Article

Effect of Anatomical Pulmonary Segmentectomy and Lobectomy under Uniportal Video-Assisted Thoracoscopic Surgery on Cardiopulmonary Function and Serum Tumor Markers in Patients with Early-Stage Non-Small Cell Lung Cancer

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AIM: In patients with early non-small cell lung cancer (NSCLC), single-port thoracoscopic anatomical segmentectomy is the primary therapeutic approach. However, the recovery of lung function is slow after operation. Conversely, anatomical segmental pneumonectomy, which excises a smaller volume of lung tissue, may facilitate more rapid functional recovery. This study aims to elucidate the comparative efficacy of these two surgical interventions by analyzing postoperative changes in cardiopulmonary function parameters and serum tumor markers.

METHODS: A retrospective analysis was conducted on 120 patients with NSCLC between October 2020 and October 2023. The cohort was classified into two groups based on the surgical intervention: the pulmonary segmentectomy group (n = 57), which underwent uniportal video-assisted thoracoscopic anatomical pulmonary segmentectomy, and the lobectomy group (n = 63), which received uniportal video-assisted thoracoscopic anatomical lobectomy. Surgical parameters and perioperative stress indicators were recorded for both groups of patients. Additionally, cardiopulmonary function indicators and serum biomarker levels of the patients before and 3 months after operation were compared.

RESULTS: The operation time of the segmentectomy group was longer than that of the lobectomy group, the intraoperative blood loss was higher, and the postoperative hospital stay, chest drainage volume and drainage tube indwelling time were shorter ($p < 0.001$). After treatment, forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC and maximal voluntary ventilation (MVV) in the segmentectomy group were higher than those in the lobectomy group ($p < 0.001$). After treatment, stroke volume (SV) and left ventricular ejection fraction (LVEF) in the segmentectomy group were higher than those in the lobectomy group ($p < 0.001$). There were no significant differences in carbohydrate antigen 50 (CA50), carcinoembryonic antigen (CEA) and cytokeratin 19 fragment antigen 21-1 (CYFRA21-1) levels between the two groups after treatment ($p > 0.05$). The levels of Epinephrine (E), Noradrenaline (NE) and Cortisol (Cor) in the segmentectomy group were lower than those in the lobectomy group at one day after operation ($p < 0.001$).

CONCLUSIONS: Compared to uniportal video-assisted thoracoscopic anatomical lobectomy, anatomical pulmonary segmentectomy for the treatment of NSCLC is more effective in reducing surgical-induced damage to cardiopulmonary function and can lower perioperative oxidative stress response. However, both surgical approaches exhibit minimal impact on serum tumor marker levels.

Keywords: NSCLC; uniportal video-assisted thoracoscopic surgery; anatomical pulmonary segmentectomy; anatomical pulmonary and lobectomy; early stage; cardiac function; pulmonary function; tumor markers

Introduction

Non-small cell lung cancer (NSCLC) is a malignant tumor originating from the epithelial cells of the bronchial mucosa or alveoli, with an increasing incidence observed in younger populations in recent years. At present, surgical treatment is the recommended therapeutic approach for patients with early-stage lung cancer, which can achieve a radical cure by removing the tumor [1]. Uniportal video-assisted thoracoscopic lobectomy has emerged as a prevalent surgical method for the treatment of early-stage NSCLC, demonstrating efficacy in lesion excision. However, postoperative pulmonary function recovery remains suboptimal in some cases, presenting a clinical challenge [2]. A previous study found that anatomical segmentectomy removes less lung tissue, facilitating quicker postoperative lung tissue expansion. This accelerated expansion contributes to enhanced patient recovery and a subsequent reduction in postoperative complications [3]. Anatomical pulmonary segmentectomy is defined as the resection of peripheral lung segments based on the location of the lesion or anatomical characteristics, performed via uniportal video-assisted thoracoscopic surgery. This technique ensures adequate resection margins while preserving adjacent pulmonary tissue [4]. However, due to strict indications, the clinical application of this procedure remains in the investigational stage. Based on this, this study aimed to compare the therapeutic effects of uniportal video-assisted thoracoscopic anatomical lung segmentectomy and anatomical pulmonary lobec-

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tomy in the treatment of NSCLC. The study utilized pre- and post-operative changes in patients' cardiopulmonary function and serum tumor markers as primary endpoints. This approach was designed to provide valuable insights into the optimal clinical treatment of this disease.

Materials and Methods

Clinical Data

The inclusion criteria were as follows: (1) Meeting the diagnostic criteria of NSCLC, and through pathological diagnosis [5]. (2) The Karnofsky score was $>$70 [6]. (3) The tumor diameter was $\leq$2 cm. (4) The clinical stage was T1N0. The exclusion criteria were as follows: (1) Patients with benign pulmonary lesions. (2) Patients who had received chemoradiotherapy or surgery before enrollment. (3) Patients with extensive pleural adhesions. (4) Patients with a history of chest surgery. (5) Patients were converted from thoracoscopic surgery to open surgery. (6) Preoperative imaging examination revealed mediastinal hilar lymph node metastasis. (7) Patient with a tumor in the middle lobe of the lung. (8) Patients who could not tolerate surgical treatment. (9) The distance of the lesion to the heart, great vessels, etc., was $<$10 mm.

According to the inclusion and exclusion criteria, patients' data from October 2020 to October 2023 were retrospectively analyzed and matched using propensity scores. A propensity scoring model was established using binary logistic regression to ensure no statistically significant baseline differences between groups. The final cohort comprised 120 patients with early-stage NSCLC. Subjects were divided into two groups: the pulmonary segmentectomy group (n = 57, patients underwent uniportal video-assisted thoracoscopic anatomical pulmonary segmentectomy) and the lobectomy group (n = 63, patients received uniportal video-assisted thoracoscopic anatomical lobectomy). This study adhered to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Institutional Medical Ethics Committee. Informed consent was obtained from all participants before the inclusion in the study.

Surgical Operation

To mitigate potential confounding variables related to surgical expertise and technical variations, all procedures in this study were performed by the same group of surgeons. This standardization aimed to eliminate the influence of interoperator variability on surgical outcomes.

Patients in the segmentectomy group underwent uniportal thoracoscopic anatomical segmentectomy. Anesthesia was uniformly administered across all patients, consisting of general anesthesia facilitated by double-lumen endotracheal intubation, ensuring optimal lung isolation and surgical field exposure. The patient was positioned in the lateral decubitus position. A 2 cm incision was made in the fourth intercostal space along the mid-axillary line. A 30° video-assisted thoracic cavity was inserted through this incision, facilitating both instrument manipulation and visual guidance operated through this port, a technique known as uniportal video-assisted thoracoscopic surgery. Following localization of the lung segment containing the lesion, the segmental pulmonary vasculature and bronchus were dissected and exposed. The intercostal fissure of the resected segment was treated with a thoracoscopic linear cutting stapler. The resected lung segments were subjected to intraoperative pathological examination. The vessels and bronchi corresponding to the target lung segment, as well as the intersegmental cleft, were dissected using a linear cutting stapler or ligated with sutures in combination with an ultrasonic scalpel.

The patients in the lobectomy group underwent uniportal video-assisted thoracoscopic anatomical lobectomy. Both anesthesia administration and thoracoscope insertion were conducted in the same manner as in the lung segmentectomy group. The lobar arteries, veins, and bronchi associated with the lesion were dissociated and exposed. Subsequently, the target blood vessels and bronchi were transected using a linear stapler. The diseased lung lobe was removed, and any underdeveloped interlobar fissures were transected using either a linear cutter or an ultrasonic scalpel.

For both groups of patients, the following criteria should be met for the removal of the chest drainage tube: (1) the drainage volume should be less than 150 mL within 24 h postoperatively, and (2) the postoperative chest X-ray should show good lung re-expansion without pleural effusion.

Clinical Efficacy

After 3 months of treatment, the same group of surgeons conducted a comprehensive evaluation of clinical efficacy in accordance with the World Health Organization's Response Evaluation Criteria in Solid Tumors (WHO RECIST) [7]. The assessment categorized outcomes into four distinct classifications: complete remission (CR) (all target lesions disappeared), partial response (PR) (reduction in the sum of target lesion diameters by a minimum of 30% from baseline measurements), stable disease (SD) (reduction in target lesion size insufficient to qualify as PR or increase insufficient to qualify as progressive disease; representing an intermediate state between PR and PD), and progressive disease (PD) (increase in the sum of target lesion diameters by at least 20% from baseline measurements). Two primary metrics were utilized to quantify treatment efficacy: (1) disease control rate (DCR) = CR + PR + SD, and (2) objective response rate (ORR) = CR + PR.

Indicators of Observation

Indicators Related to the Operation

The following perioperative parameters were compared between the segmentectomy and lobectomy groups: operation

Table 1. Comparison of the clinical data between the two groups.

Classification		Segmentectomy group (n = 57)	Lobectomy group (n = 63)	χ^2/t	*p*
Sex (case)	male	31	36	0.092	0.761
	female	26	27		
Age		61.38 ± 6.24	62.04 ± 6.31	0.575	0.566
Smoking		24	23	0.393	0.530
Alcohol consumption		15	19	0.218	0.641
Combined hypertension		9	7	0.567	0.452
Diabetes mellitus		8	12	0.541	0.462
Location of the lesion	upper lobe of left lung	15	16	0.020	0.999
	lower lobe of left lung	11	12		
	upper lobe of right lung	14	16		
	lower lobe of left lung	17	19		
Karnofsky score		91.54 ± 4.03	91.38 ± 3.95	0.219	0.827

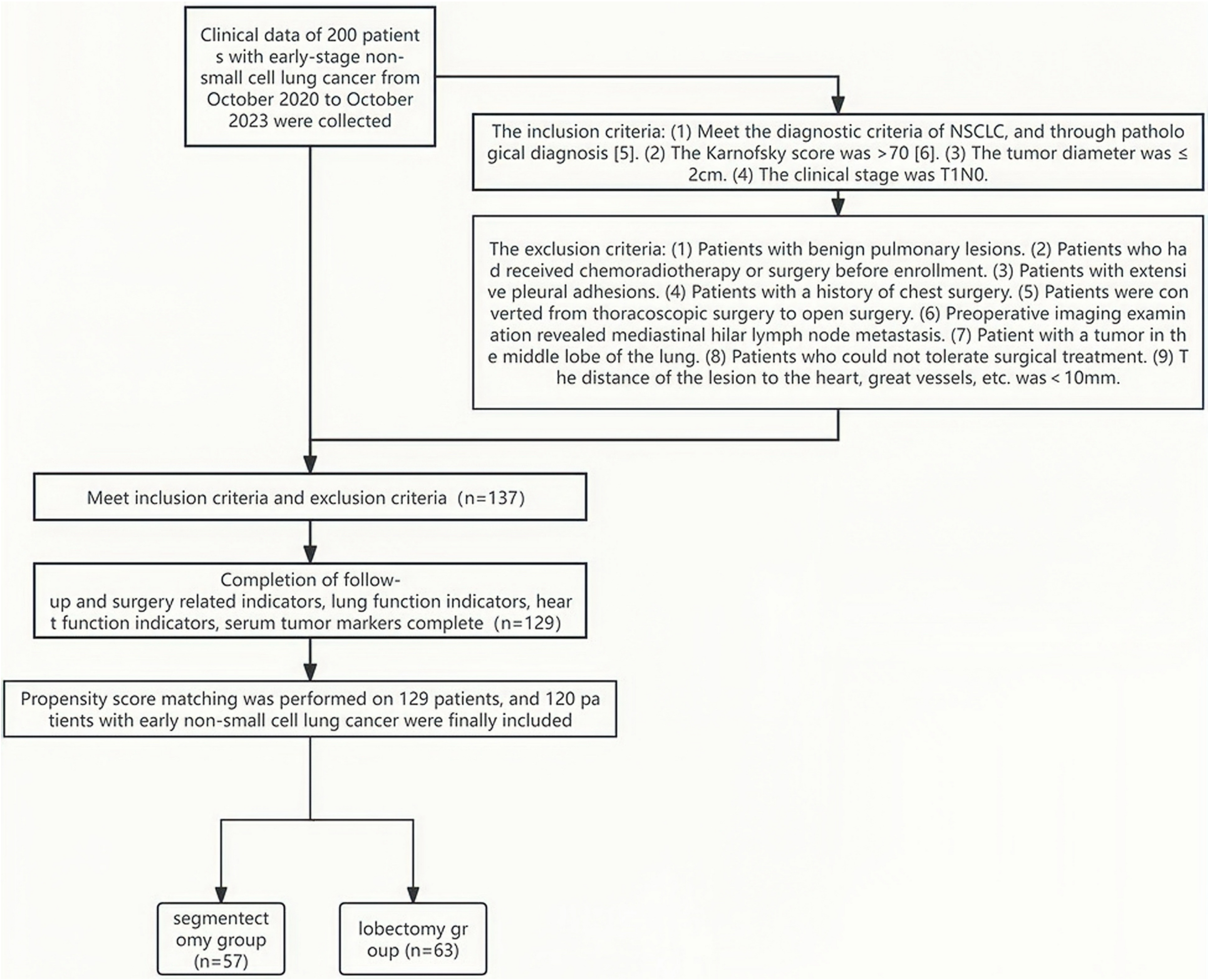

Fig. 1. Patient selection flow chart. NSCLC, non-small cell lung cancer.

time, intraoperative blood loss volume, length of hospital stay, postoperative chest lead flow and drainage tube indwelling time.

Pulmonary Function Indicators

Pulmonary function was assessed using the JAEGER MasterScreen PFT System at two time points: immediately after surgery and three months after surgery. The primary indicators evaluated were forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and maximal voluntary ventilation (MVV).

Table 2. Comparison of the efficacy between the two groups n (%).

Group	n	CR	PR	SD	PD	ORR	DCR
Segmentectomy group	57	18 (31.58)	21 (36.84)	17 (29.82)	1 (1.75)	39 (68.42)	56 (98.25)
Lobectomy group	63	15 (23.81)	22 (34.92)	21 (33.33)	5 (7.94)	37 (58.73)	58 (92.06)
χ^2						1.210	1.282
p						0.271	0.257

CR, complete remission; PR, partial response; SD, stable disease; PD, progressive disease; DCR, disease control rate; ORR, objective response rate.

Cardiac Function

EPIQ CVx color echocardiography diagnostic instrument (Philips Company) was applied to measure the heart rate (HR), stroke volume (SV), and left ventricular ejection fraction (LVEF) before and three months after treatment.

The Levels of Tumor Marker

The serum concentrations of cytokeratin 19 fragment antigen 21-1 (CYFRA21-1, national instrument registration: 20153401237) were quantified in the two groups using an electrochemiluminescence immunoassay. Carbohydrate antigen 50 (CA50, national instrument registration: 20153400050) and carcinoembryonic antigen (CEA, national instrument registration: 20163402679) levels were measured by radioimmunoassay. All assay kits were obtained from Zhengzhou Antu Biological Engineering Co., Ltd., Zhengzhou, China.

Perioperative Stress Indicators

Venous blood samples (3 mL per subject) were obtained from both groups following an overnight fast. Samples were centrifuged using a Z206A medical centrifuge (German Hermle Biotechnology, Wehingen, Germany) to isolate serum. Serum concentrations of Epinephrine (E), Noradrenaline (NE) and Cortisol (Cor) were quantified by radioimmunoprecipitation method (Shanghai Xinfan Biotechnology) before and 1 day after operation.

Statistical Analysis

Statistical analysis was conducted using SPSS version 22.0 (International Business Machines Corporation, Armonk, NY, USA). Categorical variables were presented as %, and the differences were compared by χ^2 test. The measurement data were expressed as ($\bar{x} \pm$ s) after normality test, and the differences between groups were compared using the *t* test. A *p*-value < 0.05 was considered statistically significant.

Results

Comparison of the Clinical Data between the Two Groups

A retrospective analysis was conducted on 120 patients with NSCLC (Patient selection flow chart, as shown in Fig. 1). There were no significant differences in gender, age, lesion location, and other clinical data between the two groups ($p > 0.05$), as shown in Table 1.

Comparison of the Efficacy between the Two Groups

There was no significant difference in ORR and DCR between the two groups ($p > 0.05$), as shown in Table 2.

Comparison of Surgical-Related Indicators between the Two Groups

The operation time of the segmentectomy group was longer than that of the lobectomy group, the intraoperative blood loss was higher than that of the lobectomy group, and the postoperative hospital stay, chest drainage volume and drainage tube indwelling time were shorter than those of the lobectomy group ($p < 0.001$) (Fig. 2).

Comparison of Lung Function between the Two Groups

There were no statistically significant differences in FEV_1, FVC, FEV_1/FVC and MVV between the two groups before treatment ($p > 0.05$). After treatment, FEV_1, FVC, FEV_1/FVC and MVV in the segmentectomy group were higher than those in the lobectomy group ($p < 0.001$) (Fig. 3).

Comparison of Cardiac Function Index between the Two Groups

There were no significant differences in HR, SV and LVEF between the two groups before treatment. The SV and LVEF after treatment in the segmentectomy group were higher than those in the lobectomy group ($p < 0.001$) (Fig. 4).

Comparison of Tumor Markers between the Two Groups

There were no statistically significant differences in the serum concentrations of CA50, CEA, and CYFRA21-1 between the two groups before treatment ($p > 0.05$). After treatment, the levels of CA50, CEA, and CYFRA21-1 in the two groups were significantly lower than those before treatment ($p < 0.001$). There was no significant difference in CA50, CEA and CYFRA21-1 levels between the two groups after treatment ($p > 0.05$) (Fig. 5).

Comparison of Perioperative Stress Indicators between the Two Groups

No statistically significant differences were observed in the preoperative levels of E, NE, and Cor between the two groups ($p > 0.05$). However, one day after surgery, the segmentectomy group exhibited significantly lower concentrations of E, NE, and Cor compared to the lobectomy group ($p < 0.001$) (Fig. 6).

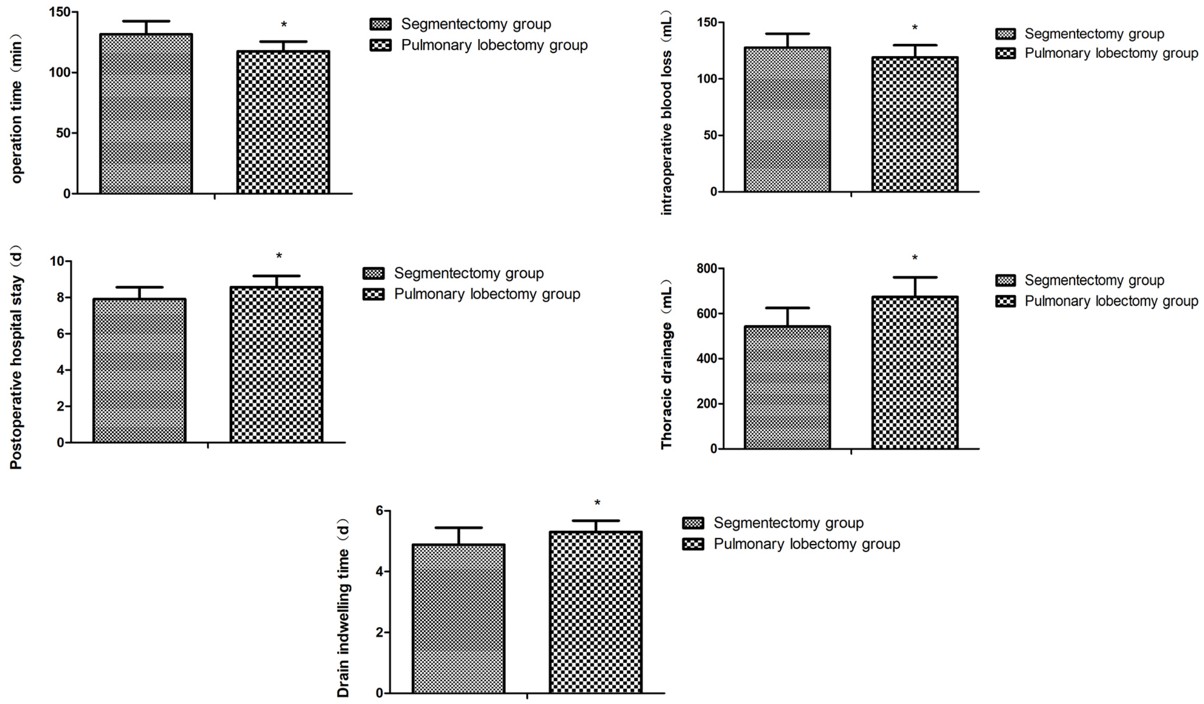

Fig. 2. Comparison of surgical-related indicators between the two groups. ($\bar{x} \pm$ s) (Note: compared with the segmentectomy group, *$p < 0.001$).

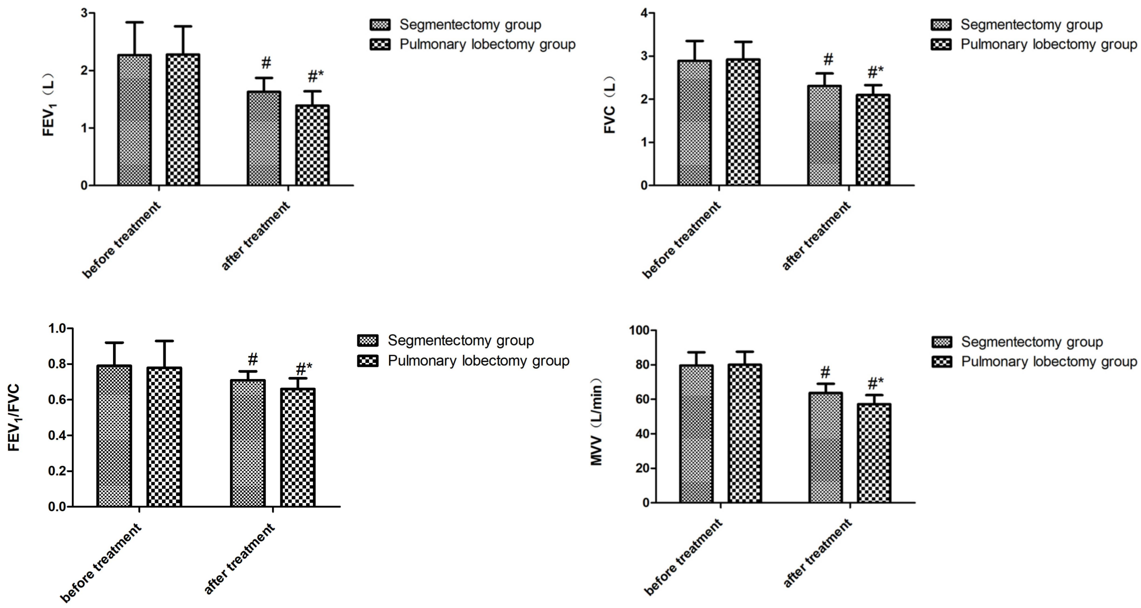

Fig. 3. Comparison of lung function between the two groups. ($\bar{x} \pm$ s) (Note: compared with preoperative, $^{\#}p < 0.05$; compared with segmentectomy group, *$p < 0.001$). FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; MVV, maximal voluntary ventilation.

Comparison of Postoperative Complications between the Two Groups

There was no significant difference in the incidence of postoperative complications between the two groups ($p > 0.05$) (Table 3).

Discussion

NSCLC is a kind of malignant tumor originating from bronchial mucosal epithelial cells, which is related to smoking, air pollution, ionizing radiation and other factors. In the early stage, patients have no obvious symptoms, but

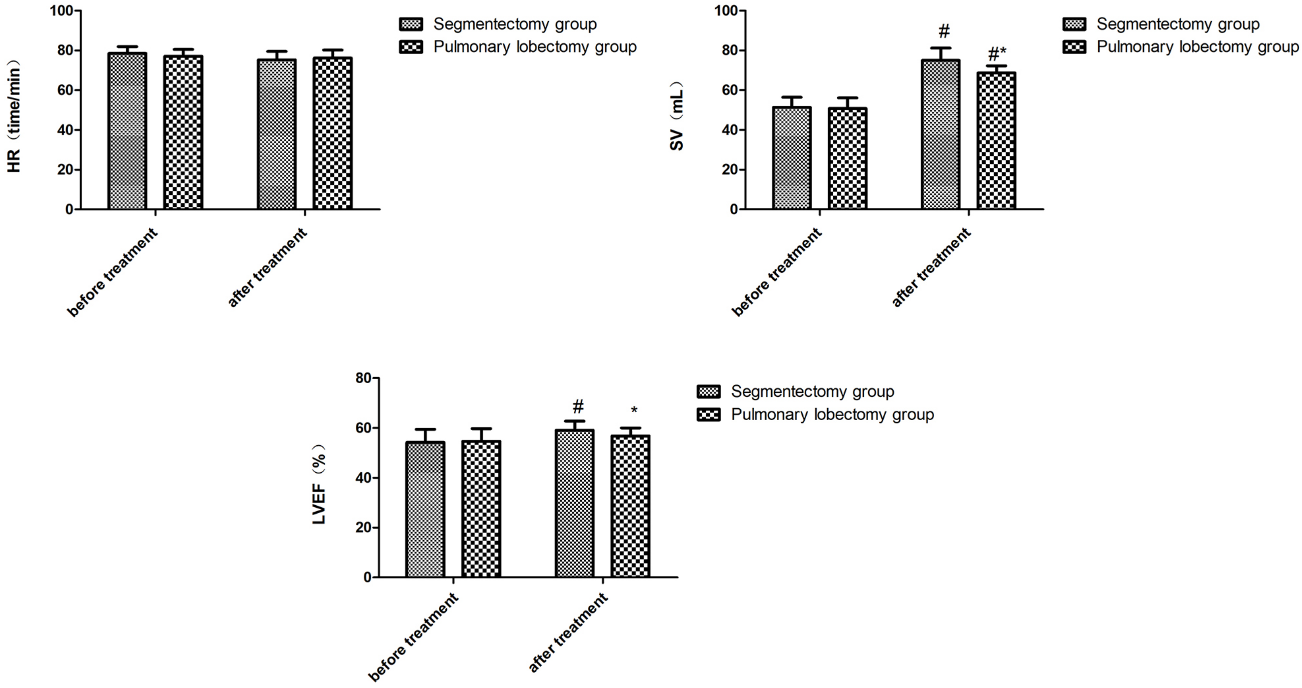

Fig. 4. Comparison of cardiac function index between the two groups. ($\bar{x} \pm$ s) (Note: compared with preoperative, $^{\#}p < 0.05$; compared with segmentectomy group, $^{*}p < 0.001$). HR, heart rate; SV, stroke volume; LVEF, left ventricular ejection fraction.

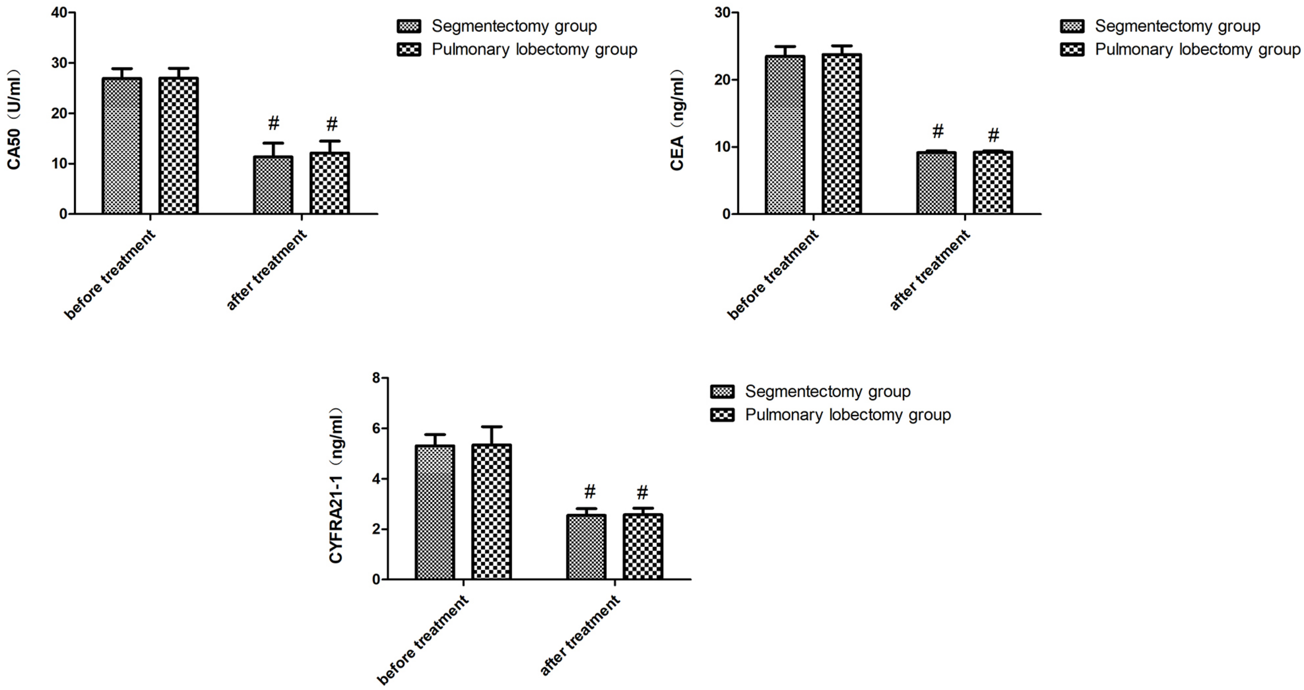

Fig. 5. Comparison of tumor markers between the two groups. ($\bar{x} \pm$ s) (Note: compared with the segmentectomy group, $^{\#}p < 0.001$). CA50, carbohydrate antigen 50; CEA, carcinoembryonic antigen; CYFRA21-1, cytokeratin 19 fragment antigen 21-1.

some patients may have clinical manifestations such as cough and expectoration [8]. At present, surgical intervention remains the primary treatment modality for NSCLC. Video-assisted thoracoscopic lobectomy has been widely used both domestically and internationally for the treatment of early-stage NSCLC, with its safety, minimally invasive, and efficacy well-established in the literature [9,10]. In recent years, there has been a notable increase in the clinical application of anatomical pulmonary resection techniques [11]. Anatomical studies on lung segments have found that each lung segment has its own separate blood vessel and bronchus, and adjacent segments share a single vein,

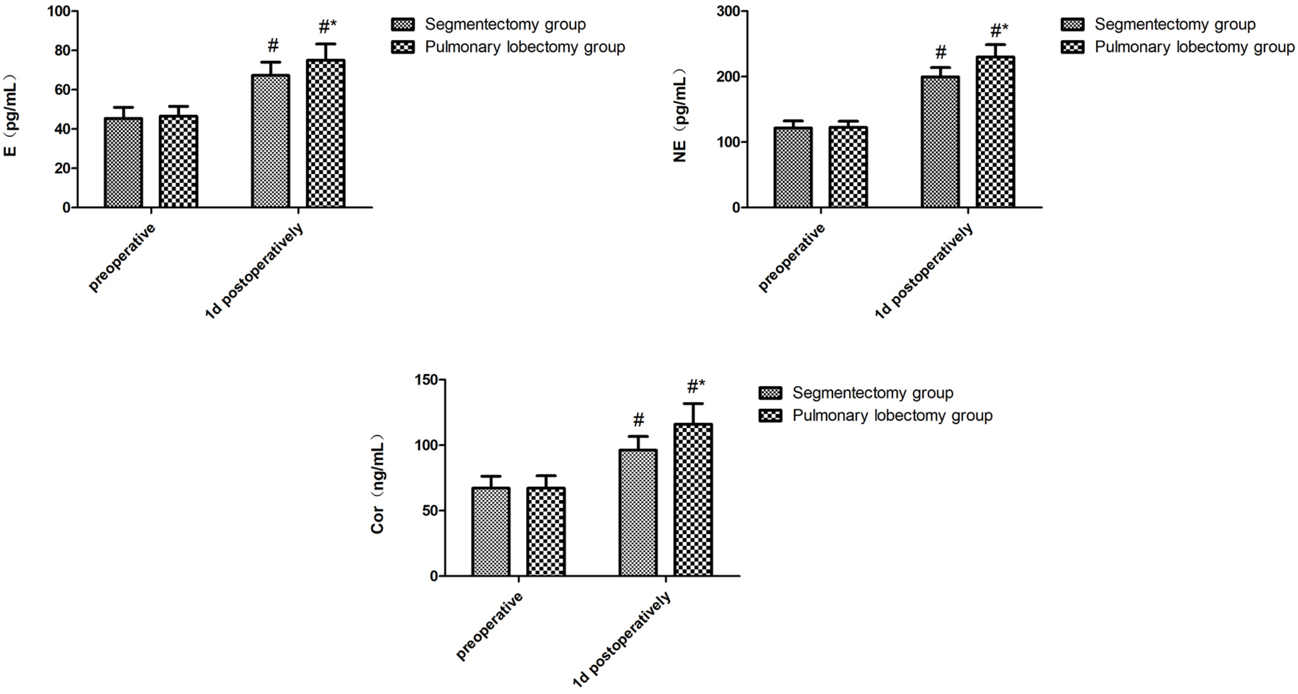

Fig. 6. Comparison of perioperative stress indicators between the two groups. ($\bar{x} \pm$ s) (Note: compared with preoperative, $^{\#}p <$ 0.001; compared with segmentectomy group, $^{*}p < 0.001$).

Table 3. Comparison of postoperative complications between the two groups n (%).

Group	n	Pulmonary infection	Arrhythmology	Atelectasis of lung	Overall incidence
Segmentectomy group	57	1 (1.75)	0 (0.00)	1 (1.75)	2 (3.51)
Pulmonary lobectomy group	63	2 (3.17)	2 (3.17)	1 (1.59)	5 (7.94)
χ^2					0.414
p					0.520

with relatively independent blood supply circulation systems and separate bronchial branches. Therefore, it is feasible to anatomically separate the bronchi and blood vessels of lung segments and remove the corresponding lung tissue. Previous studies have demonstrated that anatomical segmentectomy yields favorable therapeutic outcomes [12,13]. Tumor markers serve as crucial parameters for assessing the severity of tumor and their therapeutic effect. CA50 is a commonly used tumor marker in clinical practice, exhibiting enhanced sensitivity for lung cancer diagnosis. CYFRA21-1, a proteolytic product of CK19, is mainly expressed in lung squamous cell carcinoma and lung adenocarcinoma and can be used for early diagnosis of NSCLC. CEA remains the most frequently used tumor marker in clinical practice, which is highly expressed in a variety of tumor diseases [14]. Clinical study has found that tumor marker levels decrease in patients undergoing tumor resection or experiencing lesion shrinkage, underscoring their significance in evaluating therapeutic efficacy [15]. In this study, no statistically significant differences were observed in ORR, DCR, or post-treatment tumor marker levels between the two groups. This finding suggests comparable therapeutic efficacy of both surgical approaches for early-stage NSCLC, primarily attributable to the effective resection of tumor lesions achieved by both methods. Related studies have found that the variation of segmental lung structure is diverse, with deep positions of segmental lung vessels and bronchi. This anatomical complexity often impedes complete exposure of these structures, thereby increasing the technical challenges associated with intraoperative dissection. Consequently, this anatomical intricacy may contribute to prolonged operative durations [16]. This study found that the operation time for the segmentectomy group was longer than that for the lobectomy group, intraoperative blood loss was higher than that for the lobectomy group, and postoperative hospital stay, chest drainage volume, and duration of drainage tube placement were shorter than those for the lobectomy group. The results showed that segmentectomy was associated with prolonged operative duration and increased intraoperative blood loss. However, patients recovered well after the operation, which was consistent with the above study results. The reason is that compared to lobectomy, anatomical segmentectomy is more difficult to dissect the segmental vessels due to the variation between the segmental vessels, which leads to more complicated surgical procedures, and therefore the operation takes longer time and requires more intraoperative blood loss. However, segmentectomy has less impact on the lung tissue because of the small lesion, which can promote the postoperative recovery of patients [17].

The current scientific consensus suggests that the early recovery of pulmonary function following surgical intervention is crucial for the effective clinical treatment of early-stage NSCLC [18]. The results of this study show that the values for FEV_1, FVC, FEV_1/FVC, and MVV were higher in the segmentectomy group compared to the lobectomy group after treatment, indicating that anatomical segmentectomy can reduce the damage of lung function during the treatment of NSCLC, which is mainly related to the preservation of a greater volume of lung tissues. Anatomical segmentectomy can not only ensure the size of the resection range but also retain more lung tissue. It can reduce the occurrence of complications such as pain caused by thoracotomy, intercostal muscle incision, rib injury and atelectasis, postoperative pulmonary infection, and respiratory insufficiency, which is conducive to the recovery of postoperative pulmonary function. In addition, due to the small extent of lung tissue resection and the small expansion compensation effect, the lung function is less affected by the change of bronchial angle, and the lung function can also be protected to a certain extent [19]. This study also found that the SV after lung resection in the segmentectomy group was significantly higher compared to the lobectomy group, suggesting that anatomical lobectomy for NSCLC has a greater negative impact on postoperative cardiac function. This is mainly because more pulmonary arteries and veins need to be blocked in lobectomy compared to segmentectomy, which leads to a greater reduction of heart blood flow. At the same time, the amplitude of mediastinal deviation after lobectomy is larger than that of segmentectomy, resulting in greater impairment of postoperative cardiac function.

Surgical treatment can induce stress reactions in patients due to the effects of anesthesia drugs and surgical stimuli on the body. Several key stress indicators are commonly measured, including E, NE, and Cor. These hormones play a key role in several stress responses. When the body is stimulated by surgery, it can increase the levels of glucocorticoid and the secretion of adrenocortical hormone [20]. Patients who experience prolonged high levels of stress after surgery may exhibit reduced adaptability, which can impact postoperative rehabilitation [21,22]. The results of this study showed that the concentrations of E, NE, and Cor in the segmentectomy group were significantly lower than those in the lobectomy group one day after surgery. These findings suggest that anatomical segmentectomy can reduce the perioperative oxidative stress response, primarily due to the reduced extent of lung tissue resection during segmentectomy. Consistent with previous research, anatomical lung segmentectomy has been shown to preserve a greater amount of lung tissue, thereby facilitating easier postoperative re-expansion of lung tissue. Consequently, the incidence of postoperative complications is lower [23]. The results of this study revealed no statistically significant difference in the prevalence of postoperative complications between the two groups, suggesting that the lobectomy intervention does not increase the incidence of postoperative complications, which is inconsistent with the result of related study [23]. This discrepancy may be related to the limited sample size of patients included in this study. Consequently, further analysis is needed in the future.

Conclusions

Compared to uniportal video-assisted thoracoscopic anatomical lobectomy, anatomical pulmonary segmentectomy for the treatment of NSCLC is more effective in reducing surgical-induced damage to cardiopulmonary function and can lower perioperative oxidative stress response. Conversely, both surgical approaches demonstrate minimal impact on clinical efficacy and serum tumor marker levels. However, this study still has some limitations. Due to strict indications for uniportal video-assisted thoracoscopic anatomical lung segmentectomy, the number of cases treated with this surgery is lower compared to the lobectomy group and the follow-up time for patients is short. Therefore, it is necessary to increase the sample size and extend the observation time in the later stage for further research to address these limitations.

Availability of Data and Materials

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

Author Contributions

YTS and SX designed the research study and wrote the manuscript. YTS performed the research. SX provided help and advice on the electrochemiluminescence immunoassay and radioimmunoassay experiments. YTS analyzed the data. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study adhered to the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Ningbo No.2 Hospital Ethics Committee (approval number: PJ-NBEY-KY-2024-104-01). Informed consent was obtained from all participants before the inclusion in the study.

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Conflict of Interest

The authors declare no conflict of interest.

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