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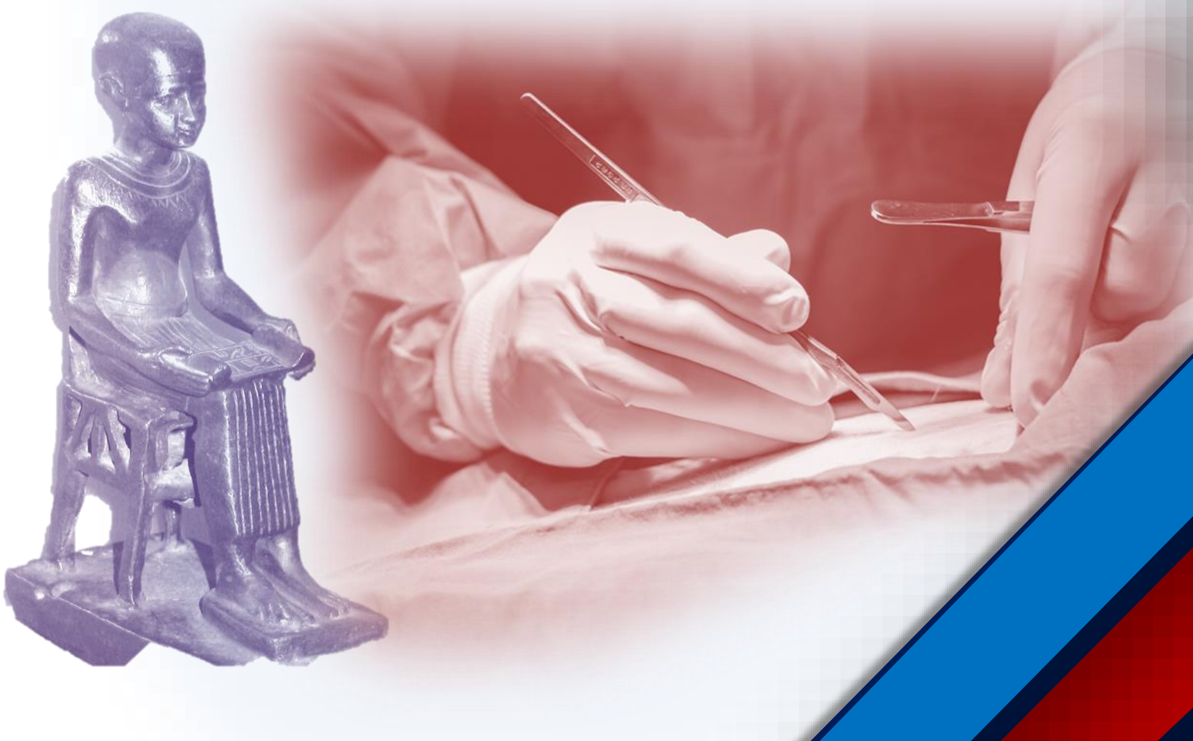

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Original Article

Role of Thermal Ablation in Pulmonary Metastases of Hepatobiliary and Gastrointestinal Malignancies

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ABSTRACT

Background: Pulmonary oligometastases from hepatobiliary and gastrointestinal primary cancers are associated with poor prognosis and limited treatment options. While local surgical resection and systemic therapies remain the mainstay, thermal ablation techniques, have emerged as effective local therapies for managing oligometastatic disease. These techniques offer a minimally invasive approach to manage pulmonary oligometastases in patients who are ineligible for resection.

Aim of the work: It was to evaluate the role of local thermal ablative therapy specifically microwave ablation in management of metastatic lung tumors from hepatobiliary and gastrointestinal origin.

Patients and methods: It was a prospective study performed on 60 patients [40 females and 20 males, Mean age 53.53] underwent computed tomography-guided percutaneous Microwave ablation for pulmonary oligometastases from hepatobiliary and gastrointestinal primaries. Outcomes included technical effectiveness, local tumor control, disease-free interval, overall survival, progression-free survival and complications.

Results: The mean hospital stay was 1.68 day per session. Pneumothorax incidence was 50% with only 3.9% requiring chest tube placement. There was a significant association between number of needle punctures [p value 0.02] and lateral position [p value <0.001] and pneumothorax incidence. The technique effectiveness rate was 97.5%. Complete response was 92.5%, 87.5% and 75% at 1, 3 and 6 months respectively. The mean follow-up period was nearly 1 year. The mean disease free interval was 9.1months. Six- month and one-year overall survival rates were 87.6% and 69.3%, while six-month and one-year progression free survival probability was 58.8%. Ground-glass opacity greater than 5 mm around the nodule was substantially associated with progression-free survival [P value 0.011].

Conclusion: Thermal ablation is a viable alternative option for patients with pulmonary oligometastasis who are not eligible for surgery. It boasts a strong safety profile and provides effective local tumor control.

Keywords: Pulmonary Oligometastases; Thermal Ablation; Microwave Ablation; Computed Tomography.

INTRODUCTION

Lung metastases are among the most frequent sites of metastasis for patients with extrapulmonary primary cancers [1]. Various cancers, including colon cancer, sarcomas, melanoma, breast cancer, urinary tract tumors and other malignancies, have the potential to metastasize to the lungs [2].

Metastatic cancer was previously regarded as the ultimate stage of the disease. Currently, a multi-modal and multi-disciplinary strategy is being used to try to improve these patients' prognosis [3].

In selected patients with pulmonary oligometastases, surgical resection is the gold standard. However, even after a complete resection, patients often experience high recurrence rates and may need multiple surgeries [4].

Image-guided tumor ablation uses thermal or electrical energy to control and destroy solid neoplasms. It is a cost-effective, minimally invasive alternative to surgical resection, allowing for greater preservation of normal lung parenchyma [5].

This study investigated the evidence supporting the use of local thermal ablation, specifically microwave ablation [MWA], in the management of pulmonary metastases originating from hepatobiliary and gastrointestinal primaries. This area has not been extensively discussed in clinical practice as the complex nature of these cancers and their pattern of metastatic spread.

THE AIM OF THE WORK

The aim of this study was to evaluate the role of local thermal ablative therapy specifically microwave ablation in management of metastatic lung tumors from hepatobiliary and gastrointestinal origin.

PATIENTS AND METHODS

The study was a prospective intervention hospital based study performed on 60 patients [40 females and 20 males, Mean age 53.53 and Range 28-76 years] underwent computed tomography [CT]-guided percutaneous Microwave ablation [MWA] for pulmonary oligometastases from hepatobiliary and gastrointestinal primaries. MWA was performed on 80 nodules in 60 patients over 76 sessions. Forty-four patients underwent one session, while eight patients underwent two sessions.

The study, conducted from June 2022 to November 2024, approval was granted by the institutional ethics committee, and written informed consent was obtained from all patients.

Patients:

Inclusion criteria consisted of oligometastatic pulmonary nodules from controlled hepatobiliary and gastrointestinal primary cancers. Lesions had to be ≤ 5 in number, each with a maximal diameter of ≤ 4 cm, and patients unfit for surgery with an adequate baseline bleeding profile were included. Exclusion criteria encompassed uncontrolled primary malignancy, severe lung emphysema, life expectancy of less than 3 months, and uncorrectable coagulopathy [6, 7].

Pre-ablation assessment:

The multidisciplinary team developed the treatment plan, taking a complete clinical history, performing a physical examination, reviewing recent imaging data, and thoroughly discussing the procedure's indications, risks, and benefits.

Pre-procedural laboratory tests, including a complete blood count, coagulation profile, and tumor markers, were conducted. Twenty-six patients underwent contrast-enhanced chest CT and thirty-four had PET/CT. Among these, 14 cases were confirmed by Tru-Cut biopsy using 16 gauge semi-automatic needles. The evaluation assessed pulmonary nodule characteristics [number, size, location, margin, enhancement, FDG uptake] and ablation parameters [applicator length, patient position, puncture site based on tumor size and location].

Ablation procedure:

MWA procedures were performed percutaneously with CT guidance [Somatom biograph 128; Siemens Healthineers, Erlangen, Germany], using Microwave Ablation device [Canyon microwave device; Model KY-2000A, China]. The MWA antennas [SureTip® REF; KY-2450B, China] were used in continuous mode, with a 16-gauge antenna and a length of 10 or 20 cm, depending on the lesion's depth from the skin."

All ablation procedures were conducted by two experienced interventional radiologists with 10 years' experience in pulmonary ablation. The procedure was performed under complete aseptic conditions.

All subjects were treated under general anesthesia. After localizing the nodule, the skin entry site was selected to ensure the shortest and safest pathway, avoiding major blood vessels, significant bronchi, bronco-vascular bundles, bullae, and inter-lobar fissures.

The successful central placement of the antenna into the center of the lesion was confirmed. The ablative area was planned to be large enough to cover the entire nodule with ablative safety margins around of at least 5 mm all over the nodule. At the end of the procedure, needle track coagulation was performed to prevent malignant cells seeding and to induce local hemostasis.

Post-Ablation:

A final CT scan of the entire chest was typically conducted immediately after antenna removal to verify the lesion's appearance and check for complications such as hemorrhage or pneumothorax. Each patient remained under hospital observation for at least one night.

Follow up protocol:

All patients involved in the study were subjected to immediate post-procedural CT chest without contrast and CECT after 1 month, while CECT or PET/CT at 3 and 6 months. Immediately post-ablation: the characteristic halo signs of GGO surrounding the treated tumor. If it exceeds 5mm in each direction, it indicates successful ablation. After one month: All patients were evaluated with CT chest with IV contrast.

After three months: 28 patients were evaluated with CECT and 32 patients were evaluated with PET/CT. 6 cases were confirmed with Tru-Cut biopsy. After six months: 22 patients were evaluated with CECT and 38 patients were evaluated with PET/CT.

The inhomogeneous contrast enhancement pattern [>15 HU] at CECT and inhomogeneous FDG uptake at PE/CT more than 3 were considered indicative of residual or recurrent disease. The local tumor response, estimation of the peri-procedural complications with analysis of the associated risk factors and post-ablation survival rate were the essential parameters in this study.

Statistical analysis:

Continuous variables with normal distribution were expressed as Mean ± SD. One-way ANOVA followed by Tukey post hoc analysis to compare between groups. Continuous variables with non-normal distribution were expressed as the median and interquartile range [IQR], and Wilcoxon rank sum test was performed to compare between groups. Categorical data were presented as frequencies and percentage and analyzed using the Fisher's Exact Tests. Survival was analyzed using the Kaplan–Meier method and survival comparisons between the groups were implemented using the log-rank test. Univariate analysis was done using a Cox-proportional hazards regression model to predictors of survival. Logistic regression analysis was used to identify the independent prognostic factors for local progression. A two-tailed P-value of less than 0.05 was statistically significant. All analyses were processed with R Software version 4.1.2 [R Foundation for Statistical Computing, Vienna, Austria].

RESULTS

Demographics [Table 1].

In this study, MWA was performed on 60 patients, 80 nodules at 76 MWA sessions, 74 denovo and 6 recurrent nodules. It included 40 females [66.67%] and 20 males [33.3%] and their age ranged between 28 and 76 years with Median [IQR] 56 [39.75, 64.50]. The mean age was 53.53 years. The primary malignancy was CRC at 48 patients [80%], 6 patients [10.00%] with pancreatic cancer, 4 patients [6.67%] with HCC and 2 patients [3.33%] with sarcoma. 24 out of 60 patients [40%] underwent local ablation only, while 36 patients [60%] were on adjuvant chemo or/and radiotherapy. MWA was performed on 80 pulmonary nodules: 52 in the right lung and 28 in the left. There were 50 nodules in the lower lobes, 16 in the upper lobes, and 14 in the middle lobe. Most nodules [90%] were peripheral, while 10% were central. In 77.5% of cases, the nodules were unilateral, and in 22.5%, they were bilateral. Regarding sizes, range was 8-35mm with a mean of 19.98mm. Among the patients, 54 had one nodule, 4 had two nodules, and 2 had three nodules

Procedure:

In this study, 76 MWA sessions were performed on 60 patients; 16 patients required two sessions, while 44 required one. One lesion was treated in 72 sessions and two lesions in 4 sessions. All procedures were CT-guided and performed under general anesthesia using 16-gauge microwave antennas. Session times ranged from 3 to 10 minutes, with a mean of 5.9 minutes, and the MWA power ranged from 40 to 100W. Patients were positioned prone in 29 sessions, lateral in 38 sessions, and supine in 9 sessions. Needle track length ranged from 38 to 83 mm, with a mean of 4 pleural needle punctures [range: 1-12]. Post-ablation hospital stay was one day for 72 sessions [94.74%], one week for 2 cases, and three weeks for 2 cases, with a mean stay of 1.68 days per session.

Safety and Complications:

No mortality was reported during or within the first month following the procedure. Various complications were observed [see Table 2], with pneumothorax being the most concerning. The overall incidence of pneumothorax was 50%, including 48.68% peri-procedural and one case of delayed pneumothorax after 7 days due to broncho-pleural fistula. Most peri-procedural pneumothoraces were mild [35 out of 37 sessions], while moderate pneumothorax occurred in two cases, requiring chest tube insertion.

Pulmonary infections occurred in 13.5% of cases, with two cases of lung abscesses requiring medical treatment and a prolonged hospital stay of about 7 days. No pulmonary hemorrhage was observed, and hemoptysis occurred in about 5% of sessions. Pleural effusion was experienced by 10% of cases, while 13% experienced pain lasting more than 7 days. No skin burns were observed, and rib fractures occurred in about 5% of cases. All studies are interested in identifying factors related to post-ablation pneumothorax to reduce its incidence. In Table 3, we observed a significant association between the number of needle punctures and the incidence of pneumothorax [p-value 0.02], with an increased number of needle punctures correlating with a higher incidence of pneumothorax. Patient position during the ablation procedure was also a significant factor; the study found an increased incidence of pneumothorax with the lateral position [p-value <0.001]. No significance was observed with the length of the needle track or the lesion's location in our study.

Technical success and effectiveness

Immediately post ablation, the GGO was more than 5 mm in 80% of sessions, 5mm in 17.5% of sessions and less than 5mm in 2.5% of sessions. The technique effectiveness in our study was 97.5%. [Figure 1]. Complete local response was 92.5%, 87.5% and 75% at 1, 3 and 6 months respectively, incomplete response was 5%, 7.5% and 15% and no response was 2.5%, 5% and 10% at 1, 3 and 6 months respectively. Recurrence of the same target lesion was observed in 13.33% of cases.

Survival Outcomes

The mean disease-free interval [DFI] was 9.1months with Median [IQR]: 6 [6-11.2 months] and range: 1-24 months. The mean follow-up period was nearly 1 year. Univariate analysis of factors associated with local progression, such as age, sex, primary tumor type, peri-abaltion adjuvant treatment, size, number, location and distribution of pulmonary metastases, and the GGO surrounding the lesion immediately post ablation, showed no significant association with these parameters. Six-month and one-year overall survival [OS] rates were 87.6% and 69.3% respectively. [Figure 2]

Univariate analysis of predictors associated with survival, such as age, sex, primary tumor type, peri-abaltion adjuvant treatment, size, number, location and distribution of pulmonary metastases and the disease free interval, showed no significant association with these parameters.

Six-month and one-year progression free survival [PFS] probability [Figure 3] was 58.8%. The univariate Analysis of predictors associated with progression-free survival in our study revealed that the GGO more than 5 mm around the nodule immediately post-ablation is significantly associated with PFS probability [Figure 4]. Other parameters, such as age, sex, primary tumor type, peri-ablation adjuvant treatment, size, number, location and distribution of pulmonary metastases, showed no significant association with PFS in our statistical analysis.

Table [1]: Demographic data, characteristics of primary tumors [N=60] and characteristics of metastatic pulmonary lesions [N=80].

		Patients N=60
Age [years]	**Mean;** **Median [IQR] ;** **Range**	53.53; 56 [39.75, 64.50]; 28-76
Sex	**Male**	20 [33.33%]
	Female	40 [66.67%]
Primary tumor Type	**Colorectal cancer**	48 [80.00%]
	Pancreatic cancer	6 [10.00%]
	HCC	4 [6,67%]
	Sarcoma	2 [3.33%]
Peri-ablation TTT	**Chemotherapy**	32 [53.33%]
	Chemotherapy and radiotherapy	4 [6.67%]
	No [Ablation only]	24 [40.00%]
		Lesions N=80
Pulmonary lesion condition	**Denovo**	74 [92.50%]
	Recurrent	6 [7.50%]
Side	**Right**	52 [65.00%]
	Left	28 [35.00%]
Lobe	**Lower**	50 [62.5%]
	Middle	14[17.50%]
	Upper	16 [20.00%]
Location	**Central**	8 [10.00%]
	Peripheral	72 [90.00%]
Size	**Mean ± SD** **Range**	19.98 ± 8.33 8-35
Laterality	**Bilateral**	18 [22.50%]
	Unilateral	62 [77.50%]
Shape	**Oval**	4 [5.00%]
	Round	76 [95.00%]
Margin	**Lobulated**	50 [62.50%]
	Speculated	30 [37.50%]
CT with IV contrast		
Enhancement	**Yes [nodular]**	40 [50.00%]
PET/CT		
Activity	**Yes [nodular]**	40 [50.00%]
SUVmax	**Mean ± SD; Range**	6.13 ± 3.41; 1.4-12

Table [2]: Complications among the ablation sessions [N=76].

		N=76
Pneumothorax	**Periprocedural pneumothorax**	37 [48.68%]
	Delayed pneumothorax	1 [1.31%]
Soft tissue emphysema		34 [44.74%]
Hemorrhage		0
Hemoptysis		4 [5.26%]
Plural effusion		8 [10.53%]
Pain	**Post-operative pain**	76 [100.00%]
	Pain 1-3 days	50 [65.79%]
	Pain 3-7 days	14 [18.42%]
	Pain >7 days	10 [13.16%]
Pulmonary infection		10 [13.16%]
Lung abscess		2 [2.63%]
Skin burn		0
Rib Fracture		4 [5.26%]
Broncho pleural fistula		1 [1.31%]

Table [3]: Factors affecting post-ablation pneumothorax among the studied patients**.**

		Pneumothorax N=38	No N=38	Test of significance	P-value
Length of needle track from skin to the lesion [mm]	**Median [IQR]** **Range**	55 [44.5 - 58.5] 39-66	54 [43 - 63.5] 38-83	W=188.5	0.826
Number of pleural needle punctures	**Median [IQR]** **Range**	4 [3.5 - 7] 3-12	3 [3 - 4] 1-5	W=104	0.020*
Patient position	**Lateral**	30 [78.95%]	8 [21.05%]	Fisher's Exact Test	<0.001*
	Prone	3 [7.9%]	26 [68.42%]		
	Supine	5 [13.15%]	4 [10.53%]		
Location	**Central**	0	6 [15.79%]	Fisher's Exact Test	0.230
	Peripheral	38 [100%]	32 [84.21%]		

W; Wilcoxon rank sum test. * p <0.05.

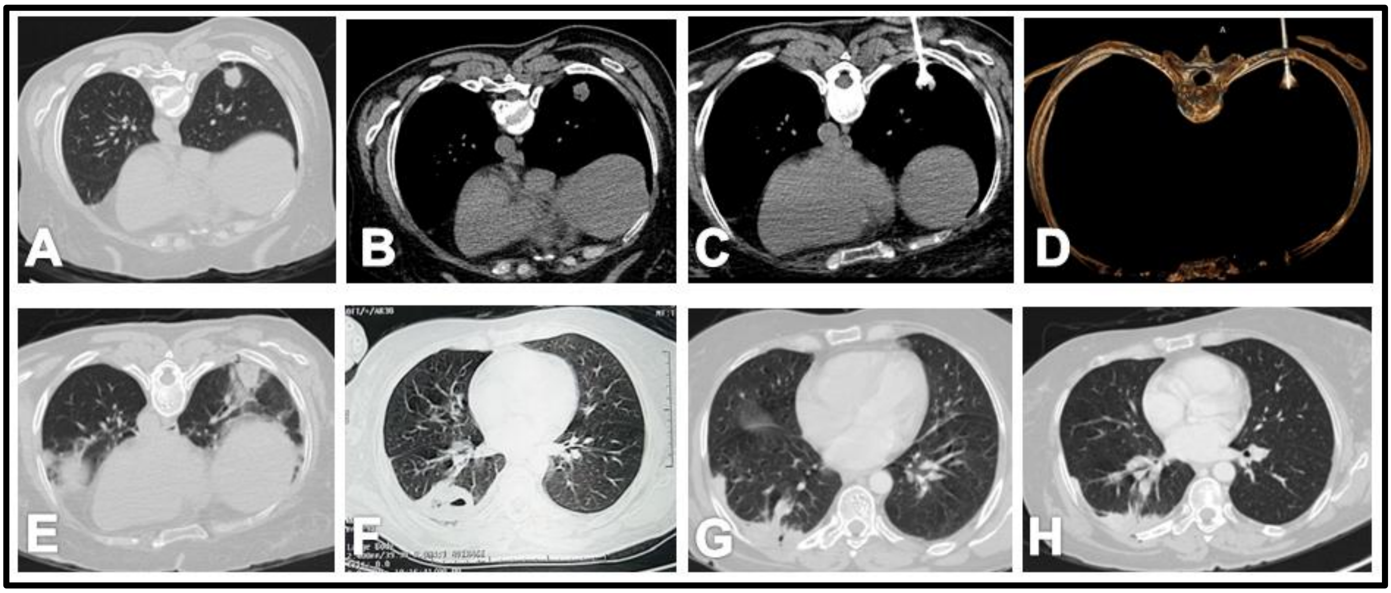

Figure [1]: A 51-years-old female had a nodule at the right lower lung lobe, 12 months after whipple operation for pancreatic head cancer. [A]&[B] axial CT cuts, lung and mediastinal window [prone] revealed 18mm round nodule at the right lower lung lobe. [C] reconstructed axial CT cuts &[D] 3D image at prone position reveled MWA antenna at the center of the nodule. [E] Immediately post-ablation, evidence of GGO all around the nodule. [F] 1 month after ablation, evidence of cavitation surrounded with consolidation. [G] 3 months after ablation, loss of cavitation with replacing atelectasis. [H] 6 months' post-ablation, the atelectasis shrank with no evidence of lesions.

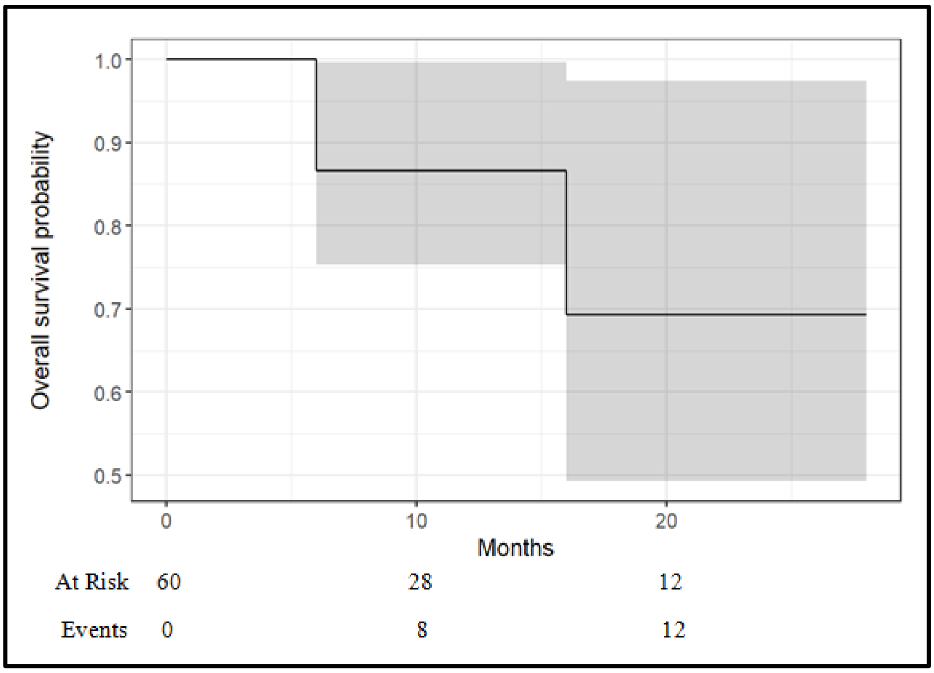

Figure [2]: Kaplan-Meier curve for survival rate after ablation.

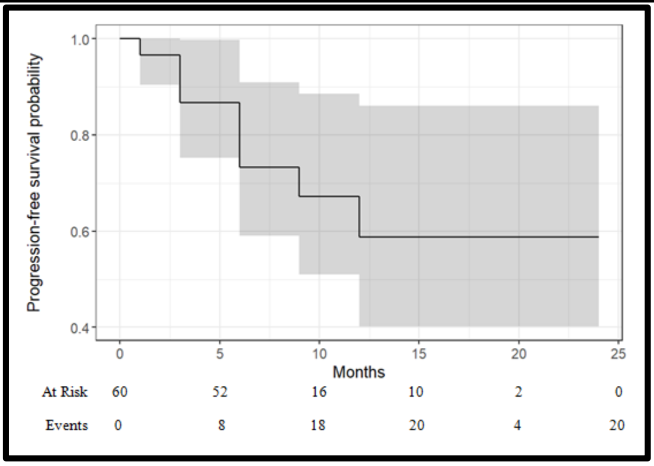

Figure [3]: Kaplan-Meier curve for progression-free survival probability after ablation.

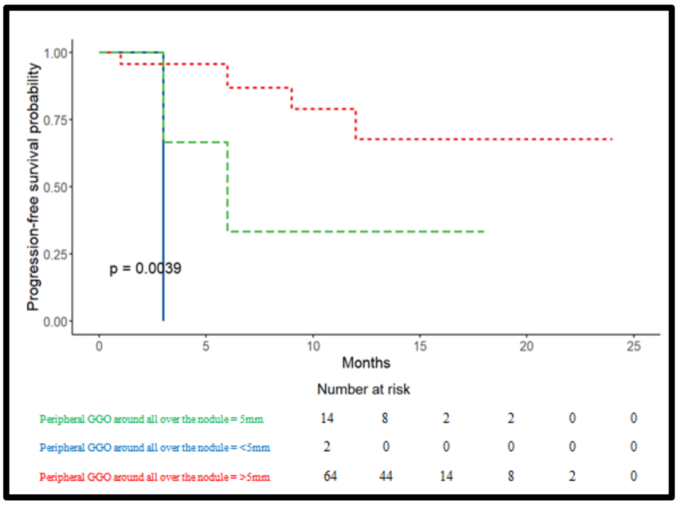

Figure [4]: Kaplan-Meier curve for progression-free survival probability by peripheral ground glass opacity immediately post ablation [green line for GGO=5mm, blue line for GGO<5mm and red line for GGO>5mm]

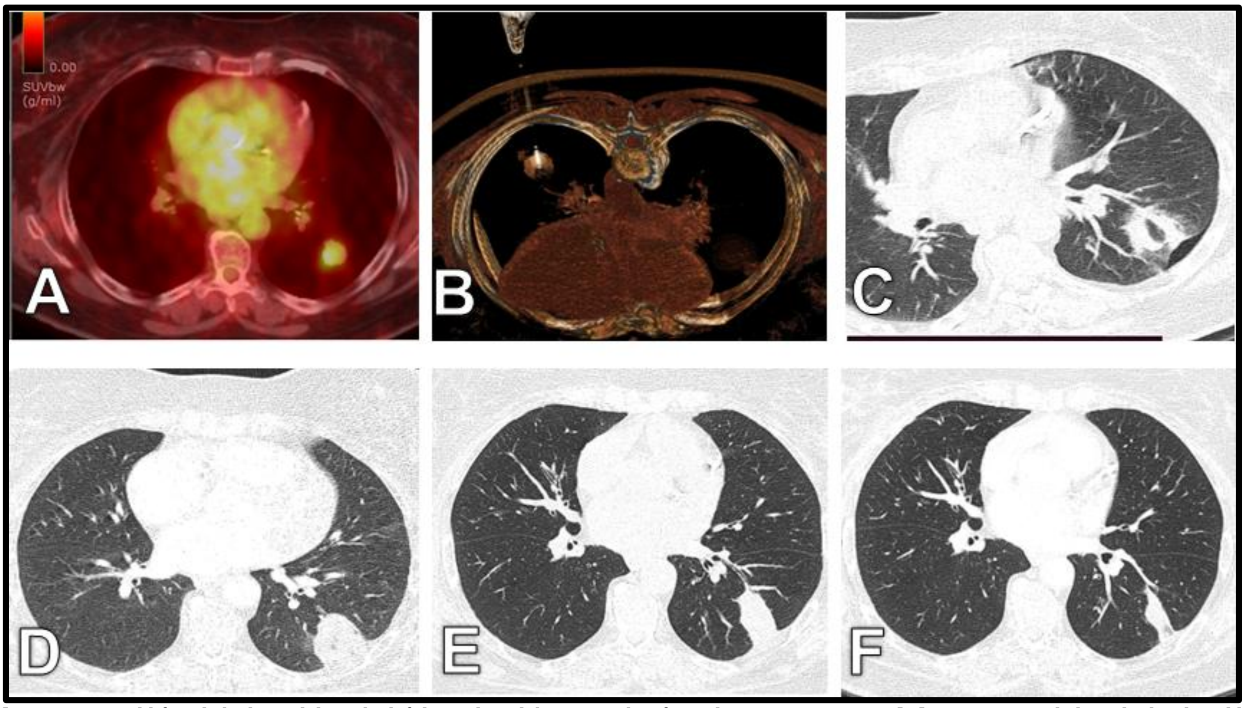

Figure [5]: A 62-years-old female had a nodule at the left lower lung lobe, 6 months after colon cancer resection. [A] PET-CT revealed newly developed left lower lobe lung nodule [16 mm in diameter with SUVmax 5.2]. [B] 3D image at prone position reveled MWA antenna at the center of the nodule. [C] Immediately post-ablation, evidence of GGO all around the nodule with mild amount of pneumothorax. [D] 1 month after ablation, evidence of enlarged size with small central cavitation. [E] 3 months after ablation, loss of cavitation with decreasing size. [F] 6 months' post-ablation, the lesion shrank to fibrous cord.

DISCUSSION

The lungs are the second most frequent metastatic organs, after the liver, in which malignant tumors develop [8].

Although a long-standing evidence-based strategy has made surgery the gold standard, innovative minimally invasive techniques have been used in an effort to preserve lung parenchyma in patients with numerous comorbidities or inadequate pulmonary reserve. As alternative remedies, non-surgical methods such percutaneous thermal ablation and stereotactic body radiation therapy have been suggested [9, 10].

In the current prospective study, CT-guided MWA was performed on 60 patients, 80 nodules at 76 MWA sessions, while at **Lassandro *et al.*** [11] study, 40 CT-guided ablation sessions were conducted on 42 lesions in 26 patients with lung metastases and **Baère *et al.*** [12] studied larger number of 566 patients with 1037 metastases.

Primary malignancies included 80% colorectal carcinoma, 10% pancreatic cancer, 6.67% hepatocellular carcinoma, and 3.33% sarcoma.

In comparison, **Baère *et al.*'s study** [12] reported primary tumors in the colon [34%], rectum [18%], kidney [12%], soft tissue [9%], and miscellaneous [27%] cases." Most patients [54] had 1 nodule, 4 patients had 2 nodules and 2 patients had 3 nodules. Oligometastases were unilateral in 77.5% of patients and bilateral in 22.5% of patients.

In **Baère *et al.*'s** study [12], oligometastases were unilateral in 75% and bilateral in 25% of patients, 53% of patients had 1 metastasis, 25% had 2, 14% had 3, 5% had 4 and 3% had 5.

Regarding the maximum lesion diameter, the mean diameter was 19.98mm and the range was from 8 to 35 mm, at **Han *et al.*** [13] diameter mean ± standard deviation was 1.5 ± 0.8 and range was 05-3.0cm. The session time Range in our study was 3 to 10 minutes with mean time 5.9 minutes and Median [IQR]: 5 [5, 8]. The power Range was 40 to 100 W with mean: 74.7 W. Chan et al. [14] reported that the median ablation time was 10 minutes [IQR: 7–14, range: 2–19], and mean ablation power was 42.9 W [SD= 13.8 W].

In this study, the post-ablation hospital stay was only one day at 72 sessions [94.74%], with a mean hospital stay of 1.68 days per session and a median of 1 day. This parameter is a significantly valuable factor in assessing the quality of the procedure. These results align with those of Taher et al. [15], where the median hospital stay was 1 day [IQR, 1–2 days; range, 1–19 days]. However, the study by **Aufranc *et al.*** [16], comparing RFA and MWA, reported longer hospital stays: the mean length of stay was 4.5 ± 3.7 days [range: 1–25 days] in the RFA group and 4.7 ± 4.6 days [range: 2–25 days] in the MWA group.

Complication rates are critical in evaluating the quality and safety of the procedure. Major complications after thermal ablation include pneumothorax, hemorrhage, and infections. In this study, the pneumothorax incidence was 50%, but 92% of cases were mild [Figure 5], and chest tubes were required in only 3 cases [3.9%], indicating the procedure's safety. In comparison, **Chan *et al.*** [14] reported pneumothorax in 54.7% of cases, with chest tubes needed in 35.2%.

Several technical modifications were implemented to reduce the incidence of pneumothorax and different factors were studied to modulate the procedure as shown at table 3. We observed the significant association between the number of needle punctures and pneumothorax with p value 0.02. This was consistent with **Wang *et al.*** [17] investigation that revealed a solid association between the number of punctures and both pneumothorax and pleural effusion.

The patient's position during the ablation procedure was also a significant factor, with an increased incidence of pneumothorax observed in the lateral position [$p < 0.001$]. We suggest that outcome due to the unstable lateral position, which is associated with multiple punctures and re-angulation.

This finding is inconsistent with the study by **Yamagami *et al.*** [18], which reported no significant association between patient position and pneumothorax. The follow- up period is a crucial limitation in our study with a mean nearly 1 year [Median [IQR]: 9 [6-17.5 months] and range, 6-24 months].

In comparison, **Baère *et al.*** [12] median follow-up was 35.5 months [interquartile range = 20–53 months], while Yan et al. [19] median follow-up period was 24 months [range, 6–40 months]. The mean DFI was 9.1 months, with a median [IQR] of 6 months [6–11.2 months] and a range of 1–24 months.

In the study by **Ambrogi *et al.*** [20], comparing wedge resection and RFA, with a statistically significant difference [p=0.01], the DFI at 1, 2, and 5 years was 87%, 63%, and 55% for RFA and 96%, 90%, and 76% for wedge resection.

For the studied group of pulmonary oligometastases, six-month and one-year overall survival rates of 87.6% and 69.3%, respectively, were comparable to previous series, though long-term results were limited. **Lencioni *et al.*** [21] reported overall survival rates of 92% at one year and 64% at two years.

In another study, **Akhan *et al.*** [22] reported long-term outcomes of RF ablation of pulmonary metastases, with overall survival rates of 60% at three years and 45% at five years.

Regarding PFS probability, six-month and one-year PFS probability was 58.8% which is better than the rates reported by Baère et al. [12]. They observed PFS rates of 40.2% [SE = 2.1], 23.3% [SE = 1.9], 16.4% [SE = 1.7] and 13.1% [SE = 1.7] at 1, 2, 3 and 4 years, respectively.

Han *et al.*[13] reported survival rates of 45.2% at one year, 32.3% at two years, 25.8% at three years, and 22.6% at five years.

The univariate Analysis of predictors associated with PFS revealed that a GGO of more than 5 mm around the nodule immediately post-ablation is significantly associated with progression-free survival probability. This association allows us to predict the probability of progression and survival immediately after the ablation session, enabling proper evaluation of the ablation's success and the need for additional overlapping ablation if necessary.

Limitations

It includes the relatively small sample size and heterogeneity of tumor types, which may affect the robustness and generalizability of conclusions. While the studied oligometastases represent common hepatobiliary and gastrointestinal primaries, they do not include tumors like bile duct or gastric cancers, which may have distinct biological behaviors and metastatic patterns. Furthermore, the follow-up duration was limited, focusing on six-month and one-year survival parameters for local effectiveness and tumor control. Assessing the impact of local ablation on long-term survival outcomes is crucial for comparison with other treatment modalities.

Conclusion:

This study highlights local thermal ablation as a potential effective treatment for pulmonary oligometastases from hepatobiliary and gastrointestinal cancers. The results show promising local tumor control and a favorable safety profile compared to previous studies and more invasive treatments. While MWA offers a minimally invasive, curative and repeatable alternative for oligometastases, the prospect of combining MWA with other treatment modalities, such as immunotherapy, targeted therapies, and radiation, warrants further investigation to enhance the therapeutic outcomes and address the systemic nature of metastatic disease.

Conflict of interest and financial disclosure: None.

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