Patient-Reported Outcomes of Radiofrequency Ablation versus Video-Assisted Thoracoscopic Surgery for Stage IA NSCLC: A Longitudinal Cohort Study

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Abstract

Background

Radiofrequency ablation (RFA), a less invasive modality, demonstrates promising oncologic outcomes for early stage lung cancers. However, existing RFA data on patient-reported outcomes (PROs) remain scarce, particularly regarding postoperative recovery trajectories. To address this, an analysis of PROs from a cohort study was conducted to evaluate postoperative symptom burden and functional recovery RFA and VATS.

Methods

A single-center, real-world study was conducted, including 244 stage IA NSCLC patients treated between December 2023 and October 2024. PRO data were collected via the MD Anderson Symptom Inventory–Lung Cancer module (MDASI-LC) at baseline, postoperative days 1–7, and 1-, 3-month follow-ups. The primary outcomes were postoperative symptom burden and functional impairment. Mixed-effects models analyzed differences in symptom severity over time, while Kaplan–Meier analysis assessed recovery duration.

Results

RFA patients reported significantly milder symptoms at postoperative day 7, including pain (5.66% vs 38.96%, $p < 0.0001$), fatigue (5.66% vs 32.47%, $p < 0.0001$), and shortness of breath (8.81% vs 41.56%, $p < 0.0001$). Functional impairment in daily activities, work, and mobility was also lower in the RFA group at both day 7 and day 30 (all $p < 0.0001$). Mixed-effects modeling confirmed a protective effect of RFA on symptom burden and recovery, especially on pain (Estimate = -2.29583, $p < 0.0001$), fatigue (Estimate = -1.59997, $p < 0.0001$), general activity (Estimate = -1.77213, $p < 0.0001$), and work (Estimate = -1.56664, $p < 0.0001$). RFA patients had significantly shorter recovery times for key symptoms compared to VATS (all $p < 0.0001$).

Conclusions

RFA results in milder symptoms, faster recovery, and improved postoperative quality of life. These findings support RFA as a less invasive, patient-friendly alternative for early-stage NSCLC.

Introduction

While surgical resection remains the recommended treatment for pulmonary tumors without lymph node metastasis[1, 2], thermal ablation (such as RFA, MWA), with its faster postoperative recovery and minimal invasiveness, holds potential for application in the treatment of multiple primary lung cancers[3, 4].

As a minimally invasive local therapy, thermal ablation has been recommended by the NCCN NSCLC Guidelines (2025 V1) as the second-line treatment after stereotactic body radiation therapy (SBRT) for inoperable stage IA NSCLC patients[1, 5, 6], demonstrating promising oncological efficacy while better preserving pulmonary function[7]. The cost-effectiveness of ablation techniques, attributable to their relatively lower consumable costs, positions them as a viable alternative to surgical intervention[8, 9].

Traditional clinical practice has predominantly relied on objective indicators (postoperative CT findings, laboratory tests, drainage volume, and length of hospital stay) rather than patient-reported outcomes to assess postoperative recovery, leading to an incomplete evaluation of different surgical treatments[10–13]. In recent years, there has been increasing recognition of patient-reported outcomes (PROs) as essential clinical endpoints[14–23], with the U.S. Food and Drug Administration approving their use in drug labeling-claim trials[24]. PROs provide critical insights into patients' authentic perceptions of symptom alleviation and functional recovery across different treatment modalities[19, 25, 26]. Previous studies by Wei et al. demonstrated through electronic PRO (ePRO) systems that VATS resulted in reduced postoperative symptom burden and minimized daily functional impairment compared to thoracotomy in locally advanced lung cancer[27, 28]. However, few previous studies have used PROs to evaluate the application of

RFA. This study aimed to delineate the postoperative recovery trajectory of patients undergoing RFA by observing their PROs within a cohort study, using data from conventional uniportal VATS as a reference. The findings are intended to provide a unique perspective on the postoperative symptom management for patients receiving RFA.

Patients and Methods

Study Design and Patients

The 244 subjects were selected from a single-center real-world study which included NSCLC patients who presented to our center and underwent either uniportal video-assisted thoracoscopic surgery (VATS) or radiofrequency ablation (RFA) between December 2023 and October 2024. The real-world study was approved by the Ethics Committee of National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (IRB No. 23/050-3789). All participants provided written, informed consent. Figure 1 illustrates the patient selection process.

The inclusion criteria for extracted cases were as follows: (1) age ≥ 18 years; (2) Clinical stage T1aN0M0 NSCLC; (3) Pathologically confirmed non-small cell lung cancer (NSCLC) or malignancy suspected on PET-CT/CECT (For RFA cases); (4) Active request for radiofrequency ablation therapy and deemed feasible by physician evaluation(For RFA cases); (5) Eastern Cooperative Oncology Group (ECOG) performance status score: 0–2; (6) Ability to provide written informed consent (ICF), with understanding and willingness to comply with study requirements and assessment schedules.

The exclusion Criteria were as follows: (1) Previous treatment for the target lesion(s); (2) Clinical or radiological suspicion of lymph node metastasis; (3) Tumor stage greater than stage IA or those whose postoperative pathology confirmed non-malignant lung cancer; (4) Severely compromised cardiopulmonary function or high risk of pneumothorax due to severe emphysema; (5) Surgeries were canceled due to acute conditions, such as poor blood pressure control or menstruation onset.(6) Other conditions that can not conduct surgical interventions.

Researchers participated in the real-world study had been trained with the standard operating procedure to ensure the accuracy of data collection.

Data were collected and recorded on the ePRO data platform of National Cancer Center. PRO data, Demographic characteristics, preoperative characteristics, surgical information, postoperative pathological diagnosis (postoperative pathological staging was based on the eighth edition of the TNM classification for lung cancer), postoperative complications, and other clinical information were collected.

Baseline variables with statistically significant differences, such as demographic characteristics and preoperative characteristics, were adjusted in the subsequent Mixed Effect Model (MEM) analysis.

Surgical Approaches

Image guided radiofrequency ablation (RFA)

Patients were positioned on the CT examination bed before hybrid surgery. CT-guided surface marking technique was performed with metal grid paper to confirm the position of GGNs and puncture sites. Patients were locally anesthetized with ropivacaine and lidocaine and were ventilated using a mask airway. The puncture path was confirmed multiple times using chest CT. Experienced surgeons adjusted ablation parameters based on tumor size, location, morphology, adjacent structures, puncture path, and vessel diameter near the nodule. Subsequently, the RFA was conducted using the STARmedTM Radiofrequency Ablation System (STARmed, Korea) with VIVA RF Electrode (STARmed, Korea) cooled by water circulation. Additionally, RFA was performed with a host working frequency of 480 kHz, median power of 60 W, for 3–5 minutes or longer in our study. Finally, Chest CT was repeated to evaluate the sufficiency of ablation after RFA. If the post-ablation target zone (PTZ) was not at least 5 mm larger than the gross tumor region (GTR)[29], supplemental ablation was conducted.

Uniportal VATS

In this study, VATS refer to single-port VATS, which usually involved a 3–4-cm incision in the fourth or fifth intercostal space between the anterior axillary line and the middle axillary line[30, 31]. Under general anesthesia, the patient was ventilated using a double-lumen endotracheal tube and underwent disinfection according to the standard procedures for VATS in thoracic surgery.

Outcome Measures

Patient-reported outcome

The MD Anderson Symptom Inventory–Lung Cancer module (MDASI-LC) is a disease-specific MDASI module comprising two parts. Part I includes 13 core symptoms and 3 lung cancer-specific symptoms (coughing, constipation, and sore throat); Part II includes 6 interfered items. MDASI-LC is a valid, reliable, and sensitive symptom assessment that can be used to assess symptom status in lung cancer patients and in epidemiological and prevalence studies of symptom severity[32–35]. The severity of symptoms were rated by patients on a 0–10 scale, as 0 was “absence of symptom”, 10 was “the worst symptoms one thinks”. Similarly, degree to which daily life is affected by symptoms were also rated on a 0–10 scale. Items scoring ≥ 4 were considered as moderate-to-severe symptoms or functional impairment.

The MDASI-LC scale were completed through electronic questionnaires or phone interviews if patients can not read or use mobile phone. ePRO assessments were scheduled preoperatively (as baseline), postoperatively daily (up to 7 days), day 10, 14, 17, 21, 30, 42, 56, 60, 70, 90 after Surgical treatment[36].

Complications

Postoperative complications were recorded for up to 4 weeks after discharge or until the start of postoperative cancer treatment using the Clavien–Dindo classification[37].

Statistical Analysis

The patients were from 2 cohort (RFA and VATS cohort) according to the surgical treatment confirmed through the shared-decision making process.

Continuous variables following a normal distribution are expressed as the mean ± standard deviation. Categorical variables are presented as numbers, percentages, or proportions. Baseline and clinical characteristics were compared between the VATS and RFA groups. For continuous variables, the t-test was applied to normally distributed data, while the Mann–Whitney U test was used for non-normally distributed data. Chi-square tests with Yates' correction and Fisher’s exact test were used for categorical variables.

Longitudinal ePRO data were analyzed at baseline (POD 0), POD 1–7, 10, 14, 17, 21, 24, 30, 42, 56, 60, 70, 90 follow-ups. We calculated the completion rate of the questionnaire at each assessment point to ensure the validity of the ePRO results. The prevalence of moderate-to-severe symptoms (defined as scoring ≥ 4 points on the assessment scale at a time point) was quantified every time point (POD 0–7, 10, 14, 17, 21, 24, 30, 42, 56, 60, 70, 90) and reported as proportions of patients with 95% confidence intervals[38, 39].

Mixed-effect models were used to assess whether **scores** differed significantly over time (POD 0–7, 10, 14, 17, 21, 24, 30, 42, 56, 60, 70, 90) between the different surgical treatment (RFA vs VATS). In these models, the independent variable was the score of each item as a continuous variable, and the dependent variables were time, treatment groups, interaction between time and treatment groups, hospital duration (in days), and baseline variables (which differed between groups in the univariate analysis). Additionally, The relative risks (RR) for moderate-to-severe symptoms and functional outcome on postoperative day 7 and day 30 were calculated using a mixed-effects model. Variables with statistical differences between the two groups were included in the mixed-effect model for adjustment.

Postoperative recovery was defined as symptoms returning to none/mild level (0–3 on a 0–10-point scale). Between-group comparisons of recovery trajectory (Since the proportion of patients with moderate-to-severe symptoms in two groups were different, only patients with moderate-to-severe symptoms or function impairment were analysed.) based on surgical approach were conducted using Kaplan–Meier analysis with log-rank test.

Two-sided p-value <0.05 was considered to be statistically significant. Analyses were performed using SAS 9.4 and Graphpad PRISM 10.

Result

Patient Characteristics

Ultimately, a total of 244 patients were included in the analysis (Fig. 1). The mean age was comparable between groups (RFA: 57.69 ± 12.48 years vs. VATS: 57.15 ± 10.54 years; p = 0.4350). The proportion of patients aged ≤ 60 and > 60 years was also similar across both cohorts (p = 0.6079). 164 and 80 patients underwent RFA and VATS, respectively. A significant sex distribution difference was observed (p = 0.0005), with a higher proportion of male patients in the RFA group (62.20%), whereas the VATS cohort had a higher proportion of female patients (62.50%). There were no significant differences observed in Employment status, Smoking status, Comorbidity, Lobular location, Lesion morphology from preoperative chest CT (all p>0.05). Given that nearly half of the patients were unwilling to disclose their annual household income, the observed significant difference may not be meaningful. Due to the fact that RFA is the preferred modality for smaller nodules with a minimal solid portion, whereas VATS is typically reserved for larger (> 10 mm) mGGNs characterized by a greater solid component, A baseline discrepancy in Maximum diameter of lesion was observed in this two groups, the mean maximum lesion diameter was significantly larger in the VATS group (17.06 ± 8.994 mm) compared to the RFA cohort (11.15 ± 4.05 mm, p < 0.0001). Similarly, among patients with solid components (nRFA = 44, nVATS = 28), the mean maximum diameter of the solid portion was markedly greater in the VATS group (14.36 ± 10.96 mm) than in RFA (6.243 ± 4.179 mm, p < 0.0001). To account for this initial imbalance, the aforementioned baseline discrepancy was statistically controlled for in all subsequent analyses. The consolidation-to-tumor ratio (CTR) showed no significant difference between the groups (p = 0.1834). The histopathological distribution of lesions among patients in the VATS group (n = 80) is summarized in Table 1. Consequently, none of the lesions treated with RFA had pathological results.

Table 1
Patient Characteristics

Characteristics	RFA n = 164	VATS n = 80	p value
Age, years, mean(SD)	57.69(12.48)	57.15(10.54)	0.4350[a]
Age, years, n(%)			0.6079[b]
≤ 60	85(51.83%)	45(56.25%)	
> 60	79(48.17%)	35(43.75%)	
Sex, n(%)			**0.0005[b]**
Female	62(37.80%)	50(62.50%)	
Male	102(62.20%)	30(37.50%)	
Educational level, n(%)			0.9554[b]
≤high school	78(47.56%)	37(46.25%)	
>high school	86(52.44%)	43(53.75%)	
Employment status, n(%)			0.9838[b]
Full or part-time	70(42.68%)	35(43.75%)	
Not currently working	94(57.32%)	45(56.25%)	
Annual household income, n(%)			**< 0.0001[b]**
< 100,000 CNY	56(34.15%)	25(31.25%)	
≥ 100,000 CNY	11(6.71%)	29(36.25%)	
Reluctance to disclose	97(59.15%)	36(45.00%)	
Smoking status, n(%)			0.2642[b]
Current or former	34(20.73%)	15(19.75%)	
Never	130(79.27%)	65(81.25%)	
Comorbidity (CCI), n(%)			0.5224[b]
0	128(78.05%)	66(82.50%)	
≥ 1	36(21.95%)	14(17.50%)	
Lesion Characteristics			
Lobular location			0.5881[c]
Right upper lobe, n(%)	48(29.27%)	20(25.00%)	
Right middle lobe, n(%)	10(6.10%)	7(8.75%)	
Right lower lobe, n(%)	37(22.56%)	13(16.25%)	
Left upper lobe, n(%)	42(25.61%)	23(28.75%)	
Left lower lobe, n(%)	27(16.46%)	17(21.25%)	
Lesion morphology from preoperative chest CT			0.3152[c]
Pure ground-glass opacity, n(%)	75(45.73%)	28(35.00%)	
Mixed ground-glass opacity, n(%)	31(18.90%)	20(25.00%)	

Characteristics	RFA n = 164	VATS n = 80	p value
Solid, n(%)	10(6.10%)	8(10.00%)	
Multiple lesions, n(%)	48(29.27%)	24(30.00%)	
Maximum diameter, mm, mean (SD)* **	11.15(4.05)	17.06(8.994)	**< 0.0001[d]**
Maximum diameter of solid component, mm, mean (SD)*	6.243(4.179)	14.36(10.96)	**< 0.0001[d]**
Consolidation-to-tumour ratio, ratio, mean(SD)*	0.5105(0.3120)	0.6111(0.3060)	0.1834[d]
N stage from chest CT**			
N0	164	80	
N1 or N2	0	0	
Postoperative length of stay, days, median	5(2–11)	5(1–11)	**< 0.0001[a]**
Histopathological Characteristics, n(%)			
AIS	16(20.00%)	N/A	
MIA	7(8.75%)	N/A	
Adenocarcinoma	54(67.50%)	N/A	
non-Adenocarcinoma	3(3.75%)	N/A	
*n(RFA) = 44, n(VATS) = 28 patients' lesions had solid components			
**Positive lymph nodes on CT chest defined as: mediastinal, hilar lymph nodes > 1cm in short diameter			
***In case of multiple lesions, the largest lesion is measured			
[a] Mann–Whitney U test			
[b] Chi-square tests with Yates' correction,			
[c] Fisher exact probability test			
[d] t-test			

Complications

Postoperative pneumothorax occurred in 4.88% of RFA patients and 1.25% of VATS patients (p = 0.2938). Pleural effusion was observed in 9.76% of RFA cases and 6.25% of VATS cases (p = 0.5006). Fever > 38°C, pneumonia, atelectasis, hemoptysis, and subcutaneous emphysema were reported only in the RFA group, with low incidence. Due to small event counts, statistical comparisons were not performed (**Supplemental Table 5**).

No significant differences were found between RFA and VATS in postoperative complications. All of the aforementioned complications were classified as Clavien-Dindo grade I and required no clinical intervention.

The longitudinal follow-up of PRO data

All the 244 patients provided MDASI-LC at the baseline(0 day). The completion rates of the MDASI-LC questionnaire were 100% at baseline, 98.77% to 96.72% during the 1–7 postoperative days, and from 95.49% to 86.07% in the follow-up (**Supplemental Table 1**).

Patient-reported outcomes

The proportion of moderate-to-severe items

The 10 most severe symptoms reported in both groups during the postoperative days (POD) 1–7 were disturbed sleep (21.09%), pain (19.21%), fatigue (18.30%), shortness of breath (17.87%), constipation (16.72%), dry mouth (13.19%), psychological distress

(13.13%), coughing (12.34%), drowsy (10.76%), and remembering(forgetfulness) (10.15%) based on 1645 symptom assessments conducted throughout the postoperative period (**Supplemental Table 2**). There was no significant difference between groups at baseline (day 0). At the POD 7, the proportion of patients with moderate-to-severe symptoms (RFA vs VATS) pain, RR = 0.11(0.05_to_0.28) ,5.66% vs 38.96%, p < 0.0001; fatigue, RR = 0.16(0.07_to_0.4), 5.66% vs 32.47%, p < 0.0001; disturbed sleep, RR = 0.22(0.1_to_0.5), 8.18% vs 32.47%, p = 0.0003; distressed, RR = 0.13(0.03_to_0.47), 2.52% vs 19.48%, p = 0.0020; shortness of breath, RR = 0.13(0.06_to_0.29), 8.81% vs 41.56%, p < 0.0001; lack of appetite, RR = 0.13(0.03_to_0.48), 1.89% vs 18.18%, p = 0.0023; drowsy, RR = 0.12(0.03_to_0.45), 1.89% vs 18.18%, p = 0.0017; dry mouth, RR = 0.25(0.09_to_0.66), 4.40% vs 19.48%, p = 0.0056; sad, RR = 0.13(0.07_to_0.62), 3.77% vs 19.48%, p = 0.0050; coughing, RR = 0.12(0.04_to_0.31), 5.03% vs 32.47%, p < 0.0001; sore throat, RR = 0.12(0.02_to_0.64), 1.89% vs 10.39%, p = 0.0129 was lower in the RFA group than in the U-VATS group after adjustment for age, maximum of tumor diameters, and other baseline variables with statistical differences (Fig. 2, **Supplemental Table 3**). Given that the clinical indications for these two treatment modalities are not perfectly aligned, the comparative data from the VATS cohort is intended solely to serve as a benchmark for the level of symptomatic changes observed in the patient-reported outcomes (PROs) of the RFA group

However, some symptoms showed no difference between groups at postoperative day 7 (nausea, 1.22% vs 8.75%, p = 0.0525; remembering, 4.88% vs 16.25%, p = 0.0558; vomiting, 1.22% vs 3.75%, p = 0.4774; numbness, 3.66% vs 8.75%, p = 0.2440; constipation, 9.76% vs 22.5%, p = 0.1298).

As for proportion of patients with moderate-to-severe functional impairment, no between-group differences were observed at baseline (day 0),. Patients in the RFA group reported less moderate-to-severe functional impairment in all the functional items at postoperative day 7 and day 30 (Fig. 3, **Supplemental Table 3, 4**), especially in the general activity (RR = 0.12(0.05_to_0.3), 6.10% vs 36.25%, p = 0.0008), mood (RR = 0.14(0.05_to_0.38), 4.27% vs 28.75%, p = 0.0204), relations (RR = 0.08(0.02_to_0.38), 1.83% vs 20.00%, p = 0.0043), Work(RR = 0.21(0.1_to_0.45), 9.15% vs 38.75%, p < 0.0001) at day 7.

However, all the difference had shrunked at POD 90, no significance were observed in symptoms (**Supplemental Table 7**). The proportion of all the symptoms and functional impairment from day 0 to day 90 were shown in **Supplemental Fig. 1** (p-value showed the significance of difference between group comparison at day 30).

In the RFA group, the proportion of patients experiencing moderate-to-severe symptoms and functional impairment remained relatively low. Notably, several moderate-to-severe symptoms—such as shortness of breath, lack of appetite, sadness, coughing, and sore throat—fluctuated in the postoperative period, rather than following the typical pattern of continuous decline after Postoperative Day 1 (POD1). Based on whether the proportion of moderate-to-severe symptoms rebounded postoperatively, symptoms were classified into two distinct patterns: a 'Sustained Resolution' group and a 'Short-Term Fluctuation' group. In contrast to RFA, the primary symptom trajectory for VATS was an 'oscillatory decline,' characterized by an initial decrease followed by subsequent fluctuations. (**Supplemental Fig. 1**)

The mixed-effects model analysis of patient-reported outcomes revealed associations between treatment modality (RFA versus VATS), time, and the interaction term across all measured items. The RFA cohort demonstrated protective effects on most symptoms and functions as expected, especially on pain (Estimate = -2.29583, p < 0.0001), fatigue (Estimate = -1.59997, p < 0.0001), general activity (Estimate = -1.77213, p < 0.0001), and work (Estimate = -1.56664, p < 0.0001). .These treatment advantages became progressively more pronounced over time, ultimately surpassing the temporal effects observed in the study (Table 2, **Supplementary Table 6**).

Table 2
PRO 0-7day Mixed effect model outcomes

Items	RFA versus VATS								
	Group			Time			Group*Time		
Symptom	Estimate	SE	p value	Estimate	SE	p value	Estimate	SE	p value
pain	-2.29583	0.18937	**< 0.0001**	-0.00536	0.00179	**0.00277**	0.02387	0.00318	**< 0.0001**
fatigue	-1.59997	0.21865	**< 0.0001**	-0.00261	0.00166	0.11609	0.01713	0.00296	**< 0.0001**
nausea	-0.68910	0.13837	**< 0.0001**	-0.00113	0.00124	0.36295	0.00480	0.00221	**0.02983**
disturbed.sleep	-1.38701	0.24480	**< 0.0001**	-0.00443	0.00199	**0.02605**	0.01170	0.00354	**0.00096**
distressed	-1.23720	0.22086	**< 0.0001**	-0.00132	0.00157	0.40099	0.01040	0.00280	**0.00022**
shortness.of.breath	-1.45477	0.20871	**< 0.0001**	-0.00119	0.00166	0.47218	0.01095	0.00295	**0.00021**
remembering	-0.32755	0.21935	0.13697	-0.00076	0.00135	0.57312	-0.00173	0.00241	0.47218
lack.of.appetite	-1.01971	0.18539	**< 0.0001**	-0.00046	0.00139	0.74271	0.00877	0.00248	**0.00042**
drowsy	-1.00785	0.18945	**< 0.0001**	-0.00098	0.00148	0.50804	0.01063	0.00264	**0.00006**
dry.mouth	-0.62106	0.25152	**0.01439**	-0.00278	0.00164	0.08987	0.00786	0.00292	**0.00720**
sad	-0.79138	0.22058	**0.00042**	0.00091	0.00136	0.50071	0.00813	0.00241	**0.00077**
vomiting	-0.39562	0.12342	**0.00157**	-0.00031	0.00102	0.75757	0.00302	0.00181	0.09530
numbness	-0.73304	0.16168	**< 0.0001**	0.00055	0.00122	0.65065	0.00073	0.00217	0.73770
coughing	-1.36741	0.18530	**< 0.0001**	-0.00174	0.00154	0.25996	0.00473	0.00275	0.08572
constipation	-1.09563	0.23381	**< 0.0001**	-0.00659	0.00194	**0.00071**	0.01010	0.00346	**0.00353**
sore.throat	-0.69894	0.15503	**< 0.0001**	-0.00092	0.00130	0.48091	0.00739	0.00231	**0.00140**
General.activity	-1.77213	0.20804	**< 0.0001**	-0.00341	0.00168	**0.04282**	0.01139	0.00300	**0.00015**
Mood	-1.18898	0.22019	**< 0.0001**	-0.00097	0.00144	0.50167	0.00735	0.00257	**0.00422**
Work	-1.56664	0.26820	**< 0.0001**	-0.00616	0.00200	**0.00216**	0.00561	0.00357	0.11641
Relations	-0.70170	0.19654	**0.00045**	0.00135	0.00132	0.30487	0.00158	0.00235	0.50056
Walking	-1.48828	0.22267	**< 0.0001**	-0.00241	0.00168	0.15010	0.01041	0.00299	**0.00050**
Statistically significant values are given in bold (p <0.05)									
Adjusted variables: Sex, postoperative hospital duration, Annual household income, Maximum diameter.									
Group*time refers to the interaction between groups and the total time									

Items	RFA versus VATS								
	Group			Time			Group*Time		
Symptom	Estimate	SE	p value	Estimate	SE	p value	Estimate	SE	p value
Enjoyment	-1.15578	0.23562	**< 0.0001**	-0.00043	0.00157	0.78199	0.00757	0.00280	**0.00689**
Statistically significant values are given in bold (p <0.05)									
Adjusted variables: Sex, postoperative hospital duration, Annual household income, Maximum diameter.									
Group*time refers to the interaction between groups and the total time									

The score in MDASI-LC were illstrated in **Supplementary Fig. 3**, showing a trend similar to that in **Supplementary Fig. 2**.

Discussion

Previous studies have primarily focused on comparisons between uniportal and multiportal video-assisted thoracoscopic surgery (VATS), VATS versus thoracotomy, and surgery versus radiotherapy[27, 40, 41]. In this study, we delineate the recovery trajectories and patterns for moderate-to-severe symptoms and functional impairment in patients following RFA, using uniportal VATS as a reference. A direct comparison of PROs between RFA and VATS is subject to significant bias due to their differing clinical indications. Nevertheless, the VATS cohort was included as a comparator in this study to contextualize the relative symptom burden in RFA patients and to offer a familiar benchmark for the thoracic surgery community.

Through the analysis of postoperative symptoms for these two surgical techniques, we identified distinct recovery patterns. In the RFA cohort, which was characterized by a lower overall proportion of moderate-to-severe symptoms, we classified two primary trajectories: a 'Sustained Resolution' pattern and a 'Short-Term Fluctuation' pattern. In contrast, the VATS cohort exclusively exhibited a single trajectory: the 'oscillatory decline'. The observed differences can be attributed to the minimally invasive nature of RFA[42, 43], which avoids thoracic incisions, leading to reduced surgical trauma and a lower systemic inflammatory response[44, 45]. This may also be attributed to the fact that a drainage tube is typically placed after VATS, whereas it is generally not required following radiofrequency ablation (RFA). Additionally, VATS is performed under general anesthesia, whereas RFA is conducted under local anesthesia.

Consequently, the RFA group exhibited a significantly shorter recovery time for key functional items such as general activity, walking, and work (Figure 3, **Supplemental Fig. 2**). This suggests that RFA may offer a more favorable postoperative recovery trajectory, particularly for working individuals who seek a quicker return to occupational and daily responsibilities.

Our study offers several distinct contributions to the literature on post-RFA recovery. First, to our knowledge, this is the first investigation to apply the MDASI-LC instrument for a comprehensive evaluation of symptom burden and functional outcomes specifically in patients undergoing thoracic RFA. This approach identified a unique symptom profile—primarily involving constipation, shortness of breath, sleep disturbance, pain, fatigue, and memory impairment—that differs notably from those reported after conventional thoracic surgery[41].Second, our prospective, multi-time-point data collection within the first 90 postoperative days, coupled with a high data acquisition rate, allowed for a high-resolution characterization of the recovery trajectory. This robust methodology enabled us to clearly demonstrate the rapid pace of symptom resolution following RFA.

This study has several limitations that should be acknowledged. First and foremost, inherent differences exist between the RFA and VATS cohorts. The two procedures have distinct clinical indications, and the associated levels of surgical trauma and methods of anesthesia are not directly comparable. Therefore, while the VATS data provides a useful benchmark for contextualizing the recovery trajectory after RFA, its direct comparative value is limited. Second, a potential for selection bias exists, as preoperative histopathological confirmation was not routinely performed for RFA cases. This is largely because the majority of RFA-treated lesions were small ground-glass nodules (mGGNs/pGGNs), for which preoperative biopsy is often technically challenging. The use of percutaneous needles carries a risk of hemorrhage, which can obscure imaging and complicate subsequent ablation targeting. Third, the 90-day follow-up period may not be sufficient to capture the full spectrum of long-term symptomatic recovery. However, we contend that the primary advantage of RFA—its rapid early recovery—may reduce the clinical relevance of symptom comparisons in

the longer term. Finally, ongoing randomized controlled trials with extended follow-up will be crucial for further validating the long-term benefits of RFA.

Conclusion

Our findings suggest that RFA is a less functionally impairing and more patient-friendly treatment alternative to VATS for early-stage NSCLC. The superior symptom recovery and functional outcomes associated with RFA support its broader clinical adoption, particularly for patients prioritizing a swift return to work and daily activities in this rapidly running era.

Abbreviations

Abbreviation	Full Term
NSCLC	Non-Small Cell Lung Cancer
RFA	Radiofrequency Ablation
VATS	Video-Assisted Thoracoscopic Surgery
PRO	Patient-Reported Outcomes
MDASI-LC	MD Anderson Symptom Inventory–Lung Cancer module
CT	Computed Tomography
PET-CT	Positron Emission Tomography-Computed Tomography
CECT	Contrast-Enhanced Computed Tomography
ECOG	Eastern Cooperative Oncology Group
GGN	Ground-Glass Nodule
PTZ	Post-Ablation Target Zone
GTR	Gross Tumor Region
MWA	Microwave Ablation
SBRT	Stereotactic Body Radiation Therapy
CTR	Consolidation-to-Tumor Ratio
SAS	Statistical Analysis Software
FDA	Food and Drug Administration
ePRO	Electronic Patient-Reported Outcomes
POD	Postoperative Day

Declarations

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was conducted at the Department of Thoracic Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College. It was approved by the Research Ethics Committee of the Cancer Hospital, Chinese Academy of Medical Sciences (23/050-3789). All participants provided written, informed consent.

Consent for publication: Not applicable

Availability of data and materials: The datasets generated and analyzed during this study are available from the corresponding authors upon reasonable request. Due to patient privacy protections under the ethical approval granted by the Research Ethics

Committee of the Cancer Hospital, Chinese Academy of Medical Sciences (Approval No. 23/050-3789), access to de-identified data requires formal approval from the institutional review board. Researchers interested in utilizing the data may submit a detailed proposal to the Ethics Committee via the corresponding authors.

Competing Interests: The authors declare no potential conflicts of interest.

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Figures

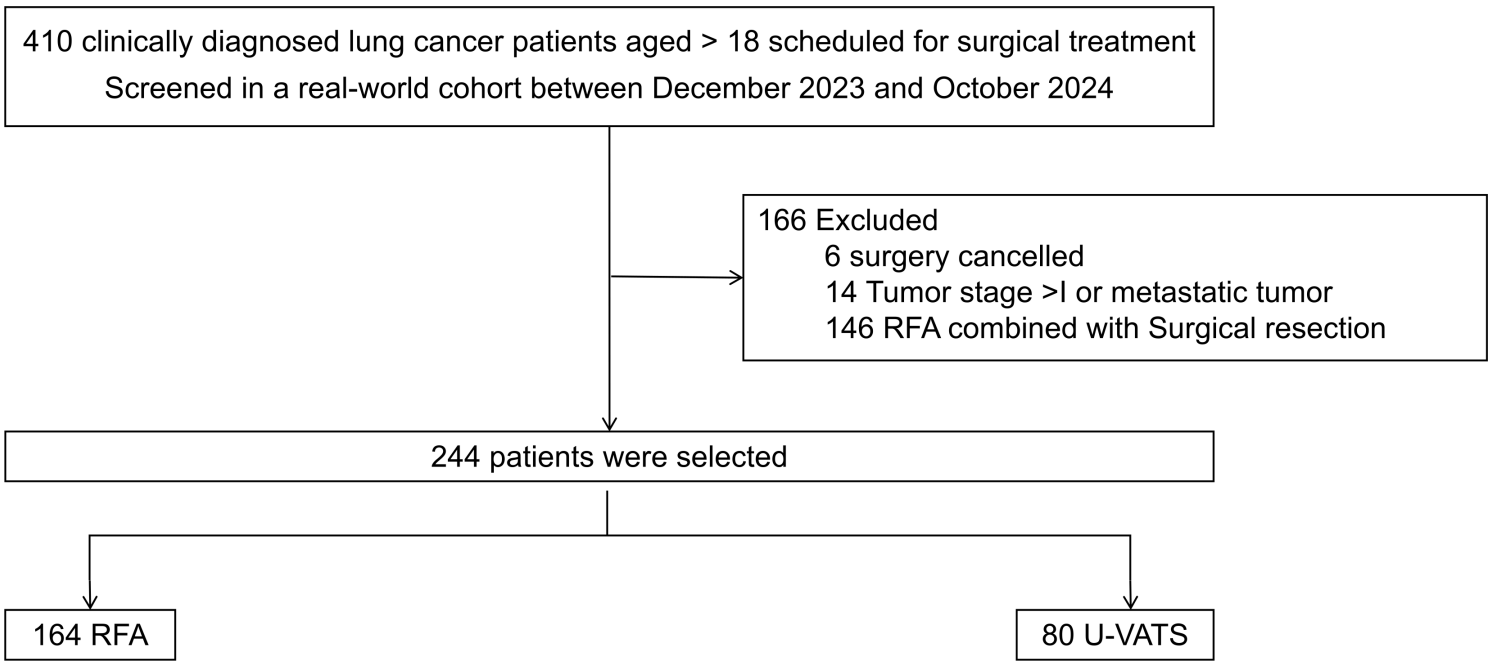

Figure 1

Flow chart of patient selection.

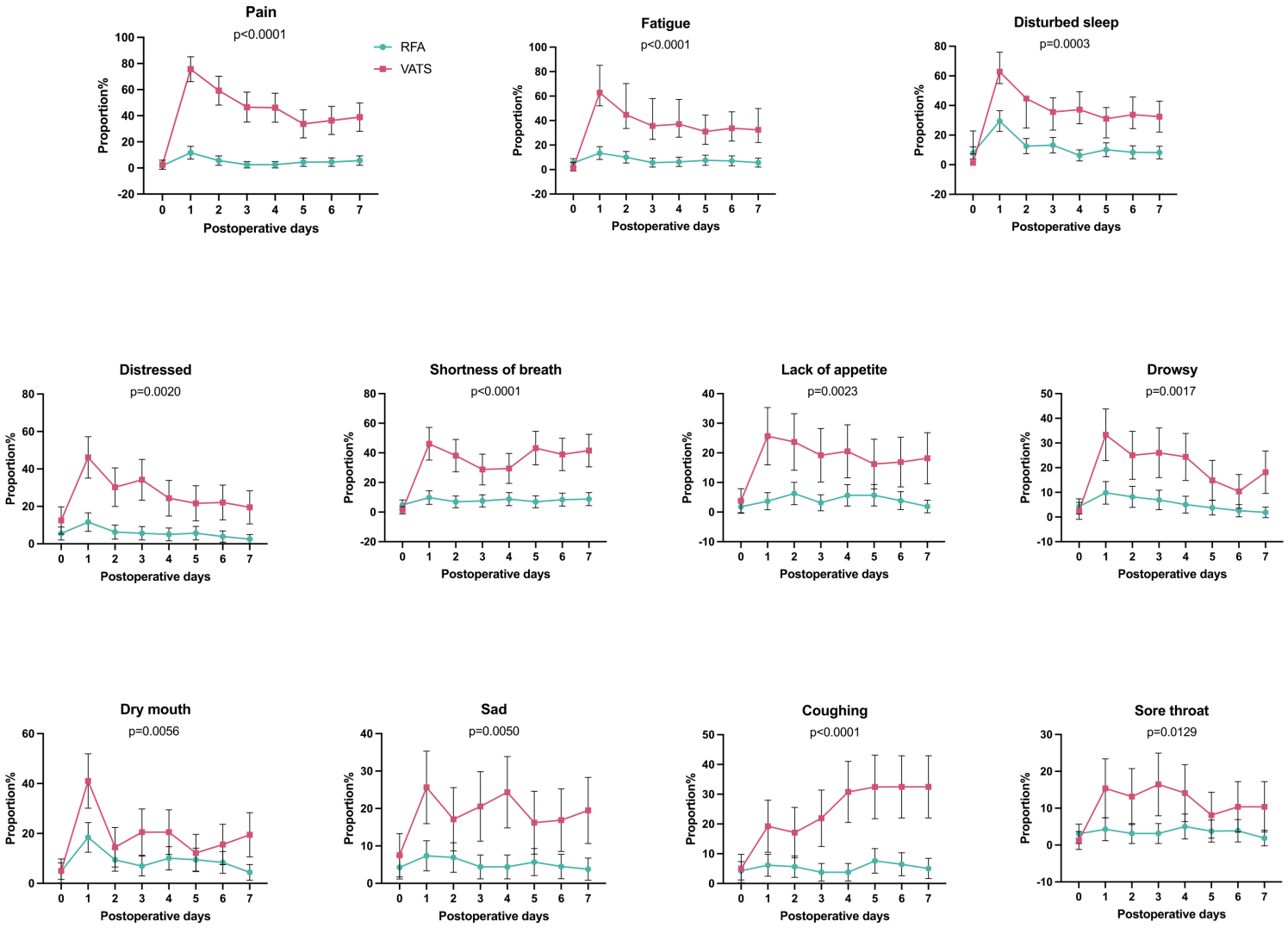

Figure 2

Postoperative 11 Siginificant Symptom Burden Over the First 7 Days in RFA vs. VATS Groups

compares the proportion of patients reporting moderate-to-severe symptoms (score ≥4/10) over the first seven postoperative days following radiofrequency ablation (RFA) or video-assisted thoracoscopic surgery (VATS) for stage IA NSCLC. Symptoms include pain, fatigue, shortness of breath, disturbed sleep, distress, and others. Mixed-effects logistic regression adjusted for baseline factors, and Chi-square tests were used for analysis at POD 7, p-values shows the significance of difference at POD 7 . RFA patients had significantly lower symptom burdens across multiple items (e.g., pain, p<0.0001; shortness of breath, p<0.0001), suggesting a more favorable recovery profile compared to VATS.

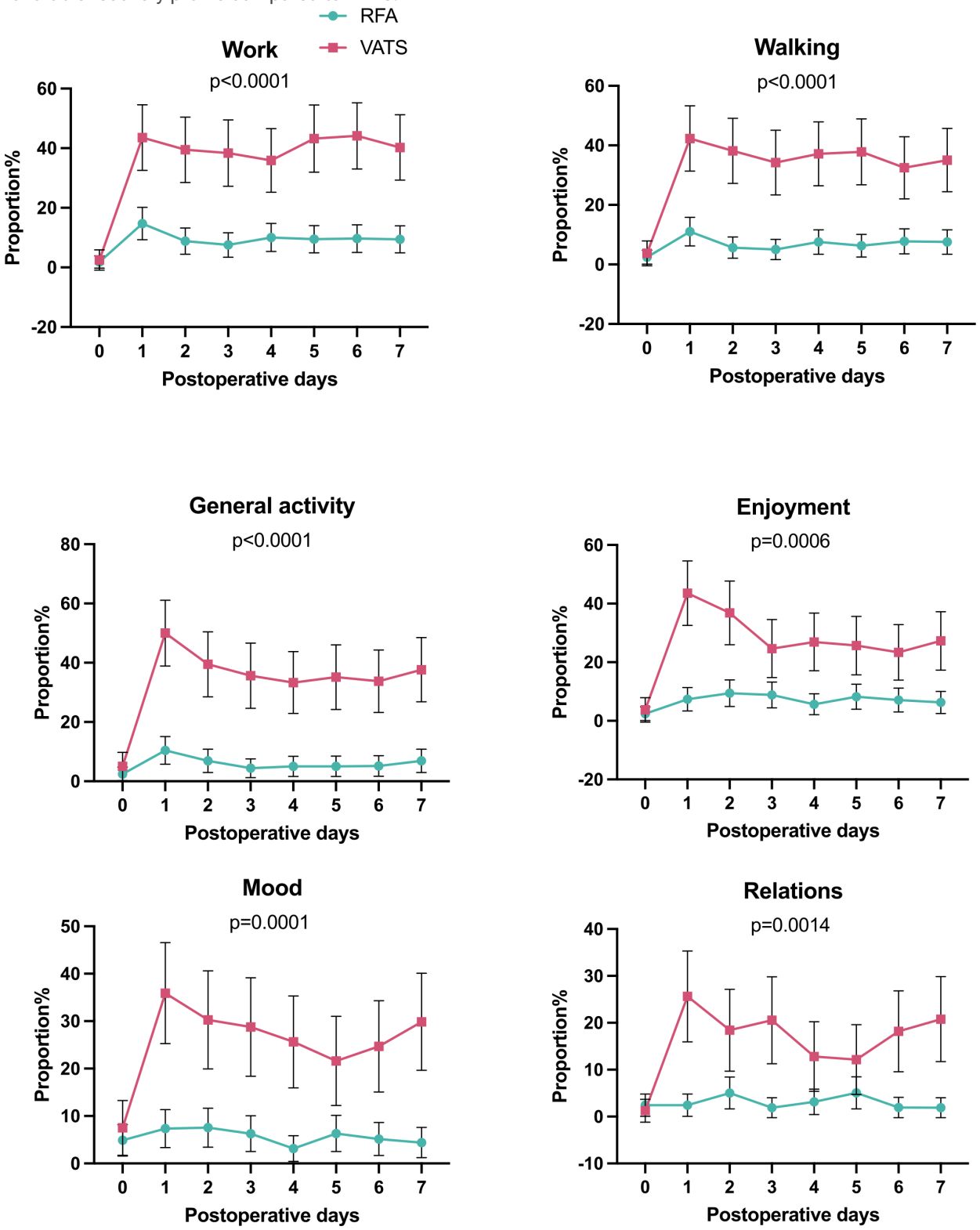

Figure 3

Postoperative Functional Impairment Over the First 7 Days in RFA vs. VATS Groups

compares proportions of patients with moderate-to-severe functional impairment (score ≥4/10) in six items—work, walking, general activity, enjoyment, mood, and relationships—over the first seven postoperative days in RFA and VATS patients with stage IA NSCLC. Mixed-effects logistic regression adjusted for baseline factors, and chi-square tests assessed between-group differences at POD 30, p-values shows the significance of difference at POD 30(e.g., work, $p<0.0001$; walking, $p<0.0001$). RFA patients had significantly lower impairment rates across all functions, indicating faster recovery and better postoperative functional outcomes compared to VATS.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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- SupplementaryFigure2combinedrecoverycurves1to90.pdf
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