

Sublobectomy versus lobectomy for postoperative cough-related quality of life and recovery in early-stage non-small cell lung cancer patients: a longitudinal study.

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Abstract

Background

To quantitatively evaluate postoperative cough regarding changes in health-related quality of life (HRQOL) and recovery trajectory with the Leicester Cough Questionnaire in Mandarin-Chinese (LCQ-MC) in patients undergoing video-assisted thoracic surgery (VATS) for early-stage non-small cell lung cancer (NSCLC).

Methods

Overall, 156 patients with NSCLC underwent either VATS lobectomy or VATS sublobectomy; LCQ-MC was used to report the impact of postoperative cough on HRQOL for 6 months after discharge. Recovery from postoperative cough was defined as LCQ-MC scores returning to preoperative levels. The sensitivity of LCQ-MC to changes in postoperative cough recovery over time was evaluated via its ability to distinguish between surgery types.

Results

The VATS sublobectomy group reported significantly higher mean LCQ-MC scores 1 month after discharge, but without no significant differences postoperatively at 3 and 6 months after discharge, and returned to preoperative physical (69 vs. 99 days), psychological (67 vs. 99 days), social (50 vs. 98 days) and total (69 vs. 99 days) scores faster than the VATS lobectomy group (all $p < 0.05$).

Conclusion

The LCQ-MC can adequately assess the impact of postoperative cough on HRQOL. Routine monitoring of postoperative cough recovery through LCQ-MC scores could be added to enhanced recovery after surgery.

Background

Non-small cell lung cancer (NSCLC) patients who undergo surgery experience an acute systemic inflammatory, neuroendocrine, and metabolic stress response. This response often encompasses a cluster of nonspecific and organ-specific symptoms. Postoperative cough is a common organ-specific symptom that impacts physical, psychological, and social aspects of daily living; contributes to pain, fatigue, insomnia, and dyspnoea; increases anxiety in patients; and leads to social isolation[1]. Video-assisted thoracic surgery (VATS) is becoming the preferred surgical procedure over open thoracotomy for early-stage NSCLC. The prevalence of postoperative cough varies widely from 39.8–46.0%[2–4].

Morbidity and distress levels due to postoperative cough have been underestimated, especially after discharge, representing an unmet clinical need[5]. Recovery from postoperative cough is a complex process that involves physical, psychological, and social domains.

To grasp the potential impact of enhanced recovery after surgery (ERAS) and new operative concepts, the effects of such techniques on a reasonable outcome, such as changes in the status of postoperative cough symptoms over time, must first be understood. However, previous studies have focused on lobectomy rather than sublobectomy and have lacked a standard measure to assess recovery from cough symptoms after surgery or discharge. According to the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology for NSCLC, sublobectomy (segmentectomy or wedge resection) is appropriate in selected patients with pure adenocarcinoma in situ histology, nodules with a ≥ 50 ground-glass appearance on computed tomography or nodules with a long doubling time (≥ 400 days) confirmed through radiologic surveillance.

We therefore performed a longitudinal study to compare postoperative cough and recovery from VATS lobectomy versus sublobectomy in patients with early-stage NSCLC. We chose the Leicester Cough Questionnaire in Mandarin-Chinese (LCQ-MC) as the instrument for the investigation and follow-up. This longitudinal study was performed in accordance with the STROCSS Reporting Checklist[6].

Methods

Subjects

A total of 166 patients who underwent VATS performed by a single medical team between May 2019 and October 2020 at the Department of Thoracic Surgery, Fujian Provincial Hospital were enrolled. Patients were included according to the following criteria: (1) aged 18 years or older, (2) had postoperative cough but no cough symptoms within the 2 weeks prior to surgery, (3) provided a signed informed consent form, (4) presented with resectable TNM stage I lung cancer, (5) underwent VATS, and (6) had postoperative pathological findings indicative of NSCLC. Patients were excluded according to the following criteria: (1) underwent bilateral pulmonary surgery, (2) underwent conversion to open thoracotomy or experienced bleeding exceeding 1,000 mL, (3) were transferred to the intensive care unit after surgery, or (4) refused to answer the survey or dropped out.

Surgical procedures

Single utility port VATS lobectomy or sublobectomy was performed[7]. Systematic mediastinal lymphadenectomy was performed in accordance with the Chinese guidelines for the diagnosis and treatment of primary lung cancer (2015)[8]. Sublobectomy achieved parenchymal resection margins ≥ 2 cm or \geq the size of the node and sampled the appropriate N1 and N2 lymph node stations. Mediastinal lymphadenectomy included stations 2R, 4R, and 7-9 for right-sided cancer and 4L and 5-9 for left-sided cancer[9]. Lymph node dissection included the N1 and N2 nodes with a minimum of 3 N2 stations sampled or complete dissection[10].

A 30 Fr chest tube was placed in the observation port for postoperative drainage (7th or 8th intercostal space), while a 22 or 30 Fr chest tube was placed in the 2nd intercostal space at the midclavicular line (usually upper lobectomy).

The patients were encouraged to engage in ambulation soon after surgery, and a chest X-ray was scheduled for postoperative day (POD) 1. The chest tube withdrawal criteria included the absence of air leakage through the chest tube, a pleural fluid drainage of <200 mL in 24 hours, and no pneumothorax, haemothorax or chylothorax. The chest tubes were removed as early as possible on POD 1.

Assessment measurements and endpoint

The LCQ-MC, which assesses the impact of cough on health-related quality of life (HRQOL), consists of 19 items divided into three domains: physical (8 items), psychological (7 items), and social (4 items). A 7-point Likert scale was used to score the individual domains. The total scores ranged from 3 to 21, with a higher score indicating better health[11, 12]. Patients completed the LCQ-MC before discharge and at multiple timepoints during the 6 months after discharge. We defined “recovery from postoperative cough” when the patients reported three domain score or a total LCQ-MC score that had returned to the preoperative (baseline) level.

The endpoint was 6 months after discharge or the disappearance of postoperative cough symptoms. The last LCQ-MC was completed when the patients’ postoperative cough symptoms disappeared during the follow-up period.

Postoperative diagnoses were determined using the 2015 World Health Organization Classification of Lung Tumours and the eighth edition of the Union for International Cancer Control /American Joint Committee on Cancer lung cancer staging classification guidelines[13, 14]. Regional lymph node classification was based on the International Association for the Study of Lung Cancer lymph node map[15].

Data collection

Inpatients completed paper questionnaires while in the wards with the assistance of our investigators before discharge. Postoperative follow-up was performed by telephone or outpatient review at 1, 3, and 6 months after discharge. All data were uploaded to a network database for management and analysis (jinshuju, a data collection and management platform, <https://jinshuju.net/>).

Statistical analysis

Patient characteristics are presented as the mean \pm standard deviation (SD) for continuous variables and as relative frequencies for categorical variables. We performed t-tests, Pearson’s χ^2 tests and Yates’s correction for continuity, as appropriate, to identify differences between the lobectomy and sublobectomy groups. All comparisons were 2-sided, and differences with $p < 0.05$ were considered statistically significant. Recovery duration from each surgery type was estimated for each interference item using Kaplan–Meier analysis, and log-rank tests were used to compare time to recovery by surgery type.

Statistical analyses were performed using IBM SPSS Statistics, version 23.0 (Statistical Package for the Social Sciences, Chicago, IL, USA) and GraphPad Prism, version 9.0 (GraphPad Software, San Diego, CA, USA).

Results

Patient characteristics

A total of 166 patients consented to participate in the study, and 156 patients completed follow-up (attrition rate 6.02%, 10/166 patients). Eight patients withdrew during the follow-up period (2 in month 1, 5 in month 3, and 1 after month 6), and 2 patients underwent bilateral pulmonary surgery. Approximately 42% (65/156) of the patients underwent VATS sublobectomy, and there were no significant differences in the baseline data between groups. Table 1 shows the baseline demographic and clinical characteristics of the patients.

Table 1
Clinical characteristics and demographic

	Lobectomy(n=91)	Sublobectomy(n=65)	P value
Age, years	59.82±10.01	57.08±11.17	0.111
Sex, <i>n</i> (%)			
Male	31(34.1)	23(35.4)	0.499
Female	60(65.9)	42(64.6)	
Smoking history, <i>n</i> (%)			
Yes	20(22.0)	13(20.0)	0.463
No	71(78.0)	52(80.0)	
Lung function			
FEV1(L)	2.47±0.55	2.50±0.53	0.816
FVC(L)	3.04±0.67	3.26±0.66	0.144
Operated side	51(56.0)	34(52.3)	0.382
Right	40(44.0)	31(47.7)	
Left			
Pathological diagnosis, <i>n</i> (%)			
Adenocarcinoma	85(93.4)	62(95.4)	0.418
Squamous carcinoma	6(6.6)	3(4.6)	
Data are presented as mean ± SD or <i>n</i> (%).			

Longitudinal profiles of postoperative cough

The median times until postoperative cough developed in patients who underwent VATS lobectomy and patients who underwent VATS sublobectomy were 1 day (interquartile range [IQR], 0-2) and 2 days (IQR, 1-2), respectively. The median duration of postoperative cough in patients who underwent VATS lobectomy was 98 days (IQR, 39–155), and 15 patients (15/91, 16.5%) still had postoperative cough symptoms at 6 months after discharge. The corresponding median duration in the VATS sublobectomy group was 65 days (IQR, 35-107), and 5 patients (5/65, 7.7%) had postoperative cough symptoms at 6 months after discharge.

Figure 1 shows that the individual domain score and total LCQ-MC score decreased rapidly after surgery and then returned to preoperative levels over time. The VATS sublobectomy group reported significantly higher mean physical, psychological, and total LCQ-MC scores than the VATS lobectomy group at 1

month after discharge (all $p < 0.05$). Of note, the mean LCQ-MC scores of the VATS sublobectomy group were higher than those of the VATS lobectomy group postoperatively and at postoperative 3 and 6 months after discharge, but the differences were not significant. The dynamic changes and detailed scores are shown in Figure 1 and Table 2.

Table 2
The mean LCQ-MC scores after surgery and follow-up

Postoperative LCQ-MC	Lobectomy(n=91)	Sublobectomy (n=65)	P value
Physical	4.92±0.73	5.06±0.86	0.268
Psychological	5.16±0.95	5.08±1.08	0.643
Social	5.56±1.00	5.67±1.10	0.516
Total	15.63±2.27	15.80±2.65	0.657
LCQ-MC at 1 month	Lobectomy(n=91)	Sublobectomy (n=65)	
Physical	5.80±1.05	6.19±0.80	0.014
Psychological	5.53±1.26	5.94±1.16	0.038
Social	6.00±1.04	6.18±0.99	0.257
Total	17.33±3.14	18.32±2.82	0.045
LCQ-MC at 3 months	Lobectomy(n=67)	Sublobectomy (n=38)	
Physical	6.14±0.95	6.39±0.81	0.160
Psychological	6.01±1.15	6.16±1.17	0.561
Social	6.33±0.85	6.46±0.73	0.426
Total	18.49±2.83	19.00±2.61	0.356
LCQ-MC at 6 months	Lobectomy(n=36)	Sublobectomy (n=17)	
Physical	6.58±0.66	6.71±0.58	0.472
Psychological	6.48±0.91	6.51±0.91	0.933
Social	6.68±0.70	6.71±0.54	0.876
Total	19.74±2.19	19.93±1.98	0.766
Data are presented as mean ± SD.			

Recovery time from postoperative cough as measured by the LCQ-MC

Table 3 shows that the physical, psychological, and total LCQ-MC scores returned to preoperative levels for all patients at approximately 3 months. The social score of the LCQ-MC took only 2 months recover. Figure 2 presents the profiles of and significant differences in the physical, psychological, social, and total aspects recovery from postoperative cough between VATS lobectomy and VATS sublobectomy by Kaplan–Meier analysis, confirming the sensitivity of LCQ-MC for indicating recovery after VATS. Compared with patients who underwent VATS lobectomy, patients who underwent VATS sublobectomy needed significantly less time to return to baseline levels of the physical aspect (69 vs. 99 days, $p = 0.024$), psychological aspect (67 vs. 99 days, $p = 0.006$), social aspect (50 vs. 98 days, $p = 0.046$) and total aspect (69 vs. 99 days, $p = 0.024$) of postoperative cough (Table 3).

Table 3
Kaplan–Meier estimated postoperative cough recovery time (days from surgery)

LCQ-MC	Median days to recovery (95% confidence interval) ^a				P
	Overall	Lobectomy	Sublobectomy		
Physical	97(85-109)	99(98-100)	69(35-103)		0.024
Psychological	96(78-114)	99(97-101)	67(36-98)		0.006
Social	66(37-95)	98(72-124)	50(27-73)		0.046
Total	97(85-109)	99(98-100)	69(35-103)		0.024
Data are presented as median(95%CI).					
^a Recovery of postoperative cough was defined as the patient having reported LCQ-MC individual domain or total score at the preoperative (baseline) level.					

Discussion

This longitudinal study demonstrated the potential utility of the LCQ-MC, a cough-specific instrument to assess impact on HRQOL, for evaluating postoperative cough in patients who undergo VATS for early-stage NSCLC and for detecting differences in recovery from postoperative cough by type of procedure (VATS lobectomy vs. VATS sublobectomy)[16]. To the best of our knowledge, this study is the first to define the recovery from postoperative cough using the LCQ-MC as an outcome measure and compare this recovery between VATS lobectomy and VATS sublobectomy.

The LCQ-MC enables real-time reporting of the impact of postoperative cough on HRQOL in terms of physical, psychological and social domains to the surgeon or health care provider, which may improve the likelihood of effectively evaluating ERAS[17]. Patient satisfaction after surgery is largely dependent on his or her recovery experience[18]. Postoperative cough, one of the most common respiratory symptoms after surgery, can adversely affect HRQOL[19]. In severe postoperative cough, patients experience disrupted sleep and difficulty talking, which increases their psychological burden and worsens their HRQOL[2, 20, 21]. The LCQ-MC is a flexible, easily completed, valid instrument that can be deployed

in various ways, including through paper and pencil, smartphones, and other electronic data capture methods. The LCQ-MC can be completed in less than 5 minutes with any of these modes. Accurate and convenient evaluations of the impact of postoperative cough on HRQOL are important for ensuring early and effective treatment[22]. We previously showed that the LCQ-MC reliably assessed postoperative cough in patients with NSCLC who underwent VATS[23]. This instrument can be used to guide effective treatment, accelerate the recovery from postoperative cough, and achieve the objective of ERAS[24].

As expected, VATS sublobectomy had more favourable effects on postoperative recovery and morbidity than VATS lobectomy[25, 26]. This may be related to a combination of factors associated with VATS lobectomy, such as greater stress on the cardiovascular system, larger change in the bronchial angle and more stimulation to cough receptors[27–29]. Postoperative cough symptoms peaked immediately after surgery and were prevalent on PODs 1-2, representing a combined effect from surgical trauma and perioperative care. The patients who underwent VATS lobectomy reported significantly higher physical, psychological, and total LCQ-MC scores at 1 month after discharge than those who underwent VATS sublobectomy. Nevertheless, the LCQ-MC scores at 3 and 6 months after discharge were not significantly different between the two surgery types. Our finding of the different impacts of postoperative cough on HRQOL between the two groups, as measured by LCQ-MC, mirrors previous studies that have reported that the severity of postoperative cough in early-stage NSCLC patients after VATS sublobectomy was lower or similar to that in patients after VATS lobectomy[17, 30, 31]. This demonstrates that the LCQ-MC is sufficiently sensitive to differentiate postoperative cough by type of procedure.

In patients who underwent VATS sublobectomy, the postoperative cough returned to preoperative levels after approximately 3 months (median time for the physical score: 69 days, psychological score: 67 days, and social score: 50 days). In patients who underwent VATS lobectomy, the postoperative cough had a somewhat different pattern of recovery in this study and recovered more slowly (median time for the physical score: 99 days, psychological score: 99 days, and social score: 98 days) (Figure 2, Table 3). Using LCQ-MC as an indicator of the status of postoperative cough symptoms, we not only defined the impact of postoperative cough on HRQOL in this study but also defined the time course of postoperative cough recovery after VATS for early-stage NSCLC. In the current study, repeated LCQ-MC measurements were acquired at selected critical timepoints, beginning with a preoperative assessment, thus sufficiently and sensitively capturing significant differences in the impact of postoperative cough on HRQOL over time and the time needed to return to preoperative levels between two different surgery types for early-stage NSCLC. The minimal clinically important difference (MCID) is the smallest change in the quality-of-life score considered to be clinically meaningful[32]. The mean (SD) total LCQ MCID was 1.3 (3.2), the MCIDs for each domain were as follows: physical: 0.2 (0.8), social: 0.2 (1.1) and psychological: 0.8 (1.5) [33]. In the current study, the differences between the immediately postoperative individual physical, psychological, and social domain scores as well as total LCQ-MC scores and those acquired 1 month after discharge were 0.96 (0.96), 0.53 (1.29), 0.43 (1.12) and 1.92 (2.99), respectively, suggesting a clinically meaningful difference.

This study had several limitations. First, the sample size was limited, and the sample was a homogenous group of patients with early-stage NSCLC. Future studies with a more diverse sample are warranted to identify potential risk factors and define the trajectory of postoperative cough recovery to increase the generalizability of the results. Second, we usually administered the LCQ-MC on the day of discharge and did not collect the LCQ-MC scores on PODs 1-3 or 1 week after discharge. The differences in postoperative cough symptoms between VATS lobectomy and VATS sublobectomy that were observed clinically may have been even more striking if these data had been included in the analysis. Third, in addition to charting the return to preoperative levels, the study lacked another objective measure of cough by which to define recovery to a “good” level of postoperative cough symptoms (both cut-off points and MCID), which could be more practical for further decision-making about ongoing cough-specific treatment, and there would be no need for a baseline LCQ-MC assessment.

In conclusion, this study is among the first to describe the nature of and changes in postoperative cough in patients with early-stage NSCLC after VATS during the first 6 months after discharge. The LCQ-MC is a clinically relevant and user-friendly instrument for assessing the patient’s perspective of the impact of postoperative cough on HRQOL. Routine monitoring of postoperative cough recovery with LCQ-MC scores could be a novel addition to ERAS that has the potential to improve standard practice after the patients are discharged after VATS.

Abbreviations

HRQOL, health-related quality of life; LCQ-MC, Leicester Cough Questionnaire in Mandarin-Chinese; NSCLC, early-stage non-small cell lung cancer; VATS; video-assisted thoracic surgery; ERAS, enhanced recovery after surgery; POD, postoperative day; SD, standard deviation; IQR, interquartile range; MCID, minimal clinically important difference.

Declarations

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Authors’ contributions

RJL, WC, XJP were involved in the research conception. Study was conceptualized by all 4 authors. RJL and WC was the principal investigator and responsible for the data collection, entry and analysis with RJL and LLZ for manuscript preparation. All authors read and approved the final manuscript. RJL and WC contributed equally to this work and should be considered co-first authors

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The authors have no conflicts of interest to declare.

Availability of data and materials

This is part of a larger study. The dataset generated and analysed during the current study is not publicly available but may be obtained from the corresponding author

Ethics approval and consent to participants

This longitudinal study conformed to the provisions of the Declaration of Helsinki and was approved by the Chinese Clinical Trial Registry (Clinicaltrials.gov number: ChiCTR1900023419; approval date: May 20, 2019) and Chinese Ethics Committee of Registering Clinical Trials (approval no. from the ethics committee: ChiECRCT20190084). The primary sponsor is West China Hospital, Sichuan University, and the secondary sponsor is Fujian Provincial Hospital. All participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests

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Tables

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Postoperative LCQ-MC	Lobectomy(n=91)	Sublobectomy (n=65)	P value
Physical	4.92±0.73	5.06±0.86	0.268
Psychological	5.16±0.95	5.08±1.08	0.643
Social	5.56±1.00	5.67±1.10	0.516
Total	15.63±2.27	15.80±2.65	0.657
LCQ-MC at 1 month	Lobectomy(n=91)	Sublobectomy (n=65)	
Physical	5.80±1.05	6.19±0.80	0.014
Psychological	5.53±1.26	5.94±1.16	0.038
Social	6.00±1.04	6.18±0.99	0.257
Total	17.33±3.14	18.32±2.82	0.045
LCQ-MC at 3 months	Lobectomy(n=67)	Sublobectomy (n=38)	
Physical	6.14±0.95	6.39±0.81	0.160
Psychological	6.01±1.15	6.16±1.17	0.561
Social	6.33±0.85	6.46±0.73	0.426
Total	18.49±2.83	19.00±2.61	0.356
LCQ-MC at 6 months	Lobectomy(n=36)	Sublobectomy (n=17)	
Physical	6.58±0.66	6.71±0.58	0.472
Psychological	6.48±0.91	6.51±0.91	0.933
Social	6.68±0.70	6.71±0.54	0.876
Total	19.74±2.19	19.93±1.98	0.766

Data are presented as mean ± SD.

Table 3 Kaplan–Meier estimated postoperative cough recovery time (days from surgery)

	Median days to recovery (95% confidence interval) ^a			
LCQ-MC	Overall	Lobectomy	Sublobectomy	P
Physical	97(85-109)	99(98-100)	69(35-103)	0.024
Psychological	96(78-114)	99(97-101)	67(36-98)	0.006
Social	66(37-95)	98(72-124)	50(27-73)	0.046
Total	97(85-109)	99(98-100)	69(35-103)	0.024

Data are presented as median(95%CI).

^aRecovery of postoperative cough was defined as the patient having reported LCQ-MC individual domain or total score at the preoperative (baseline) level.

Figures

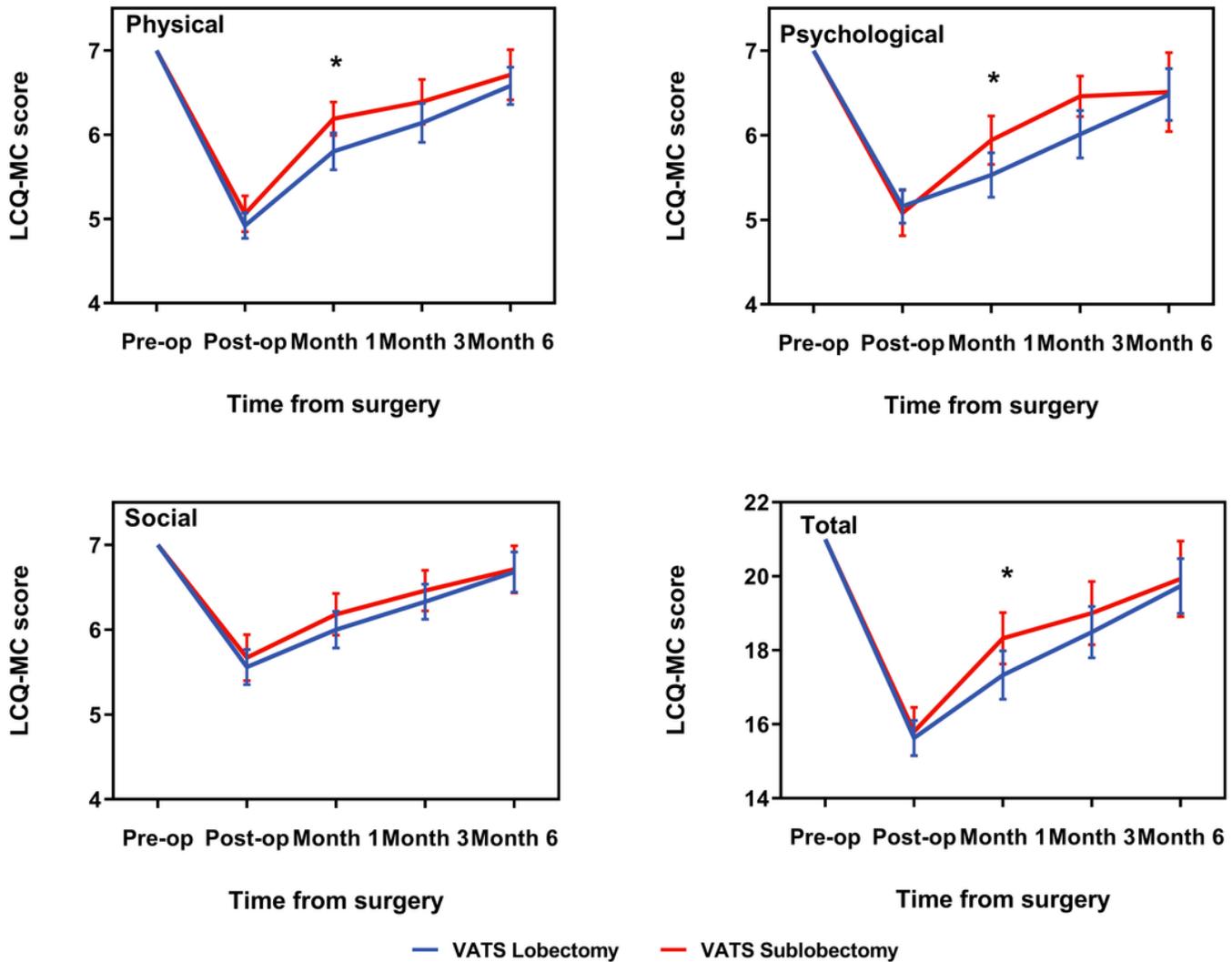


Figure 1

Change in average LCQ-MC scores during the 6 months after discharge by surgery type. *, $p < 0.05$. LCQ-MC, Leicester Cough Questionnaire in Mandarin-Chinese; VATS, video-assisted thoracic surgery.

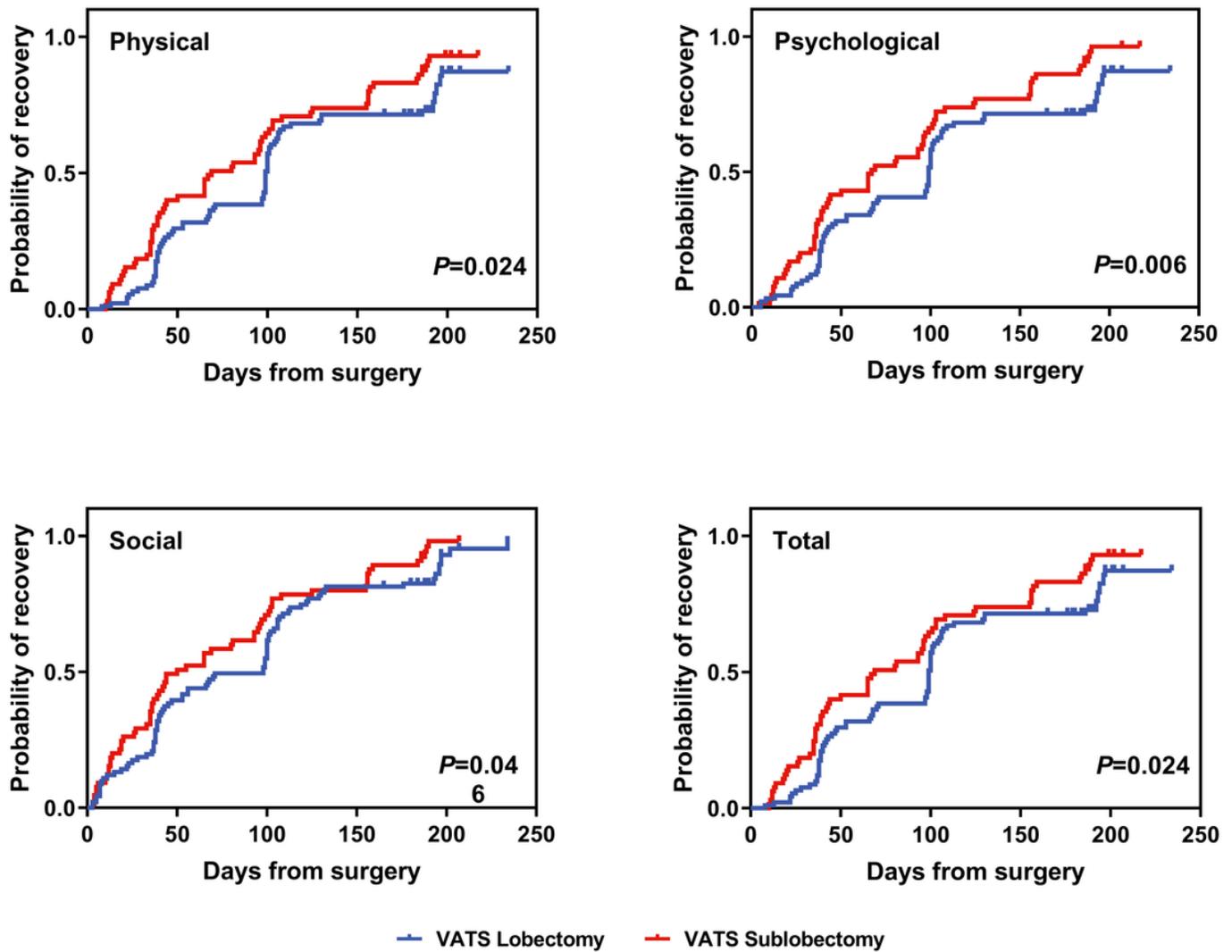


Figure 2

The recovery trajectories of postoperative cough by surgery type. P value by log-rank test. VATS, video-assisted thoracic surgery.