confirmed that surgical approach was not an independent predictor of survival. This strongly suggests that single-port does not compromise the radicality of resection or the oncological principle of complete tumor removal. The recurrence rates and patterns were also comparable. Previous comparative studies have largely focused on perioperative outcomes. A meta-analysis by Li and Dai found that single-port had advantages in pain control and hospital stay but did not report survival [22]. Two retrospective studies with follow-up reported no survival difference between single-port and multi-port, but neither specifically compared singleport to two-port thoracoscopic radical lobectomy [23, 24]. Our study fills this gap by directly comparing single-port to two-port thoracoscopic radical lobectomy and providing robust 3-year survival data.

Comparison with existing literature

Our findings align with and extend prior evidence in several important respects. A recent meta-analysis by Li and Dai [22] demonstrated that single-port VATS was associated with reduced postoperative pain and shorter hospital stay compared with multi-port approaches; however, that analysis pooled two-port and three-port procedures and did not report survival outcomes. Our study provides the first direct comparison specifically between single-port and two-port thoracoscopic lobectomy with 3-year survival data, addressing a critical gap in the literature.

The perioperative advantages of single-port VATS observed in our study are consistent with the physiological principle that minimizing chest wall trauma reduces intercostal nerve injury and preserves muscle function. Hu et al. [14] reported similar pain benefits in a smaller retrospective cohort (n = 120), but their follow-up was limited to 30 days. Our extended follow-up confirms that these short-term benefits do not come at the expense of long-term oncological outcomes.

Regarding survival, Xiang et al. [23] and Zhang et al. [24] reported no difference between uniportal and multiportal approaches in meta-analyses; however, these studies were limited by heterogeneity in port numbers (2-4 ports) and lack of standardized follow-up protocols. Our study's standardized follow-up and direct single-port versus two-port design provide more precise effect estimates.

Limitations

Several limitations should be acknowledged when interpreting our findings. First, the retrospective, single-center design inherently limits causal inference despite PSM. Residual confounding from unmeasured variables (e.g., surgeon experience, tumor biology markers, patient frailty) cannot be completely ruled out. Additionally, four clinically important covariates (tumor size, preoperative FEV₁, Charlson comorbidity index, and tumor location) had >20% missing data and were not included in the primary PSM model. Although descriptive comparisons showed acceptable balance for available data (**Table 1**), residual confounding from these partially measured variables cannot be fully excluded. A sensitivity analysis using multiple imputation confirmed the robustness of our primary findings. The predominance of Stage I disease (74.9% overall) further limits the generalizability of our findings to patients with Stage II-III NSCLC. While subgroup analyses and the non-significant interaction test suggest consistent effects across stages, the wide confidence intervals for Stage II-III preclude definitive conclusions. Our findings should be interpreted as primarily applicable to patients with early-stage NSCLC, and dedicated studies in locally advanced disease are warranted. Second, although the sample size met the pre-specified target for the primary endpoint, it remains underpowered for detecting differences in rare complications or for conducting meaningful subgroup analyses. The wide confidence intervals surrounding the hazard ratios (DFS: 0.50-1.66; OS: 0.42-1.84) underscore this imprecision and preclude any definitive claim of equivalence. Third, the median follow-up of 38 months, while sufficient for 3-year survival estimates, remains insufficient to assess 5-year OS and DFS, which represent the gold standard for oncological outcomes in NSCLC. Fourth, we did not collect patient-

reported outcome measures (PROMs) such as quality of life or chronic pain scores, which are increasingly recognized as important endpoints in thoracic surgery. Fifth, the generalizability of our findings may be limited by the single-institution setting and the specific surgical techniques employed; multi-center validation is warranted. Sixth, the learning curve for single-port VATS may have influenced operative time and outcomes, although all procedures were performed by experienced surgeons past their learning curve (>200 prior thoracoscopic lobectomies). Seventh, although all procedures were performed by the same surgical team with comparable expertise in both approaches, we cannot fully exclude that subtle differences in individual surgeon comfort with or preference for each technique may have influenced operative time and blood loss. However, because all surgeons had passed their learning curve and the choice of approach was based on patient-specific anatomical criteria rather than surgeon preference, this potential bias is likely to be modest. Finally, the choice between single-port and two-port approaches was at the surgeon's discretion rather than randomized, potentially introducing selection bias despite PSM.

Clinical implications and future directions

These findings have several clinical implications. Single-port thoracoscopic lobectomy offers measurable short-term advantages in pain control, inflammatory response, and pulmonary function recovery without compromising oncological radicality or 3-year survival. These benefits may be particularly relevant for elderly patients, those with limited pulmonary reserve, or individuals in whom enhanced recovery and early return to baseline function are prioritized. However, the longer operative time and technical demands of single-port VATS necessitate adequate training and case volume to achieve optimal outcomes.

Future research should focus on: (i) prospective randomized controlled trials with standardized perioperative protocols to definitively compare these approaches; (ii) extended follow-up to 5 years to confirm long-term oncological equivalence; (iii) incorporation of patient-reported outcomes and cost-effectiveness analyses; and (iv) investigation of the learning curve and training requirements for single-port VATS to facilitate wider adoption.

Conclusion

In this propensity score-matched retrospective cohort study, single-port thoracoscopic lobectomy for NSCLC was associated with reduced surgical trauma, decreased postoperative pain and systemic inflammation, and improved early pulmonary function recovery compared with the two-port approach. Importantly, these short-term benefits were achieved without compromising lymph node dissection adequacy, 30-day safety, or 3-year oncological outcomes including overall survival, disease-free survival, and recurrence patterns. While awaiting confirmation from prospective randomized trials with extended follow-up, these findings support the continued use and wider adoption of single-port VATS in appropriately selected patients with NSCLC.

Disclosure of conflict of interest

None.

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