

# Pulmonary function changes after thoracoscopic lobectomy versus intentional thoracoscopic segmentectomy for early-stage non-small cell lung cancer

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**Background:** Thoracoscopic segmentectomy is increasingly used in the surgical treatment of early-stage non-small cell lung cancer. However, it remains unclear whether pulmonary function loss after thoracoscopic lung resection is in direct proportion to the number of resected segments, and thus intentional thoracoscopic segmentectomy has the function-preserving advantage over thoracoscopic lobectomy.

**Methods:** In this prospective observational study, spirometry tests were performed preoperatively and 6 months postoperatively. The observed functional loss was compared with the expected loss estimated by the segment counting method. Resection extent index was introduced as the number of resected segments to total number of segments in the corresponding lobe. Spirometry changes after thoracoscopic lobectomy and intentional thoracoscopic segmentectomy were compared using propensity score matching.

**Results:** There were 338 thoracoscopic lobectomies and 321 thoracoscopic segmentectomies. Overall, the observed pulmonary function loss after segmentectomy was significantly less than after lobectomy. But the observed functional loss was significantly greater than the expected loss after segmentectomy. And pulmonary function loss per segment resected was almost doubled after segmentectomy comparing to lobectomy. For segmentectomies with a resection extent index less than 0.5, especially single segmentectomies, pulmonary function loss was significantly less than after corresponding lobectomies. Otherwise, no significant differences in spirometry changes between lobectomies and segmentectomies were detected.

**Conclusions:** Pulmonary function loss after thoracoscopic lung resection cannot be accurately evaluated by the number of resected segments. According to the resection extent index, intentional thoracoscopic segmentectomy may help preserve more pulmonary function than thoracoscopic lobectomy only when less than half of the corresponding lobe are resected.

Keywords: Lobectomy; pulmonary function; segmentectomy; video-assisted thoracic surgery (VATS)

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# Introduction

Lung cancer remains one of the leading causes of cancer incidence and mortality worldwide (1). Over the past decades, lobectomy with systemic lymph node dissection has been the gold standard for surgical treatment of stage IA non-small cell lung cancer (NSCLC). With the increasing use of low-dose computed tomographic screening, lung cancers tend to be diagnosed at an earlier stage (2). Sublobar resection such as segmentectomy, which used to be applied only in functionally compromised patients (3), is now increasingly used as an intentional procedure in goodrisk surgical candidates. The two phase III multicenter prospective randomized trials comparing lobectomy and sublobar resections (JCOG0802/WJOG4607L and CALGB/ALLIANCE 140503) have already reported their perioperative outcomes (4,5), showing little difference between lobectomy and segmentectomy in the perioperative mortality and morbidity in functionally fit patients. Recently, JCOG0802/WJOG4607L trial has reported its follow-up results, revealing that segmentectomy might offer survival and functional benefits over lobectomy (6).

One of the major reasons for performing segmentectomy instead of lobectomy in good-risk patients is that segmentectomy may help preserve more pulmonary function than lobectomy, which is based on the assumption that postoperative pulmonary function loss is in direct proportion to the number of lung parenchyma units resected (7). In this study, we aimed to verify the consistency between expected and postoperative function loss actually observed after video-assisted thoracic surgery (VATS) in good-risk patients, taking into account that postoperative pulmonary function changes may be affected by the various factors including baseline lung function, the interval between surgery and the postoperative spirometry test, surgical incisions, different compensatory lung expansion after various extent of resections and location of the resected lobes (8). In addition, we further investigated which VATS segmental resections would be truly superior to its corresponding VATS lobectomy in pulmonary function preservation, as according to our previous findings, VATS segmentectomy was associated with better pulmonary function preservation in general, but was also associated with more function loss per segment resected than VATS lobectomy (9). We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/tlcr-21-661).

#### Methods

# Study design

This was a prospective observational study in consecutive patients who underwent thoracoscopic lobectomy or segmentectomy for clinical stage IA NSCLC according to the eighth edition TNM stage classification (10) by a single team of surgeons at the Shanghai Chest Hospital during 2012 to 2018. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethical committee of the Shanghai Chest Hospital (No. ks11014) and informed consent was taken from all individual participants. All patients included in this study were functionally fit for standard lobectomy. Exclusion criteria were as follows (Figure 1): patients with a history of previous lung surgery on the ipsilateral side, lesions in the right middle lobe or need multiple resections in different lobes. Patients in whom postoperative adjuvant therapies were considered necessary were also excluded for fear that follow-up treatment might have certain impact on pulmonary function recovery (11). Patients who suffered severe postoperative complications were not included, such as bronchopleural fistula, respiratory failure, pulmonary embolism, etc. And those who had inadvertent phrenic nerve injury during surgery were also not included (12). The indications for intentional segmentectomy in the current study followed the National Comprehensive Cancer Network guideline, which were peripherally located nodules  $\leq 2$  cm whereby a safe resection margin could be achieved by sublobar resection, together with at least one of the following factors: pure adenocarcinoma in situ, nodules with  $\geq$ 50% ground-glass appearance on computed tomography, radiologic surveillance confirmed a long doubling time (≥400 days) (13). Otherwise, a lobectomy was considered necessary. Both procedures were conducted by three-port VATS. Segmental pulmonary veins, arteries, and bronchus were divided separately during segmentectomy. Staplers were used to divide the intersegmental plane according to an inflation-deflation line (14). Single segmentectomy was defined as resection of only one segment, while combined segmentectomy referred to resection of two or more adjacent segments.

# Postoperative course and follow-up

After the surgery, all the patients were encouraged to become ambulatory and do the respiratory function

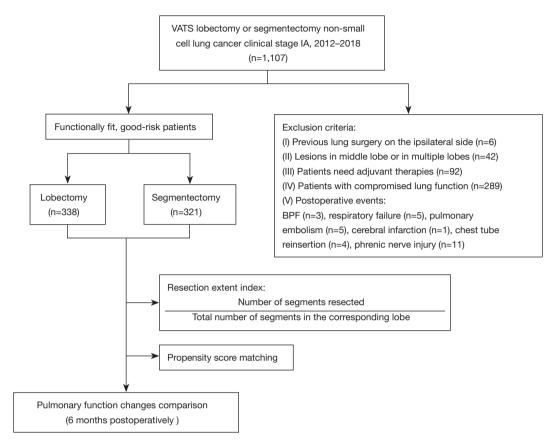


Figure 1 The flow chart of the patients in this study. BPF, bronchopleural fistula; VATS, video-assisted thoracic surgery.

training, and they were discharged with good lung expansion. No reoperation or readmission occurred in patients included in this study. And the postoperative surveillance included check up of recovery and evaluation of potential adjuvant therapies one month after surgery, chest CT scan, serum tumor markers, neck and abdominal ultrasonography performed every 6 months during the first 2 years and then annually.

## **Pulmonary function tests**

Pulmonary function tests were performed according to American Thoracic Society standards (15) preoperatively and repeated 6 months postoperatively upon follow-up at out-patient clinic, including 3 parameters: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and diffusing capacity of the lungs for carbon monoxide (DLCO). The expected postoperative pulmonary function was calculated based on the conventional segment counting method:

The total number of segments was deemed to be 18 in both lungs, including 3 in the right upper lobe, 2 in the right middle lobe, 5 in the right lower lobe, and 4 in the left upper and lower lobes each (16). The following formulas were used to evaluate the observed or expected pulmonary function loss after surgery and average pulmonary function loss per segment resected, respectively:

Pulmonary function loss  
= 
$$\frac{Postoperative function - preoperative function}{Preoperative function} \times 100\%$$
 [2]

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The ratio of the observed to expected postoperative pulmonary function loss (O/E ratio) was then calculated by the following formula:

$$O/E \ ratio = \frac{The \ observed \ pulmonary \ function \ loss}{The \ expected \ pulmonary \ function \ loss}$$
[4]

Resection extent index (listed in Table S1) was calculated as follows:

Since average functional loss per segment resected was found to be almost doubled after segmentectomies than after lobectomies in our previous study (9), indicating that when the number of resected segments was reaching half of the corresponding lobe, the potential functional benefit of segmentectomy would become negligible. Thus, the cutoff point for resection extent index in this study was set at 0.5.

#### Statistical analysis

Categorical variables were expressed as count and percentage, while continuous variables were presented as mean ± standard deviation. Differences in categorical variables were assessed by Chi-squared test, while Student's t-test was used to compare continuous variables. The consistency between observed and expected pulmonary function loss was evaluated by intraclass correlation coefficients (ICC) for single measures with a two-way random model and absolute agreement, and the ICC value greater than 0.70 was considered acceptable (17). Since this was not a randomized trial, 1:1 propensity score matching (PSM) was adopted via the nearest neighbor method, no replacement and 0.05 caliper width between the imbalanced groups to diminish the potential influences on pulmonary function preservation from the following variables: sex, age, smoking history, chronic obstructive pulmonary disease (COPD) and tumor location (lobe of resection). The indications for surgery such as tumor size or radiological features, which were not associated with outcomes due to the hypothesis in this study, were not included into the PSM model (18). Statistical significance was defined as P value <0.05. Standardized mean difference was used to evaluate the degree of baseline variable balance, representing a high degree of balance when the difference was no more than 0.1 (19). SPSS v22.0 and R Project v4.0.3 were used for analysis. GraphPad Prism v8.0 and Photoshop v2020 were used for graphics production.

#### **Results**

Altogether 659 patients were enrolled, including 338 patients with VATS lobectomy and 321 patients with VATS segmentectomy. In the VATS segmentectomy group, there were 200 single segmentectomies and 121 combined segmentectomies, including 120 cases of twosegment resection and one case of four-segment resection (Table S1). No significant difference existed in demographic characteristics between the two groups, including smoking history (P=0.683) and COPD (P=0.779). No significant difference was detected in the baseline pulmonary function between the two groups (FVC: P=0.079; FEV1: P=0.128; DLCO: P=0.533). More segments were resected in the lobectomy group than in the segmentectomy group (P<0.001). Tumors in the segmentectomy group were of smaller sizes (P<0.001), in earlier T stages (P<0.001), and were of lower grade histology (P<0.001) than those in the lobectomy group (Table 1).

Poor consistency between the observed and expected pulmonary function loss was identified by the very low ICC values in *Table 2* (none of them greater or even close to the acceptable value of 0.70). The observed functional loss was significantly less than the expected loss after VATS lobectomy (FVC: P<0.001; FEV1: P=0.003; DLCO: P<0.001), but greater than the expected loss after VATS segmentectomy (FVC: P<0.001; FEV1: P<0.001; DLCO: P=0.001). The O/E ratio decreased accordingly as the number of resected segments increased (*Figure 2* and Table S2).

Overall, the observed pulmonary function loss after segmentectomy was significantly less than after lobectomy (FVC: P<0.001; FEV1: P<0.001; DLCO: P<0.001), while average pulmonary function loss per segment resected was significantly greater after segmentectomy than after lobectomy (FVC: P<0.001; FEV1: P<0.001; DLCO: P<0.001, Table 2). According to the resection extent index, 205 segmentectomies with a resection extent index less than 0.5 and 55 segmentectomies with a resection extent index no less than 0.5, paired with lobectomies respectively, were included after PSM (Figures 3,4). The baseline characteristics between the matched groups were well balanced (Figure S1), and a high degree of overlap in the distribution of propensity scores was demonstrated in Figure S2. FVC, FEV1 and DLCO loss were significantly greater after lobectomies than after single segmentectomies (FVC: P<0.001; FEV1: P<0.001; DLCO: P<0.001, Figure 4A) or after segmentectomies with a resection

Table 1 Clinical characteri	stics in natients r	eceiving VATS lobect	omy and VATS segmentectomy
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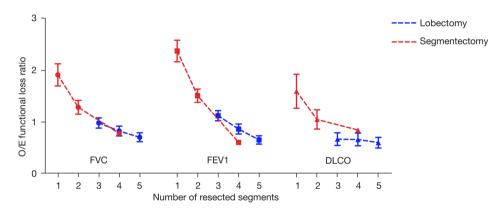
Variables	Lobectomy (n=338)	Segmentectomy (n=321)	P value
Sex, n (%)			0.751
Male	123 (36.4)	113 (35.2)	
Female	215 (63.6)	208 (64.8)	
Age (year), mean ± SD	59.1±9.2	57.7±9.5	0.065
BMI (kg/m²), mean ± SD	23.0±3.0	23.3±2.9	0.363
Smoking history, n (%)			0.683
Never smoker	274 (81.1)	264 (82.2)	
Former smoker	64 (18.9)	57 (17.8)	
Comorbidities, n (%)			
COPD	25 (7.4)	22 (6.9)	0.779
Hypertension	124 (36.7)	96 (29.9)	0.069
Diabetes	42 (12.4)	27 (8.4)	0.099
Baseline pulmonary function, mean $\pm$ SD			
FVC (%)	95.6±12.1	97.4±13.1	0.079
FEV1 (%)	94.3±13.7	96.0±14.5	0.128
DLCO (%)	98.8±17.0	99.6±15.8	0.533
Mean number of resected segments, mean $_{\pm}$ SD	3.7±0.8	1.4±0.5	<0.001
Duration of chest tube drainage (days), nean ± SD	4.45±2.57	3.89±2.16	0.003
Autologous blood pleurodesis, n (%)	7 (2.1)	1 (0.3)	0.069
īumor size (cm), mean ± SD	1.8±0.6	1.3±0.5	<0.001
stage, n (%)			<0.001
Tis	14 (4.1)	26 (8.1)	
T1mi	48 (14.2)	79 (24.6)	
T1a	26 (7.7)	50 (15.6)	
T1b	153 (45.3)	148 (46.1)	
T1c	97 (28.7)	18 (5.6)	
Histology, n (%)			<0.001
AIS	14 (4.1)	26 (8.1)	
MIA	48 (14.2)	79 (24.6)	
Invasive adenocarcinoma	264 (78.1)	212 (66.0)	
Squamous cell carcinoma	11 (3.3)	4 (1.2)	
Adenosquamous carcinoma	1 (0.3)	0	

VATS, video-assisted thoracic surgery; SD, standard deviation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity of the lungs for carbon monoxide; AIS, adenocarcinoma in situ; MIA, minimally invasive adenocarcinoma.

Parameters	Expected PFT loss (%)	Observed PFT loss (%)	Observed PFT loss per segment (%)	P value*	ICC
Lobectomy (n=338)					
FVC	-20.7±4.5	$-17.8 \pm 10.6^{\dagger}$	$-4.9{\pm}3.1^{\dagger}$	<0.001	0.086
FEV1	-20.7±4.5	$-18.9 \pm 10.4^{\dagger}$	$-5.3\pm3.2^{\dagger}$	0.003	0.007
DLCO	-20.7±4.5	$-13.6\pm13.0^{\dagger}$	$-3.7\pm3.7^{\dagger}$	<0.001	0.087
Segmentectomy (n=321)					
FVC	-7.7±2.8	$-12.1\pm8.6^{\dagger}$	$-9.3\pm7.4^{\dagger}$	<0.001	0.101
FEV1	-7.7±2.8	$-14.6\pm8.3^{\dagger}$	$-11.4\pm7.4^{\dagger}$	<0.001	0.075
DLCO	-7.7±2.8	$-9.9 \pm 12.2^{\dagger}$	$-7.8 \pm 10.9^{\dagger}$	0.001	0.050

 Table 2 Differences between the observed and expected postoperative pulmonary function changes in patients receiving VATS lobectomy and VATS segmentectomy

<sup>†</sup>, significant differences were observed in the corresponding pulmonary function parameters between VATS lobectomy and VATS segmentectomy. \*, P value for the difference between observed and expected PFT loss. VATS, video-assisted thoracic surgery; PFT, pulmonary function test; ICC, intraclass correlation coefficient; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity of the lungs for carbon monoxide.



**Figure 2** The ratio of the observed to the expected (O/E ratio) postoperative pulmonary function loss based on the number of resected segments. The dots represent the mean values of the ratios, while the upper and lower whiskers represent 95% confidence intervals. The dashed lines connecting each dot depict the tendency of change in the O/E ratio. DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

extent index less than 0.5 (FVC: P<0.001; FEV1: P<0.001; DLCO: P<0.001, *Table 3* and *Figure 4B*). When the resection extent index was equal to or greater than 0.5, no significant difference in the functional loss was detected between segmentectomy and lobectomy (FVC: P=0.125; FEV1: P=0.145; DLCO: P=0.357, *Table 3* and *Figure 4C*) after PSM.

## Discussion

Segmentectomy is now increasingly used in the surgical

treatment for early-stage lung cancer. But its advantages over lobectomy remain unclear, especially as an intentional procedure for good-risk patients. The Lung Cancer Study Group trial found limited functional benefits of sublobar resection compared with lobectomy at 6 months after surgery (20). But the result was controversial due to the enrollment of wedge resection, insufficient data on pulmonary function, and the open surgical approach. The JCOG0802/WJOG4607L trial has just reported its followup results, showing a very limited functional benefit (2–3%) of segmentectomy over lobectomy (6).

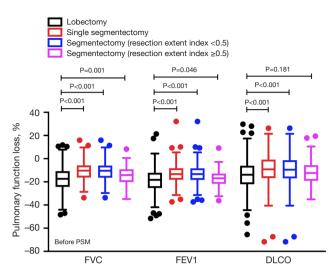


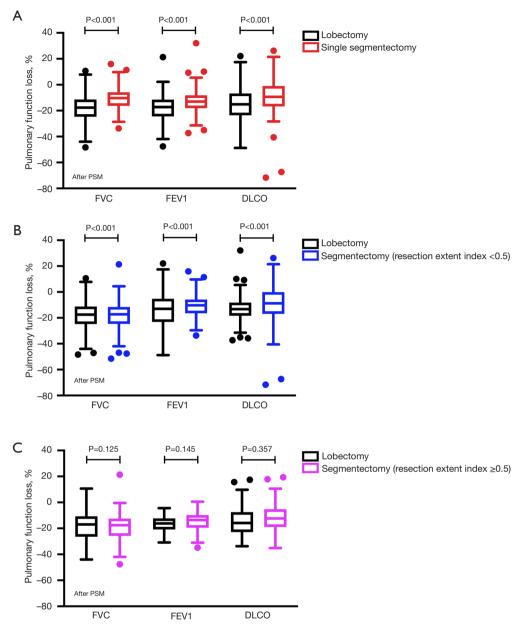
Figure 3 Comparison of pulmonary function changes between VATS lobectomy and VATS segmentectomy according to the resection extent index before propensity score matching. The upper and lower borders of the box represent the upper and lower quartiles, and the middle horizontal line represents the median, while the upper and lower whiskers represent the maximum and minimum values of non-outliers. The outliers are represented by the extra dots. DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; PSM, propensity score matching; VATS, video-assisted thoracic surgery.

Traditionally, pulmonary function loss after lung resection is thought to be in direct proportion to the number of resected segments, leading to the assumption that segmentectomies might preserve more function than lobectomies. However, previous studies have noticed that pulmonary function after lung resection might be inaccurately predicted by the segment counting method due to various factors including the baseline lung function, different intervals between surgery and the postoperative spirometry test (8,21,22), impacts from the surgical incisions (23,24), different compensatory lung expansion after various extent of resections and various lobes resected (25). In this study, we compared the expected pulmonary function loss with the actual loss observed at a fixed interval between spirometry tests after VATS lung resection in functionally fit patients. We found that all the ICC values were much less than the acceptable value of 0.70. The observed pulmonary function loss was significantly less than the expected loss after VATS lobectomy, but was greater than the expected loss after VATS segmentectomy. This means that actual

pulmonary function loss would be overestimated after VATS lobectomy, but underestimated after VATS segmentectomy, if the segment counting method was used. The gradual decline in the O/E ratio along with the increased number of resected segments indicated that the accuracy of prediction by the segment counting method would be greatly affected by the extent of resection. Thus, it is unwise to assume that pulmonary function loss after VATS lung resection would be in direct proportion with the extent of resection.

Only a limited number of retrospective small-sample studies have compared functional changes after lobectomy and segmentectomy in the VATS setting (24-30), among which few explored pulmonary function changes after different segmentectomies (25,29). Tane et al. noticed that FEV1 could be better preserved after single segmentectomy than after combined segmentectomy (25). However, due to the limited sample size, they did not compare pulmonary function changes after different segmentectomies with the corresponding lobectomies. Kuroda et al. detected significant differences in FEV1 preservation after VATS left upper lobe resections between 4 and 5-7 resected subsegments, and between 5-7 and 10 resected subsegments (29). But their study did not embark on resections of other lobes. In our prospective observational study, a much larger number of patients were included. All patients were functionally fit for lobectomy, and those receiving VATS segmentectomy were operated on with an intention-to-treat. Moreover, FVC, FEV1 and DLCO loss were all examined. Our results showed that pulmonary function loss after VATS segmentectomy was significantly less than after VATS lobectomy in general. But in consistency with the results of our previous study (9), average pulmonary function loss per segment resected after VATS segmentectomy was almost doubled than after VATS lobectomy. These results mean that less lung parenchyma resected under VATS would not necessarily translate into better function preservation, which might be potentially caused by less satisfactory re-expansion of the residual lobe after segmentectomy (9). Another reason might be that the remaining lobe(s) in the ipsilateral or contralateral lung after lobectomy expanded and compensated better than after segmentectomy, as suggested by Kim et al. (26).

To explore which VATS segmentectomies might be functionally beneficial than its corresponding VATS lobectomies, resection extent index was introduced to evaluate the loss of parenchyma and pulmonary function after surgery. And considering the impact on pulmonary function changes from different lobes resected (26,31), tumor location was also included into the PSM model so



**Figure 4** Comparison of pulmonary function changes after propensity score matching between lobectomy and single segmentectomy (A), segmentectomy with a resection extent index <0.5 (B), segmentectomy with a resection extent index  $\geq 0.5$  (C). The upper and lower borders of the box represent the upper and lower quartiles, and the middle horizontal line represents the median, while the upper and lower whiskers represent the maximum and minimum values of non-outliers. The outliers are represented by the extra dots. DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; PSM, propensity score matching.

that functional changes after segmentectomies would be compared directly to their corresponding lobectomies, together with the other characteristics including sex, age, smoking history and COPD. We found that for segmentectomies with a resection extent index less than 0.5, especially single segmentectomies, FVC, FEV1 and DLCO loss were all significantly less than after corresponding lobectomies. Otherwise, no significant functional advantage could be detected after segmentectomies with a resection extent index equal to or greater than 0.5. To our knowledge,

Table 3 Pulmonary function changes after VATS lobectomy and VATS segmentectomy evaluated according to the resection extent index before and after propensity score matching

Parameters –	Before PSM			After PSM		
	Lobectomy	Segmentectomy	P value	Lobectomy	Segmentectomy	P value
Resection extent index <0.5	n=338	n=214		n=205	n=205	
FVC loss (%)	-17.8±10.6	-10.8±8.5	<0.001	-18.5±10.7	-10.7±8.6	<0.001
FEV1 loss (%)	-18.9±10.4	-13.3±8.4	<0.001	-18.1±10.6	-13.2±8.5	<0.001
DLCO loss (%)	-13.6±13.0	-9.1±12.9	<0.001	-14.1±12.5	-9.0±13.1	<0.001
Resection extent index ≥0.5	n=338	n=107		n=55	n=55	
FVC loss (%)	-17.8±10.6	-14.6±8.1	0.001	-17.7±12.3	-14.7±7.7	0.125
FEV1 loss (%)	-18.9±10.4	-17.0±7.5	0.046	-18.8±12.3	-16.0±6.4	0.145
DLCO loss (%)	-13.6±13.0	-11.8±10.5	0.181	-13.7±12.3	-11.5±11.1	0.357

VATS, video-assisted thoracic surgery; PSM, propensity score matching; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity of the lungs for carbon monoxide.

this is the first prospective observational study comparing pulmonary function changes according to different resection extent indexes after VATS lobectomy and its corresponding VATS segmentectomy solely in good-risk patients. This makes our results more convincing and helpful in predicting potential functional benefits when considering segmentectomy for early-stage lung cancers.

The present study has several limitations. This was not a randomized trial. There might have been imbalances among patients included, even with stringent efforts to diminish their impacts by PSM. The purpose for this study was to evaluate the functional benefits of segmentectomy as an intentional procedure for good-risk patients. Patients who had poor lung function were excluded during the study design. Therefore, quantitative ventilation-perfusion scans would be not essential in this study (32-34), and the results could not be extrapolated to patients with poor lung function. Then segmental planes were divided by staplers in our patients. Thus, the results may not be extrapolated to segmentectomies using energy devices to divide segmental planes (35). Meanwhile, whether the pulmonary function changes are affected by the postoperative complications such as prolonged air leakage, which is treated with autologous blood pleurodesis in the current study remains unclear (36,37). Long-term pulmonary function changes may not be absolutely consistent with the results on functional changes evaluated at 6 months after surgery in this study, although longterm pulmonary function changes seem to vary little

6 months or later after surgery, as reported previously (38).

# Conclusions

Pulmonary function loss after thoracoscopic lung resection is not in direct proportion to the number of resected segments. VATS segmentectomy may help preserve more pulmonary function than VATS lobectomy in general. However, average pulmonary function loss per segment resected is greater after segmentectomy than after lobectomy. Which thoracoscopic segmentectomies would be truly beneficial in pulmonary function preservation can be estimated by the resection extent index. Only for segmentectomies with a resection extent index less than 0.5, especially single segmentectomies, more postoperative pulmonary function is preserved than the corresponding lobectomies.

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# Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://dx.doi. org/10.21037/tlcr-21-661

#### Chen et al. Spirometry changes after lobectomy versus segmentectomy

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi. org/10.21037/tlcr-21-661). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethical committee of the Shanghai Chest Hospital (No. ks11014) and informed consent was taken from all individual participants.

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