

Original Research Article

Computed Tomography for Evaluation and Follow up of Hepatocellular Carcinoma after Microwave Ablation

Abstract:

Background: When surgical procedures are not possible, image-guided HCC tumor ablation provides curative treatment or acceptable therapeutic choices in appropriately selected patients. Post-ablation tumor response evaluation is critical for assessing treatment effectiveness and further therapy. Ultrasound (US) and computed tomography (CT) are critical in the follow-up of patients who have undergone liver thermal ablation therapy. The purpose of this study was to evaluate the role of computed tomography for evaluation and follow up of hepatocellular carcinoma following Microwave ablation.

Methods: This prospective study was carried out on 30 patients radiologically proved with hepatocellular carcinoma.

Results: Triphasic CT imaging arterial phase revealed homogenous enhancement lesions in 46.7% of patients and heterogeneous enhancement in 53.35% of patients. All the lesions showed early washout in Porto venous and delayed phases with patent portal vein in all patients. The diameter of ablated area was different according to duration of ablation. 60 W was applied for 8-10 minutes, resulting in ablation zones of 3.5-4 x 4.7-5.2 cm whereas applications of 60 W for 10-15 minutes resulting in ablation zones with a size of 4.5 - 5.5 x 5.6-6.5 cm. Triphasic CT was performed after 1 month and revealed that the success rate was 93.8% for tumors measuring ≤ 3 cm 92.9% for tumors measuring 3-5cm. Local tumor progression was shown in 2 patients (6%) after 1 month, in 3 patients (10%) after 3 months, and in 5 patients (16.7%) after 6 months of follow up. There was an intrahepatic distant recurrence in 9 patients (30%) after 1 month, in 15 patients (50%) after 3 months, and in 18 patients (60%) after 6 months of follow up.

Conclusions: Percutaneous microwave ablation guided by ultrasound for the treatment of challenging HCC tumors up to 5 cm in diameter, including exophytic or subcapsular targets as well as those located in the hepatic dome or close to the diaphragm / hepatic hilum /heart, shown satisfactory efficacy and safety rates. For both technical and clinical success, selecting the proper approach is critical.

Keywords: Computed Tomography, Hepatocellular Carcinoma, Microwave Ablation

Introduction

The standard therapeutic options of hepatocellular carcinoma (HCC) consist of surgical resection, ablation, trans-arterial therapy (chemoembolization or radiotherapy). Hepatectomy, liver transplantation, and percutaneous thermal ablation are all potentially curative therapies. The remaining therapeutic options are mostly palliative with positive impact on survival (Bruix and Sherman, 2011).

Microwave ablation (MWA) utilizes electromagnetic energy (up to 2 cm surrounding the antenna); in the absence of current flow, the electromagnetic field rapidly and uniformly heats the tissue, resulting in coagulation necrosis. Tissue with a high water content has the highest heating effect whereas fat has the worst. Ionic polarization is considered another mechanism of MWA, which results in the conversion of kinetic energy into heat. MWA can be CT or US guided (Brace, 2009). MWA is effective in the treatment of 5-8 cm HCC. In addition, MWA permits simultaneous tumor ablation or even combination resection and ablation. In a multicenter effort that collect data for patients treated with MWA for tumors of any origin, Microwave ablation has many advantages over RF ablation, including a shorter total period of microwave application for each lesion (median: 4 minutes/lesion), the use of fewer microwave applications for each ablated lesion, and the capability to coagulate blood vessels more efficiently and an important advantage of MWA over RF ablation is a less severe heat sink effect (Livraghi et al., 2012, Lloyd et al., 2011).

CT plays an important role before and after MWA of HCC. CT imaging is done before ablation to determine size, number, location and relation to vascular structures and immediately after ablation to detect any potential complications. Follow up by CT at 1, 3, 6 and 12 months post ablation and annually ever since are done for assessment of tumor response to prove efficacy of ablation or detect residual activity (Kelekis and Filippiadis, 2016). The modified Response Evaluation Criteria in Solid Tumors (mRECIST) is used nowadays to assess tumor response after MWA. It includes evaluation of response in both target lesions and non-target lesions as well as potential new lesions. It defines the diameter of viable tissue of target lesion by contrast enhancement in arterial phase (Lencioni and Llovet, 2010). The purpose of this work was to evaluate the role of computed tomography in evaluation and follow up of HCC after microwave ablation.

Patients and Methods

30 patients were enrolled in this prospective study who were radiologically proved with hepatocellular carcinoma, who were referred to Diagnostic Radiology and Medical Imaging Department at Tanta University Hospitals and Liver Institute at Kafr-Elsheikh. Abdominal ultrasonography & triphasic CT scan were performed for all patients. The inclusion Criteria for percutaneous US guided MWA: Presence of unresectable hepatocellular carcinoma, the tumor away from GB, bile ducts, gut and large blood vessels, maximum three intrahepatic nodules with average size from 1 to 5, absence of extra hepatic metastases, patent main portal vein and its branches, patients with Child-Pugh classification A or B and Satisfactory liver and renal functions. Exclusion Criteria for CT study: Pregnant females, patients with previous allergy to the contrast media, renal impairment (serum creatinine > 2mg/dl), patients with hepatic failure and patients who refuse the examination. The exclusion criteria for percutaneous US guided MWA: Age, patients above the age of 80, presence of vascular involvement, more than three intrahepatic nodules, evidence of extra hepatic metastases, patients with severe hemodynamic instability, patients with serious coagulation disorder or an acute sepsis or cardiac patients, severely debilitated patients and patients with renal insufficiency. This study was approved by our local research ethical committee. An informed written consent before participation of the study was collected from all patients. The patients were subjected to the following: Complete history taking: Personal history that include sex, age and special habits as smoking, alcoholism, current illness's history with special concern on right hypochondrial pain or swelling and history of viral hepatitis and cardiac or renal trouble. The patients were asked about any previous imaging procedures (abdomino-pelvic ultrasound and abdomino-pelvic CT). **Clinical examinations:** All the patients were subjected to clinical abdominal and surgical examinations. Vital signs as blood pressure (BP), respiratory rate (RR) and pulse rate (PR). Airway, breathing, circulation, and disability are all evaluated according to the role of A B C D. **Laboratory investigations:** Liver functions: serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), serum albumin and total bilirubin level, complete blood picture, coagulation profile including International Normalized Ratio (INR), Prothrombin time and concentration and Alpha-fetoprotein level: It was done before and after 1, 3 and 6 months after ablation.

Imaging techniques: Pelvi-abdominal US for evaluation of: (Focal lesions (site, shape, size, number and echogenicity), biliary or vascular invasion and the percutaneous approach possibility - Exclusion of Splenomegaly- extra-hepatic metastases especially porta hepatis or paraaortic lymph node enlargement- Presence of ascites and if present evaluation of its amount- Color Doppler US is used to determine the patency of the portal vein. For all

patients, a triphasic CT scan of the liver is performed: The aim was to study the enhancement pattern of the focal lesion.

The satellites presence and vascular or biliary invasion was also evaluated, exclusion of extrahepatic metastases. It was done before ablation, and repeated after 1, 3 and 6 months from the ablation. Evaluation of previous tri phasic CT, abdominal ultrasound and colored doppler imaging.

Multi-slice CT: The CT was performed by using of multi-slice 16 detectors CT Toshiba.

Patient preparation: No specific patient preparation was requested except fasting for 6 hours before performing the procedure, fill the stomach and bowel by water to help proper subtraction techniques and visualization of the target vessels. All instructions were given to the patients about table movement, voice messages, timing and manner of breath holding.

Patient position: The patients were laid down on the couch in the supine position, headfirst with the arms elevated above the head from the level of the tracheal carina down to the level of the symphysis pubis.

Gonadal shielding was used in all patients.

Using a detector collimation of 1.2 mm and voltage 120 kV, thin slice images were obtained with slice thickness 2 mm, an increase of 1 mm then transferred to an independent workstation.

In antero-posterior view, one scout was acquired. Pre and post contrast sequences were planned on these scouts from the level of the top of the right diaphragmatic copula (hepatic dome) to about 20 cm caudally or to the iliac crest with a slice thickness of around 6-8 mm.

Interventional procedure US guided microwave ablation (one session was done for twenty-eight patients & two sessions for two patients with incomplete ablation in our study).

Patient preparation: Patients fast overnight. Patients were admitted on the day of the procedure in the morning. Peripheral pulses and blood pressure were observed. Random blood sugar was measured. IV cannula was administrated to gain an intravenous access. Prophylactic antibiotics (1 gm of cefazolin, 500 mg of metronidazole) and antiemetics (24 mg of ondansetron hydrochloride), 10 mg of dexamethasone, 50 mg of diphenhydramine (avil) were administered.

Ablation technique:

Sedation and anesthesia: Microwave ablation were performed with the use of IV anesthesia for all patients (short-acting anesthesia)

Equipment: Microwave coagulator and thermal monitoring system:

Technique:

Before beginning of treatment, a detailed plan describing the electrode placement. On a tumor-by-tumor basis, the emission time and power output setting were determined. The

tumour and the 0.5–1.0 cm of normal-appearing liver tissue that surrounding it were to be eradicated during therapy. Microwave ablation for lesions located in the right lobe was conducted under real-time US guidance utilizing a 3.5 MHz probe by free hand technique, Intercostal approaches with the patient in the left lateral decubitus posture were more frequently employed, whereas subcostal approaches were most frequently used for lesions found in the left lobe. In order to establish local anesthetic, 10 ml of 2% xylocaine is used to anaesthetize the skin, subcutaneous tissue, muscles, and the liver capsule along the assumed track of entry, after povidone iodine has been used as a contact medium, using sonographic guidance, a 16-gauge 15-cm guide needle with an antenna was inserted and placed at the targeted tumour location. The active tip was entered into the deepest portion of the tumour and attached to the microwave generator. The energy application was then initiated. To avoid damage to surrounding structures such as gastrointestinal tract, the diaphragm, or gallbladder, the microwave ablation electrode was inserted into the tumour perpendicular to the surrounding structure. Power output and time emission was variable according to the site and the size of the tumor. The applications of 60 W for 8-10 minutes were effective for treatment of tumors <3cm and applications of 60 W for 10-15 minutes was effective for treatment of tumors 3-5cm. The needle track was cauterised for 10 seconds prior to removing the antenna, to avoid seeding of tumours. Throughout the procedure, vital signs as heart rate, blood pressure, rate of respiration, and the levels of oxygen saturation were regularly monitored.

After care: Complete bed rest for 12 hours. Observation of blood pressure and pulse for every 30 minutes for 2 hours and then every 2 hours for 12 hours. Analgesic (Panadol 500 mg 3 times/day for 5 days) to control any pain experienced after the procedure. Intravenous administration of antibiotics (Ciprofloxacin 200mg /12h) was routinely used for 3 days. Patients were discharged following a six-hour hospitalization with stable vital signs.

Evaluation of therapeutic efficacy and follow-up: To determine the responsiveness of tumours to microwave ablation therapy:

Triphasic CT: Before ablation to determine the location and size of HCC (concerning vascular structures and hepatic segments) and and post-contrast enhancement criteria. After ablation at 1, 3 and 6 months to determine the response to the ablation and any complications. Following treatment, patients who achieved complete ablation had follow-up, whereas those who did not achieve complete ablation were scheduled for further therapy. Regrowth of tumour inside or adjacent to the nodule that had previously been totally ablated was defined as local tumour progression (LTP) whereas the emergence of additional lesions in the liver

parenchyma or elsewhere was described as distant tumour progression (DTP). **Serum alpha-fetoprotein level** was checked at 1, 3 and 6 months after MWA.

Statistical Analysis

The data were collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis, version 21 (SPSS Inc, Chicago, IL, USA). As appropriate, data were input numerically or categorically. Two different types of statistical analysis were conducted: Descriptive statistics: Qualitative data were expressed as frequency and percent at 95% confidence interval (95% CI) and quantitative data were shown as range, SD, and mean.

Results:

Demographic data of the studied groups, risk factors for HCC and clinical presentation of the study participants are shown in table 1.

Table 1: Demographic data of the studied groups, risk factors for HCC and clinical presentation of the study participant

		Study participants (n =30)	Sex	
			Male	Female
Age (years)	40 - <50	8 (26.7%)	6	2
	50 - <60	13 (43.3%)	10	3
	60 - <70	7 (23.3%)	6	1
	70 - 80	2 (6.7%)	2	0
Risk factor		Total (n =30)		
HCV		25 (83.3%)		
HBV		4 (13.33%)		
Diabetes mellitus		18 (60%)		
Smoking		9 (30%)		
Clinical Presentation		Study participants (n =30)		
Pain		15 (50%)		
Jaundice		10 (33.3%)		
Loss of weight and appetite		10 (33.3%)		
Fever		8 (26.6%)		

HCV: hepatitis c virus, HBV: hepatitis B virus

Liver function tests of the study participants shown in table 4

Table 2: Liver function tests of the study participants

Test	Level	Study participants (n =30)
Albumin level (g/dL)	> 3.5	18 (60%)
	2.8 - 3.5	12 (40%)

Total Bilirubin level (mg/dL)	≤ 1	20 (66.7%)
	<1-2	10 (33.3%)
SGOT [AST] (IU/L)	≤ 40	14 (46.7%)
	> 40	16 (53.3%)
SGPT [ALT] (IU/L)	≤ 40	14 (46.7%)
	> 40	16 (53.3%)
Prothrombin concentration (%)	> 80	13 (43.3%)
	50-80	17 (56.7%)
INR	≤ 1.4	14 (46.7%)
	>1.4-2	16 (53.3%)

SGOT: serum glutamic-oxaloacetic transaminase, AST: Aspartate transaminase, SGPT: serum glutamic-pyruvic transaminase, ALT: alanine aminotransferase, INR: international normalized ratio.

Child Pugh classification of the study participants shown in Figure 1.

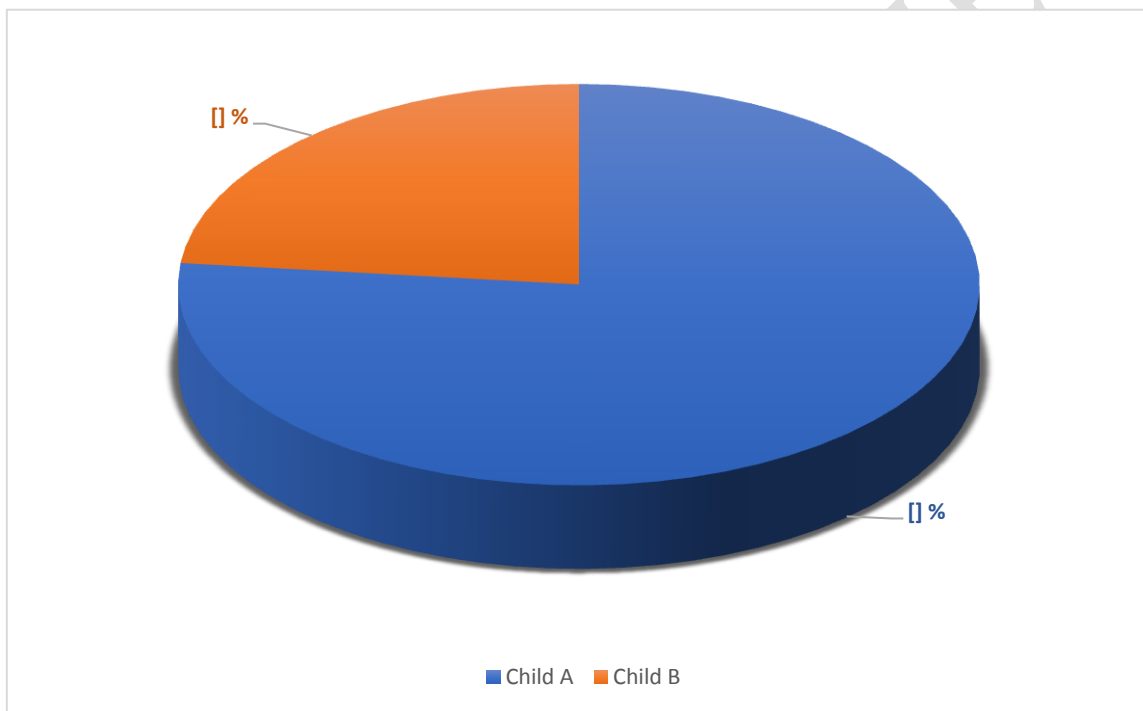


Figure 1: Child Pugh classification of study participants

US findings of the study participants shown in Table 3

Table 3: US findings of the study participants

US examination		Study participants (n =30)
Cirrhotic liver		30 (100%)
Liver size	Enlarged	4 (13.3%)
	Average	20 (66.7%)
	Shrunken	6 (20%)
Patent portal vein		30 (100%)
Splenomegaly	Average	2 (6.67%)
	Mild	11 (36.67%)
	Moderate	6 (20%)

	Marked	3 (10%)
Splenectomy		8 (26.67%)
Ascites	Minimal ascites	6 (20%)
	No ascites	24 (80%)

US: ultrasound

US and CT criteria of hepatic focal lesions and segmental distribution of hepatic focal lesions (hepatocellular carcinoma) of the study participants are shown in Table 4

Table 4: US and CT criteria of hepatic focal lesions and segmental distribution of hepatic focal lesions (hepatocellular carcinoma) of the study participants.

	Criteria of the lesion		Study participants (n =30)
US criteria	Echogenicity	hypoechoic	18 (60%)
		hyperechoic	3 (10%)
		heterogenous	9 (30%)
	Size	≤3cm	16 (53.3%)
		3-5cm	14 (46.7%)
	Lesion location	Right lobe	17 (56.6%)
		Left lobe	4 (13.3%)
Right and left lobes		9 (30%)	
CT criteria	Arterial enhancement	Homogenous	14 (46.7%)
		Heterogeneous	16 (53.35%)
	Patent portal vein	30 (100%)	
Hepatic segment		Study participants (n =30)	
II		6 (20%)	
III		7 (23.3%)	
IV		3 (10%)	
V		4 (13.3%)	
VI		5 (16.7%)	
VII		6 (20%)	
VIII		8 (26.7%)	

US: ultrasound, CT: Computed Tomography

Diameters of Coagulation Zones at different power output and duration according to the tumor size. Table 5

Table 5: Diameters of Coagulation Zones at different power output and duration according to the tumor size

Tumor Size	The electrode & Power output (W)	Microwave ablation duration (min)	Diameter of coagulation zone (cm)	
			Short axis	Long-axis
≤ 3cm	16G/60W	8-10	3.5-4	4.7-5.2
3-5cm	16G/60W	10-15	4.5- 5.5	5.6 -6.5

HCC can be treated locally utilising microwave ablation with cooled shaft antennas.

Table 6

Table 6: Local effectiveness of microwave ablation with cooled shaft antennas for treatment of HCC

Tumor size (cm)	No. of Patients	Ablation zone size (cm)		Complete ablation %
		Short Axis	Long Axis	
≤ 3 cm	16	3.5-4	4.7-5.2	93.8% (15/16)
>3 – 5 cm	14	4.5–5.5	5.6 -6.5	92.9% (13/14)

HCC: hepatocellular carcinoma

Recurrence of HCC in the study participants. Distribution of studied sample according to AFP, after 1 months, it showed significant decline. Table 7

Table 7: Recurrence of HCC and distribution of studied sample according to AFP in the study participants.

		Study participants (n =30)			
1-month	LTP	2 (6%)			
	IDR	9 (30%)			
3-month	LTP	3 (10%)			
	IDR	15 (50%)			
6-month	LTP	5 (16.7%)			
	IDR	18 (60%)			
		Baseline	1 month	3 months	6 months
AFP	Mean ± SD	438.24 ± 270.561	95.93 ± 55.974	105.83 ± 64.541	116.43 ± 66.478
	Range	100 – 1060	14 – 210	15 – 257	9.5 – 309
	P value		<0.001*	0.229	0.321

HCC: hepatocellular carcinoma, AFP: alpha-fetoprotein

Different complications occurred after microwave ablation in the studied thirty patients.

Table 8

Table 8: Different complications occurred after microwave ablation in the studied thirty patients

	Complications	Study participants (n =30)
Minor complications: Immediate	Pain	30 (100%)
	Skin burn requiring no treatment	15 (50%)
	Mechanical damage to the probe tip	1 (3.3%)
	Fever	18 (60%)
	Asymptomatic pleural effusion	7 (23.3%)
	Mild subcapsular bleeding	5 (16.7%)

Periprocedural	Asymptomatic thickening of gallbladder wall	2 (6.7%)
Major complications after Microwave ablation	Ablation lesion infection (liver abscess)	1 (3.3%)
	Pneumothorax	1 (3.3%)
	Hydropneumothorax	2 (6.7%)
	Hematoma	4 (13.3%)

Discussion

This study showed that overall, Males had a more than 4-fold increased incidence of HCC compared to females. Consistent with previous data from Liu et al., 2017 and Zang et al., 2020 studies (Liu et al., 2017, Zhang et al., 2020), For those patients with an age over 70 years, the magnitude of male predominance was the lowest. According to these findings sex hormones and reproductive factors may have a vital role in HCC development. in HCC risk. Elevated estrogens levels are believed to have a role in protecting against the development of HCC, while elevated androgen levels may promote tumorigenesis (Ren et al., 2016). However, even among those over 70 years, males had a nearly 2-fold increased risk of developing HCC compared to females. Males have higher rates of HCV infection and heavy alcohol use than females, which may explain the male prevalence in HCC, despite the fact that hormonal and reproductive factors may explain some of the sex effect in HCC.(Zhang et al., 2020).

Our results were supported by what was reported by Puoti, 2018 (Puoti, 2018), that the age between 50 and 69 showed the highest incidence of HCC. Our findings are in agreement with (Baghdady et al., 2014), who found that the age range of HCC patients was 42 to 70 years, and also with Shaker et al., 2013 who found that, in Egypt the most frequently affected age category by HCC was between 51 and 60 years. The age of onset of HCC is variable according to different locations of the world. In North America, Japan, and Europe, where the onset average age is more than 60 years, HCC is more likely to develop later in life. By contrast, the majority of African countries and parts of Asia, according to Yang et al., 2019 (Yang et al., 2019) HCC is most frequently diagnosed in participants between the ages of 30 and 60. Burnot et al., 2016 (Brunot et al., 2016) explained HCC onset in middle-aged and elderly populations in their study. They reported that the increasing prevalence of noninfectious cirrhosis liver, which is mostly associated with HCC, is a result of the disease

developing later in life. Additionally, Antiviral medications and vaccination have improved long-term management of chronic HBV or HCV infection, but have also delayed the onset of liver cirrhosis and hepatocellular carcinoma development. Furthermore, HCV infection occurs more often in adults and has more severe consequences in the elderly, including severe histological damage and increased liver cirrhosis, The latter is a significant contributor to the development of HCC in the elderly.

Yang et al., 2019 (Yang et al., 2019) documented that chronic HBV and HCV infection has been shown to be the primary cause of HCC, accounting for approximately 80% of patients of HCC worldwide. In Eastern Asia and the majority of Africa, chronic HBV infection is thought to be the primary cause of HCC, with the exception of northern Africa, where HCV is more prevalent. This is supporting our findings, which are in agreement also with what has been established by Blachier et al., 2013 (Blachier et al., 2013) that HCV infected patients have a 15-20-fold risk of developing HCC compared with HCV negative patients.

Concerning diabetes mellitus, Rashed et al., 2020 (Rashed et al., 2020) mentioned that several genome-wide association studies (GWAS) have revealed various locations associated with an increased risk of type 2 diabetes. The link between type 1 diabetes and an increased risk of developing (HCC) is currently unclear. There are several probable explanations for the association between diabetes and an increased risk of hepatocellular carcinoma (HCC). One of the metabolic syndrome components which may cause NASH and HCC after it, is diabetes. Also, Yang et al., 2017 (Yang et al., 2017) mentioned that persistently elevated insulin levels in type 2 diabetes patients result in both increase in insulin-like growth factor-1 (IGF-1) levels and insulin resistance (IR) in the majority of tissues, including the liver, which may improve the development of carcinogenesis. Moreover, hepatocyte damage and oxidative stress might be caused by prolonged hyperglycemia. In aligning with Fenoglio et al., 2013 and Aljumah et al., 2016 (Aljumah et al., 2016, Fenoglio et al., 2013) studies. They reported that most patients in their studies were of Child Pugh class A. Evaluation of liver function is particularly important in clinical trials because it is perceived that cirrhosis is a competing cause of mortality. Many HCC therapy trials are confined to patients with C-P grade A to isolate the effect of a particular HCC medication on survival. In match with these findings, Holah et al., 2015 (Holah et al., 2015) study also revealed that HCC cases were virtually equal in the left and right lobes (50.0 and 44.6%, respectively) while only 5.4 % of HCC cases affected both lobes. This may be explained by that their study population lesions were mainly of the fibrolamellar type, with its documented left lobe predominance. In accordance, Zhou et al., 2013 (Zhou et al., 2013) reported that microwave ablations with ≥ 5

minutes time duration can induce coagulation zones with clinically desirable ablation shape at power from 40 W to 80 W. Guan, 2015 (Guan, 2015) found that with tumor sizes ranging from 3 to 5 cm in diameter, microwave power for ablation is set at 50-60 W for 5-15 min. Nevertheless, our figures are relatively distant from those of Liu et al. 2013 and Poggi et al. 2013 (Ding et al., 2013, Poggi et al., 2013) which may be attributed to the use of different microwave machines.

Our data are comparable to previous studies. Dawoud et al., 2019 (Dawoud. T et al., 2019) revealed that total complete response was achieved in 92.3% of patients, Alexander et al., 2015 (Alexander et al., 2015) reported technical success rates of 95.3%, Xu et al., 2017 (Xu et al., 2017) reported primary local efficiency of 95.2% and also Hetta et al., 2011 (Hetta. OM et al., 2011) reported complete ablation in 96% of nodules. In the study of Dawoud et al., 2019 (Dawoud. T et al., 2019), tumor size was the single significant predictor of initial complete ablation.

Our results emphasized the previously concluded association between the HCC status and AFP levels such as in the studies of **Toro et al., 2014** and **Wang et al., 2016** (Toro et al., 2014, Wang et al., 2016).Yolk sac cells, Fetal hepatocyte and gastrointestinal cells produce α -Fetoprotein, which is considered an oncofetal protein. AFP is generated by dedifferentiated HCC cells in comparison to normal hepatocytes. Thus, even in the absence of evident cancer, dedifferentiation and carcinogenesis in hepatocytes can be predicted by an increase in AFP serum levels. In addition to the persistence of HCC, elevated AFP levels following RFA show that the non-cancerous liver is in a highly carcinogenic condition. (Dohi et al., 2016).

Pain and fever occurred in the present study are expected and mostly resulted from an inflammatory response to the necrotic tissue with cytokines production (Chao. W-C et al., 2015). The presence of pleural effusion following thermal ablation was previously attributed to temporary pleurisy caused by the thermal effect. Direct thermal damage to the pleural membranes may cause an increase in pleural capillary filtration and interference with the evacuation of parietal pleural fluid, resulting in the creation of a pleural effusion. (Lu et al., 2003).

For the treatment of malignant liver tumors, MW ablation is a well-tolerated therapy with an acceptable risk of significant complications (Lahat et al., 2014). In variable distances from our findings, Over a 13-year period, a large-scale study conducted by **Liang et al. 2009** found that the rate of significant complications is approximately 2.6 % ⁽¹⁵²⁾. Fever was the most often reported adverse effect, occurring in 83.4 % of participants in the study of **Liang et al. 2009**. **Livraghi et al., 2012** (Livraghi et al., 2012) stated the safety of MWA as reported 0%

mortality, 7.2% minor complications and 2.9% major complications. **Mobarak et al., 2020** (Mobarak et al., 2020) reported no major complications or mortality was related to the MWA procedure, and only minor complications in the form of right hypochondrial pain (12%) were reported. In the study of **Li et al., 2012** (Li et al., 2012) moderate to massive pleural effusion occurred in 3.1% of patients and **Huang et al., 2014** (Huang et al., 2014) reported one case of portal vein thrombosis (0.7%) and two cases of tumor seedling (1.4%) out of 139 perivascular lesions.

Conclusion

Percutaneous microwave ablation guided by ultrasound for the treatment of challenging HCC tumors up to 5 cm in diameter, including exophytic or subcapsular targets as well as those located in the hepatic dome or close to the diaphragm / hepatic hilum /heart, shown satisfactory safety and efficacy rates. For both technical and clinical success, selecting the proper approach is critical.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References<Dawoud et al.pdf>.

ALEXANDER, E. S., WOLF, F. J., MACHAN, J. T., CHARPENTIER, K. P., BELAND, M. D., IANNUCILLI, J. D., HAAS, R. H. & DUPUY, D. E. 2015. Microwave ablation of focal hepatic malignancies regardless of size: A 9-year retrospective study of 64 patients. *Eur J Radiol*, 84, 1083-90.

ALJUMAH, A. A., KURIRY, H., ALZUNAITAN, M., AL GHOBAIN, M., AL MUAIKEEL, M., AL OLAYAN, A., AZZUMEEA, F., ALMUTAIRI, B.,

- ALALWAN, A. & ALGHAMDI, H. 2016. Clinical Presentation, Risk Factors, and Treatment Modalities of Hepatocellular Carcinoma: A Single Tertiary Care Center Experience. *Gastroenterol Res Pract*, 2016, 1989045.
- BAGHDADY, I., FOUAD, F., SAYED, M., SHOAB, A., SALAH, Y., ELSHAYEB, E. & HASAN, A. 2014. Serum markers for the early detection of hepatocellular carcinoma in patients with chronic viral hepatitis C infection. *Menoufia Medical Journal*, 27, 544-550.
- BLACHIER, M., LELEU, H., PECK-RADOSAVLJEVIC, M., VALLA, D. C. & ROUDOT-THORAVALL, F. 2013. The burden of liver disease in Europe: a review of available epidemiological data. *J Hepatol*, 58, 593-608.
- BRACE, C. L. 2009. Radiofrequency and microwave ablation of the liver, lung, kidney, and bone: what are the differences? *Curr Probl Diagn Radiol*, 38, 135-43.
- BRUIX, J. & SHERMAN, M. 2011. Management of hepatocellular carcinoma: an update. *Hepatology*, 53, 1020-2.
- BRUNOT, A., LE SOURD, S., PRACHT, M. & EDELINE, J. 2016. Hepatocellular carcinoma in elderly patients: challenges and solutions. *J Hepatocell Carcinoma*, 3, 9-18.
- CHAO, W-C, LIU, C-Y & LIN, C-C 2015. Pleural effusion after percutaneous radiofrequency Ablation for hepatic malignancies. *J Cancer Res Pract*, 2, 22-30.
- DAWOUD, T., HEFEDA, M & EL-SHAFFEY, K 2019. Ultrasound-Guided Microwave Ablation of Unresectable Hepatocellular Carcinoma: Short Term Response and Predictors of Success. *Med J Cairo Univ*, 87, 5009-20.
- DING, J., JING, X., LIU, J., WANG, Y., WANG, F., WANG, Y. & DU, Z. 2013. Comparison of two different thermal techniques for the treatment of hepatocellular carcinoma. *Eur J Radiol*, 82, 1379-84.

- DOHI, C., NOUSO, K., MIYAHARA, K., MORIMOTO, Y., WADA, N., KINUGASA, H., TAKEUCHI, Y., KUWAKI, K., ONISHI, H., IKEDA, F., NAKAMURA, S., SHIRAHA, H., TAKAKI, A. & OKADA, H. 2016. Potential of alpha-fetoprotein as a prognostic marker after curative radiofrequency ablation of hepatocellular carcinoma. *Hepatol Res*, 46, 916-23.
- FENOGLIO, L., SERRAINO, C., CASTAGNA, E., CARDELLICCHIO, A., POMERO, F., GROSSO, M. & SENORE, C. 2013. Epidemiology, clinical-treatment patterns and outcome in 256 hepatocellular carcinoma cases. *World J Gastroenterol*, 19, 3207-16.
- GUAN, Y.-S. 2015. Microwave coagulation therapy of hepatocellular carcinoma. *Hepatoma Research*, 1, 159-164.
- HETTA. OM, SHEBRYA. NH & AMIN. SK 2011.). Ultrasound-guided microwave ablation of hepatocellular carcinoma: Initial institutional experience. *EJRNM*, 42, 343-9.
- HOLAH, N., EL-AZAB, D., AIAD, H. & SWEED, D. 2015. Hepatocellular carcinoma in Egypt: epidemiological and histopathological properties. *Menoufia Medical Journal*, 28, 718-724.
- HUANG, S., YU, J., LIANG, P., YU, X., CHENG, Z., HAN, Z. & LI, Q. 2014. Percutaneous microwave ablation for hepatocellular carcinoma adjacent to large vessels: a long-term follow-up. *Eur J Radiol*, 83, 552-8.
- KELEKIS, A. & FILIPPIADIS, D. 2016. Computed Tomography and Ultrasounds for the Follow-up of Hepatocellular Carcinoma Ablation: What You Need to Know. *Diagnostics (Basel)*, 6.
- LAHAT, E., ESHKENAZY, R., ZENDEL, A., ZAKAI, B. B., MAOR, M., DREZNIK, Y. & ARICHE, A. 2014. Complications after percutaneous ablation of liver tumors: a systematic review. *Hepatobiliary Surg Nutr*, 3, 317-23.

- LENCIONI, R. & LLOVET, J. M. 2010. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. *Semin Liver Dis*, 30, 52-60.
- LI, M., YU, X. L., LIANG, P., LIU, F., DONG, B. & ZHOU, P. 2012. Percutaneous microwave ablation for liver cancer adjacent to the diaphragm. *Int J Hyperthermia*, 28, 218-26.
- LIANG, P., WANG, Y., YU, X. & DONG, B. 2009. Malignant liver tumors: treatment with percutaneous microwave ablation--complications among cohort of 1136 patients. *Radiology*, 251, 933-40.
- LIU, P., XIE, S. H., HU, S., CHENG, X., GAO, T., ZHANG, C. & SONG, Z. 2017. Age-specific sex difference in the incidence of hepatocellular carcinoma in the United States. *Oncotarget*, 8, 68131-68137.
- LIVRAGHI, T., MELONI, F., SOLBIATI, L. & ZANUS, G. 2012. Complications of microwave ablation for liver tumors: results of a multicenter study. *Cardiovasc Intervent Radiol*, 35, 868-74.
- LLOYD, D. M., LAU, K. N., WELSH, F., LEE, K. F., SHERLOCK, D. J., CHOTI, M. A., MARTINIE, J. B. & IANNITTI, D. A. 2011. International multicentre prospective study on microwave ablation of liver tumors: preliminary results. *HPB (Oxford)*, 13, 579-85.
- LU, D. S., RAMAN, S. S., LIMANOND, P., AZIZ, D., ECONOMOU, J., BUSUTTIL, R. & SAYRE, J. 2003. Influence of large peritumoral vessels on outcome of radiofrequency ablation of liver tumors. *J Vasc Interv Radiol*, 14, 1267-74.
- MOBARAK, L., YOSSIF, A. F., KHATER, H., ZARAD, C. A., ZAKARIA, Z., SHOKRY, A. A. & EL AGAWY, W. 2020. The role of microwave ablation in treatment of small and medium sized hepatocellular carcinoma. *Medicine Updates*, 3, 46-59.

- POGGI, G., MONTAGNA, B., P, D. I. C., RIVA, G., BERNARDO, G., MAZZUCCO, M. & RICCARDI, A. 2013. Microwave ablation of hepatocellular carcinoma using a new percutaneous device: preliminary results. *Anticancer Res*, 33, 1221-7.
- PUOTI, C. 2018. New insights on hepatocellular carcinoma: epidemiology and clinical aspects. *Hepatoma Research*, 4.
- RASHED, W. M., KANDEIL, M. A. M., MAHMOUD, M. O. & EZZAT, S. 2020. Hepatocellular Carcinoma (HCC) in Egypt: A comprehensive overview. *J Egypt Natl Canc Inst*, 32, 5.
- REN, J., CHEN, G. G., LIU, Y., SU, X., HU, B., LEUNG, B. C., WANG, Y., HO, R. L., YANG, S., LU, G., LEE, C. G. & LAI, P. B. 2016. Cytochrome P450 1A2 Metabolizes 17 β -Estradiol to Suppress Hepatocellular Carcinoma. *PLoS One*, 11, e0153863.
- SHAKER, M. K., ABDELLA, H. M., KHALIFA, M. O. & EL DORRY, A. K. 2013. Epidemiological characteristics of hepatocellular carcinoma in Egypt: a retrospective analysis of 1313 cases. *Liver Int*, 33, 1601-6.
- TORO, A., ARDIRI, A., MANNINO, M., ARCERITO, M. C., MANNINO, G., PALERMO, F., BERTINO, G. & DI CARLO, I. 2014. Effect of pre- and post-treatment α -fetoprotein levels and tumor size on survival of patients with hepatocellular carcinoma treated by resection, transarterial chemoembolization or radiofrequency ablation: a retrospective study. *BMC Surg*, 14, 40.
- WANG, T., LU, X. J., CHI, J. C., DING, M., ZHANG, Y., TANG, X. Y., LI, P., ZHANG, L., ZHANG, X. Y. & ZHAI, B. 2016. Microwave ablation of hepatocellular carcinoma as first-line treatment: long term outcomes and prognostic factors in 221 patients. *Sci Rep*, 6, 32728.

- XU, H., LI, X., H., GAO, Y., PAN, M., WANG, L. & GAO, P. 2017. Diabetes mellitus increases the risk of hepatocellular carcinoma in treatment-naïve chronic hepatitis C patients in China. *Medicine (Baltimore)*, 96, e6508.
- YANG, J. D., HAINAUT, P., GORES, G. J., AMADOU, A., PLYMOTH, A. & ROBERTS, L. R. 2019. A global view of hepatocellular carcinoma: trends, risk, prevention and management. *Nat Rev Gastroenterol Hepatol*, 16, 589-604.
- YANG, J. D., MOHAMED, E. A., AZIZ, A. O., SHOUSHA, H. I., HASHEM, M. B., NABEEL, M. M., ABDELMAKSOU, A. H., ELBAZ, T. M., AFIHENE, M. Y., DUDUYEMI, B. M., AYAWIN, J. P., GYEDU, A., LOHOUÈS-KOUACOU, M. J., NDAM, A. W., MOUSTAFA, E. F., HASSANY, S. M., MOUSSA, A. M., UGIAGBE, R. A., OMUEMU, C. E., ANTHONY, R., PALMER, D., NYANGA, A. F., MALU, A. O., OBEKPA, S., ABDO, A. E., SIDDIG, A. I., MUDAWI, H. M., OKONKWO, U., KOOFFREH-ADA, M., AWUKU, Y. A., NARTEY, Y. A., ABBEW, E. T., AWUKU, N. A., OTEGBAYO, J. A., AKANDE, K. O., DESALEGN, H. M., OMONISI, A. E., AJAYI, A. O., OKEKE, E. N., DUGURU, M. J., DAVWAR, P. M., OKORIE, M. C., MUSTAPHA, S., DEBES, J. D., OCAMA, P., LESI, O. A., ODEGHE, E., BELLO, R., ONYEKWERE, C., EKERE, F., IGETEI, R., MAH'MOUD, M. A., ADDISSIE, B., ALI, H. M., GORES, G. J., TOPAZIAN, M. D. & ROBERTS, L. R. 2017. Characteristics, management, and outcomes of patients with hepatocellular carcinoma in Africa: a multicountry observational study from the Africa Liver Cancer Consortium. *Lancet Gastroenterol Hepatol*, 2, 103-111.
- ZHANG, X., EL-SERAG, H. B. & THRIFT, A. P. 2020. Sex and Race Disparities in the Incidence of Hepatocellular Carcinoma in the United States Examined through Age-Period-Cohort Analysis. *Cancer Epidemiol Biomarkers Prev*, 29, 88-94.

ZHOU, W., LIANG, M., PAN, H., LIU, X., JIANG, Y., WANG, Y., LING, L., DING, Q. & WANG, S. 2013. Comparison of ablation zones among different tissues using 2450-MHz cooled-shaft microwave antenna: results in ex vivo porcine models. *PLoS One*, 8, e71873.

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