Percutaneous Image-Guided Microwave Ablation for Treating Postsurgical Intrapulmonary Oligometastases or Oligorecurrence

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ABSTRACT

Objective: To assess the clinical efficacy of microwave ablation (MWA) in treating tumour patients with postsurgical intrapulmonary oligometastases or oligorecurrence (PIORO).

Study Design: Descriptive study.

Place and Duration of the Study: Departments of Thoracic Surgery and Oncology, Jinan Central Hospital and Qilu Hospital, Jinan, China, from January 2014 to June 2023.

Methodology: Clinical data of 31 patients with PIORO receiving treatment with MWA were retrospectively analysed. After undergoing MWA, the patients were followed up for computed tomography (CT) examination on the 7th day, 1st month, and every 3 months, respectively. The Kaplan-Meier method was conducted to evaluate the clinical outcomes; overall survival (OS), progression-free survival (PFS), and time to local progression (TTLP).

Results: All patients with PIORO were successfully treated with MWA. The 3-year survival rate of patients was 35.5%. The median OS was 26.0 months, the median PFS was 11.1 months, and the median TTLP was 14.4 months. Patients with oligometastatic or oligorecurrent tumours ≤3 cm in diameter showed better PFS (≤3 cm, 14.261 m *vs.* >3 cm, 7.786 m; p <0.01) and TTLP (≤3 cm, 19.522 m vs. >3 cm, 12.214 m; p <0.05) than those with tumours >3 cm in diameter. Clinical characteristics of the patients were not significantly correlated with OS.

Conclusion: MWA, as a topically therapeutic method, is an effective procedure for tumour patients with PIORO, especially in cases of oligometastatic or oligorecurrent tumours ≤3 cm in diameter.

Key Words: *Microwave ablation, Thermal ablation, Oligometastases, Oligorecurrence, Progression-free survival, Survival.*

How to cite this article: Zheng QM, Li YY, Zuo TY, Li CH, Sun ZG. Percutaneous Image-Guided Microwave Ablation for Treating Postsurgical Intrapulmonary Oligometastases or Oligorecurrence. *J Coll Physicians Surg Pak* 2024; **34(02)**:178-182.

INTRODUCTION

Metastasis and recurrence of tumours are considered a stage near the end of life. Most patients with tumour metastasis or recurrence have previously received systemic therapy, and oncotherapy has improved topical and systemic treatment recently. In 1995, Hellman *et al.* put forward the concept of oligometastases for the first time,[1] and then Niibe *et al.* revised it as oligorecurrence in 2006.[2]

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Received: July 13, 2023; Revised: December 30, 2023; Accepted: January 26, 2024
DOI: https://doi.org/10.29271/jcpsp.2024.02.178

The term oligometastases refers to distant metastases between one and five that can be treated locally to have long-term survival. The term oligorecurrence refers to distant metachronous metastases between one and five that could be used as local treatment, in the case of a controlled primary tumour. These concepts are the first to classify the metastasis or recurrence of cancer to help distinguish subgroups with long-term survival.

For local therapy of neoplasms, thermal ablation is an accurate and minimally invasive method, which utilises biothermal effects to directly cause irreversible damage or necrosis of tumour cells.[3] Radiofrequency ablation (RFA) is currently the most widely used thermal ablation method in tumour treatment.[4] Microwave ablation (MWA) is another thermal ablation method that has been applied for local treatment of cancer patients. Compared to RFA, MWA could enlarge ablative regions and shorten treatment time. Multiple studies have shown that MWA may be an alternative way to treat patients with early stage lung cancer who are at high risk of surgery and could lead

to a favourable prognosis for patients.[4,5] The purpose of this study was to assess the clinical outcomes of percutaneous image-guided MWA for the treatment of tumour patients with postsurgical intrapulmonary oligometastases or oligorecurrence (PIORO).

METHODOLOGY

From January 2014 to June 2023, 31 patients with PIORO were enrolled in the Departments of Thoracic Surgery and Oncology of Jinan Central Hospital and Qilu Hospital. Before receiving MWA, all patients were diagnosed with PIORO according to the literature.[6] All oligometastatic or oligo-relapsed lesions were treated with MWA, and all patients received regular follow-ups. Those patients with a life expectancy of less than 3 months, severe cardiovascular and cerebrovascular disease who could not tolerate MWA, and cachexia were excluded from this study. All patients consented to the study and it was approved by the Research Ethics Committee of Jinan Central Hospital (Reference 2022-157-01). The data for this study were retrospectively collected from workstations with picture archiving and communication system (PACS) facilities.

Patients fasted for 4 hours prior to MWA. The surgical puncture point was determined by computed tomography (CT) images. Local anaesthesia was performed with 1% lidocaine. At the beginning of ablation, all patients received intravenous anaesthesia with 1.5-2 mg/kg propofol.

All patients received MWA under CT guidance. The ECO-100C MWA system (ECO Microwave Electronics Research Institute, Nanjing, China; Registration standard: YZB/National 3388 - 2011; China: Use SFDA certification No.20113251473) was used. The transmission frequency of microwave was 2450 ± 50MHz, and the output level was in the continuous wave range of 0~150W. The ablation power was 60-70W for 4-8 minutes. Based on changes in imaging results, the operators modified and repositioned the antenna until the tumour was completely covered. After MWA, CT scans were performed to assess treatment response and immediate postoperative complications.

Patients underwent chest CT before treatment and received the same follow-up visits after MWA at the seventh day, the first month and every three-month, and the follow-up time was up to 3 years. Outcome indicators include overall survival (OS), progression-free survival (PFS), and time to local progression (TTLP). OS refers to the time that the first lesion was ablated until the patient died. PFS refers to the time that the first lesion was ablated until the imaging examination or the disease progression (local or remote) at the time of death. TTLP is analysed per lesion, which refers to the time from the first ablation of each lesion to the local tumour progression on imaging. At the last imaging session, the authors censored surviving patients who showed no evidence of progression.

For all statistics, the authors used SPSS (version 13; SPSS, Inc., Chicago, IL, USA) for analysis. Continuous variables were expressed as mean and SD, and categorical variables were expressed as counts and percentages. The survival curves were performed by Kaplan-Meier survival curves. The log-rank test was used to calculate the OS, PFS, and TTLP. The volume of $p < 0.05$ indicated a statistically significant difference.

RESULTS

A total of 31 patients were successfully treated with CT-guided percutaneous MWA. Among them, 18 (58.1%) cases were lung cancer, 25 (80.6%) cases were adenocarcinoma, 26 (83.9%) cases accepted surgery and chemotherapy before MWA, and 5 cases accepted only surgery before MWA. In 14 cases (37.8%), the diameter of oligometastatic or oligorecurrent tumours was greater than 3 cm. Table I shows the clinicopathologic features of the patients. Additionally, MWA-associated complications were found in 4 patients (12.9%). They included pneumothorax (3 cases) and chest pain (1 case). Prior to discharge, the patient was cured of all complications (Figure 1).

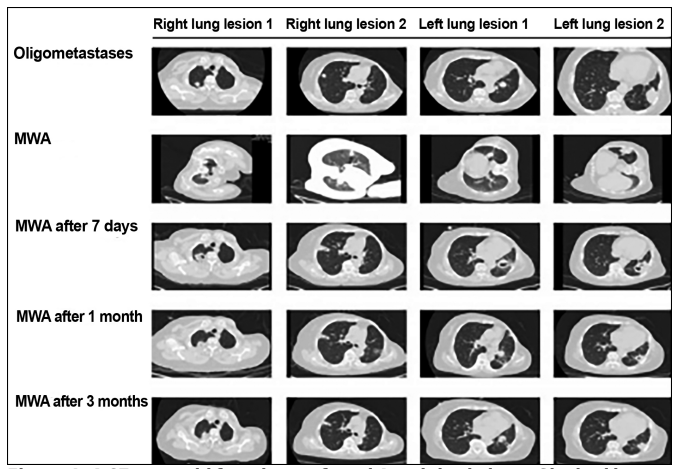

Figure 1: A 67-year-old female was found 4 nodules in lung. She had breast cancer and accepted surgery and chemotherapy. The pulmonary nodule was affirmed by mammary metastatic adenocarcinoma by biopsy pathology. The antenna was modified and repositioned according to imaging changes until the tumour was covered completely. The tumour has shrunken, fibrosis has developed and an irregular cavity has been formed from the CT image at 7 days, 1 month and 3 months after MWA.

Table I: Clinicopathologic features of 31 patients.

Clinical features	Number of patients	Percentage (%)
Gender		
Male	20	64.5
Female	11	35.5
Age, year		
≤65	15	48.4
>65	16	51.6
Primary tumour		
Lung	18	58.1
Extrapulmonary organs	13	41.9
Histological type		
ADC	25	80.6
SCC	6	19.4
Treatment before MWA		
Surgery+Chemotherapy	26	83.9
Surgery	5	16.1
Number of PIORO		
1	27	87.1
2-4	4	12.9
Size of PIORO, cm	Number of PIORO	
≤3 cm	23	62.2
>3 cm	14	37.8

MWA, Microwave ablation; SCC, Squamous cell carcinoma; ADC, Adenocarcinoma; PIORO, Postsurgical intrapulmonary oligometastases or oligorecurrence.

Table II: Univariate analysis with respect to OS, PFS, and TTIP of the patients.

Clinical features	Patients	3-year TTIP Patients	Median time (m)	p	3-year PFS Patients	Median time (m)	p	3-year OS Patients	Median time (m)	p
	31	2	14.419		2	11.129		11	25.968	
Gender				0.269			0.330			0.369
Male	20	0	13.200		0	9.750		6	24.850	
Female	11	2	16.636		2	13.636		5	28.000	
Age, year				0.339			0.336			0.568
≤65	15	2	15.867		2	12.600		5	24.000	
>65	16	0	13.063		0	9.750		6	27.813	
Primary tumour				0.505			0.468			0.222
Lung	18	2	15.556		2	12.333		8	27.556	
Extrapulmonary organs	13	0	12.846		0	9.462		3	23.769	
Histological type				0.208			0.218			0.963
ADC	25	2	15.160		2	11.880		9	25.800	
SCC	6	0	11.333		0	8.000		2	26.667	
Treatment before MWA				0.914			0.720			0.744
Surgery+Chemotherapy	26	2	14.500		2	11.038		10	25.962	
Surgery	5	0	14.000		0	11.600		1	26.000	
Number of PIORO				0.099			0.308			0.115
1	27	1	13.296		1	10.407		8	24.815	
2-4	4	1	22.000		1	16.000		3	33.750	
Size of PIORO, cm	Number of PIORO	6		0.021	2		0.009	16		0.210
≤3 cm	23	6	19.522		2	14.261		11	29.696	
>3 cm	14	0	12.214		0	7.786		5	23.500	

P: Log-rank test; MWA, Microwave ablation; SCC, Squamous cell carcinoma; ADC, Adenocarcinoma; PIORO, Postsurgical intrapulmonary oligometastases or oligorecurrence; OS, Overall survival; PFS, Progression-free survival; TTLP, Time to local progression.

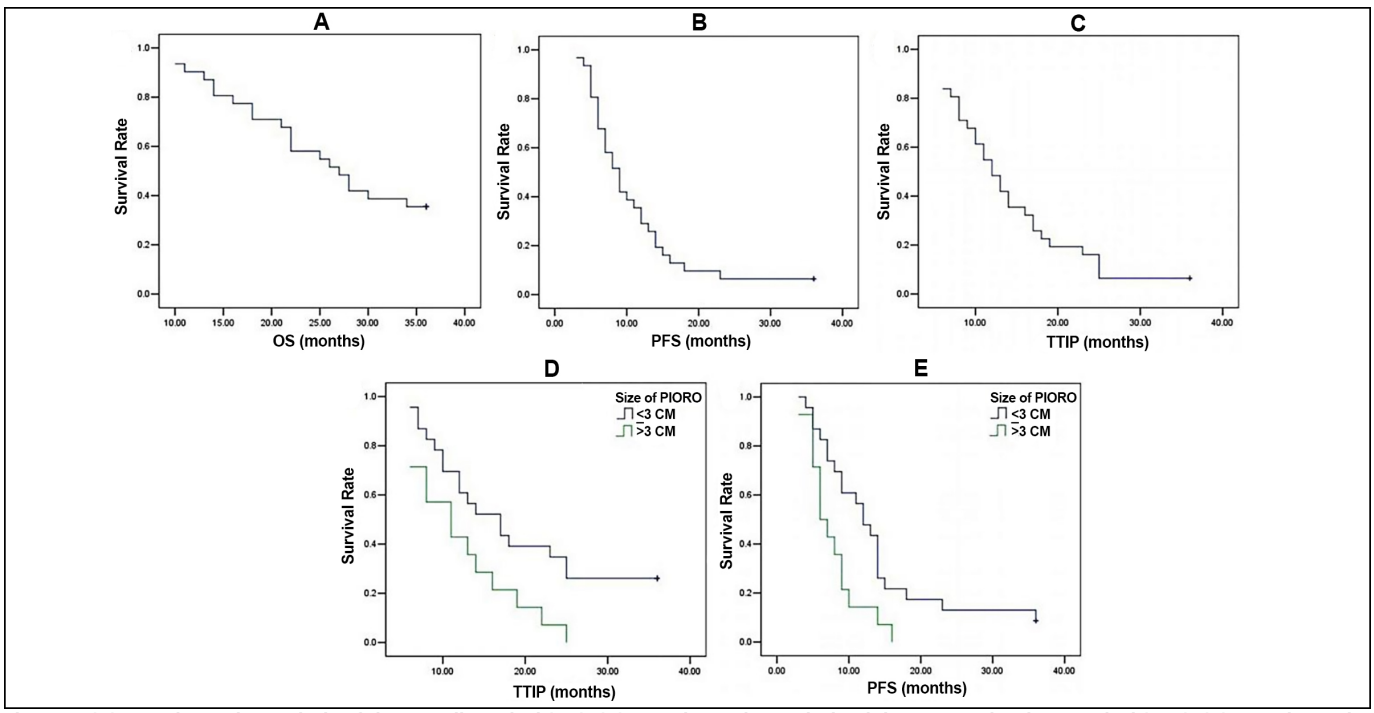

Figure 2: (A) A Kaplan-Meier analysis of the overall survival (OS). (B) A Kaplan-Meier analysis of the progression-free survival (PFS). (C) A Kaplan-Meier analysis of the time to local progression (TTLP). (D) A Kaplan-Meier analysis of time to local progression (TTLP) in patients with tumour size. (E) A Kaplan-Meier analysis of the progression-free survival (PFS) in patients with tumour size.

All patients were followed up for three years and the follow-up rate was 100%. The 3-year survival rate of the patients was 35.5% (cut-off = 3 years). The median OS was 26.0 months, the median PFS was 11.1 months, the median TTLP was 14.4 months. Patients with oligometastatic or oligorecurrent tumours ≤3 cm in diameter had better PFS (≤3 cm, 14.261m *vs.* >3 cm, 7.786 m; p <0.01) and TTLP (≤3 cm, 19.522m *vs.* >3 cm, 12.214 m; p <0.05) than those with tumours >3 cm in diameter (Figure 2). The clinical features of these patients were not significantly correlated with OS (Table II).

DISCUSSION

Oligometastasis or oligorecurrence is often depicted as an intermediate state before widespread metastasis of malignant tumour. When tumour metastasis or recurrence is confined to the lungs, reoperation is considered the treatment of choice for longer survival.[7] Considering many factors such as old age and cardiopulmonary dysfunction, those patients with PIORO who cannot tolerate surgery usually receive local treatment.[8] Among them, chemotherapy, radiotherapy, and radiochemotherapy are effective in treating

patients with postoperative local recurrence of non-small cell lung cancer (NSCLC).[9] In a report by Kelsey *et al.* for patients with NSCLC, 29 patients with PIORO accepted radiotherapy, with or without chemotherapy, whose median survival after therapy was 17 months.[10] However, chemotherapy, radiotherapy and radiochemotherapy require multiple treatments to achieve the desired results. As a result, thermal ablation, which offers low cost, rapid treatment, and similar efficacy, has come into focus.

The advent of thermal ablation has changed the landscape of localised tumour treatment to some extent. In fact, RFA has been widely used in the treatment of NSCLC with high success rate and safety. In recent decades, MWA has also been applied to tumour therapy. It produces more energy than RFA and ablates tumour necrosis in a shorter surgical time. Furthermore, the treatment effect is not affected by the heat sink effect of large vessels.[4] Especially, multiple MWA antennas could maximise the ablation zone size.[11] In relevant clinical studies, MWA has been shown to be effective in stage IA NSCLC,[12] and it can significantly improve the prognosis of patients receiving chemotherapy for advanced NSCLC.[13] Although a multicentre study showed that MWA should be considered an effective and safe treatment option for selected patients with oligopulmonary recurrence after radical resection of NSCLC,[6] there are still relatively few studies on MWA in tumour patients with PIORO. In this study, the results of 31 tumour patients with PIORO showed the 3-year survival rate was 35.5%. The median OS was 26.0 months, the median PFS was 11.1 months, the median TTLP was 14.4 months. Previous studies on different tumours have found that tumour diameter is an important factor affecting the efficacy of MWA.[14,15] When the tumour diameter is more than 3cm, it is necessary to adjust the antenna position for multiple ablations or use multiple antennas at the same time to expand the ablation range, resulting in poor treatment effect.[16] Similar results were found in this study, where the PFS and TTLP of patients with oligometastatic or oligorecurrent tumours ≤3 cm in diameter were better than those with tumours >3 cm in diameter. No clinical characteristics of the patients were significantly associated with OS. Notably, patients who received MWA did not get any treatment before the tumour progressed, which made the results of PFS more objective.

The present results of this study showed MWA was a relatively safe treatment. Common complications of MWA in the treatment of lung tumours include pneumothorax and chest pain.[17] Pneumothorax is one of the most common complications, with a frequency of 10-67%.[18] Ablation of some tumours near the pleura can easily cause chest pain, and opioids or nonsteroidal anti-inflammatory drugs can be used for symptomatic treatment. In the present study, 3 patients developed postoperative pneumothorax, and 2 cases required closed thoracic drainage. Additionally, 2 patients developed chest pain after surgery. After analgesia, chest pain symptoms improved within 3 days. All patients with complications of MWA were cured before discharge.

There were some limitations to this study. Firstly, due to the small sample size and the retrospective nature of the study, the results should be viewed reasonably. Given that MWA has rarely been reported as a local therapy for tumour cases with PIORO, this promising conclusion might append to the evidence-based medicine in this field and could help to implement prospective studies with larger sample sizes to further substantiate its effects. Secondly, some patients received chemotherapy, radiotherapy or targeted therapy after tumour progression. These different treatment options might affect patients' OS. Thirdly, in clinical practice, physicians provide treatment options for patients with PIORO, and the final decision also depends on the wishes of the patients and their families. This study excluded patients who refused any treatment, which may have biased the results. However, despite these limitations, this study could help us better understand the effectiveness of MWA for the treatment of tumour patients with PIORO. Large sample size, prospective, randomised controlled studies should be considered in further research.

CONCLUSION

MWA, as a topically therapeutic method, is a safe and effective procedure for tumour patients with PIORO, especially for those with oligometastatic or oligorecurrent tumours ≤3 cm in diameter.

FUNDING:
This work was supported by the science and technology projects of the Jinan Health Committee (Grant No. 2019-2-04).

ETHICAL APPROVAL:
The study was approved by the Ethics Committee of Jinan Central Hospital, Shandong, China (No. 2022-157-01, Date: 2022.08.24).

PATIENTS' CONSENT:
Informed consents were obtained from all patients.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
QMZ: Design, acquisition and analysis of data, and manuscript writing.
YYL, TYZ, CHL: Result interpretation and discussion.
ZGS: Study design, accountable for all aspects of the work.
All authors approved the final version of the manuscript to be published.

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