



Effective and Safe Treatment of Risky Localized Liver Tumors Using Microwave Ablation in Patients with Comorbid Lung Diseases Unfit for Deep Anesthesia

Akciğer Hastalıkları Nedeni ile Derin Anesteziye Alınamayan Hastalarda Riskli Lokalizasyonda Yerleşimli Karaciğer Tümörlerinin Perkütan Mikrodalga Ablasyon Yöntemi ile Güvenli ve Etkin Tedavisi

id Murat ASIK

Istanbul Medeniyet University Faculty of Medicine, Department of Radiology, Istanbul, Turkey

ABSTRACT

Objective: To assess the safety and efficacy of percutaneous microwave ablation (MWA) in treating high-risk localized liver tumors in patients unable to undergo deep anesthesia because of comorbid lung diseases.

Methods: Between January 2019 and January 2022, percutaneous MWA procedures were performed for 50 liver tumors. These lesions were situated in close proximity to anatomically essential structures, with a maximum distance to surrounding structures being 10 mm. Because of comorbid lung diseases, patients could not undergo deep anesthesia. Regular follow-ups were performed using blood tests and dynamic contrast-enhanced computed tomography or magnetic resonance imaging.

Results: The patient cohort consisted of 30 (68%) men and 14 (32%) women, with a mean age of 64.36±11.65 years (range: 40-80 years). The lesions were challenging to access and were located in proximity to critical structures such as the diaphragm (32, 64%), gallbladder (8, 16%), major vessels (5, 10%), and heart (5, 10%). During the follow-up period, 10 patients (23%) had local tumor recurrence and 14 (32%) had new primary foci in a different location and metastasis [liver (10) and non-liver organs (4)]. No major complications developed, and 21 of 44 patients experienced minor complications, which were treated with local medications during follow-up.

Conclusions: Percutaneous MWA results in very low mortality and morbidity, coupled with high complete ablation rates for liver cancer. Most liver tumors can be treated safely and effectively with percutaneous MWA, even in cases of high-risk localization, without the need for deep anesthesia.

Keywords: Hepatocellular carcinoma, liver metastases, microwave ablation, comorbid lung diseases, deep anesthesia

ÖZ

Amaç: Eşlik eden akciğer hastalıkları nedeniyle derin anestezi uygulanamayan hastalarda riskli lokalizasyonlarda yerleşimli karaciğer tümörlerinin tedavisinde perkütan mikrodalga ablasyon (MWA) yönteminin etkinliğini ve güvenilirliğini değerlendirmektir.

Yöntemler: Ocak 2019 ve Ocak 2022 tarihleri arasında 50 karaciğer tümörüne perkütan MWA işlemi uygulandı. Lezyonlar anatomik olarak önemli organlara çok yakındı. Eşlik eden akciğer hastalıkları nedeniyle derin anestezi alınamıyordu. Hastalar düzenli aralıklarla olarak kan testleri ve dinamik kontrastlı bilgisayarlı tomografi veya manyetik rezonans görüntüleme ile takip edildi.

Bulgular: Hasta grubu 30 (%68) erkek ve 14 (%32) kadından oluşmakta olup yaş ortalaması 64,36±11,65 yıl (aralık: 40-80 yıl) idi. Lezyonlara erişim zordu ve lezyonlar diyafram (32, %64), safra kesesi (8, %16), büyük damarlar (5, %10) ve kalp (5, %10) gibi kritik yapıların yakınında bulunuyordu. Takip süresi boyunca 10 hastada (%23) lokal tümör nüksü, 14 hastada (%32) farklı lokasyonda yeni bir primer odak ve metastazlar [karaciğer (10) ve karaciğer dışı organlar (4)] görüldü. Herhangi bir majör komplikasyon gelişmedi ve 44 hastanın 21'inde takip sırasında gelişen minör komplikasyonlar lokal tedaviler ile tedavi edildi.

Sonuçlar: Perkütan MWA karaciğer tümörlerinin tedavisinde yüksek tam ablasyon oranları ile çok düşük mortalite ve morbiditeye sahiptir. Çoğu hastada tümörler riskli lokalizasyonda olup ve hastalara derin anestezi verilemese de MWA ile çok güvenli ve etkili bir şekilde tedavi edilebilir.

Anahtar kelimeler: Hepatoselüler karsinom, karaciğer metastazi, mikrodalga ablasyonu, eşlik eden akciğer hastalıkları, derin anestezi

Address for Correspondence: M. Asik, Istanbul Medeniyet University Faculty of Medicine, Department of Radiology, Istanbul, Turkey

E-mail: muratasik81@gmail.com **ORCID ID:** orcid.org/0000-0002-5267-1602

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INTRODUCTION

Hepatocellular carcinoma (HCC), the third leading cause of death among all types of cancer, constitutes approximately 90% of liver tumors¹. Furthermore, the liver is the organ most commonly affected by metastatic involvement². Various medical, surgical, and locoregional treatment methods are available for primary and metastatic liver tumors. The choice of treatment depends on factors such as the general health condition, comorbid diseases of the patients, clinical and laboratory findings, and radiological imaging features, including the number, size, and location of the lesions.

In the locoregional treatment group, thermal ablation methods such as radiofrequency ablation (RFA), microwave ablation (MWA), irreversible electroporation, and high-intensity focused ultrasound (USG) are increasingly preferred for the treatment of liver tumors because of their less invasive nature. Consequently, these techniques are associated with shorter hospital stays and faster recovery than other methods. Locoregional therapy also boasts lower complication rates than standard surgical treatments and can be safely repeated if necessary^{3,4}.

Thermal ablation of lesions located near essential anatomical structures, such as the heart, gallbladder, diaphragm, and vascular system, could lead to severe complications⁵⁻⁸. In contrast to RFA, MWA does not exhibit the heat sink effect, making it particularly suitable for lesions near the heart and major vascularity. The absence of a cooling effect from flowing blood in the MWA ensures that the ablation volume does not reduce. Another advantage of MWA is its ability to achieve a larger ablation zone within a shorter procedure time. This feature is especially beneficial for patients with comorbid lung disease who cannot undergo deep anesthesia and cannot hold their breath for an extended period⁹.

In tumors located in high-risk areas of the liver, MWA can be performed without significant complications using real-time USG imaging or computed tomography (CT) guidance in different planes. Several studies have demonstrated that liver tumors situated in high-risk areas can be entirely and safely ablated. This study aimed to assess the safety, efficacy, and feasibility of MWA treatment in patients with serious lung diseases that preclude deep anesthesia and in tumors located in high-risk areas such as the diaphragm, inferior vena cava (IVC), portal vein (PV), and gallbladder.

MATERIALS and METHODS

The Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee approved our study (decision no: 2020/0398, date: 24.06.2020). Before undergoing MWA, detailed information about the procedure was provided to all patients, and informed consent was obtained.

Patient Population

A retrospective analysis was conducted on forty-four patients, totaling 50 lesions, who underwent MWA at a single center for liver tumors, including HCC or metastases, between January 2019 and January 2022. The diagnosis of HCC followed the guidelines of the American Association for the Study of Liver Diseases. Cases of HCC not determined through clinical findings and imaging underwent confirmation through percutaneous biopsy¹⁰. The same diagnostic procedure was applied to all liver metastases.

All patients were referred for MWA treatment based on decisions made by the multidisciplinary tumor board. Because of the presence of cardiorespiratory system impairments, all patients were considered unsuitable for general anesthesia or deep sedation. Consequently, the decision was made to treat them using moderate sedation along with MWA.

All liver lesions that underwent MWA with USG or CT guidance were situated in challenging and hard-to-reach areas, including the liver dome, left lobe near the heart, hilum near the PV (Figure 1), adjacent to the gallbladder, close to the IVC (Figure 2), and near the diaphragm (Figure 3). To confirm that the lesions were adjacent to these critical anatomic structures, the distance between the lesions and these structures was no more than 10 mm in any of the three planes obtained with CT or magnetic resonance (MR) before the MWA procedure.

The study excluded patients eligible for surgery with extrahepatic metastasis, those in Child-Turcotte-Pugh (CTP) class C, and those with coagulation disorders. In addition, patients with more than three lesions or any lesions larger than 5 cm were excluded.

Of the 44 patients, 32 were classified as CTP class A, and 12 were classified as CTP class B. Among the 50 lesions, 27 were HCC, with 18 related to hepatitis B and 6 to hepatitis C. The remaining three patients had no history of viral hepatitis or alcohol use. Furthermore, 23 of the 50 lesions were identified as liver metastases.

Patient and Lesion Assessment Before the MWA Procedure

Laboratory and imaging findings were assessed approximately 2 weeks before the procedure. Laboratory tests included CBC, liver function tests, bilirubin values, coagulation parameters, and tumor markers such as alpha-fetoprotein, carcinoembryonic antigen, cancer antigen 19-9 (CA 19-9), and CA 125.

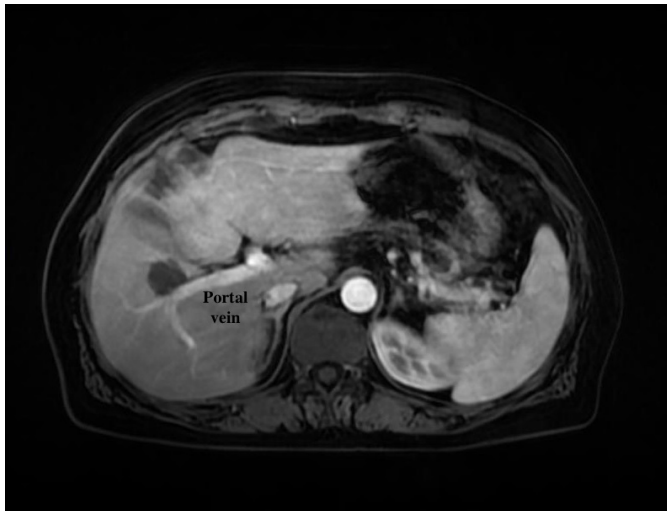


Figure 1. Mass without contrast enhancement in front of the right portal vein on axial MRI after MWA.

MRI: Magnetic resonance imaging, MWA: Microwave ablation

During the pre-ablation anesthesia examination, the decision was made to administer moderate sedation instead of deep sedation to patients with chronic obstructive lung diseases such as emphysema and asthma, as well as sleep apnea syndrome.

Before the MWA procedure, in addition to characterizing the lesions, their anatomic locations and relationships with adjacent structures were assessed. This evaluation used triphasic contrast-enhanced CT with a 128-detector-row single-source CT system scanner (Optima CT 660, GE Healthcare, USA) or dynamic contrast-enhanced magnetic resonance imaging (MRI) with a 1.5 T scanner (Optima MR 450w, GE Healthcare, Waukesha, WI).

Patients opting for MWA underwent USG assessment using an Aplio 500 US system (Toshiba Medical Systems Corporation, Tochigi, Japan) to verify the ablation route. The axial, sagittal, and coronal images from CT/MRI and USG images were separately analyzed. This analysis aimed to assess the relationship between the lesion and adjacent structures, determine access to the lesion with USG, and verify the compatibility of the CT/MRI images of the lesions with USG images.

As lesions situated in the dome of the liver are better visualized when patients hold their breath, compliance with breath-holding commands was essential during the placement of the ablation needle. Patients underwent MWA only after performing breath-holding exercises

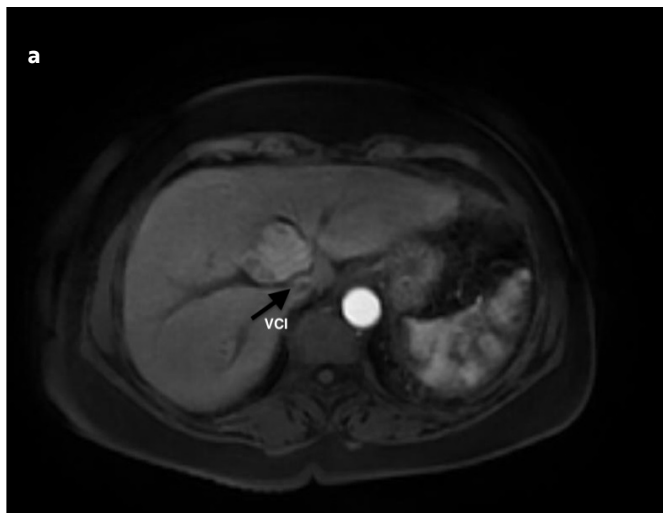


Figure 2. a. Pre-ablation axial contrast-enhanced T1W magnetic resonance imaging (MRI) shows diffuse homogenous contrast enhancement in HCC adjacent to VCI and hepatic veins. b. No contrast enhancement is seen in the coronal contrast-enhanced T1W MRI of the same patient one month after ablation.

VCI: Vena cava inferior, HCC: Hepatocellular carcinoma

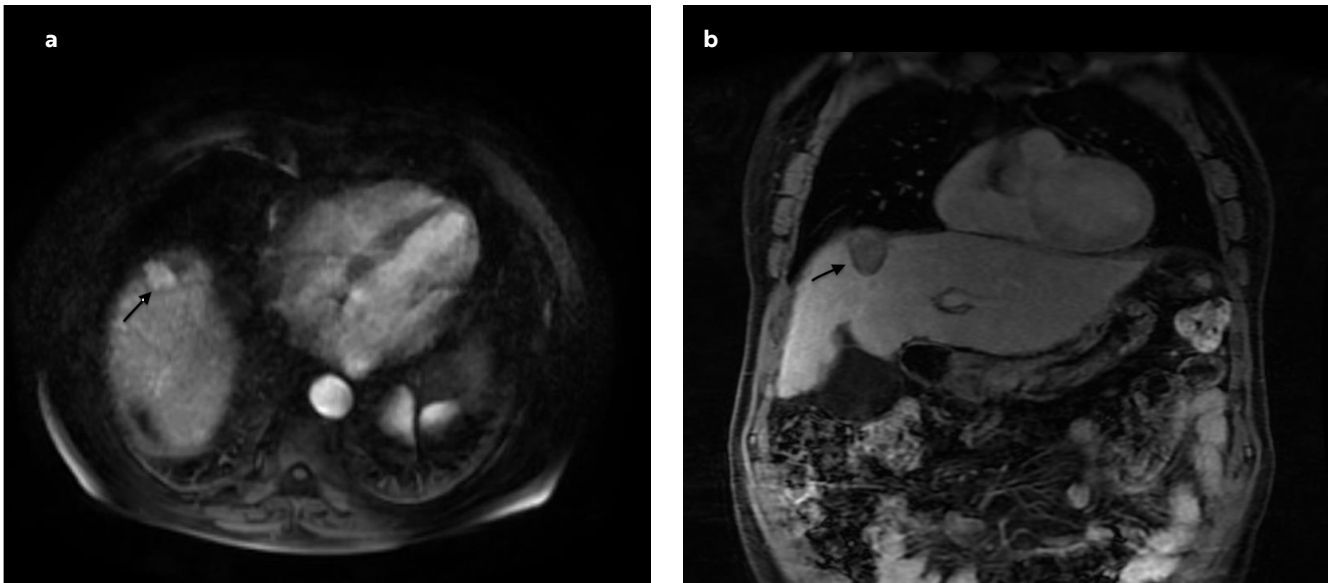


Figure 3. a. Pre-ablation axial contrast-enhanced T1W magnetic resonance imaging (MRI) demonstrates diffuse homogenous contrast enhancement in HCC adjacent to the diaphragm. b. There is no contrast enhancement in the coronal contrast-enhanced T1A MRI of the same patient after ablation.

several times. For lesions that could not be safely visualized or reached with USG, CT guidance was employed during MWA.

MWA System and Procedure

All ablation procedures were performed percutaneously with USG guidance (n=45) or CT guidance (n=8) by two expert radiologists with more than 10 years of experience in interventional radiology. Patients were placed in the supine or left lateral decubitus position depending on the location of the lesion and the most accessible position for targeting. In all ablation procedures, tumor size was considered, and the time and given energy were adjusted to encompass an ablation zone of at least 5 mm into the intact liver tissue surrounding the tumor.

For the MWA procedure, a 14-G antenna with a 15-cm shaft length equipped with a tissue feedback control mechanism (Seronova-AngioDynamics, Queensbury, NY, USA) was used. Continuous or intermittent ablation was performed using a generator frequency ranging from 902 to 928 MHz and power levels between 10 and 32 W. The generator featured an automatic shutdown mechanism triggered by excess energy return from the tissue, facilitated by feedback control.

Lesions larger than 3 cm were ablated either with two probes simultaneously or with a second procedure following the initial one to ensure complete lesion ablation. Throughout the ablation, the ablated area

and the position of the MWA probe were continuously monitored until the completion of the procedure. Adjustments to the probe position were made when necessary.

Throughout the ablation, patients were monitored using electrocardiography, pulse oximetry, and blood pressure measurements overseen by an anesthesiologist. After determining the skin entry point, typically from the intercostal or subcostal area, the entry site was disinfected with povidone-iodine, and local anesthesia was administered by injecting 2% lidocaine into the subcutis.

Given that most lesions were subdiaphragmatic, patients were required to hold their breath for optimal probe positioning, especially during the initial minutes of the procedure. Consequently, moderate sedation was initiated after placing the ablation probe in patients with subdiaphragmatic lesions. For this purpose, 0.03-0.1 mg/kg dormicum, 1 mg/kg ketamine, and, when necessary, propofol at 0.5 mg/kg/h were used.

Artificial ascites was not employed to avoid prolonging the procedure, especially in older patients who faced challenges with breath-holding. Additionally, the literature has demonstrated no significant differences in terms of diaphragm damage, post-ablation pain, and local recurrence between patients who undergo artificial ascites and those who do not¹¹.

Patients experiencing difficulty maintaining prolonged breath holding were occasionally granted short breaks, and the probe positioning process was intermittently resumed. To prevent damage to the vascular structures, Doppler USG evaluation was conducted at short intervals. Throughout the entire ablation procedure, the needle position, which might shift with the patient's breathing, was monitored using USG or CT in various planes.

At times, the direction of the probe was intentionally adjusted slightly or it was re-inserted to ensure comprehensive coverage of the entire tumor area by the ablation zone. The presence of an expanding hyperechoic area with USG or a hypodense zone with CT was used to determine the form of the ablation zone during the procedure. A minimum of 5 mm oncologic margins were considered, and a spherical ablation zone was aimed to cover all tumor tissue as extensively as possible.

Technical success was acknowledged when a newly formed hyperechoic or hypodense ablation area within the tumoral tissue and surrounding parenchyma was detected using USG or CT. To prevent tumor seeding and provide coagulation, at the end of the ablation process, the probe was withdrawn back at low energy (20 W) at a rate of 1 cm/sec, and tract ablation was performed.

Follow-up

After ablation, patients were observed for 24 h. At the 24th h, follow-up USG and CBC, along with general biochemistry tests, were conducted to assess the development of any complications using the Society of Interventional Radiology (SIR) Existing Adverse Event Classification system¹². Patients without major complications were discharged 24 h after the procedure.

In addition to the examination of tumor markers, all patients underwent contrast-enhanced CT or MRI to assess the ablated areas. Local tumor progression (LTP) was defined as the presence of enhancement in the ablation area, indicating newly formed tumoral tissue, observed from the 1st to 3rd months after the ablation.

Patients were evaluated every 3 months for up to 1 year after the procedure using CT or MRI, CBC, general biochemical tests, and tumor markers to monitor for residue or recurrence. The median follow-up period was 12.22±6.82 standard deviation (SD) months (range: 3-30).

Statistical Analysis

The normality of the variables was assessed using the Shapiro-Wilk test. Mean and SD were calculated for continuous variables, whereas median, frequency,

and interquartile range were calculated for categorical variables. Percentages were used for categorical variables. For comparing means, Student's t-test was used for continuous variables, and the Mann-Whitney U test was used for ordinal variables. A significance level of p<0.05 was considered statistically significant. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 26.0 software (IBM SPSS Inc., Armonk, NY, USA).

RESULTS

The study included 44 patients, consisting of 30 men and 14 women, with an average age of 64.36 years (range: 40-80; SD: 11.65). A total of 50 liver tumors were enrolled in the study. Of the 50 liver tumors, 27 (54%) were HCC, while the remaining 46% were metastases (Table 1).

Table 1. Lesion characteristic.	
Lesions	Values
Tumor type	
HCC	27 (54%)
Metastasis	23 (46%)
HCC etiology	
Hepatitis B	18
Hepatitis C	6
Cryptogenic	3
Metastatic tumor type	
Colon	12 (24%)
Pancreas	6 (12%)
Breast	1 (2%)
Small intestine	1 (2%)
Gastric	1 (2%)
Lung	2 (4%)
Long axes of tumor (mm)	
Mean	29.27±8.57
Range	15-50
HCC: Hepatocellular carcinoma	

Table 2. Localisation of lesions.			
Critical structure near the lesion	HCC n (%)	Metastasis n (%)	Total n (%)
Diaphragm	15 (30%)	17 (34%)	32 (64%)
Gallbladder	6 (12%)	2 (4%)	8 (16%)
Major vascularity	4 (8%)	1 (2%)	5 (10%)
Heart	2 (4%)	3 (6%)	5 (10%)
Total	27 (54%)	23 (46%)	50 (100%)
HCC: Hepatocellular carcinoma			

All patients underwent percutaneous MWA, and all lesions were situated in anatomically challenging access areas close to critical structures (within 5-10 mm). These critical structures included the diaphragm, gallbladder, heart, and major vascular structures (Table 2).

Lesions larger than 30 mm (n=14) were simultaneously ablated using two MWA probes. The average duration of ablation sessions was 8.20 ± 3.48 SD min (range: 5-21 min). Complete ablation was achieved in 45 of 50 lesions (90%). However, residue was detected in 5 lesions (10%) during the 1st-month follow-up in CT or MRI. A second ablation was performed for three patients with residual tumors. In the remaining two patients, residual lesions were visible on contrast-enhanced MRI but not on USG or CT. Therefore, systemic chemotherapy was chosen as the treatment option (Table 3).

During the approximately 30-month follow-up period, recurrence was detected in 10 patients (23%). In patients with detected recurrence, the distance of the tumoral lesion to critical organs was 6 ± 1.05 SD (range: 5-8 mm), whereas in those without recurrence, it was found to be 6.18 ± 1.01 SD (range: 6-10 mm). There was no statistically significant difference in the distances of tumoral lesions to critical organs between patients with and without recurrence ($p=0.623$).

Among the 14 patients (32%) with newly developed metastatic lesions, 10 were in the liver and 4 originated from other organs. Comparison between HCC and metastases revealed no statistically significant difference in terms of LTP ($p=0.860$).

Complications and Treatments

No major or life-threatening complications were encountered, resulting in 0% disease-specific mortality during this limited period. A total of 21 minor complications (SIR category A/B) occurred. One patient developed an asymptomatic abscess detected on USG in the first week, which was subsequently drained by

catheter drainage. Two patients with tumors located in the liver dome developed asymptomatic pleural effusion after the procedure, but no intervention was required. Additionally, erythematous changes over the puncture wound occurred in two patients treated with topical medications.

During the procedure, six patients experienced pain radiating from the right/left upper quadrant of the abdomen, and 10 patients reported such pain immediately after the procedure. The pain was relieved using analgesics after an average of 3 days.

DISCUSSION

Local thermal ablation is a viable treatment option for patients ineligible for surgery because of liver tumors. The two most commonly used methods are RFA and MWA. RFA has limitations, especially in lesions near the heart and vessels larger than 3 mm, where the heat sink effect can result in insufficient ablation, allowing residual tumor tissue to persist^{13,14}. Furthermore, wider ablation zones in RFA may not achieve as high intratumoral temperatures as MWA^{15,16}. MWA provides more uniform heating in the ablated areas and can cover larger areas in a shorter time, making it a preferred choice, especially for older patients with difficulties holding their breath^{17,18}. Rapid and effective ablative treatment is crucial, particularly in procedures that may be painful, and it is especially important for patients with comorbid lung diseases who cannot undergo deep sedation.

In this study, patients who were unable to undergo surgical treatment because of anatomical location or comorbidity or who were planned to undergo MWA because of the patients' refusal for surgical treatment were enrolled. However, all tumors planned for ablation were located in hard-to-reach areas in the liver or adjacent to essential organs. It was sometimes thought that, for tumors very close to vital structures, percutaneous ablation procedures could be harmful and contraindicated because of the possibility of either mechanical or thermal damage^{5,6,19,20}. This thought could be an obstacle to the treatment of patients. In this study and the literature, percutaneous MWA was shown to be a feasible and effective method, even for these lesions, by evaluating several planes on USG or CT and cooperating with patients^{11,21-26}.

MWA was employed as a local thermal ablation therapy for tumors adjacent to vital anatomic structures. No major complications were encountered during either the early or long-term follow-up period after the procedure.

Table 3. Features of the ablation procedures and follow-up.

Ablation procedure	Values
USG guidance ablation (n)	45
CT guidance ablation (n)	8
Ablation time (minutes)	
Mean	8.20 ± 3.48
Range	5-21
Follow-up (months)	
Mean	12.22 ± 6.82
Range	6-30
USG: Ultrasound, CT: Computed tomography	

The recommended ablation zone should encompass at least 5 mm of non-tumor parenchyma because small satellite lesions, not visible on CT/MR, may be present²⁷. It has been emphasized that including the surrounding tissue in the ablation area is crucial for preventing LTP²⁸. In our study, achieving this expanded ablation area was not possible in all lesions due to a distance of less than 5 mm between normal tissue and the tumor in some patients. This might explain why our local recurrence rates (20%) were slightly higher. In the literature, several studies have reported local recurrence rates after thermal ablation ranging from 10% to 30% in liver tumors²⁹.

Heat uniformly transfers within the ablation zone, assuming a spherical form, enabling more effective and safer ablation of both the tumor and surrounding normal tissue with MWA. The heat sink effect is minimal or nonexistent in MWA because of tissue permittivity control. MWA systems, with their specific features, can be used for the treatment of liver tumors, even those situated in challenging areas such as the dome, subcapsular region, adjacent to hepatic vessels, and gallbladder.

During MWA, hydro-dissection can be employed to prevent damage to important anatomic structures surrounding lesions, such as the diaphragm, heart, and gallbladder. However, in our approach, several reasons led us to refrain from performing hydrodissection at the ablation site. General anesthesia or deep sedation was not initiated for MWA because most patients needed to consciously hold their breath for an extended period during probe placement under local anesthesia. In addition, the absence of sufficient fatty tissue or empty space for hydro-dissection around the lesion influenced the decision against creating artificial ascites. Stabilizing the injected liquid was also challenging because of the movements of the heart and diaphragm. Numerous studies in the literature have demonstrated the success of ablation procedures for HCC located in the left lobe adjacent to the heart and diaphragm without employing hydro-dissection. These studies reported no significant difference in complications and recurrence rates between groups with and without hydro-dissection in MWA procedures³⁰. Furthermore, evidence from both human and animal studies suggests that the use of artificial ascites is more beneficial in RFA and is not as effective in MWA, which operates on a different mechanism^{12,25,31}.

In the thermal ablation of lesions adjacent to the heart and major vascular structures, concerns often arise about the potential heat sink effect, which prevents complete ablation and increases local recurrence rates. However, both in our study and in the literature, it has been demonstrated that the rates of complete ablation in tumors near vital structures are not statistically different from those in other locations^{9,22,25,32,33}.

Although serious complications such as perforation or cholecystitis are possible in tumors close to the gallbladder, numerous studies in the literature have reported high success rates and low complication rates for MWA in tumors adjacent to the gallbladder²⁶.

MWA in this series was well tolerated, with no postoperative deaths and few complications related to the procedure. None of the patients in this series exhibited evidence of internal bleeding, bile duct damage, or significant systemic imbalances. When compared with previous reports of RFA with complication rates ranging from 9.2% to 33%^{23,34}, MWA emerges as a favorable method. In our study, 16 patients with tumors on the liver dome subcapsular area experienced pain in the right upper quadrant, which was alleviated by oral analgesics. Two patients with tumors in the liver dome developed asymptomatic pleural effusion that required no interventional treatment. Erythematous changes over the puncture wound occurred in two patients after ablation and were treated with topical care.

Our study has some limitations. First, being a retrospective study conducted in a single center with a relatively small number of patients may have limited the effective evaluation of survival rates and reliable long-term results. Second, our study serves as a preliminary analysis focusing on the technical efficacy and safety of MWA in liver tumors located in risky areas; therefore, we did not address long-term disease-free survival. Third, the ablated lesions comprised a heterogeneous group of HCC and metastases situated in various locations. The decision not to perform hydrodissection during ablation could be a parameter that potentially negatively influences the results of the procedure.

CONCLUSION

MWA has emerged as an effective and safe treatment option for risky localized liver tumors in patients with comorbid lung diseases who are unsuitable for deep anesthesia. This offers patients a significant opportunity because MWA can be performed effectively and safely for liver tumors in areas where surgery is challenging due to their location. Importantly, patients with comorbidities that preclude surgery can be safely treated with MWA. Although the initial results are promising, long-term outcomes and delayed complications related to MWA should be analyzed in larger prospective, longer follow-up studies.

Ethics

Ethics Committee Approval: The Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee approved our study (decision no: 2020/0398, date: 24.06.2020).

Informed Consent: Informed consent was obtained.

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