Original Article

Computed tomography-guided microwave ablation for non-small cell lung cancer patients on antithrombotic therapy: a retrospective cohort study

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Background: For non-small cell lung cancer (NSCLC) patients on antithrombotic therapy who are treated with microwave ablation (MWA), the transient interruption of antithrombotic agents may increase the risk of thromboembolism, and continuation of antithrombotic agents may increase the risk of intraprocedural hemorrhage. This retrospective cohort study aimed to explore the safety of MWA in patients with NSCLC on antithrombotic therapy.

Methods: A total of 572 patients with NSCLC (antithrombotic therapy group: n=84, Group A; control group: n=488, Group B) who received MWA were included. Antithrombotic agent use was suspended before MWA and resumed as soon as possible after MWA. Hemorrhagic (hemothorax and hemoptysis) and thromboembolic complications (pulmonary embolism, cerebral infarction, and angina) were compared. Logistic regression analyses were used to investigate the predictors of hemorrhagic complications after MWA.

Results: Hemorrhagic complications occurred in 8 participants (9.5%) from Group A and 33 participants (6.8%) from Group B, and no statistically significant difference was found (P=0.365). There were 3 participants (0.5%) who developed thromboembolic complications, including 1 case (1.2%, 1/84) of pulmonary embolism in Group A, and 2 cases (0.4%, 2/488) of cerebral infarction or angina in Group B; no significant difference was found (P=0.923). In the subgroup analyses of Group A, no statistically significant difference of hemorrhagic (P>0.999) or thromboembolic complications (P>0.999) was found between patients who received and did not receive bridging anticoagulation with heparin. Logistic regression analyses revealed that direct contact of a tumor with vessels ≥2 mm was a predictor of hemorrhagic complications [hazard ratio (HR) =2.318; 95% confidence interval (CI): 1.215–4.420; P=0.011], while antithrombotic therapy was irrelevant.

Conclusions: With the appropriate cessation and resumption of antithrombotic agents, patients with NSCLC on antithrombotic therapy have comparable incidence rates of hemorrhagic and thromboembolic complications after MWA to those of patients who are not on antithrombotic therapy. Therefore, with appropriate cessation, MWA appears to generally be safe for NSCLC patients on antithrombotic therapy.

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Introduction

Primary lung cancer ranks second in cancer incidence and is the leading cause of cancer fatality worldwide, with more than 2.2 million new cases and 1.79 million deaths estimated in 2020 (1). In China, 85% of lung cancer diagnoses are non-small cell lung cancer (NSCLC) (2,3), and most NSCLC patients have already advanced beyond the optimal time-window for surgical treatment at first diagnosis (4). Thermal ablation aims to cause coagulative necrosis conforming to the tumor and its margins and has been used in recent years as a primary treatment option for early-stage NSCLC and/or adjuvant to systemic treatments for advanced-stage NSCLC (5,6). Microwave ablation (MWA) has advantages over radiofrequency ablation (RFA), with a higher temperature, a larger ablation zone, and a shorter ablation duration (7).

Cancer has been reported to increase the risk of venous and arterial thrombosis (8,9). Several studies have shown that patients with lung cancer are at heightened risk of developing stroke or pulmonary embolism compared with cancer-free individuals (10,11). Similarly, Kato *et al.* (12) demonstrated that the incidence of cardiac infarction is elevated in advanced or postoperative NSCLC. Antithrombotic therapy, including antiplatelet agents and anticoagulants, is increasingly being used for the prevention of thromboembolism (13). Management with peri-invasive procedures in these circumstances is arduous, because transient interruption of antithrombotic agents may increase the risk of thromboembolism, while continuation may increase the risk of intraprocedural hemorrhage (14-16). According to the consensus guidelines for the management of thrombotic and bleeding risk in patients undergoing percutaneous image-guided interventions, thermal ablation is categorized as a procedure with high bleeding risk, and previous antithrombotic agents are recommended to be suspended (17,18). Uchino *et al.* (19) analyzed over 10,000 RFA treatments in 3,485 patients with liver cancer and found minor incidence rates of hemorrhagic and thromboembolic complications after an appropriate cessation of antithrombotic therapy. However, the safety of MWA in NSCLC patients on antithrombotic therapy remains unclear. Therefore, a retrospective cohort study was conducted to compare the hemorrhagic and thromboembolic complications after MWA between patients with NSCLC with and without antithrombotic therapy and to explore the safety of MWA in patients with NSCLC on antithrombotic therapy. We present the following article in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-21-1043/rc).

Methods

Patient criteria

This single-center retrospective cohort study included all patients with NSCLC who underwent MWA in Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences. The institutional ethics review board approved this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was waived due to the retrospective nature of this study. Patients with NSCLC who could not tolerate or refused surgery and received MWA between August 2016 and April 2021 were allocated to the antithrombotic therapy group (Group A) or control group (Group B) based on the prescriptions of antithrombotic agents before MWA. The patient inclusion criteria were as follows: (I) aged ≥18 years; (II) confirmed to have NSCLC, and undergoing treatment with MWA; (III) Eastern Cooperation Oncology Group (ECOG) score of 0–2; and (IV) platelet count $\geq 50\times10^9$/L. The patient exclusion criteria were as follows: (I) antithrombotic therapy was ceased more than 1 month before MWA; (II) incomplete data; (III) the presence of hemothorax or/and hemoptysis before MWA; (IV) lost to follow up; and (V) other concomitant therapies performed during the MWA procedure, such as radioactive seeds

implantation.

As described previously (20), all cases underwent chest computed tomography (CT) (CT590; GE Healthcare, Chicago, IL, USA) before the MWA procedure to evaluate the location, quantity, and size of tumors. Positron emission tomography (PET) or contrast-enhanced CT was performed to evaluate the lymph nodes and distant metastases. The NSCLC tumor stage was identified via the clinical tumor-node-metastasis (TNM) staging system of the Union for International Cancer Control (8th edition) (21). All laboratory examinations were conducted 1–4 days before MWA.

Peri-MWA management of antithrombotic therapy

Electronic medical records were comprehensively searched to identify patients who received antithrombotic therapy. Antithrombotic agents included aspirin, clopidogrel, and sarpogrelate as antiplatelet agents, and warfarin and rivaroxaban as anticoagulants. Telephone follow-up was performed to obtain detailed information on prescriptions and medication as needed. Antithrombotic agents were withheld from all participants before the MWA procedure. Discontinuation of antithrombotic agents, timing of antithrombotic therapy cessation, and the need for bridging anticoagulation therapy were determined by the multidisciplinary treatment team and followed the guidelines of the Society of Interventional Radiology (SIR) (17,18). Generally, aspirin, clopidogrel, and sarpogrelate were withheld at least 5 days before MWA; warfarin, 3 days with international normalized ratio (INR) <3.0 before MWA; and rivaroxaban, 1 day before MWA. The bridging anticoagulation of heparin was performed for patients with a high risk of thromboembolism, especially for those where cardiocerebrovascular diseases had occurred within 3 months before MWA. Blood transfusion was considered when patients presented with unstabilized hemodynamics, and vitamin K or fresh frozen plasma was administered to correct coagulopathy as needed. Antithrombotic agents were resumed after confirming the recovery and/or in the absence of complications after MWA via CT reexamination.

Definition of hemorrhagic and thromboembolic complications

There were no specific definitions of hemorrhagic and thromboembolic complications based on SIR criteria (22). Hemorrhagic complications in this study were defined as hemoptysis and hemothorax, as per expert consensus in China (23). Hemoptysis was defined as the expectoration of blood to the mouth or nose that originated from the respiratory tract during or after MWA, while hemothorax was diagnosed when an echo-free space or high-density fluid was detected in the thorax on CT scans (19). In addition, thromboembolic complications were defined as ischemic heart disease, cerebral infarction, or pulmonary embolism after MWA (19). The severity of complications was classified as per the SIR criteria (22). Tumor adjacency to vessels ≥2 mm was defined as the tumors having direct contact with vessels ≥2 mm or the distance between tumors and vessels being ≤5 mm and was evaluated using transverse images or/and multiplanar reformation on CT images.

MWA procedure and follow-up

The MWA procedures followed the SIR guidelines (22) and were performed by several experienced interventional radiologists. As described previously (20), an MTC-3C MWA system (Vison Medicine, Nanjing, China) or an ECO-100A1 MWA system (ECO Medical Instruments, Nanjing, China) was used, with a microwave emission frequency of 2,450±50 MHz and an adjustable continuous wave output power of 20–80 W. The MWA antennas (Vison or ECO) were 15–18 cm in effective length and 15–17 G in outside diameter according to the tumor location and distance to the pleura, with a 15 mm active tip. Preprocedural CT was performed to inform the treatment plan and to clarify the suitable position, puncture site location, optimal puncture trajectory, and the number of MWA antennas. Local anesthesia was used for most patients, while intravenous anesthesia was used for patients requiring more pain control. Antennas were introduced into the planned site, and MWA was performed with the planned power and duration, with adjustments of suitable power and duration being carried out according to the intraprocedural location of MWA antennas as needed. The procedure was terminated when the ablation zone included a 5–10 mm rim of ground glass opacification beyond the lesion boundary. Finally, a repeat chest CT scan was performed to evaluate the ablation zone and detect possible complications. For patients without a histopathological subtype, a 15 G coaxial introducer needle (Co-Axial Introducer Needle; Argon Medical Devices, Athens, Greece) was first advanced into the tumor, and then the stylet was replaced with a 16 G full-core biopsy needle (BioPince; Argon Medical Devices) through the cannula. A 17 G MWA antenna (Vison or

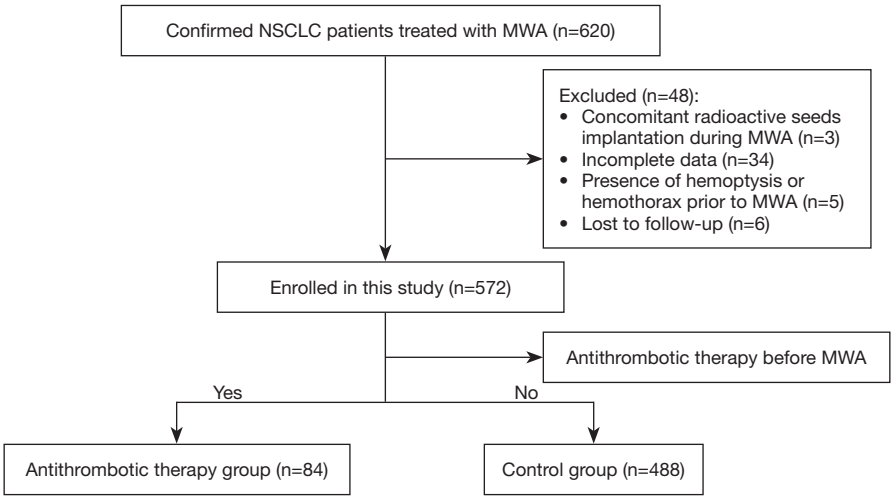

Figure 1 Patient selection flowchart. NSCLC, non-small cell lung cancer; MWA, microwave ablation.

ECO) was introduced into the tumor through the cannula. For patients with advanced-stage NSCLC, subsequent systemic treatments were performed at least 2 weeks after MWA.

Follow-up with CT was conducted 1–5 days after MWA during hospitalization and 3–4 weeks after MWA to detect postprocedural complications. Pneumothorax was classified as mild if it presented with the retraction of lung surface less than 2 cm from the pleura, moderate if it presented with retraction of 2–4 cm, and severe if it presented with retraction of more than 4 cm. Chest tube placement was performed for patients with moderate and severe pneumothorax, pleural effusion, or hemothorax and was terminated when the retraction of the lung surface or pleural effusion or/and hemothorax disappeared.

Statistical analysis

Categorical variables were described as frequencies and percentages, and continuous variables were described as means or medians ± SD. Statistical analyses were performed using SPSS 25.0 for Windows (IBM Corp., Armonk, New York, NY, USA). Baseline characteristics and hemorrhagic and thromboembolic complications were compared using the Student's *t*-test or the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables to compare 2 groups. A P value <0.05 was considered statistically significant. For the subgroup analyses of Group A, the hemorrhagic and thromboembolic complications were compared between patients with and without bridging anticoagulation. The possible predictors for hemorrhagic complications were analyzed using univariate logistic regression analyses, including 21 parameters on demographics, treatment history, ablation factors, and radiological features. Variables with P<0.05 in the univariate analyses were entered into the multivariate logistic regression analyses as candidate variables.

Results

Patient characteristics

There were 572 patients with NSCLC (84 in Group A and 488 in Group B; *Figure 1*) who underwent MWA and were included in this study. The baseline characteristics are presented in *Table 1*. A total of 267 patients (46.7%) receiving synchronous coaxial-cannula biopsy and MWA, including 37 patients (44.0%) in Group A and 230 patients (47.1%) in Group B, were included, and no significant differences were found (P=0.601). Patients in Group A were significantly older than those in Group B (P<0.001). More male patients were included in Group A (P=0.020). In addition, the proportion of patients with underlying cardiovascular diseases (P<0.001), cerebrovascular diseases (P<0.001), and pulmonary embolism or deep vein thrombosis (DVT; P=0.007) were higher in Group A. Patients in Group A had a slightly higher white blood cell count (P=0.024). Compared with those in Group B, patients in Group A had a slightly longer ablation time (P=0.037). The mean follow-up was 23.8±9.6 months.

Table 1 Clinical characteristics between Group A and Group B treated with MWA

Variables	Overall (n=572)	Group A (n=84)	Group B (n=488)	P value
Age (years)	68.5±10.8	73.2±9.1	67.6±10.9	<0.001
Gender				0.020
Male	350 (61.2%)	61 (72.6%)	289 (59.2%)	
Female	222 (38.8%)	23 (27.4%)	199 (40.8%)	
Underlying diseases				
Cardiovascular diseases	102 (17.8%)	64 (76.2%)	38 (7.8%)	<0.001
Cerebrovascular diseases	36 (6.3%)	16 (19.0%)	20 (4.1%)	<0.001
Pulmonary embolism or DVT	4 (0.7%)	3 (3.6%)	1 (0.2%)	0.007
Other malignancies	54 (9.4%)	6 (7.1%)	48 (9.8%)	0.436
Cirrhosis	4 (0.6%)	1 (1.2%)	3 (0.6%)	0.471
CCV adverse events within 3 months	14 (2.4%)	12 (14.3%)	2 (0.4%)	<0.001
CCV adverse events beyond 3 months	85 (14.9%)	61 (72.6%)	24 (4.9%)	<0.001
Tumor subtypes				0.095
Adenocarcinoma	415 (72.6%)	53 (63.1%)	362 (74.2%)	
Squamous cell carcinoma	127 (22.2%)	26 (31.0%)	101 (20.7%)	
Others	30 (5.2%)	5 (6.0%)	25 (5.1%)	
Tumor stage				0.396
I	238 (41.6%)	38 (45.2%)	200 (41.0%)	
II	68 (11.9%)	8 (9.5%)	60 (12.3%)	
III	104 (18.2%)	19 (22.6%)	85 (17.4%)	
IV	162 (28.3%)	19 (22.6%)	143 (29.3%)	
Laboratory test				
WBC ($\times10^9$/L)	6.3±2.3	6.8±2.2	6.2±2.3	0.024
Hb (g/L)	127.7±17.4	125.3±18.6	128.1±17.2	0.184
PLT ($\times10^9$/L)	217.9±73.2	215.7±77.3	218.3±72.5	0.772
PT (s)	11.4±1.9	11.8±2.6	11.3±1.8	0.073
Treatment history				
Previous surgery	52 (9.1%)	6 (7.1%)	46 (9.4%)	0.501
Previous chemotherapy	57 (10.0%)	3 (3.6%)	54 (11.1%)	0.055
Previous radiotherapy	20 (3.5%)	1 (1.2%)	19 (3.9%)	0.355
Previous TKIs	77 (13.5%)	8 (9.5%)	69 (14.1%)	0.252
Previous immunotherapy	12 (2.1%)	1 (1.2%)	11 (2.3%)	0.829
Radiological features				
Tumor diameter (cm)	3.3±2.1	3.6±2.2	3.3±2.1	0.252

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Overall (n=572)	Group A (n=84)	Group B (n=488)	P value
Location				0.173
Upper lobe	315 (55.1%)	52 (61.9%)	263 (53.9%)	
Middle or lower lobe	257 (44.9%)	32 (38.1%)	225 (46.1%)	
Distance to pleura (mm)	9.7±10.8	7.9±9.7	1.0±1.1	0.103
Direct contact of tumor with vessels ≥2 mm	225 (39.3%)	31 (36.9%)	194 (39.8%)	0.621
Extrapulmonary metastases	98 (17.1%)	11 (13.1%)	87 (17.8%)	0.288
Number of metastases				0.160
<2	497 (86.9%)	77 (91.7%)	420 (86.1%)	
≥2	75 (13.1%)	7 (8.3%)	68 (13.9%)	
Ablation factors				
Size of instruments				0.226
17 G	153 (26.7%)	21 (25.0%)	132 (27.0%)	
16 G	62 (10.8%)	5 (6.0%)	57 (11.7%)	
15 G	357 (62.4%)	58 (69.0%)	299 (61.3%)	
Maximum power (W)	48.5±12.4	49.3±12.4	48.4±12.4	0.538
Ablation time (min)	10.3±5.5	11.4±6.0	10.1±5.3	0.037
Number of pleural punctures	1.4±0.6	1.4±0.7	1.4±0.6	0.544

Frequencies and percentages are reported for categorical variables and means ± SDs are reported for continuous variables. Group A, antithrombotic therapy group; Group B, control group. MWA, microwave ablation; DVT, deep vein thrombosis; CCV, cardiocerebrovascular; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; PT, prothrombin time; TKIs, tyrosine kinase inhibitors.

Profiles of antithrombotic therapy

Detailed prescriptions of antithrombotic agents are shown in *Table 2*. Among the 84 patients from Group A, 64 cases (76.2%) received single-agent therapy, and 20 cases (23.8%) received dual-agent therapy. In Group A, 71 cases (84.5%) received antiplatelet agents, and 13 cases (15.5%) received anticoagulants. Aspirin was the predominant antiplatelet agent (73.8%), while warfarin was the most frequent anticoagulant (9.5%). The main indications of antithrombotic therapy were ischemic heart disease (54.8%), cerebrovascular disease (10.7%), and peripheral vascular disease (10.7%). There were 12 patients (2.1%) who received bridging anticoagulation of heparin after the cessation of antithrombotic therapy. The antithrombotic therapy was resumed 5.6±2.4 days after MWA.

Complications

The detailed complications in Groups A and B are presented in *Table 3*. Hemorrhagic complications were diagnosed 0.5±0.8 days after MWA in 41 cases (7.2%); of these, hemothorax occurred in 27 cases (4.7%) and hemoptysis in 21 (3.7%) cases. There were 4 cases (0.7%) with hemothorax who received chest tube placement. A hemorrhagic complication was diagnosed in 8 cases (9.5%) in Group A and 33 cases (6.8%) in Group B, and there were no statistically significant differences (P=0.365), although Group A had a slightly higher incidence rate. There were 2 cases (0.3%) who received a blood transfusion, while no cases received transcatheter arterial embolization. In addition, none of the hemorrhagic complications were classified as a severe adverse events or above.

Table 2 Profiles of antithrombotic therapy (n=84)

Variables	Number (%)
Number of agents	
Single agent	64 (76.2)
Two agents	20 (23.8)
Antiplatelet agents	
Aspirin	62 (73.8)
Clopidogrel	28 (33.3)
Sarpogrelate	1 (1.2)
Anticoagulants	
Warfarin	8 (9.5)
Rivaroxaban	5 (6.0)
Indications for antithrombotic therapy	
Ischemia heart diseases	46 (54.8)
PCI without stent	21 (25.0)
PCI with stent	20 (23.8)
CABG	1 (1.2)
CABG and PCI with stent	4 (4.8)
Valvular heart disease	3 (3.6)
Arrhythmia	8 (9.5)
Cerebrovascular disease	9 (10.7)
Peripheral vascular disease	9 (10.7)
Pulmonary embolism or DVT	3 (3.6)
Other or unspecified	6 (7.1)

PCI, percutaneous coronary intervention; CABG, cardiac artery bypass graft; DVT, deep vein thrombosis.

Thromboembolic complications were diagnosed in 3 cases (0.5%); of these, 1 was pulmonary embolism (1.2%, 1/84) in Group A, 1 was a cerebral infarction (0.2%), and 1 was angina (0.2%) in Group B, and there no statistically significant differences (P=0.923), although Group A had a slightly higher incidence rate. A patient without continuous antithrombotic therapy before MWA developed a stroke 3 days after MWA, and aspirin was prescribed in a timely manner. A patient who experienced chest pain after MWA was diagnosed with stable angina and underwent treatment with aspirin but without percutaneous coronary intervention. Pulmonary infarction was diagnosed in 1 case; antithrombotic therapy and intensive care were provided in a timely manner, and their symptoms improved 4 days after MWA.

The details of hemorrhagic and thromboembolic complications in patients undergoing antithrombotic therapy with and without bridging anticoagulation after MWA are presented in *Table 4*; no statistically significant differences in hemorrhagic complications (P>0.999) or thromboembolic complications (P>0.999) were found between the 2 subgroups.

Predictor of hemorrhagic complications after MWA

Logistic regression analyses for hemorrhagic complications are shown in *Table 5*. The predictor of hemorrhagic complications after MWA was direct contact of a tumor with vessels ≥2 mm [hazard ratio (HR) =2.318; 95% confidence interval (CI): 1.215–4.420; P=0.011; *Figure 2*].

Table 3 Detailed complications between Group A and Group B after MWA

Variables	Overall (n=572)	Group A (n=84)	Group B (n=488)	P value
Main complications				
Pneumothorax	161 (28.1%)	17 (20.2%)	144 (29.5%)	0.081
Pleural effusion	40 (7.0%)	5 (6.0%)	35 (7.2%)	0.686
Hemorrhagic complications	41 (7.2%)	8 (9.5%)	33 (6.8%)	0.365
Hemothorax	27 (4.7%)	6 (7.1%)	21 (4.3%)	0.257
Hemoptysis	21 (3.7%)	4 (4.8%)	17 (3.5%)	0.794
Thromboembolic complications	3 (0.5%)	1 (1.2%)	2 (0.4%)	0.923
Pulmonary embolism	1 (0.2%)	1 (1.2%)	0	0.147
Cerebral infarction	1 (0.2%)	0	1 (0.2%)	>0.999
Angina	1 (0.2%)	0	1 (0.2%)	>0.999

Group A, antithrombotic therapy group; Group B, control group. MWA, microwave ablation.

Table 4 Detailed hemorrhagic and thromboembolic complications between antithrombotic therapy patients with and without bridging anticoagulation after MWA

Variables	Bridging anticoagulation (n=12)	Without bridging anticoagulation (n=72)	P value
Hemorrhagic complications	1 (8.3%)	7 (9.7%)	>0.999
Hemothorax	1 (8.3%)	5 (6.9%)	>0.999
Hemoptysis	1 (8.3%)	3 (4.2%)	>0.999
Thromboembolic complications	0	1 (1.4%)	>0.999
Pulmonary embolism	0	1 (1.4%)	>0.999
Cerebral infarction	0	0	–
Angina	0	0	–

MWA, microwave ablation.

Table 5 Univariate and multivariate logistic regression analyses of hemorrhagic complications in NSCLC patients treated with MWA

Variables	Univariable analyses			Multivariable analyses		
	HR	95% CI	P value	HR	95% CI	P value
Age (years)	1.019	0.988–1.050	0.228	–	–	–
Gender	1.242	0.636–2.424	0.525	–	–	–
Antithrombotic therapy	1.451	0.646–3.261	0.367	–	–	–
Tumor subtypes	1.216	0.723–2.044	0.461	–	–	–
Tumor stage	1.126	0.878–1.444	0.349	–	–	–
WBC	1.029	0.901–1.176	0.673	–	–	–
Hb	0.996	0.978–1.014	0.639	–	–	–
PLT	0.999	0.994–1.003	0.608	–	–	–
PT	1.047	0.931–1.178	0.442	–	–	–
Previous ipsilateral surgery	0.493	0.116–2.104	0.340	–	–	–
Previous chemotherapy	1.613	0.648–4.020	0.304	–	–	–
Previous radiotherapy	1.462	0.327–6.529	0.619	–	–	–
Previous TKIs	0.885	0.336–2.331	0.805	–	–	–
Tumor diameter	1.155	1.019–1.309	0.024	–	–	–
Location	0.846	0.448–1.599	0.607	–	–	–
Distance to pleura	0.878	0.637–1.209	0.424	–	–	–
Near vessels larger than 2 mm	2.318	1.215–4.420	0.011	2.318	1.215–4.420	0.011
Number of metastases	0.915	0.347–2.410	0.857	–	–	–
Maximum size of instruments	0.806	0.570–1.140	0.222	–	–	–
Maximum power (W)	1.02	0.995–1.045	0.116	–	–	–
Ablation time (min)	1.048	0.998–1.101	0.063	–	–	–

NSCLC, non-small cell lung cancer; MWA, microwave ablation; HR, hazard ratio; CI, confidence interval; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; PT, prothrombin time; TKIs, tyrosine kinase inhibitors.

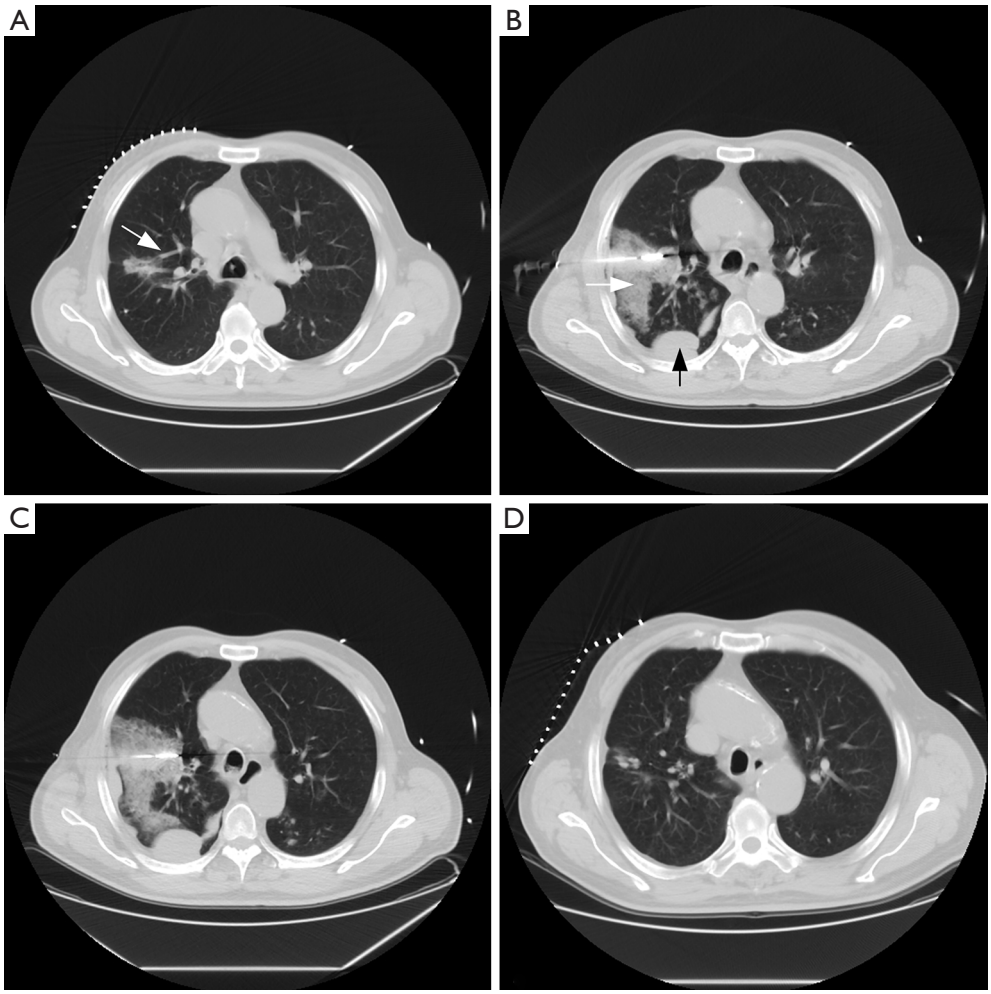

Figure 2 A case showing that direct contact of a tumor with vessels ≥2 mm is the predictor of hemorrhagic complications. (A) A suspected NSCLC patient with previous ischemic stroke who was on antithrombotic therapy of aspirin was admitted. The CT scan revealed the presence of multiple vessels in direct contact with the lesion (white arrow). Aspirin was ceased 5 days before MWA. (B) Synchronous biopsy and MWA were performed via a coaxial cannula. An intraparenchymal hemorrhage (white arrow), hemothorax (black arrow), and intraprocedural hemoptysis occurred before MWA. (C) Compared with the initial CT-scan, MWA was performed via cannula, followed by multiple adjustments to achieve complete ablation. Histopathological results proved the diagnosis of adenocarcinoma, and aspirin was resumed 5 days after MWA. (D) Hemorrhagic complications were not sustained, even though the antithrombotic agent was resumed, and thromboembolic complications occurred. One-month CT scans after MWA revealed alleviation of hemothorax. NSCLC, non-small cell lung cancer; CT, computed tomography; MWA, microwave ablation.

Discussion

In this study, the overall incidence rate of hemorrhagic complications was 7.2%. The incidence of hemorrhagic complications in Group A was 9.5%, which was slightly higher than the threshold of 9.2% in pulmonary hemorrhage recommended by SIR (22). There were no statistically significant differences in hemorrhagic and thromboembolic complications between the 2 groups, and the safety of appropriate cessation and resumption of antithrombotic therapy in patients with NSCLC treated with MWA was supported by our findings.

It has been reported that hemorrhagic complications occur in up to 15% of patients with lung tumors treated with thermal ablation, and they are predominantly hemoptysis and hemothorax. Less than 1% of patients require blood

transfusion or transcatheter arterial embolization (24). In 2021, Chi *et al.* (25) showed that 56.3% of patients with ground glass opacity lesions had hemorrhages after MWA using a sharp ablation tip. According to SIR standards, the incidence rate of pulmonary hemorrhage after thermal ablation in patients with lung tumors ranges from 6% to 9.3%, while 1.6% to 2.9% of these patients present with hemorrhage requiring interventions (26-28). Although hemorrhagic complications have not been specifically defined by the SIR criteria, an expert consensus from China defined hemorrhagic complications mainly as hemoptysis and hemothorax, which was adopted in this study (22,23). The leading reason that intraparenchymal hemorrhage was not included as the diagnostic criterion of hemorrhagic complications was that moderate intraparenchymal hemorrhage or bleeding in the puncture path are common features during MWA without symptoms of hemothorax or hemoptysis, which are typically absorbed, and no further interventions are required.

In recent years, 2 guidelines regarding the management of antithrombotic therapy in patients who undergo surgery or gastrointestinal endoscopy have been proposed (14,29). In 2019, Douketis *et al.* (30) demonstrated that appropriate cessation of anticoagulant agents for surgery is safe and tolerated. Heparin bridging is recommended for surgical candidates receiving warfarin who are considered at high thromboembolic risk (such as venous thromboembolism within 3 months) (14). According to SIR guidelines, thermal ablation was also categorized as a procedure with high bleeding risk, and previous antithrombotic agents were recommended to be withheld (17,18). In a similar study with over 10,000 RFA treatments in 3,485 patients with liver cancer, the incidence rates of hemorrhagic complications were 0.7% and 0.5% in the antithrombotic group and antithrombotic therapy-free group, respectively, while those of thromboembolic complications were 0.2% and 0.1% in the antithrombotic group and antithrombotic therapy-free group, respectively; no statistically significant differences were found, which demonstrates the safety of appropriate cessation and resumption of antithrombotic therapy in patients with liver cancer treated with RFA (19). As one of the common types of thermal ablation, MWA is generally performed percutaneously in patients with NSCLC, and direct hemostasis using surgical instruments (such as tamponade or cautery) cannot be performed. Although Uchino *et al.* (19) found a tendency of late-onset hemorrhage after RFA in patients with liver cancer on antithrombotic therapy, an identical tendency after MWA in patients with NSCLC on antithrombotic therapy was not revealed in this study. The results from this study reveal that transient cessation of antithrombotic therapy may not increase the risk of hemorrhagic and thromboembolic complications in NSCLC patients treated with MWA. In addition, the indications of bridging anticoagulation in this study were for patients receiving warfarin or/and for those developing had cardiocerebrovascular diseases within 3 months, as per the surgical guidelines mentioned above (14). Although the incidence rate of hemorrhagic complication in patients without bridging anticoagulation was slightly higher than that in patients with bridging anticoagulation, no significant differences were found between the 2 subgroups, but a comparison including a larger sample warrants further investigation.

The predictors of hemorrhagic complications in NSCLC patients treated with MWA remain debatable. Kashima *et al.* (27) reported an incidence rate of 1.6% of bleeding requiring blood transfusion in 420 patients with lung cancer involving 1,000 sessions of RFA treatment, and the predictors of bleeding after RFA were serum platelet count $\leq 180\times10^9$/L and tumor size >3 cm. As reported by another study with 164 patients with lung cancer involving 248 sessions of RFA treatment, the incidence of intraparenchymal hemorrhage and hemoptysis were 17.7% and 16.1%, respectively, and the mortality rate due to massive bleeding was only 0.4% (31). The predictors associated with intraparenchymal hemorrhage were lesions <2.5 cm located in the lower or middle lobe, pulmonary vessels being penetrated, and the use of multi-tined electrodes (31). In 2021, Uchino *et al.* (19) found no statistically significant correlation between receiving antithrombotic therapy and hemorrhagic complications patients with liver cancer treated with RFA. Similarly, direct contact of a tumor with vessels ≥2 mm was the predominant predictor of hemorrhagic complications in patients with NSCLC treated with MWA in this study, and antithrombotic therapy was not associated with hemorrhagic complications.

Several limitations of this study should be noted. First, it was a retrospective study; thus, patient-related selection bias may have existed. Second, the data from this study are from a single-center study, and the results should be validated using other datasets. Third, the types of antithrombotic agents in this study are limited, and more types and patients should be included in future investigations. Fourth, Zhu *et al.* (32) showed that pulmonary artery enlargement detected using CT was independently associated with

higher-grade pulmonary hemorrhage following CT-guided transthoracic lung biopsy, and this study lacked quantitative analysis of the identical parameters to explore the potential correlations with hemorrhagic complications following MWA. Fifth, the sample size of the antithrombotic group and the patients with hemorrhagic or thromboembolic complications are still limited, and the results require validation by future investigations involving more patients.

In conclusion, with the appropriate cessation and resumption of antithrombotic agents, patients with NSCLC on antithrombotic therapy have comparable incidence rates of hemorrhagic and thromboembolic complications after MWA compared to patients not receiving antithrombotic therapy. Therefore, MWA is generally safe for patients on antithrombotic therapy with appropriate cessation.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-21-1043/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-21-1043/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board approved this study. Written informed consent from patients was waived for this retrospective analysis.

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