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Runsen Jin, MD, PhD, Zhengyuan Zhang, MD, Yuyan Zheng, MD, Zhenyi Niu, MD, Siying Sun, MS, Yuqin Cao, MD, Yajie Zhang, MD, PhD, Abbas E. Abbas, MD, MS, FACS, Toni Lerut, MD, PhD, MPH, FACS, Jules Lin, MD, FACS, FCCP, Hecheng Li, MD, PhD, FACS

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Title page

Health-Related Quality of Life following Robotic-Assisted or Video-Assisted Lobectomy in Patients with Non-Small-Cell Lung Cancer: Results from The RVlob Randomized Clinical Trial

Runsen Jin MD, PhD[1#]; Zhengyuan Zhang MD[1#]; Yuyan Zheng MD[1#]; Zhenyi Niu MD[1]; Siying Sun MS[1]; Yuqin Cao MD[1]; Yajie Zhang MD, PhD[1]; Abbas E. Abbas MD, MS, FACS[2]; Toni Lerut MD, PhD, MPH, FACS[3]; Jules Lin MD, FACS, FCCP[4]; Hecheng Li MD, PhD, FACS[1*]

1. Department of Thoracic Surgery, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
2. Department of Thoracic Surgery, Brown Surgical Associates and Lifespan Hospitals, Warren Alpert Medical School of Brown University, Rhode Island, USA
3. Department of Thoracic Surgery, University Hospital Leuven, Leuven, Belgium
4. Section of Thoracic Surgery, University of Michigan Medical Center, Ann Arbor, Michigan, USA

#Equal Contributions: These authors contributed equally to this work.

***Corresponding Author:** Hecheng Li, MD, PhD, FACS; Department of Thoracic Surgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 197 Ruijin 2nd Road, Shanghai 200025, China; E-mail: lihecheng2000@hotmail.com.

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Disclosure: Hecheng Li is currently receiving a Robotic Research Grant from Intuitive Surgical Operations, Inc. Jules Lin is a robotic proctor for Intuitive Surgical, Inc. For the remaining authors none were declared. The authors declare no other conflict of interest.

Key Words: Non-small cell lung cancer, Robotic-assisted lobectomy, Video-assisted lobectomy, Quality of life, Postoperative pain, Randomized controlled trial.

Abstract

Background: Robotic-assisted lobectomy (RAL) is increasingly employed as an alternative to video-assisted lobectomy (VAL) for resectable non-small-cell lung cancer (NSCLC). However, there is little evidence for any difference in the postoperative health-related quality of life (HRQoL) between these two approaches.

Research Question: Is robotic-assisted lobectomy (RAL) superior to video-assisted lobectomy (VAL) in improving quality of life in patients with resectable non-small-cell lung cancer (NSCLC)?

Study design and methods: We performed a single-center, open-label randomized clinical trial from May 2017 to May 2020 with 320 patients undergoing RAL or VAL for resectable NSCLC enrolled (RVlob trial, NCT03134534). Postoperative pain was evaluated with the visual analogue score (VAS) or numeric rating score (NRS) on postoperative day 1 and at weeks 4, 24, and 48. The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30), EORTC Quality of Life Questionnaire in Lung Cancer (QLQ-LC13), and the European Quality of Life 5 Dimensions (EQ-5D) questionnaire were also administered at weeks 4, 24 and 48 after surgery.

Results: 157 patients underwent RAL and 163 had VAL. The mean pain score of patients after RAL was statistically lower at week 4 (2.097 ± 0.111 vs 2.431 ± 0.108, $p=0.032$). QLQ-C30 and QLQ-LC13 summary scores ($p>0.05$) were similar for both RAL and VAL during the

first 48 weeks of follow-up. HRQoL score assessed with the EQ-5D questionnaire was also comparable between the two groups ($p > 0.05$) during the whole study period.

Interpretation: Both RAL and VAL showed satisfactory and comparable HRQoL and postoperative pain up to 48 weeks after surgery, despite some minor statistical differences at week 4.

Clinical Trial registration: NCT03134534 (http://www.clinicaltrials.gov)

Lung cancer is the leading cause of cancer-related death in the world[1], and non-small-cell lung cancer (NSCLC) categories account for the most common pathological types of lung cancer. Video-assisted lobectomy (VAL) is a standard surgical procedure for resectable NSCLC, and uniportal lobectomy is considered one of the mainstream modalities[2]. The robotic platform, which provides technical benefits including three-dimensional, high-definition visualization and better maneuverability, has become increasingly utilized in various surgical fields since 1985[3]. Melfi *et al.* described the first robotic-assisted lobectomy (RAL) in 2002[4]. Since then, several studies have also revealed the potential benefits of robotic surgery regarding short-term outcomes compared to other modalities. Fewer studies have described the long-term oncologic efficacy of robotic lobectomy[5].

In addition to evaluating disease-free and overall survival, modern surgical research has focused on changes in postoperative life quality after oncologic surgery. The health-related quality of life (HRQoL) index was developed to evaluate a patient's physical, psychological

and cognitive status following a specific treatment. Several studies comparing the postoperative HRQoL between robotic-assisted and laparoscopic surgery for other cancer procedures such as rectal cancer resection[6], pancreatectomy[7] and hysterectomy[8] have demonstrated similar or marginally improved outcomes after robotic surgery. However, such studies on the effect of robotic surgery compare to other approaches in lung cancer have shown mixed results.

One small, retrospective study did report improved quality of life in lung cancer patients undergoing robotic-assisted resection compared to thoracoscopic surgery in the short term[9]. Meanwhile, another non-randomized prospective study reported that patients with stage I or II NSCLC who underwent VAL had improved long-term quality of life and a lower incidence of postoperative complications compared to patients who had RAL[10]. Unfortunately, approximately 40% of patients in the latter study were lost to follow-up making the results less reliable[10]. Due to this lack of clarity in the differences of HRQoL between RAL and VAL, further evidence is clearly necessary.

We have previously launched a prospective, single-center, open-label and parallel-arm randomized controlled trial (ClinicalTrials.gov identifier, NCT03134534), to compare the safety and efficacy between VAL (uniport or biport) and RAL for patients with resectable NSCLC [11]. In addition to safety, feasibility, and long-term survival, we also compared HRQoL between the two surgical modalities and investigated the potential discrepancy which could be derived from robotic-assisted surgery.

METHODS

Trial Design

RVlob was a single-center, open-label, parallel-arm, non-inferiority trial comparing the safety and efficacy of RAL and VAL. Details of inclusion and exclusion criteria, recruitment and randomization procedures have been previously reported[11]. Briefly, patients with pulmonary tumors who were identified as suitable for minimally invasive lobectomy were enrolled and randomized to receive RAL or VAL. A da Vinci S/Si surgical robot (Intuitive Surgical, Inc, Santa Clara, CA) was used to perform RAL. Five ports were placed in the following positions: a 12-mm camera port was placed in the 8th intercostal space (ICS) at the mid-axillary line; three 8-mm working ports were placed separately in the 5th ICS at the anterior axillary line (#1 arm), the 8th ICS at the posterior axillary line (#2 arm), and the 8th ICS at 2 cm lateral to the spine (#3 arm). Finally, the auxiliary port was placed in the 8th ICS between the camera port and the anterior port. VAL was performed through a 4-cm incision, which was placed in the 5th ICS at the anterior axillary line and covered with a protective sleeve. When necessary, an additional auxiliary port was placed in the 7th or 8th ICS at the mid-axillary line. All surgical instruments were inserted through the incision without spreading the ribs[11]. Study protocol and amendments were approved by the ethics committee of Ruijin Hospital, Shanghai Jiaotong University School of Medicine (approval number, 2017-58). All enrolled patients gave informed written consent before randomization. The trial was registered at ClinicalTrials.gov (NCT03134534).

HRQoL Assessments

All patients were asked to complete four validated HRQoL instruments before surgery and at weeks 4, 24, and 48 postoperatively: the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) version 3.0[12], the EORTC Quality of Life Questionnaire in Lung Cancer (EORTC QLQ-LC13)[13], the European Quality of Life 5 Dimensions questionnaire (EQ-5D)[14], and the numeric rating scale (NRS) or visual analogue score (VAS) for postoperative pain evaluation. The EORTC QLQ-C30 assesses cancer-specific QoL, including 30 items divided into four domains: functioning scales, symptom scales, single item for economic status and two items evaluating global health status (GHS). The EORTC QLQ-LC13 serves as a complement to the EORTC QLQ-C30 core cancer module. For EORTC QLQ-C30 and EORTC QLQ-LC13[15], the scores for each domain range from 0 to 100 after linear transformation of the raw scores. An EORTC QLQ-C30 summary score was calculated using the mean of 15 of the QLQ-C30 scores, while an EORTC QLQ-LC13 symptom summary score was calculated with the same method. The EQ-5D questionnaire consists of five questions (primary dimensions) including mobility, self-care, usual activities, pain and discomfort, and anxiety and depression. Each question has three possible answers (“no problems”, “some problems”, or “extreme problems”). For pain evaluation, an eleven-point VAS (on postoperative day 1) and NRS (used during follow-up) were used, where a score of 0 represents “no pain” while a score of 10 signifies the “worst pain imaginable”.

At follow-up, patients were administered these four QoL evaluation instruments during clinic visits at weeks 4, 24, and 48 postoperatively (Figure 1). If a patient missed the

scheduled postoperative follow-up at our institution, a telephone follow-up was conducted instead.

Statistical Analysis

Statistical methods for the primary analyses have been described previously[11]. No power calculation was done for HRQoL. HRQoL assessment was carried out in all randomly assigned patients who underwent RAL or VAL. The compliance rate was defined as the proportion of patients who completed the indicated questionnaires among those who were expected to complete one at each timepoint. Scores for EORTC QLQ-30 and EORTC QLQ-LC13 were calculated according to the published scoring manuals and the developer's guidelines[12,13]. The outcomes of EQ-5D questionnaires were converted by a linear formula into the utility index respectively[16]. Comparisons between the two groups were done using Student's t-test for normally distributed continuous variables which were represented as mean ± standard deviation (SD). In cases of non-compliance, continuous variables were presented as median (interquartile range [IQR]) and compared by Mann-Whitney U test between the groups. Classification data was compared using the chi-square test or Wilcoxon rank-sum test.

All statistical analysis was performed using IBM SPSS 22.0 (SPSS Inc; Chicago, IL, USA), GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, California USA, www.graphpad.com) and OriginPro, Version 2021 (OriginLab Corporation, Northampton, MA, USA). The test level between the two groups was set at α=0.05 (bilateral), and P values less than 0.05 were considered statistically significant.

RESULTS

Patient Inclusion and Questionnaire Participation

After screening, 320 patients (157 in the RAL group and 163 in the VAL group) were enrolled and randomized. Table 1 describes the clinicopathological characteristics and perioperative outcomes of both groups. Baseline characteristics were balanced between the groups including age, sex, place of residence, employment status, education level, BMI and smoking index (Table 1). There were no significant differences in pathological TNM stage, operation time, rate of conversion to thoracotomy, postoperative length of stay or postoperative complications (Table 1). And there were 21 deaths (7 RAL and 14 VAL) and 11 cases of recurrence (6 RAL and 5 VAL) by the time of 48 weeks of postoperative follow-up.

The rate of loss to follow-up was comparable in both groups; approximately 12% of patients in the RAL group and 10% in the VAL group. We received 144 (92%) questionnaires in the RAL group and 153 (94%) in the VAL group at week 4 and 139 (86%) in the RAL group and 143 (88%) in the VAL group at week 24. By week 48, 131 (83%) in the RAL group and 134 (82%) in the VAL group completed the QLQ-C30 and the QLQ-LC13. Meanwhile, 131 (83%) in the RAL group and 134 (82%) in the VAL group completed the EQ-5D at 48 weeks, and 265 patients completed the assessment for postoperative pain (131 (83%) in the RAL group and 134 (82%) in the VAL group) at week 48. Overall, there were no significant differences in survey completion or compliance rates between both groups at each timepoint (Table 2).

EORTC QLQ-C30 and QLQ-LC13 Questionnaire Scoring

To evaluate the postoperative HRQoL in detail, we applied the EORTC QLQ-C30

questionnaire mainly consisting of functioning scale (physical function, role function, emotional function, cognitive function, and social function), symptom scale (fatigue, nausea and vomiting, dyspnea, etc.) two Global Health Status (GHS)/QoL evaluating items, and the QLQ-LC13 questionnaire consisting of 13 specific symptoms for lung cancer. The mean GHS/QoL scores decreased in both RAL and VAL groups after surgery, compared with the baseline status. They maintained close levels between both groups at each time point for the entire follow-up period (Figure 2A). The mean score changes from baseline of the GHS/QoL at week 4, 24 and 48 showed no marked difference between both groups (-27.03 ± 13.34 vs -26.42 ± 13.41, -12.41 ± 18.26 vs -8.68 ± 15.57, -7.19 ± 16.60 vs -7.28 ± 17.65, respectively, $p>0.05$, Figure 2B and Supplementary Figure 1). The similarity between both groups in mean GHS/QoL score at week 48 was consistent across QLQ-C30 and QLQ-LC13 functioning/symptom scales (Figure 2B and 2C). Both groups had similar scores in physical function ($p=0.59$, Figure 2B) and coughing scores ($p=0.85$, Figure 2C) at week 48. By the end of the 1-year follow-up period, the most commonly reported postoperative symptoms were mainly fatigue, pain, dyspnea and coughing (Figure 2B and 2C). At week 48, no significant differences were found in mean score changes from baseline in both groups for any functional or symptom scales. Subgroup analyses for the GHS/QoL at weeks 4 and 48 showed no differences with the outcomes in the overall population (Supplementary Figure 2).

At week 48, fewer patients in both the RAL and VAL groups had decreased QLQ-C30 GHS/QoL scores or lower functioning and symptom scales, which indicated that more patients had stable even better feeling, compared with baseline condition before surgery. In fact, a larger proportion of patients had stable or improved status, compared to postoperative

week 4 (Figure 3). A similar proportion of patients in both groups had decreased GHS/QoL scores (RAL group, 53% and VAL group, 49%). This trend was consistent with that seen in the rest of the QLQ-C30 functional and symptom scales (Figure 3).

EQ-5D Utility Index (UI)

The EQ-5D questionnaire assesses patient quality of life from five dimensions, including mobility, self-care, usual activities, pain and discomfort, and anxiety/depression. A majority of the individual dimensions on the EQ-5D questionnaires showed no differences between the two groups at each timepoint. When specifically asked about usual activities, there were more patients who chose "some problem" in the RAL group than the VAL group (26 RAL (19.8%) vs 15 VAL (10.3%), p=0.03, Figure 4A) at week 4. At week 48, there were no significant differences in any of the specific dimensions (Figure 4B). When comparing the entire EQ-5D utility index which represents the summary scores, both RAL and VAL patients had similar scores ($p > 0.05$) at each timepoint (Figure 4C). Further analyses for EQ-5D summary scores in subgroups at weeks 4 and 48 showed the comparable results with the outcomes in the overall population (Supplementary Figure 3).

Postoperative Pain

Postoperative pain is an important component of assessing HRQoL after surgery. The VAS was used on postoperative day one while the NRS was used for baseline evaluation and after hospital discharge. Most patients (83.5%) had a relatively tolerable pain score between 0 to 3 at their first postoperative visit. Furthermore, there was a correlation between pain score and time, with both VAS and NRS scores showing a consistent decline with increasing time after surgery. Patients in the VAL group did report higher pain scores than those in the RAL

group at week 4 (2.431 ± 0.108 vs 2.097 ± 0.111, p=0.03, Figure 5A). Otherwise, there were no significant differences at other timepoints. We also recorded the use and frequency of analgesics (Supplementary Table 1). Furthermore, the outcomes at week 4 in most clinical subgroups demonstrated that the patients who underwent RAL had a lower pain score. This was evident in groups including male, thinner population and urban residents, where the patients who underwent RAL showed the trend of lower pain scores compared with the VAL (Figure 5B).

DISCUSSION

RAL has been demonstrated to achieve superior surgical outcomes to conventional open surgery[17]. An earlier report of a randomized study by this group revealed that RAL was safe and feasible compared to VAL[11]. There were also a few retrospective studies reporting the potential long-term benefits of RATS, compared with VATS[18,19]. In 2017, David *et al.* reported the HRQoL in patients undergoing robotic-assisted and conventional laparoscopic surgery for rectal cancer, and showed no difference at 6 months[6]. In 2015, Jenny *et al.* [20] demonstrated that there were no differences in postoperative pain between conventional laparoscopy and robotic-assisted surgery for gynecologic procedures. Similarly, in comparing the results of laparoscopic versus robotic-assisted prostatectomy for localized prostate cancer, Ilic *et al.* reported [21] that urinary and sexual quality of life-related outcomes appeared similar and the difference in postoperative pain was minimal. However, only two previous studies[9,10] discussed the outcomes of HRQoL and postoperative pain after RAL. Both studies suffered from small sample size and incomplete long-term follow-up. The HRQoL results of our prospective clinical trial suggested that patients who underwent RAL reported lower pain scores than the VAL group at week 4. However, the RAL group had less functionality ($p < 0.05$) in usual activities than the VAL group although the composite summary scores of EQ-5D at week 4 were the same for both groups. Besides these minor differences between the 2 groups, there were no other differences in the overall scores of HRQoL or postoperative pain.

In addition to survival, having the ability to maintain a good quality of life is an important consideration in clinical decision-making for all surgical fields, and is a key goal of treatment[22]. Bendixen *et al.* performed a randomized controlled trial to analyze QoL after

video-assisted thoracoscopic surgery (VATS) and thoracotomy in 206 patients with early-stage lung cancer[23]. During the period of observation, self-reported QoL according to the EQ-5D was significantly better after VATS. However, QoL according to QLQ-C30 was not different between the groups. Williams *et al.* reported that VAL patients received higher QLQ-C30 summary scores, due to higher social scores and decreased postoperative dyspnea at 12 months[10]. In contrast, Zheng *et al.* revealed that the QoL scores according to QLQ-C30 in the robotic-assisted thoracoscopic surgery (RATS) group were higher than those of the VATS group 6 weeks postoperatively[9]. In this study, patients received the EORTC-C30 and QLQ-LC13 questionnaire to determine their QoL scores. The EQ-5D questionnaire served as an additional enrichment to the QoL evaluation. We found that both RAL and VAL groups exhibited an obvious degree of fatigue, dyspnea, pain or coughing in the symptom scales at each timepoint postoperatively. The same trend was also observed in functioning scales (physical, role and social functioning). Meanwhile, the degree of score changes in functioning and symptom scales was not different between the 2 groups at each timepoint during the follow-up (Supplementary Figure 1 and 4). The GHS/QoL scores which represent general self-reported QoL were also consistent between both groups at each timepoint postoperatively. At long-term follow-up, both the symptom and function scores returned to near-baseline levels gradually. Our study found few differences between the 2 groups in EQ-5D individual dimensions during the study, except for the activity status at week 4, in which more patients from the RAL group reported difficulty in working. Further data analysis revealed that the proportion of patients in employment was larger in the RAL group (42.3% vs 26.7%, p=0.317) among the same patients who felt difficult in usual activities at week 4. This was

consistent with the fact that there was a higher overall proportion of patients in employment in the RAL group, compared to the VAL group (29.2% vs 21.6%, p=0.132). This may provide a reasonable explanation for this discrepancy, since the usual activity status in the EQ-5D questionnaire included study, housework and leisure activities in addition to work. Several other factors could also have affected the subjective evaluation of usual activity status, including recall bias, understanding bias, or incorrect responses during the assessment. Overall, both RAL and VAL exhibited comparable impact on the HRQoL using the above three questionnaires.

Both the VAS and NRS questionnaires are widely applied clinically as postoperative pain assessment tools[24]. Current studies demonstrate that both methods appropriately reflect the degree of pain. NRS assesses the degree of pain according to its current intensity[24,25]. However, VAS evaluates pain not only in intensity but also in its character, thus representing a more nuanced description of the symptom. VAS was administered on the first day after surgery, while NRS was used at preoperative baseline and during the follow-up period. The pain score continued to decrease with time after surgery in both groups. There were no differences between groups at the first day, week 24 and week 48 but the RAL group had significantly lower pain scores than VAL group at postoperative week 4 (2.097 ± 0.111 vs 2.431 ± 0.108, p=0.03, Figure 5A). Among other studies that compared RAL and VAL, our findings were consistent with the results of Zheng *et al.* who also showed a lesser proportion of patients feeling pain after RAL than VAL in the early postoperative period[9]. Otherwise, Testori *et al.* reported that the robotic group had a non-statistically significant superiority toward the video-assisted group concerning the postoperative pain during one-year follow-up

in their retrospective study[26]. Conversely, Novellis *et al*. reported that the VATS approach was associated with less pain 2 weeks after surgery, but the difference was very small and the clinical relevance was unclear[27]. In our study, the lower postoperative pain score at week 4 in RAL group was possibly due to less stress injury to the thoracic wall during surgical manipulations owing to the unique internal wrist rotation system. This system allows the machine arm to move more precisely and achieve a better operating angle all while remaining at a fixed point in space[28,29]. Of note, most patients in the VAL group underwent uniportal surgery, in which all the instruments were placed through a single larger incision, potentially causing more pressure and torquing on the intercostal tissues. Indeed, we found that patients underwent RAL had the similar level of postoperative pain in our clinical center, compared with patients underwent VAL, despite the minor differences in the pain evaluation.

There are several limitations in our study. Firstly, the single-center nature of this clinical trial makes it less persuasive than a multicenter study. Secondly, since no blinding to treatment assignment was incorporated into this trial, the research findings may be influenced by the subjective feelings of the patients. Thirdly, some patients were lost to follow-up at each time point, contributing to an approximately 90% survey rate at week 48. Similar prospective multi-center studies may be required to confirm and validate the long-term results.

INTERPRETATION

In conclusion, we reported the HRQoL and postoperative pain outcomes of the first prospective RCT comparing RAL and VAL in the treatment of resectable NSCLC. Both surgical modalities showed satisfactory and comparable HRQoL and postoperative pain up to 48 weeks after surgery, despite some minor statistical differences at week 4.

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Additional information: The supplementary figure and table can be found in the Supplemental Materials section of the online article.

Take-home Points

Study Question: Is robotic-assisted lobectomy (RAL) superior to video-assisted lobectomy (VAL) in improving quality of life in patients with resectable non-small-cell lung cancer (NSCLC)?

Results: 157 patients underwent RAL and 163 had VAL. The mean pain score of patients after RAL was statistically lower at week 4 (2.097 ± 0.111 vs 2.431 ± 0.108, p=0.032). QLQ-C30 and QLQ-LC13 summary scores (p>0.05) were similar for both RAL and VAL during

311 the first 48 weeks of follow-up. HRQoL score assessed with the EQ-5D questionnaire was
312 also comparable between the two groups ($p > 0.05$) during the whole study period.
313 **Interpretation:** Both RAL and VAL showed satisfactory and comparable HRQoL and
314 postoperative pain up to 48 weeks after surgery, despite some minor statistical differences at
315 week 4.
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405

406 **Table 1. Patient clinicopathological characteristics and perioperative outcomes**

407 [a]Two patients underwent bilobectomy in the video-assisted group.

408 Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; ECOG

409 PS, Eastern Cooperative Oncology Group performance score; IQR, interquartile range; LLL,

410 left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL,

411 right upper lobe.

412 **Table 2. Completion and compliance for the questionnaires**

413 Data are n (%) or n/N (%). Completion was defined as completing at least one item among the

414 total HRQoL analysis population. Compliance was defined as completing at least one item at

415 each timepoint, as listed in the numerator for each group, among patients who were expected

416 to complete at each timepoint (except for deaths, dementia, or illiteracy, etc). Abbreviations:

417 EQ-5D, The European Quality of Life 5 Dimensions; HRQoL, health-related quality-of-life;

418 NRS, numeric rating scale; QLQ-C30, quality of life questionnaire core 30 items; QLQ-LC13,

419 quality of life questionnaire lung cancer 13 items; RAL, robotic-assisted lobectomy; VAL,

420 video-assisted lobectomy.

421 **Figure 1. Patient Enrollment and Outcomes**

422 HRQoL assessments are shown according to planned procedure. Assessments were completed

423 on paper by each patient in person at clinics or telephone interview. *Baseline data had been

424 collected before surgery. Abbreviations: QoL, quality of life; RAL, robotic-assisted lobectomy;

425 VAL, video-assisted lobectomy.

426 **Figure 2. Mean scores in QLQ-C30 GHS/QoL (A), change from baseline to week 48 in (B)**

427 **QLQ-C30 functioning and symptom scales and (C) QLQ-LC13 symptoms**

428 Mean scores in QLQ-C30 GHS/QoL at baseline, weeks 4, 24 and 48 (A). For GHS and

functioning scales, higher scores denote improved functioning; for symptom scales, higher scores denote worse symptoms (B, C). Mean score changes are based on a constrained longitudinal data analysis model. Error bars represent SEs. Abbreviations: CI, confidence interval; GHS, global health status; QLQ-C30, quality of life questionnaire core 30 items; QLQ-LC13, quality of life questionnaire lung cancer 13 items; QoL, quality of life; RAL, robotic-assisted lobectomy; SE, standard error; VAL, video-assisted lobectomy.

Figure 3. Proportion of patients with improved, stable, and worse QLQ-C30 scores at week 4 (A) and 48 (B)

Abbreviations: GHS, global health status; QLQ-C30, quality of life questionnaire core 30 items; QoL, quality of life; RAL, robotic-assisted lobectomy; VAL, video-assisted lobectomy.

Figure 4. Proportion of 5 dimensions in EQ-5D at weeks 4 (A), 48 (B) and mean scores at common assessment time points for EQ-5D UI (C)

Proportion of individual dimension in EQ-5D at week 4 and 48 (A, B). Mean scores for EQ-5D UI at baseline, weeks 4, 24, 48. Mean difference between RAL and VAL groups(C). Error bars indicate SEs. Abbreviations: CI, confidence interval; EQ-5D, The European Quality of Life 5 Dimensions; RAL, robotic-assisted lobectomy; SE, standard error; UI, utility index; VAL, video-assisted lobectomy

Figure 5. Postoperative Pain Scores (A) and Subgroup Analyses Comparing Postoperative Pain Scores at week 4 (B)

VAS was used in the first day after operation and NRS was used during baseline evaluation and at weeks 4, 24, 48. Error bars indicate SEs. Chronic disease[a] included hypertension, diabetes, cardiovascular disease, etc. *$p<0.05$. Abbreviations: BMI, body mass index; CI, confidence

451 interval; NRS, numeric rating scale; RAL, robotic-assisted lobectomy; SE, standard error; VAL,

452 video-assisted lobectomy.

453

Table 1. Patient clinicopathological characteristics and perioperative outcomes

Characteristic	Robotic-assisted lobectomy (n=157)	Video-assisted lobectomy (n=163)	P
Age [year], median (IQR)	61 (54-66)	62 (53-68)	0.29
Sex, No. (%)			0.44
Male	81 (51.6)	76 (46.6)	
Female	76 (48.4)	87 (53.4)	
Place of residence, No. (%)			0.44
Urban	100 (63.7)	97 (59.5)	
Rural	57 (36.3)	66 (40.5)	
Employment status, No. (%)			0.09
Employed	47 (29.9)	35 (21.5)	
Unemployed	3 (1.9)	8 (4.9)	
Retired	103 (68.2)	120 (73.6)	
Education level, No. (%)			0.29
College	53 (33.8)	42 (25.8)	
Middle school	70 (44.6)	81 (49.7)	
Less than middle school	34 (21.6)	40 (24.5)	
BMI [kg/m^2], median (IQR)	23.4 (21.7-25.6)	22.9 (21.4-24.4)	0.05
Smoking index, No. (%)			0.66
No	110 (70.1)	110 (67.5)	
<400	14 (8.9)	12 (7.4)	
>=400	33 (21.0)	41 (25.2)	
ECOG PS, No. (%)			0.10
0	137 (87.3)	128 (78.5)	
1	19 (12.1)	32 (19.6)	
2	1 (0.6)	3 (1.8)	
COPD, No. (%)	1 (0.6)	4 (2.5)	0.37
Diabetes, No. (%)	19 (12.1)	14 (8.6)	0.40
Cardiovascular disease, No. (%)	6 (3.8)	6 (3.7)	>0.99
Hypertension, No. (%)	47 (29.9)	48 (29.4)	>0.99
Tumor location[a], No. (%)			>0.99
LLL	21 (13.4)	22 (13.5)	
LUL	36 (22.9)	35 (21.5)	
RLL	21 (13.4)	22 (13.5)	
RML	26 (16.6)	29 (17.8)	
RUL	53 (33.8)	57 (35.0)	
Pathological TNM stage, No. (%)			0.89
0	2 (1.3)	1 (0.6)	
IA1	40 (25.5)	39 (23.9)	
IA2	67 (42.7)	59 (36.2)	
IA3	15 (9.6)	20 (12.3)	

IB	12 (7.6)	13 (8.0)	
IIA	3 (1.9)	6 (3.7)	
IIB	7 (4.5)	9 (5.5)	
IIIA	10 (6.4)	14 (8.6)	
IIIB	1 (0.6)	2 (1.2)	
Operation time [min], median (IQR)	110 (95–140)	120 (97.5–150)	0.25
Blood loss [mL], median (IQR)	100 (50–100)	100 (50–150)	0.04
Conversion to thoracotomy, No. (%)	7 (4.5)	9 (5.5)	0.86
Postoperative hospital stay [d], median (IQR)	4 (4–5)	5 (4–5)	0.76
Postoperative complications, No. (%)	23 (14.6)	30 (18.4)	0.45
Clavien Dindo I-II	18 (11.5)	24 (14.7)	0.49
Clavien Dindo III-IV	5 (3.2)	6 (3.7)	>0.99

Table 2. Completion and compliance for the questionnaires

	RAL group (n=157)	VAL group (n=163)
QLQ-C30, QLQ-C13 and EQ-5D		
Baseline	157 (100%)	163 (100%)
Week 4		
Completion	144 (92%)	153 (94%)
Compliance	144/155 (93%)	153/160(96%)
Week 24		
Completion	139 (86%)	143 (88%)
Compliance	139/154 (90%)	143/158 (91%)
Week 48		
Completion	131 (83%)	134 (82%)
Compliance	131/150 (87%)	134/149 (90%)
NRS/VAS		
Baseline	157 (100%)	163 (100%)
Post-op day 1	157 (100%)	163 (100%)
Week 4		
Completion	144 (92%)	153 (94%)
Compliance	144/155 (93%)	153/160(96%)
Week 24		
Completion	139 (86%)	143 (88%)
Compliance	139/154 (90%)	143/158 (91%)
Week 48		
Completion	131 (83%)	134 (82%)
Compliance	131/150 (87%)	134/149 (90%)

Figure 1. Patient Enrollment and Outcomes

HRQoL assessments are shown according to planned procedure. Assessments were completed on paper by each patient in person at clinics or telephone interview. *Baseline data had been collected before surgery. Abbreviations: QoL, quality of life; RAL, robotic-assisted lobectomy; VAL, video-assisted lobectomy.

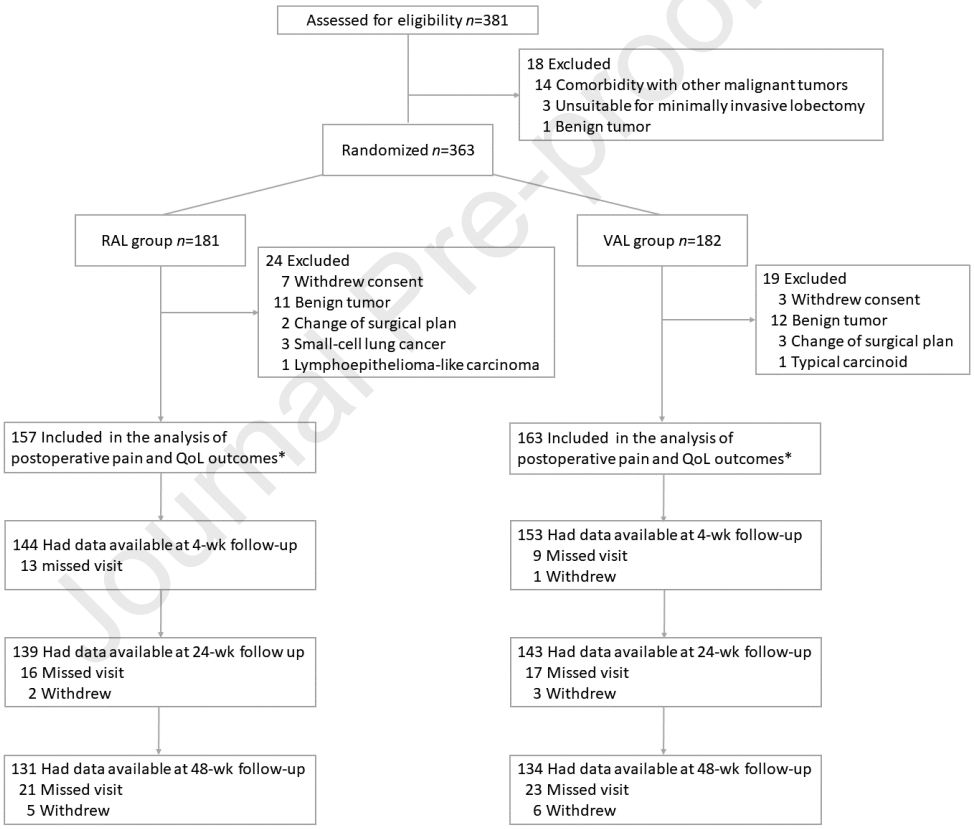


Figure 2. Mean scores in QLQ-C30 GHS/QoL (A), change from baseline to week 48 in (B) QLQ-C30 functioning and symptom scales and (C) QLQ-LC13 symptoms

Mean scores in QLQ-C30 GHS/QoL at baseline, weeks 4, 24 and 48 (A). For GHS and functioning scales, higher scores denote improved functioning; for symptom scales, higher scores denote worse symptoms (B, C). Mean score changes are based on a constrained longitudinal data analysis model. Error bars represent SEs. Abbreviations: CI, confidence interval; GHS, global health status; QLQ-C30, quality of life questionnaire core 30 items; QLQ-LC13, quality of life questionnaire lung cancer 13 items; QoL, quality of life; RAL, robotic-assisted lobectomy; SE, standard error; VAL, video-assisted lobectomy.

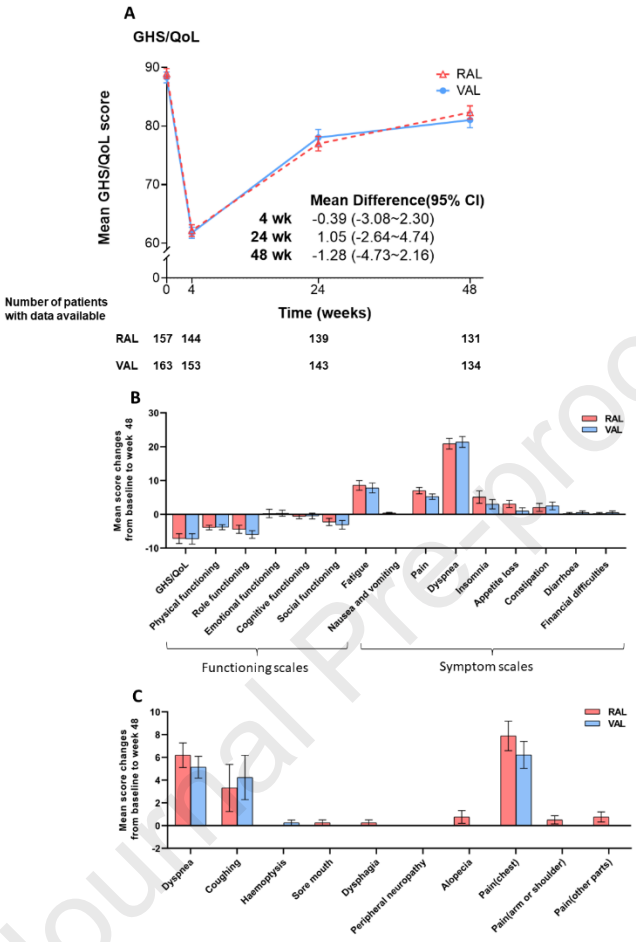


Figure 3. Proportion of patients with improved, stable, and worse QLQ-C30 scores at week 4 (A) and 48 (B)

Abbreviations: GHS, global health status; QLQ-C30, quality of life questionnaire core 30 items; QoL, quality of life; RAL, robotic-assisted lobectomy; VAL, video-assisted lobectomy.

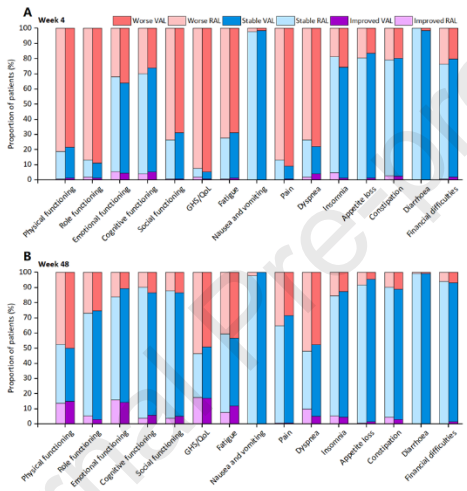


Figure 4. Proportion of 5 dimensions in EQ-5D at weeks 4 (A), 48 (B) and mean scores at common assessment time points for EQ-5D UI (C)

Proportion of individual dimension in EQ-5D at week 4 and 48 (A, B). Mean scores for EQ-5D UI at baseline, weeks 4, 24, 48. Mean difference between RAL and VAL groups (C). Error bars indicate SEs. Abbreviations: CI, confidence interval; EQ-5D, The European Quality of Life 5 Dimensions; RAL, robotic-assisted lobectomy; SE, standard error; UI, utility index; VAL, video-assisted lobectomy.

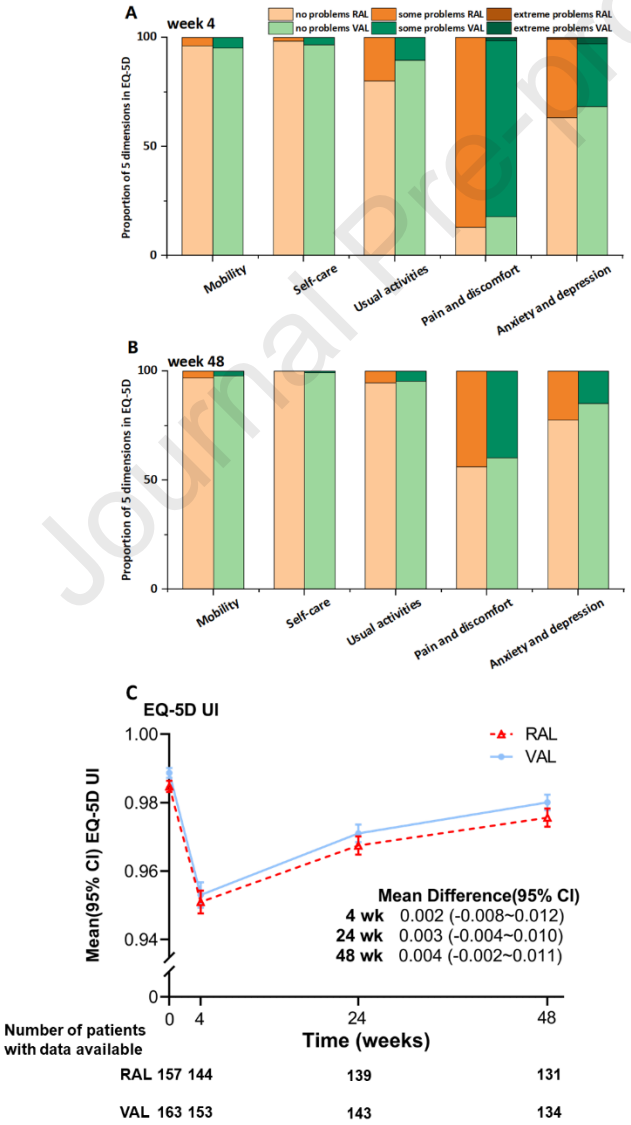
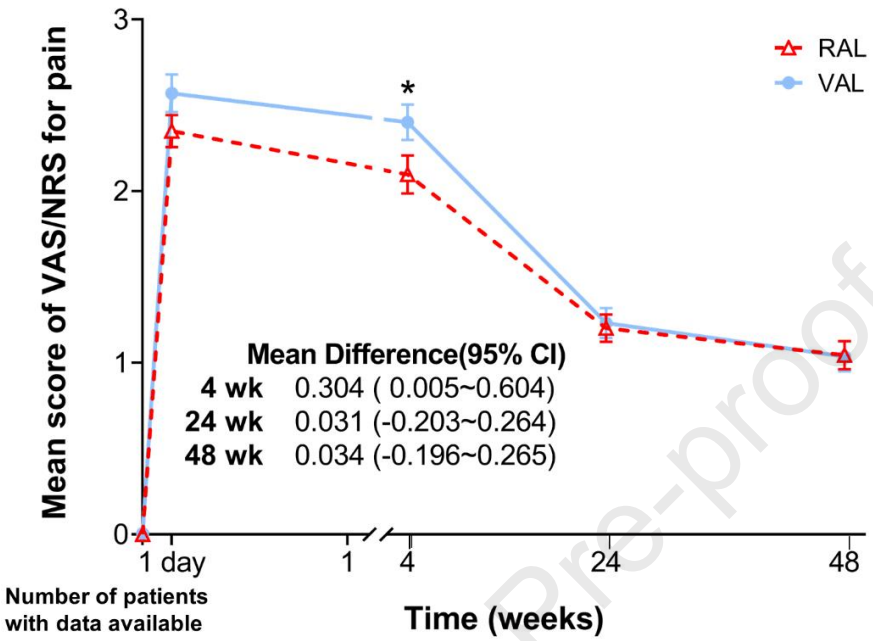


Figure 5. Postoperative Pain Scores (A) and Subgroup Analyses Comparing Postoperative Pain Scores at week 4 (B)

VAS was used in the first day after operation and NRS was used during baseline evaluation and at weeks 4, 24, 48. Error bars indicate SEs. Chronic disease[a] included hypertension, diabetes, cardiovascular disease, etc. *$p<0.05$. Abbreviations: BMI, body mass index; CI, confidence interval; NRS, numeric rating scale; RAL, robotic-assisted lobectomy; SE, standard error; VAL, video-assisted lobectomy.

A

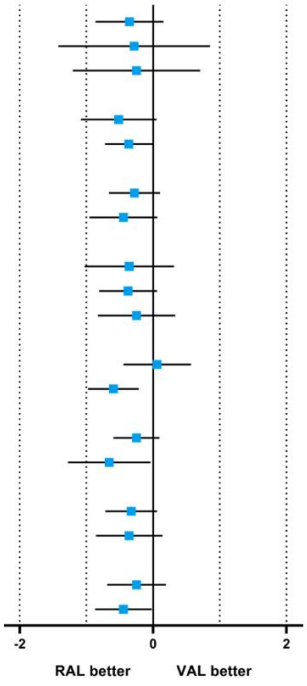


Number of patients with data available

RAL	157	144	139	130
VAL	163	153	143	134

B

Subgroup	RAL group Total N	VAL group Total N	P-value
Overall	144	153	
pTNM			
I	121	125	0.05
II	10	12	0.61
III	11	15	0.60
BMI			
24.5+	51	38	0.08
< 24.5	93	115	0.04
Chronic disease[a]			
No	91	103	0.16
Yes	53	50	0.09
Education			
College	51	41	0.40
High school	62	75	0.09
Primary school	31	37	0.29
Place of residence			
Rural	52	62	0.81
Urban	92	91	0.002
Job			
Unemployed	102	120	0.16
Employed	42	33	0.07
Age			
60+	84	94	0.10
<60	60	59	0.16
Sex			
Female	69	84	0.27
Male	75	69	0.04



Conflict of Interest and Source of Funding: Hecheng Li is currently receiving a Robotic Research Grant from Intuitive Surgical Operations, Inc. Jules Lin is a robotic proctor for Intuitive Surgical, Inc. For the remaining authors none were declared.

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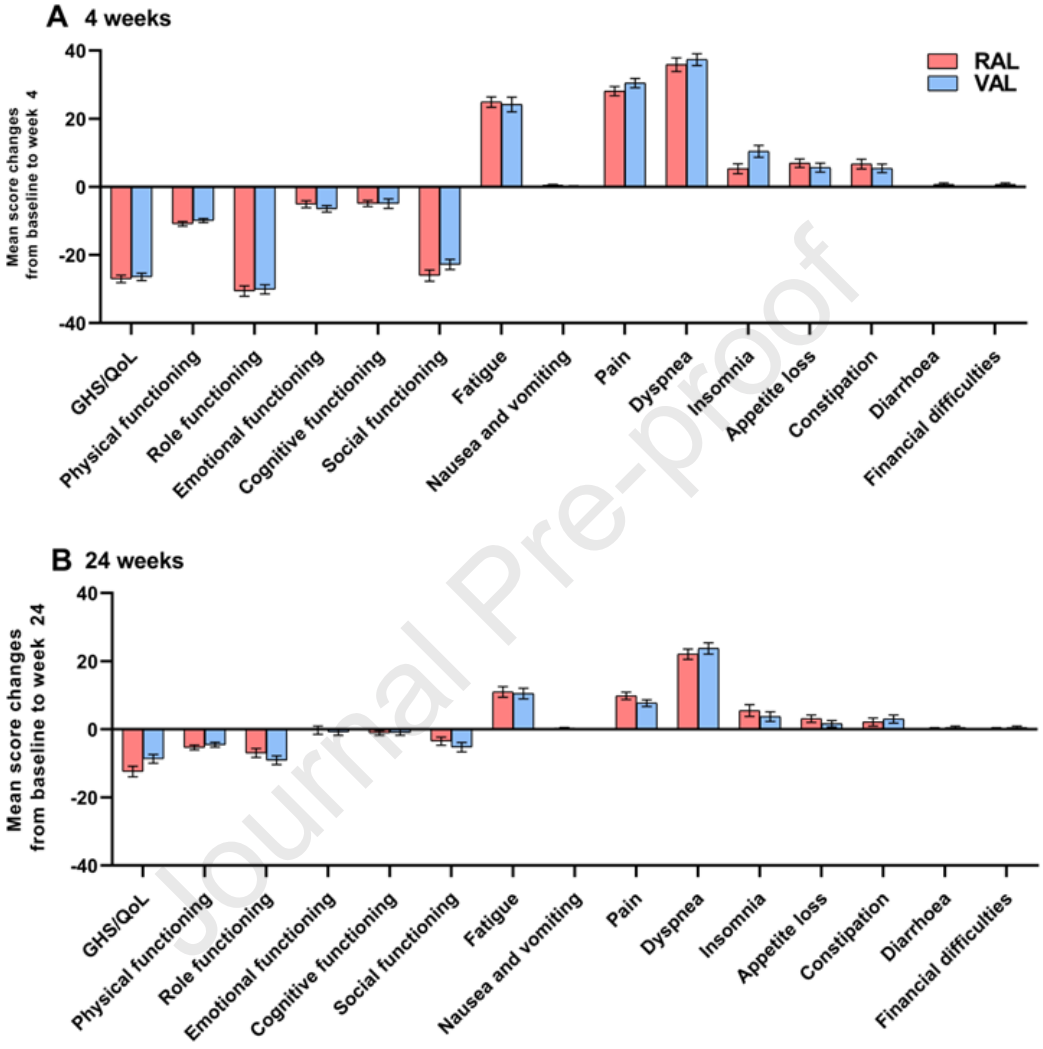
Supplementary Figure 1. Change from baseline during follow-up in QLQ-C30 functioning and symptom scales

A, B represented the outcomes at weeks 4 and 24. For GHS and functioning scales, higher scores denote improved functioning; for symptom scales, higher scores denote worse symptoms. Mean score changes are based on a constrained longitudinal data analysis model. Error bars represent SEs. Abbreviations: GHS, global health status; QLQ-C30, quality of life questionnaire core 30 items; QoL, quality of life; RAL, robotic-assisted lobectomy; SE, standard error; VAL, video-assisted lobectomy.

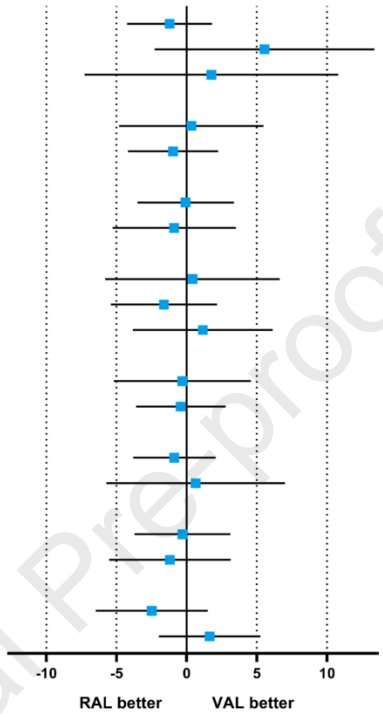


Supplementary Figure 2. Subgroup Analyses Comparing GHS/QoL at weeks 4 (A) and 48 (B)

Chronic disease[a] included hypertension, diabetes, cardiovascular disease, etc. Abbreviations: BMI, body mass index; GHS/QoL, global health status/quality of life; RAL, robotic-assisted lobectomy; VAL, video-assisted lobectomy.

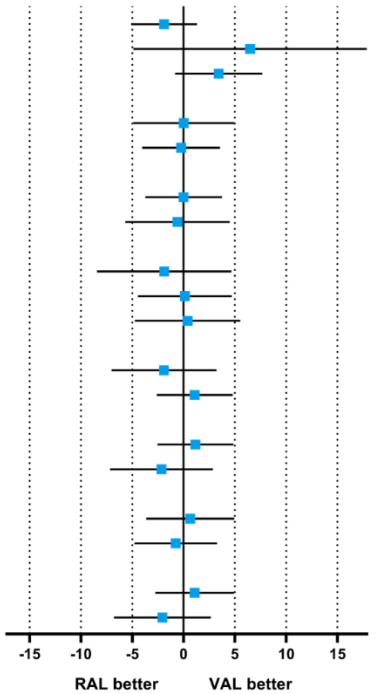
A

Subgroup	RAL group Total N	VAL group Total N	P-value
Overall	144	153	
pTNM			
I	121	125	0.43
II	10	12	0.15
III	11	15	0.69
BMI			
24.5+	51	38	0.89
< 24.5	93	115	0.55
Chronic disease[a]			
No	91	103	0.69
Yes	53	50	0.97
Education			
College	51	41	0.64
High school	62	75	0.30
Primary school	31	37	0.89
Place of residence			
Rural	52	62	0.90
Urban	92	91	0.80
Job			
Unemployed	102	120	0.56
Employed	42	33	0.84
Age			
60+	84	94	0.87
<60	60	59	0.59
Sex			
Female	69	84	0.22
Male	75	69	0.37



B

Subgroup	RAL group Total N	VAL group Total N	P-value
Overall	131	134	
pTNM			
I	111	114	0.24
II	9	11	0.25
III	9	8	0.06
BMI			
24.5+	47	32	0.99
< 24.5	84	102	0.90
Chronic disease[a]			
No	85	94	> 0.99
Yes	46	40	0.82
Education			
College	50	38	0.88
High school	60	68	0.96
Primary school	21	28	0.57
Place of residence			
Rural	44	53	0.46
Urban	87	81	0.56
Job			
Unemployed	86	101	0.54
Employed	45	33	0.39
Age			
60+	70	78	0.76
<60	61	56	0.71
Sex			
Female	62	77	0.58
Male	69	57	0.39

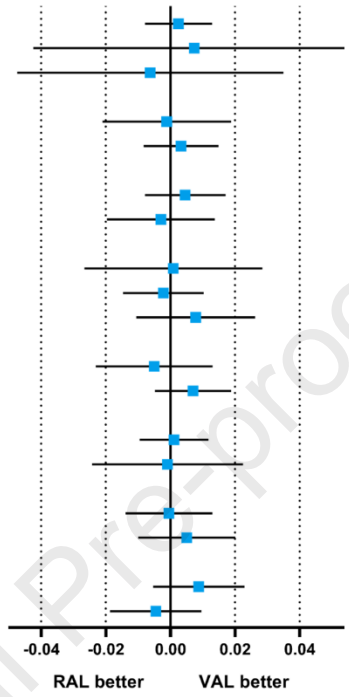


Supplementary Figure 3. Subgroup Analyses Comparing EQ-5D UI at weeks 4 (A) and 48 (B)

Chronic disease[a] included hypertension, diabetes, cardiovascular disease, etc. Abbreviations: BMI, body mass index; EQ-5D, The European Quality of Life 5 Dimensions; RAL, robotic-assisted lobectomy; UI, utility index; VAL, video-assisted lobectomy.

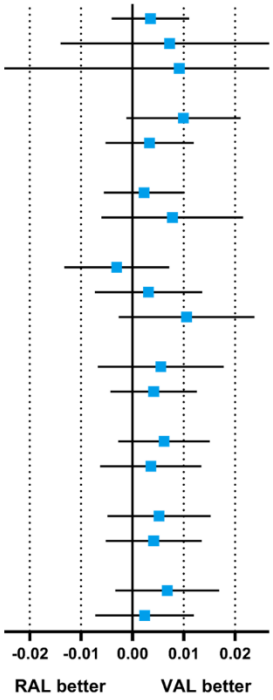
A

Subgroup	RAL group Total N	VAL group Total N	P-value
Overall	144	153	
pTNM			
I	121	125	0.64
II	10	12	0.76
III	11	15	0.75
BMI			
24.5+	51	38	0.91
< 24.5	93	115	0.57
Chronic disease[a]			
No	91	103	0.73
Yes	53	50	0.47
Education			
College	51	41	0.40
High school	62	75	0.73
Primary school	31	37	0.95
Place of residence			
Rural	52	62	0.24
Urban	92	91	0.59
Job			
Unemployed	102	120	0.47
Employed	42	33	0.94
Age			
60+	84	94	0.38
<60	60	59	0.51
Sex			
Female	69	84	0.22
Male	75	69	0.52



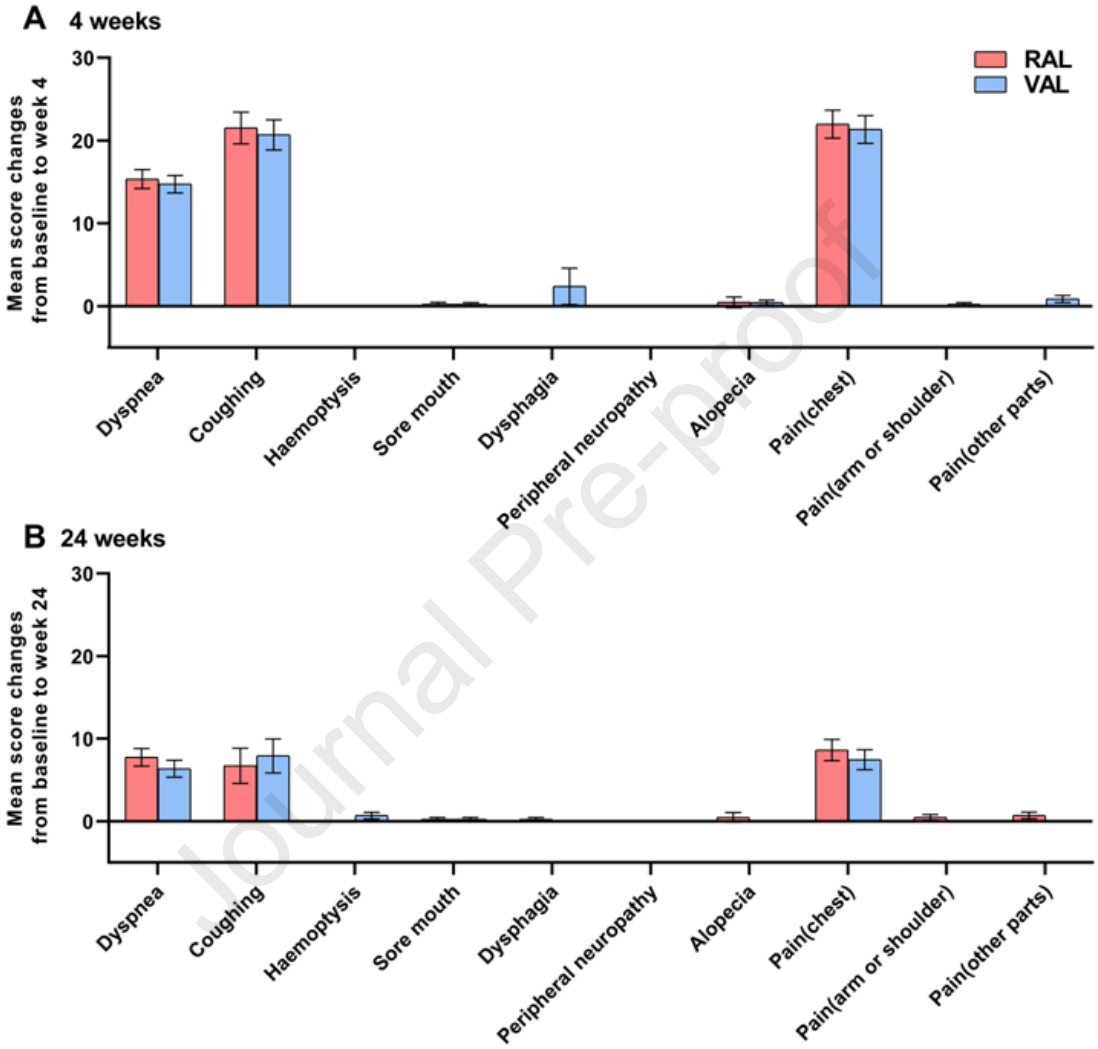
B

Subgroup	RAL group Total N	VAL group Total N	P-value
Overall	131	134	
pTNM			
I	111	114	0.36
II	9	11	0.48
III	9	8	0.60
BMI			
24.5+	47	32	0.08
< 24.5	84	102	0.46
Chronic disease[a]			
No	85	94	0.56
Yes	46	40	0.27
Education			
College	50	38	0.12
High school	60	68	0.55
Primary school	21	28	0.55
Place of residence			
Rural	44	53	0.33
Urban	87	81	0.37
Job			
Unemployed	86	101	0.17
Employed	45	33	0.83
Age			
60+	70	78	0.30
<60	61	56	0.95
Sex			
Female	62	77	0.17
Male	69	57	0.62



Supplementary Figure 4. Change from baseline during follow-up in QLQ-LC13 symptoms

A, B represented the outcomes at weeks 4 and 24. For GHS and functioning scales, higher scores denote improved functioning; for symptom scales, higher scores denote worse symptoms. Mean score changes are based on a constrained longitudinal data analysis model. Error bars represent SEs. Abbreviations: QLQ-LC13, quality of life questionnaire lung cancer 13 items; RAL, robotic-assisted lobectomy; SE, standard error; VAL, video-assisted lobectomy.



Supplementary Table 1. The frequency of analgesic drug after operation

	RAL group (n=157)	VAL group (n=163)
Analgesic drug		
Nonsteroidal		
Flurbiprofen axetil	6 (4%)	10 (6%)
Indometacin suppositories	0	1 (0.6%)
Tylox capsule	37 (24%)	25 (15%)
Ibuprofen	21 (13%)	27 (17%)
Compound Paracetamol Tablets(Ⅱ)	2 (1%)	1 (0.6%)
Opioids		
Meperidine	3 (2%)	7 (4%)
Tramadol hydrochloride	1 (0.6%)	4 (2%)
Morphine hydrochloride	0	1 (0.6%)

The table exhibited the frequency of analgesics three days after operation. Some patients used multiple analgesics.