

## ORIGINAL ARTICLE

# Computed tomography-guided microwave ablation for the treatment of non-small cell lung cancer patients with and without adjacent lobe invasion: A comparative study

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## Abstract

**Background:** The aim of the study was to explore the outcomes of computed tomography-guided microwave ablation (MWA) in non-small cell lung cancer (NSCLC) patients with adjacent lobe invasion (ALI), and to compare the outcomes of ALI-NSCLC and non-ALI NSCLC patients after MWA.

**Methods:** A total of 319 NSCLC patients and 366 tumors treated with MWA were included in the study, comprising 34 ALI-NSCLC patients and 285 non-ALI NSCLC patients. Complications, local recurrence rates, progression-free survival (PFS), and overall survival (OS) were compared. Logistic regression analyses were used to investigate the correlation between ALI and the occurrence of pneumothorax after MWA.

**Results:** The mean tumor diameter of ablated tumors was  $3.6 \pm 2.2$  cm. There were 95 (29.8%) NSCLC patients in which pneumothorax occurred after MWA, and all patients recovered. Of these, the ALI group had a significantly higher incidence rate of pneumothorax than the non-ALI group (52.9% vs. 27.0%,  $p = 0.002$ ). The median PFS and OS for the ALI group were  $12.0 \pm 10.2$  and  $15.5 \pm 9.5$  months, respectively, and that of the non-ALI group were  $13.0 \pm 10.6$  and  $17.0 \pm 11.1$  months, respectively, and no significant difference was found in PFS ( $p = 0.329$ ) nor OS ( $p = 0.394$ ) between the two groups. Local recurrence rates for ALI and non-ALI groups were 29.4% and 20.7%, respectively, and no significant difference was found ( $p = 0.244$ ). Logistic regression analyses revealed that ALI can increase the risk of pneumothorax (hazard ratio [HR], 2.867;  $p = 0.012$ ).

**Conclusions:** MWA is an effective and safe approach for ALI-NSCLC treatment. Although ALI can increase the risk of pneumothorax, ALI-NSCLC patients reveal a comparable outcome to non-ALI NSCLC patients after MWA.

## KEYWORDS

adjacent lobe invasion, microwave ablation, non-small cell lung cancer, pneumothorax, survival

## INTRODUCTION

Although lung cancer is surpassed and no longer the most common cancer worldwide, it remains the leading cause of cancer mortality, with more than 2.2 million new cases and 1.79 million deaths estimated in 2020,<sup>1</sup> and over 730 000 new cases and 610 000 deaths in China, among which non-

small cell lung cancer (NSCLC) accounts for 85% of the diagnoses.<sup>2</sup> However, over two-thirds of NSCLC patients are diagnosed at an advanced stage when they are no longer the best candidates for curative surgery.<sup>3</sup> In recent decades, thermal ablation has been reported as a primary therapeutic strategy or/and an adjuvant to other treatments for NSCLC patients, or for patients with a limited pulmonary reserve

who cannot tolerate the surgery.<sup>4</sup> Radiofrequency ablation and microwave ablation (MWA) are the two most common types of thermal ablation, while the latter has the advantages of a higher intratumoral temperature, a larger ablation scope, decreased ablation duration, and deeper penetration.<sup>5</sup>

Adjacent lobe invasion (ALI) is defined as the pulmonary lesions that invade into an adjacent lobe across the fissure. This is an uncommon condition in NSCLC, with its incidence rate reported to range from 5.5% to 17.1%.<sup>6</sup> In general, surgery is considered as the optimal therapeutic option for ALI-NSCLC,<sup>7</sup> of which complete resection of the tumor and an appropriate lymph node evaluation is undertaken during surgery.<sup>8</sup> However, whether the presence of ALI is a negative predictor of prognosis remains debatable. Demir et al.<sup>9</sup> reported the survival of ALI-NSCLC patients who underwent lobectomy was worse than those who did not receive lobectomy, and Riquet et al.<sup>10</sup> reported that ALI was an independent factor of poor prognosis in NSCLC patients. On the contrary, Yang et al.<sup>11</sup> found a better prognosis in ALI-NSCLC patients who underwent lobectomy. To the best of our knowledge, few studies have explored the efficacy and safety of MWA in ALI-NSCLC treatment. Furthermore, it seems that the MWA technique in treating ALI-tumor is more complicated than that of tumors restricted to one lobe, and whether it can cause a different prognosis between two conditions remains unclear. Therefore, a retrospective study was conducted to explore the outcomes of MWA in ALI-NSCLC patients and to compare the outcomes of ALI-NSCLC and non-ALI NSCLC patients after MWA.

## METHODS

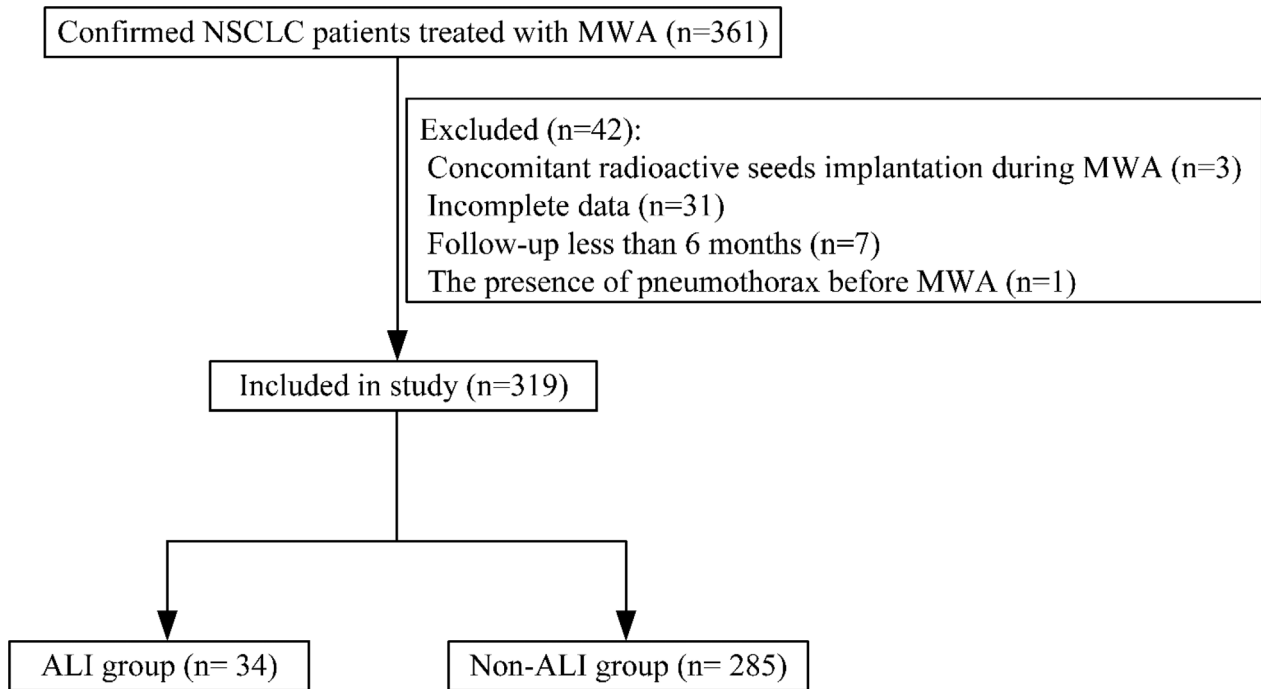
### Patient criteria

This single-center retrospective study included all NSCLC patients who underwent MWA at this institution. The institutional ethics review board approved the study, and the study protocol was conducted in accordance with the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study. NSCLC patients who were unable to tolerate or had refused surgery, and received MWA between August 2016 and May 2020, were screened for study inclusion (Figure 1) and were allocated to the ALI group and non-ALI group according to the presence of ALI-tumors. ALI is diagnosed as pulmonary lesions that invade into an adjacent lobe across the fissure on computed tomography (CT) images. Patient inclusion criteria were: (i) age older than 18 years, (ii) confirmed NSCLC patients treated with MWA, (iii) Eastern Cooperation Oncology Group score of 0–2, and (d) complete clinical and radiological data were available. Patient exclusion criteria were: (i) other concomitant therapies performed during the MWA procedure, such as radioactive seeds implantation, (ii) follow-up less than 6 months, (iii) incomplete data, and (iv) the presence of pneumothorax before MWA.

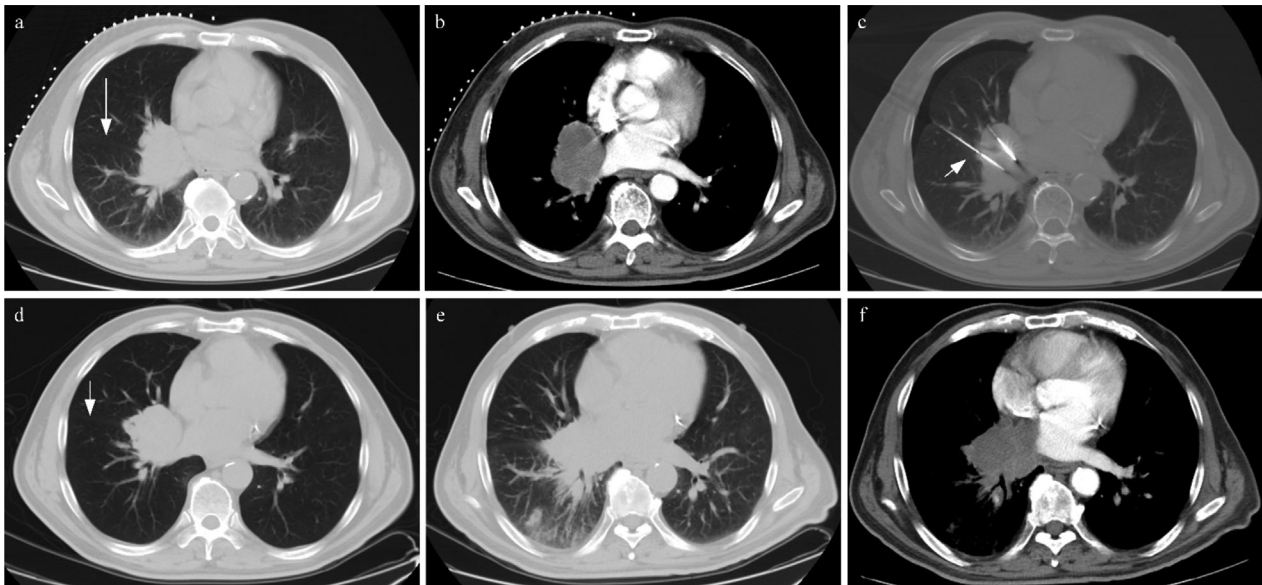
The histopathological subtypes of NSCLC were obtained according to previous percutaneous needle aspiration biopsy, fiberoptic bronchoscopy, or synchronous biopsy via a coaxial-cannula during the MWA procedure. All NSCLC patients underwent chest CT (Discovery CT590; GE Healthcare) before the MWA to evaluate the location, quantity, and size of tumors. The pre-MWA CT images were examined for the detection of ALI by two radiologists with >5 years of experience in diagnostic radiology. The diagnosis of emphysema was made according to the Goddard Visual Score.<sup>12</sup> Positron-emission-computed tomography (PET-CT) or contrast-enhanced CT was performed to evaluate the lymph node and distant metastases. The NSCLC tumor stage was identified via the clinical TNM staging system of the Union for International Cancer Control (eighth edition).<sup>13</sup> All laboratory examinations were conducted 1–4 days before MWA.

### MWA procedure

The MWA indications and procedures followed the guidelines of the Society of Interventional Radiology and were performed under CT (Discovery CT590; GE) by several experienced interventional radiologists.<sup>14</sup> An MTC-3C MWA system (Vison Medicine) or an ECO-100A1 MWA system (ECO Medical Instrument) was used, with a microwave emission frequency of  $2450 \pm 50$  MHz and an adjustable continuous wave output power of 20 to 80 W. The effective length of the microwave antennas (Vison or ECO) was 10–18 cm and the outside diameter was 15–17 G according to the tumor location and distance to the pleura, with a 15 mm radiating tip. A preprocedural CT was performed to enable successful treatment planning and to clarify the suitable position, puncture site location, optimal puncture trajectory, and the number of MWA antennas. Local anesthesia was the main option for most patients, while intravenous anesthesia with propofol was performed for patients who were unable to bear the intraprocedural pain. Antennas were introduced into the planned site, and MWA was performed at the planned power and duration, with adjustments of suitable power and duration being carried out according to the intraprocedural location of MWA antennas, as required. The procedure was terminated when the ablation zone presented a 5–10 mm rim of ground-glass opacification beyond the lesion boundary. At this institution, the techniques of MWA in ALI-NSCLC are listed as follows. For central ALI-tumors, the MWA antennas are introduced along with the direction of the pulmonary fissure, and pincer ablation is performed in entire tumors. A certain distance should be kept away from the pulmonary fissure (Figure 2), and bilateral punctures of MWA antennas along with the direction of pulmonary fissure could be considered for large tumors. For subpleural ALI-tumors, the MWA antennas could point in the direction of pulmonary fissure but the direct traversal of pulmonary fissure should



**FIGURE 1** Patient selection flowchart. ALI, adjacent lobe invasion; MWA, microwave ablation; NSCLC, non-small cell lung cancer



**FIGURE 2** A typical case of adjacent lobe invasion-non-small cell lung cancer (ALI-NSCLC) treated with microwave ablation (MWA). (a, b) An NSCLC patient with the histopathological subtype of squamous cell lung cancer was admitted. Pre-MWA computed tomography (CT) scan revealed the location and presence of ALI (white arrow). (c) MWA was performed and the tumor was ablated by two MWA antennas, one of which can be seen adjacent to the pulmonary fissure (white arrow). (d) The 2-month CT re-examination after MWA revealed a decrease in size of the tumor. (e, f) One-year CT re-examination after MWA revealed stable disease of the tumor size compared with the previous examination

be avoided. Finally, a repeat chest CT scan was performed to evaluate the ablation zone and detect possible complications. For patients without a previous histopathological subtype, a synchronous coaxial-cannula biopsy was performed if necessary. A 15 G coaxial introducer needle (Argon Medical

Devices) was first advanced into the tumor, and the stylet was then replaced by a 16 G full-core biopsy needle (BioPince; Argon Medical Devices) through the cannula. A 17G MWA antenna (Vison or ECO) was introduced into the tumor through the cannula.

## Follow-up and assessments

Short-term follow-up with CT re-examinations was conducted 1–5 days after MWA during hospitalization and 3–4 weeks after MWA at an outpatient visit to detect post-procedural complications, including pneumothorax and pleural effusion. Patients who presented with symptoms received on-time re-examinations on demand. Long-term follow-up with CT re-examinations was conducted every 1–4 months after MWA. Chest tube placement was performed for patients with moderate and severe pneumothorax or pleural effusion, and was terminated until the retraction of the lung surface or the disappearance of pneumothorax or pleural effusion.

Complications were assessed according to criteria from the Society of Interventional Radiology.<sup>14,15</sup> Nodular or central enhancement >10 mm and/or >15 HU on contrast-enhanced CT was considered a local recurrence. Radiological recurrence was assessed by two experienced radiologists who were blinded to the clinical information. Overall survival (OS) was defined as the interval from the start of MWA to death or the last follow-up (December 31, 2020). For patients who died during the follow-up period, OS was calculated as the interval from the MWA procedure to death. For patients who survived but were lost to follow-up, OS was calculated as the interval from the MWA procedure to the last follow-up. Progression-free survival (PFS) was defined as the interval from the MWA procedures to the time of objective progression, including local recurrence and/or distant metastases, which was evaluated by two independent interventional radiologists. For patients who did not die or progress, the censoring date was defined as the last clinical assessment date.

## Statistical analysis

Categorical variables are described as frequencies and percentages, and continuous variables are described as the mean/median  $\pm$  SD. Statistical analyses were performed using SPSS 25.0 for Windows (IBM). The data were compared by Student's *t*-test or the Mann–Whitney U test for continuous variables and by chi-square test for categorical variables in the ALI group and non-ALI group.  $p < 0.05$  was considered to indicate statistical significance. The possible predictors for pneumothorax were analyzed by univariate logistic regression analyses, including 19 parameters on demographics, treatment history, ablation factors, and radiological features. Variables with  $p < 0.05$  in the univariate analyses were entered as candidate variables into the multivariate logistic regression analyses.

## RESULTS

### Patient characteristics

A total of 366 MWA procedures were performed for 319 NSCLC patients, which comprised 196 males (61.4%)

and 123 females (38.6%), with a mean age of  $68.0 \pm 10.6$  years. The detailed demographic characteristics between ALI and non-ALI groups are presented in Table 1; a significant difference was found in tumor diameter ( $p = 0.003$ ), and the number of pleural punctures ( $p = 0.004$ ). The ALI group included eight (23.5%) patients with right lung horizontal interlobar fissure invasion, 11 (32.4%) patients with right lung oblique fissure invasion, and 15 (44.1%) patients with left lung oblique fissure invasion. A synchronous coaxial-cannula biopsy was performed for 108 (33.9%) patients, which consist of 16 (47.1%, 16/34) in the ALI group and 92 (32.3%, 92/285) in the non-ALI group.

### Clinical outcomes between ALI and non-ALI groups

The detailed complications and clinical outcomes between ALI and non-ALI groups treated with MWA are presented in Table 2. Pneumothorax was the predominant complication, with incidence rates of 52.9% (18/34) in the ALI group and 27.0% (77/285) in the non-ALI group, and a significant difference was found between groups ( $p = 0.002$ ). A total of 44 (13.8%) NSCLC patients underwent chest tube placement owing to pneumothorax and/or pleural effusion, including five (14.7%) ALI-NSCLC patients and 39 (13.7%) non-ALI NSCLC patients. The tubes were removed when the pneumothorax and/or pleural effusion disappeared, and all patients recovered. In addition, no MWA-associated mortality and severe complications were found within 30 days after MWA. The detailed results of univariate and multivariate logistic regression analyses for pneumothorax are presented in Table 3. The risk of pneumothorax increased when the NSCLC patients presented with ALI (hazard ratio [HR], 2.867; 95% confidence interval [CI]: 1.256–6.548;  $p = 0.012$ ; Figure 3) and emphysema (HR, 9.891; 95% CI, 5.538–17.665;  $p < 0.001$ ). New pulmonary metastases were found in five (14.7%) ALI-NSCLC patients and 21 (7.4%) non-ALI NSCLC patients. Of these, 7 (2.2%) NSCLC patients underwent secondary MWA. The local recurrence rates for ALI and non-ALI groups were 29.4% (10/34) and 20.7% (59/285), respectively, and no significant difference was found between groups ( $p = 0.244$ ). Of these patients who experienced a local recurrence, 18 (5.6%) NSCLC patients underwent secondary MWA. In a mean follow-up of  $27.2 \pm 11.8$  months, the median PFS and OS for ALI-NSCLC were  $12.0 \pm 10.2$  and  $15.5 \pm 9.5$  months, respectively, and those for non-ALI NSCLC were  $13.0 \pm 10.6$  and  $17.0 \pm 11.1$  months, respectively, and no significant difference was found in PFS ( $p = 0.329$ ) nor OS ( $p = 0.394$ ) between two groups.

## DISCUSSION

Thermal ablation is an effective therapeutic strategy for NSCLC patients aimed at inducing a zone of thermal

**TABLE 1** Clinical characteristics and outcomes between ALI and non-ALI groups treated with MWA

Variables	Overall (n = 319)	ALI group (n = 34)	Non-ALI group (n = 285)	p-value
Age (year)	68.0 ± 10.6	70.6 ± 8.8	67.7 ± 10.7	0.136
Gender				0.967
Male	196 (61.4%)	21 (61.8%)	175 (61.4%)	
Female	123 (38.6%)	13 (38.2%)	110 (38.6%)	
Histopathological subtypes				0.194
Adenocarcinoma	230 (72.1%)	20 (58.8%)	210 (73.7%)	
Squamous cell carcinoma	73 (22.9%)	12 (35.3%)	61 (21.4%)	
Others	16 (5.0%)	2 (5.9%)	14 (4.9%)	
Tumor stage				0.628
I or II	147 (46.1%)	17 (50.0%)	130 (45.6%)	
III or IV	172 (53.9%)	17 (50.0%)	155 (54.4%)	
Treatment history				
Previous surgery	36 (11.3%)	2 (5.9%)	34 (11.9%)	0.292
Previous chemotherapy	43 (13.5%)	6 (17.6%)	37 (13.0%)	0.452
Previous radiotherapy	17 (5.3%)	2 (5.9%)	15 (5.3%)	0.879
Previous TKIs	47 (14.7%)	4 (11.8%)	43 (15.1%)	0.605
Radiological features				
Tumor diameter (cm)	3.6 ± 2.2	4.7 ± 2.2	3.5 ± 2.2	0.003
Tumor number				0.385
1	281 (88.1%)	32 (94.1%)	249 (87.4%)	
≥2	38 (11.9%)	2 (5.9%)	36 (12.6%)	
Involved lobe				0.314
Upper lobe	127 (39.8%)	15 (44.1%)	112 (39.3%)	
Middle or lower lobe	192 (60.2%)	19 (55.9%)	173 (60.7%)	
Emphysema	82 (25.7%)	13 (38.2%)	69 (24.2%)	0.077
Distance to pleura (cm)	0.9 ± 1.0	0.7 ± 0.9	0.9 ± 1.0	0.454
Laboratory examinations				
WBC (×10 <sup>9</sup> mmol/l)	6.2 ± 2.3	6.7 ± 2.3	6.2 ± 2.3	0.246
Hb (g/L)	125.8 ± 16.9	125.3 ± 16.4	125.8 ± 17.0	0.865
PLT (×10 <sup>9</sup> mmol/l)	218.4 ± 72.9	200.9 ± 68.0	220.5 ± 73.3	0.138
PT (s)	11.2 ± 1.2	11.1 ± 2.0	11.3 ± 1.1	0.391
Post-MWA treatments				
Post chemotherapy	63 (19.7%)	8 (23.5%)	55 (19.3%)	0.558
Post radiotherapy	38 (11.9%)	7 (20.6%)	31 (10.9%)	0.170
Post TKIs	120 (37.6%)	14 (41.2%)	106 (37.2%)	0.650
Post immunotherapy	28 (8.8%)	3 (8.8%)	25 (8.8%)	1
Ablation factors				
Maximum power (W)	55.5 ± 11.1	57.4 ± 13.3	55.2 ± 10.8	0.290
Total ablation time (min)	10.4 ± 5.8	12.1 ± 4.8	10.2 ± 5.9	0.072
Diameter of instruments				0.112
15G	135 (42.3%)	10 (29.4%)	125 (43.9%)	
16G	50 (15.7%)	4 (11.8%)	46 (16.1%)	
17G	134 (42.0%)	20 (58.8%)	114 (40.0%)	
Number of pleural punctures	1.4 ± 0.6	1.7 ± 0.7	1.4 ± 0.6	0.004

Note: Frequencies and percentages are reported for categorical variables and mean ± SD are reported for continuous variables.

Abbreviations: ALI, adjacent lobe invasion; Hb, hemoglobin; MWA, microwave ablation; PLT, platelet; PT, prothrombin time; TKIs, tyrosine kinase inhibitors; WBC, white blood cell.



**TABLE 2** Detailed complications of ALI and non-ALI groups treated with MWA

Variables	Overall ( <i>n</i> = 319)	ALI group ( <i>n</i> = 34)	Non-ALI group ( <i>n</i> = 285)	<i>p</i> -value
Main complications				
Pneumothorax	95 (29.8%)	18 (52.9%)	77 (27.0%)	0.002
Pleural effusion	7 (2.2%)	2 (5.9%)	5 (1.8%)	0.350
Hemoptysis	9 (2.8%)	2 (5.9%)	7 (2.5%)	0.247
Local recurrence	69 (21.6%)	10 (29.4%)	59 (20.7%)	0.244
Status				
Survival	185 (58.0%)	16 (47.1%)	169 (59.3%)	0.172
Mortality	134 (42.0%)	18 (52.9%)	116 (40.7%)	
Median PFS (m)	13.0 ± 10.5	12.0 ± 10.2	13.0 ± 10.6	0.329
Median OS (m)	17.0 ± 10.9	15.5 ± 9.5	17.0 ± 11.1	0.394

Abbreviations: ALI, adjacent lobe invasion; MWA, microwave ablation.

**TABLE 3** Univariate and multivariate logistic regression analyses of pneumothorax in NSCLC patients treated with MWA

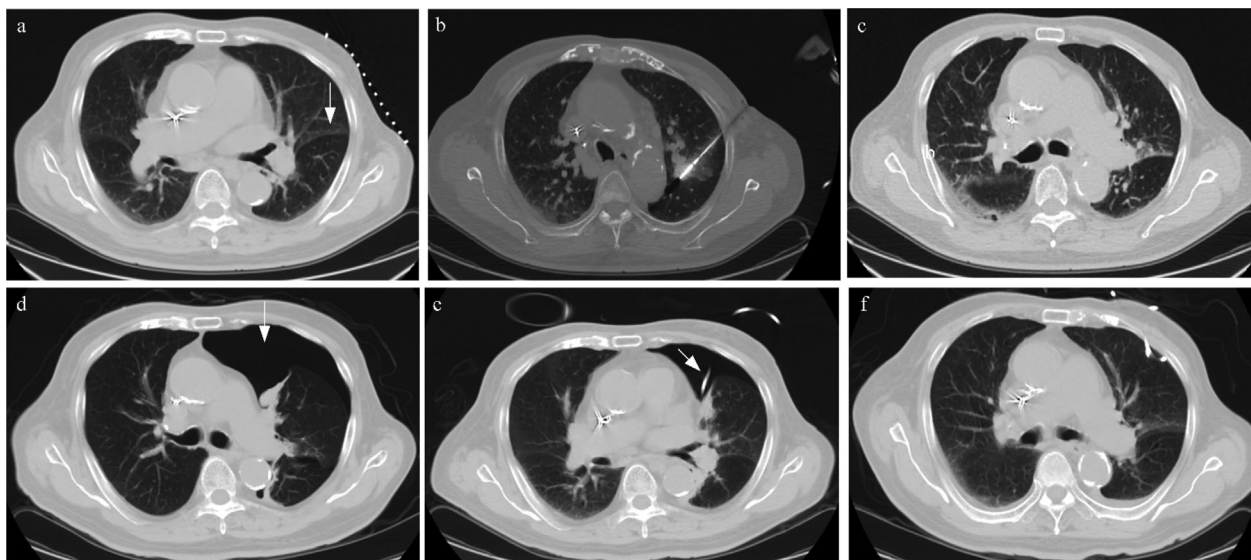
Variables	Univariable analyses			Multivariable analyses		
	HR	95% CI	<i>p</i> -value	HR	95% CI	<i>p</i> -value
ALI	3.039	1.476–6.258	0.003*	2.867	1.256–6.548	0.012*
Age (year)	0.993	0.971–1.016	0.557			
Gender	1.762	1.053–2.948	0.031*			
Tumor types	1.133	0.748–1.717	0.556			
Tumor stage	0.855	0.706–1.035	0.108			
Previous surgery	1.812	0.890–3.691	0.101			
Previous chemotherapy	1.478	0.755–2.891	0.254			
Previous radiotherapy	0.981	0.336–2.867	0.973			
Previous TKIs	1.125	0.578–2.191	0.729			
Number of metastases	0.724	0.507–1.032	0.074			
Tumor diameter (cm)	0.909	0.808–1.021	0.108			
Tumor number	0.955	0.453–2.015	0.905			
Involved lobe	0.721	0.445–1.167	0.183			
Emphysema	10.032	5.660–17.783	<0.001*	9.891	5.538–17.665	<0.001*
Distance to pleura (cm)	1.249	0.993–1.572	0.058			
Diameter of instruments	1.036	0.871–1.233	0.689			
Maximum power	0.995	0.974–1.017	0.672			
Ablation time (min)	0.995	0.955–1.038	0.825			
Number of pleural punctures	1.438	0.994–2.079	0.054			

Abbreviations: ALI, adjacent lobe invasion; MWA, microwave ablation; NSCLC, non-small cell lung cancer; TKIs, tyrosine kinase inhibitors.

\*The variables with significant difference in statistical analyses.

coagulative necrosis which encompasses the whole tumor, and a surrounding safety margin, with 3- and 5-year survival rates of 36%–88% and 25%–61%, respectively.<sup>16</sup> Although the best candidates for thermal ablation are stage I NSCLC patients who have contraindications to surgery or stereotactic radiotherapy as recommended,<sup>4,17</sup> many studies have attempted thermal ablation as a salvage therapy or as part of combination therapeutic strategies with other treatments for intermediate and advanced-stage patients.<sup>18–20</sup> ALI was detected in 10.7% (34/319) of NSCLC patients in this study, which is similar to the previously reported incidence rate of

5.5%–17.1%.<sup>6</sup> The median PFS and OS of NSCLC patients treated with MWA were 13.0 ± 10.5 months and 17.0 ± 10.9 months, respectively. These results were comparable to the PFS of 8.7–16.2 months and the OS of 10.6–71.6 months reported in other studies.<sup>21</sup> The potential mechanism of the short interval between PFS and OS was the high percentages of early-stage NSCLC patients. Of these, the median OS of ALI-NSCLC was 15.5 ± 9.5 months, which was comparable to the OS of 17.0 ± 11.1 months in the non-ALI group, which revealed a comparable prognosis in the statistical analyses. In a



**FIGURE 3** A typical case of delayed pneumothorax for adjacent lobe invasion -non-small cell lung cancer (ALI-NSCLC) treated with microwave ablation (MWA). (a) An NSCLC patient with the histopathological subtype of squamous cell lung cancer was admitted. Pre-MWA computed tomography (CT) scan revealed the location and presence of ALI (white arrow). (b) MWA was performed, with the MWA antennas being adjacent to the pulmonary fissure. (c) The instant CT re-examination after MWA revealed no presence of pneumothorax. (d) The 2-day CT re-examination after MWA revealed the presence of delayed pneumothorax. (e) Chest tube placement was performed to relieve the severe pneumothorax (white arrow). (f) The 4-day CT re-examination after MWA revealed the disappearance of the pneumothorax after chest tube placement

systemic review, David et al. reported an incidence rate of 9%–37% for local recurrence in NSCLC patients treated with MWA and 5%–19% for local recurrence among tumors smaller than 3 to 4 cm.<sup>22</sup> In this study, the local recurrence rate after MWA was 21.6% (69/319), which was comparable to the rate previously reported. The median time from MWA to the first recurrence was 45.5 months for stage I NSCLC patients, with local control rates at 1, 3, and 5 years after MWA of 96%, 64%, and 48%, respectively.<sup>23</sup> Above all, the ALI-NSCLC patients were found to have a comparable prognosis to non-ALI NSCLC patients after MWA in this study.

Previous studies have indicated the overall prognosis of patients with ALI-NSCLC is similar to those with T3 disease, although the condition is usually defined as the T2 category, according to the seventh edition of the tumor, node, and metastasis (TNM) classification.<sup>7,24</sup> According to the eighth edition of TNM staging system of lung cancer, visceral pleural invasion is considered as T2 stage, and tumors in a different ipsilateral lobe are considered as T4 stage.<sup>13</sup> It seems ALI should be classified as T2. In addition, Nonaka et al.<sup>25</sup> analyzed 28 ALI-NSCLC patients with squamous cell carcinoma and found the 5-year survival rate was similar to that of T2 disease and considered ALI-NSCLC patients should be classified as T2. However, Haam et al.<sup>26</sup> reported the OS and disease-free survival of ALI-NSCLC patients were similar to those of T3, and considered the T category should be classified as T3 rather than T2. Andreotti et al.<sup>27</sup> differentiated the ALI-NSCLC as complete and incomplete ALI, based on whether the tumor invaded the adjacent lobe across a complete fissure point, and found the latter

provided a better prognosis. Meanwhile, Ohtaki et al.<sup>28</sup> divided ALI into the invasion across complete and incomplete fissures, and found the complete fissure was associated with a better prognosis. They proposed ALI across the complete fissure should be classified as T2b, but ALI across the incomplete fissure required no adjustments to the T category.<sup>28</sup> It has been reported ALI-NSCLC patients have a 5-year OS between stages I and II after bilobectomy or a lobectomy and wedge resection,<sup>29</sup> and the incidence of squamous cell carcinoma is higher than adenocarcinoma in ALI-NSCLC.<sup>24</sup> The potential mechanisms are squamous cell carcinomas which present as the central tumors and can be closer to the fissure or require lobectomy.<sup>30</sup> The options of surgical approaches for ALI-NSCLC remain debatable. Yang et al.<sup>11</sup> found that lobectomy of the adjacent lobe provided a better survival for ALI-NSCLC, while another study demonstrated that lobectomy provided a worse prognosis for ALI-NSCLC, when compared to those patients who did not receive lobectomy.<sup>9</sup> These controversial results may be explained by the different lymph node statuses and surgical approaches. In 2014, Leuzzi et al.<sup>31</sup> compared 28 ALI-NSCLC patients who underwent anatomical lobectomy and 12 ALI-NSCLC patients who underwent nonanatomical lobectomy (lobectomy plus wedge resection) and found a similar prognosis of 5-year disease-specific survival (56% and 47%, respectively) and a close recurrence rate, which elaborated that nonanatomical resection can be considered as a feasible surgical option.

Although pneumothorax has been reported to be the most common complication with an incidence rate of 1.3%–60% after thermal ablation, according to a systemic review,<sup>32</sup>

most cases are can recover after the observation, manual evacuation, and chest tube placement. Emphysema, tumor diameter, pulmonary fissure traversed by MWA antennas, and ablation zone encompassing the pleura are the risk factors of pneumothorax, as previously reported,<sup>33–36</sup> of which emphysema is the leading predictor.<sup>36</sup> In the MWA procedure, the traversal of the pulmonary fissure was performed as needed to achieve complete ablation in tumors, especially for ALI-NSCLC patients, which may increase the risk of pneumothorax. In our study, the ALI group had a significantly higher incidence rate of pneumothorax than the non-ALI group (52.9% vs. 27.0%,  $p = 0.002$ ), but no severe adverse events were found. Moreover, a significant difference in tumor diameter was found between the two groups. Therefore, a logistic regression analysis was conducted to investigate the potential correlation between ALI and the risk of pneumothorax, which showed a correlation, whereas no association between tumor diameter and pneumothorax was found. The mechanisms of a high risk of pneumothorax in ALI-NSCLC remain ambiguous. The potential mechanisms are: (i) the antennas can create a large hole when the pulmonary fissure is traversed by antennas during the MWA procedure; these holes can be further enlarged by respiratory-induced lung motion and increase the risk of pneumothorax; (ii) in general, MWA procedures were usually terminated when the ablation zone presented a 5–10 mm rim of ground-glass opacification (GGO) beyond the lesion boundary. The ablation zone might encompass the pulmonary fissure for ALI-tumors, which may induce dehydration and reduce the elastic properties of the lung parenchyma, and increase the risk of pneumothorax.

This study has several limitations that should be noted. First, it was a retrospective study, and patient selection bias may therefore exist. Second, the sample size was still limited for ALI-NSCLC patients. Third, the mean follow-up of this study was  $27.2 \pm 11.8$  months, and a longer follow-up and comparisons are warranted in further studies. Fourth, the incomplete data of immediate contrast-enhanced CT scans after MWA prevented a comparison of the complete ablation rate between the two groups.

In conclusion, MWA is an effective and safe approach for ALI-NSCLC treatment. Although ALI can increase the risk of pneumothorax, the ALI-NSCLC patients reveal a comparable outcome to non-ALI NSCLC patients after MWA.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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