Original Article

Percutaneous radiofrequency versus microwave ablation for management of hepatocellular carcinoma: a randomized controlled trial

Ahmed Kamal, Amr Aly Abd Elmoety, Yousri Abdel Meguid Rostom, Mohamed Said Shater, Sameh Aldesoky Lashen

Hepatology Unit, Internal Medicine Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt

Contributions: (I) Conception and design: AA Elmoety, A Kamal, SA Lashen; (II) Administrative support: YA Rostom, MS Shater, AA Elmoety; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: A Kamal; (V) Data analysis and interpretation: A Kamal, SA Lashen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ahmed Kamal, MS. Assistant Lecturer of Internal Medicine and Hepatology, Hepatology Unit, Internal Medicine Department, Faculty of Medicine, Alexandria University, 1 Khartoum Square, Alexandria, Egypt. Email: ahmed.kamal.med.scientific@gmail.com; Ahmed.kamal@alexmed.edu.eg.

Background: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world and the third most common cause of cancer related deaths. Radiofrequency ablation (RFA) and microwave ablation (MWA) are effective measures for HCC management. Although MWA is usually considered to be superior to RFA in the medical community, clinical studies showed contradictory results. We aimed to compare the efficacy of both techniques using a randomized controlled trial.

Methods: We had assessed all patients with definite HCC who were referred to our unit during the period from mid-June 2017 to mid-December 2017 for inclusion in the study. After fulfilling the criteria, patients were randomized to either RFA or MWA. Achieving complete ablation was ensured. Patients were followed up every 3 months after the procedure to detect any tumor recurrence.

Results: There were no statistically significant differences between both techniques regarding complications, local tumor recurrence, development of *de novo* HCC lesions and changes in the modified Child-Pugh score. Time of ablation using MWA was significantly shorter than RFA (P<0.001).

Conclusions: RFA and MWA are comparable techniques for HCC treatment. Our group couldn't prove any superiority of MWA over RFA except for the shorter time needed for ablation.

Keywords: Radiofrequency ablation (RFA); microwave ablation (MWA); hepatocellular carcinoma (HCC)

Submitted Jan 09, 2019. Accepted for publication Jan 26, 2019.
doi: 10.21037/jgo.2019.01.34
View this article at: http://dx.doi.org/10.21037/jgo.2019.01.34

Introduction

Hepatocellular carcinoma (HCC) is one of aggressive tumors that usually arise on top of background of liver cirrhosis (1). It is the fifth most common cancer in the world (2). Also, it is the third most common cause of cancer related deaths (1). In Egypt, it is the most common malignancy among males, comprising 33% of all cancer cases and the second most common malignancy in females, coming after breast cancer, comprising 13% of all cancer cases (3). The optimal management of HCC depends on many factors including tumor size, number, distribution, the relationship of the tumor to hepatic vasculature, presence or absence of lymph nodes or distant metastases, the Child-Pugh score, the functional status of the patient, the suitability for liver transplantation and local expertise (3).

Many available treatment modalities for HCC are present including liver resection, liver transplantation, radiofrequency ablation (RFA), percutaneous ethanol

injection (PEI), microwave ablation (MWA), transarterial chemoembolization (TACE), yttrium ablation, conformal radiation therapy and systemic therapy (e.g., sorafenib) (4,5).

RFA depends on ultrasound guided delivery of high frequency current to the targeted tissue via a needle electrode (6,7).

RFA is more effective against small tumors less than 3 cm. It is difficult to destroy lesions above 5 cm using the currently available needles (6-8). A margin of 0.5–1.0 cm of non-malignant liver tissue should be ablated to ensure treatment of the peripheral tumor that includes any microscopic extension beyond the radiologically visible margins (7).

Presence of the tumor nearby a large blood vessel decreases the efficacy of RFA by the heat sink effect when thermal energy escapes from the targeted tissue to the vessels adjacent to it (9,10). Also, Tissue charring acts as electrical insulators and limit the effect of RFA through increased impedance. As a result, the size and shape of the ablation zone may be unpredictable and multiple sessions may be necessary for complete tumor ablation (9,11).

Compared to RFA, MWA is another local ablation method that is increasingly used. It depends on delivering high frequency microwave into the tumor tissue creating electromagnetic energy leading to rapid directional changes in the current causing water dipoles to oscillate with subsequent heat generation that leads to coagulative necrosis of the tumor cells (6,7).

Unlike RFA, the MWA is less affected by the heat-sink effect and increased impedance of the ablated tissue, and so the shape and size of ablated zone created by MWA is more predictable (9,11). Also, during MWA simultaneous multi-probe activation can be performed, which is not possible with RFA because of the potential electrical interference (7).

Despite the theoretical advantages of MWA over RFA, MWA still not included in the standard guidelines for HCC management. There are scarce studies comparing results of both techniques in the real life, most of which are retrospective, so our aim was to compare efficacy of RFA and MWA in management of HCC using a prospective randomized controlled trial.

Methods

Subjects and study design

All patients with definite HCC on top of liver cirrhosis related to HCV who were referred to Alexandria University Hepatobiliary Unit during the 6-month period from 15/6/2017 to 15/12/2018 whose HCC lesions are 3 or less with no lesion more than 5 cm and no vascular invasion or extrahepatic spread were enrolled to the study, with exclusion of those with positive HBsAg, history of alcohol consumption, patients with other known causes of chronic liver disease, patients who have received previous DAAs for HCV and patients who have received previous locoregional treatment for HCC. Patients were randomly assigned to either RFA or MWA. The study was conducted in accordance with the provisions of the Declaration of Helsinki, as revised in 2013, and Good Clinical Practice guidelines. It was approved by the Ethics Committee of Faculty of Medicine, Alexandria University (IRB No. 00007555). An informed consent was obtained from all subjects included in the study.

The CONSORT flow diagram of the study is shown in *Figure 1*.

Procedures

All patients included in the study were evaluated as regards Clinical Evaluation, Laboratory Investigations including complete blood picture (CBC), serum aspartate and alanine aminotransferases (AST and ALT), serum albumin, serum bilirubin, serum, alkaline phosphatase, prothrombin activity, INR, alfa fetoprotein (AFP), HCV antibodies, hepatitis B surface antigen and hepatitis B core antibody using enzyme-linked immune-sorbent assay (ELISA), HCV RNA levels in serum using real time polymerase chain reaction assay and HCV genotyping +/– subtyping if indicated. Liver disease severity was assessed based on modified Child Pugh classification (CTP) and model for end-stage liver disease.

Radiological evaluation depended on a recent Triphasic CT abdomen and/or dynamic MRI performed within 4 weeks before ablation for diagnosis of HCC based on characteristic enhancement pattern and to determine number, size and site of tumors and to exclude portal vein invasions. Hepatic lesions were classified according to LI-RADS classification (12). Definite HCC (LR-5) lesions were the only to be considered for inclusion in the study.

All included patients were randomized for HCC ablation using RFA or MWA. If multiple lesions were present, all were treated with the same method. For RFA (Angiodynamics RITA model 1,500×, USA) generator and RITA StarBurst XL needle were used complying with manufacturer's instructions. For MWA, a 14 gauge 200 mm disposable MWA probe (AMICA probe MW) and a 2.45 GHz

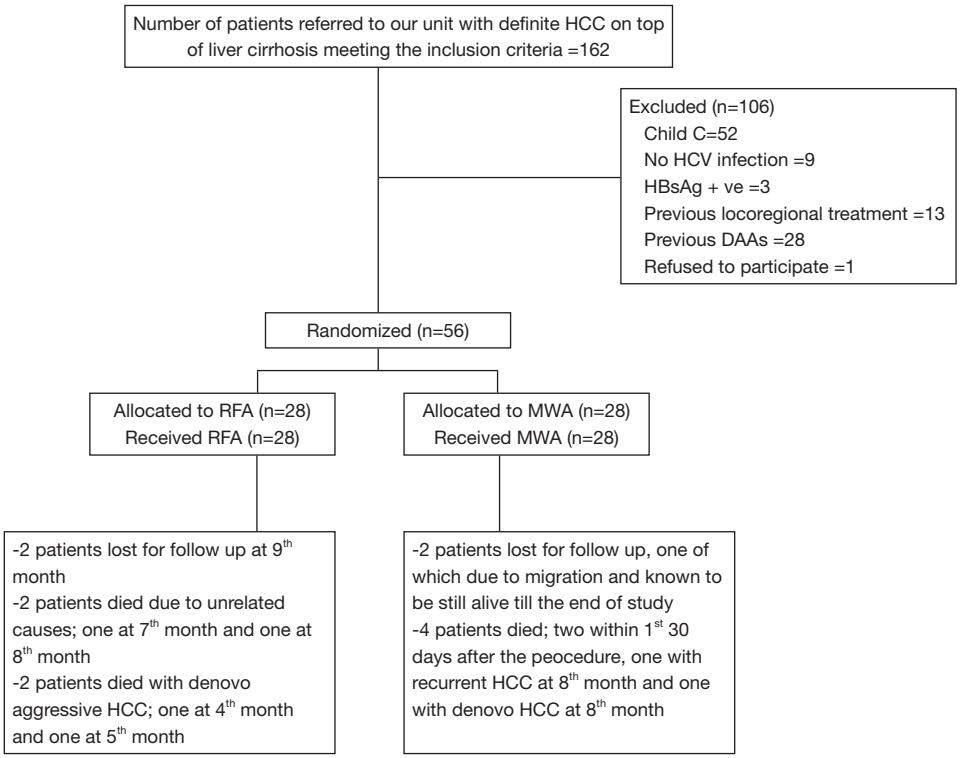

Figure 1 CONSORT flow diagram of the study. HCC, hepatocellular carcinoma; RFA, radiofrequency ablation; MWA, microwave ablation.

generator (AMICA GEN AGN-H-1.2, Italy) were used. Duration and wattage used for ablation were chosen according to the manufacturer's instructions.

Local response was assessed by triphasic CT done 4 weeks after the treatment. Those with residual activity were retreated by RFA or MWA according to the initial randomization. An extra follow up triphasic CT was performed after another 4 weeks.

All patients were followed every 3 months after the procedure to discover any HCC recurrence using triphasic CT. Response was evaluated according to modified RECIST criteria (13). Also, modified Child-Pugh score was evaluated on the same intervals.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. Chi-square test was used for categorical variables, to compare between different groups. Fisher's Exact or Monte Carlo correction for chi-square were used when more than 20% of the cells have expected count less than 5. Student *t*-test was used for normally distributed quantitative variables, to compare between two studied groups. Mann Whitney test was used for non-normally distributed quantitative variables, to compare between two studied groups. Kaplan-Meier Survival curve was used and cox regression was done for the significant relation with overall survival.

Results

There were no statistically significant differences between both groups regarding age and sex. Men were predominating in both groups (78.6% in the RFA group and 75% in the MWA group), whereas the mean age was nearly 55 years in both groups, ranging from 42 to 80 years.

There were no statistically significant differences between both groups regarding the pre-treatment

Table 1 Pretreatment important laboratory findings in the studied group

Parameter	RFA (n=28)	MWA (n=28)	Test of significance	P
PLT (×10^3/μL)			t=1.797	0.079
Range	60.0–259.0	46.0–172.0		
Mean ± SD	132.5±66.24	105.5±44.14		
Total bilirubin (mg/dL)			t=0.130	0.897
Range	0.53–2.10	0.50–2.10		
Mean ± SD	1.16±0.44	1.15±0.41		
Direct bilirubin (mg/dL)			U=379.0	0.831
Range	0.10–1.02	0.20–1.50		
Mean ± SD	0.53±0.30	0.57±0.30		
Serum albumin (g/dL)			t=1.090	0.281
Range	2.70–4.20	2.0–4.50		
Mean ± SD	3.36±0.37	3.49±0.53		
AFP (ng/mL)			U=312.50	0.192
Range	3.0–1,345.0	0.60–1,370.0		
Mean ± SD	214.8±319.0	282.4±469.7		
Total HBcAb			χ^2=0.163	FEp=1.000
Negative	25 (89.3%)	24 (85.7%)		
Positive	3 (10.7%)	4 (14.3%)		

T, Student *t*-test; χ^2, Chi square test; FE, Fisher Exact; U, Mann Whitney test; P, P value for comparing between the studied groups. PLT, platelets count; AFP, alfa fetoprotein; HBcAb, hepatitis B core antibody; RFA, radiofrequency ablation; MWA, microwave ablation.

laboratory findings including platelet counts, albumin, total bilirubin and AFP levels (*Table 1*). Also, there was no difference regarding the pre-treatment Child-Pugh score. Twenty-two patients were Child-Pugh class A *vs.* 6 patients were Child-Pugh class B in both groups. The mean Child-Pugh score was 5.86 for the RFA group *vs.* 5.79 for the MWA group (P=0.778). Performance status and MELD score were not significantly statistically different between both groups before HCC ablation (*Table 2*).

In addition, there were no statistically significant differences between both groups regarding number and sizes of HCC lesions. Twenty-two patients in the RFA group had single lesion while 6 patients had 2 lesions. In the MWA group, 24 patients had single lesion, while 2 patients had 2 lesions and the other 2 had 3 lesions (P=0.155). Eighteen patients in the RFA group had lesions that measured 3 cm or more *vs.* 16 patients in the MWA group (P=0.584). The mean size of largest lesions per patient in the RFA group was 3.28 *vs.* 3.25 in the MWA group (P=0.908) (*Table 3*).

There was no statistically significant difference between both groups regarding number of sessions needed till complete ablation of the tumor, but the duration was significantly shorter in the MWA group. The mean ablation time at RFA group was 14.21 minutes while it was 4.41 minutes at the MWA group (P<0.001) (*Table 4*).

Regarding complications after the procedure, there were no clinically significant differences between both groups. Two major complications occurred after MWA, namely bleeding from the tumor in one patient and hematemesis in the next day of the procedure in another patient, but this was not statistically significant (*Table 5*).

Local tumor recurrence didn't differ statistically between both groups. At 6 months the local recurrence was 0% at the RFA group while it was 8.3% at the MWA group (P=0.225). At 12 months, the local recurrence was 9.1% in both groups (*Table 6*).

Kaplan-Meier estimates of local tumor recurrence-free

Table 2 Comparison between the two studied groups according to the pre-treatment performance status, MELD score, modified Child-Pugh class and score

Pre-treatment status	RFA (n=28)	MWA (n=28)	Test of significance	P
Performance status, n (%)			χ^2=0.000	1.000
0	20 (71.4)	20 (71.4)		
1	8 (28.6)	8 (28.6)		
MELD score			t=1.118	0.268
Range	6.0–11.0	6.0–11.0		
Mean ± SD	8.79±2.01	8.21±1.81		
Median	9.50	8.0		
Child Pugh class, n (%)			χ^2=0.00	1.000
A	22 (78.6)	22 (78.6)		
B	6 (21.4)	6 (21.4)		
Child Pugh score			t=0.283	0.778
Range	5.0–8.0	5.0–8.0		
Mean ± SD	5.86±0.93	5.79±0.96		
Median	6.0	5.50		

χ^2, Chi square test; t, Student *t*-test; P, P value for comparing between the studied groups. RFA, radiofrequency ablation; MWA, microwave ablation.

Table 3 Comparison between the two studied groups according to pretreatment CT findings

Pre-treatment CT findings	RFA (n=28)	MWA (n=28)	Test of significance	P
Number of lesions per patient, n (%)			χ^2=3.610	MCp=0.155
1	22 (78.6)	24 (85.7)		
2	6 (21.4)	2 (7.1)		
3	0 (0.0)	2 (7.1)		
Size of largest lesion per patient, n (%)			0.299	0.584
<3	10 (35.7)	12 (42.9)		
≥3	18 (64.3)	16 (57.1)		
Size of largest lesion per patient (cm)			t=0.117	0.908
Range	1.70–4.50	2.0–5.0		
Mean ± SD	3.28±0.91	3.25±0.92		
Median	3.75	3.0		
Ascites, n (%)			χ^2=0.747	FEp=0.669
No ascites	26 (92.9)	24 (85.7)		
Mild ascites	2 (7.1)	4 (14.3)		

χ^2, Chi square test; MC, Monte Carlo; FE, Fisher Exact; t, Student *t*-test; P, P value for comparing between the studied groups. RFA, radiofrequency ablation; MWA, microwave ablation.

Table 4 Comparison between the two studied groups according to duration of sessions and Number of sessions per lesion till complete ablation

Parameter	RFA (n=34)	MWA (n=34)	Test of significance	P
No. of sessions (%)			χ^2=0.731	FEp=0.673
1	30 (88.2)	32 (94.1)		
2	4 (11.8)	2 (5.9)		
Duration			U=67.0	<0.001
Range	4.0–31.0	3.0–10.0		
Mean ± SD	14.21±9.12	4.41±1.73		
Median	10.0	5.0		

n, number of all HCC lesions; χ^2, Chi square test; FE, Fisher Exact; U, Mann Whitney test; P, P value for comparing between the studied groups. RFA, radiofrequency ablation; MWA, microwave ablation; HCC, hepatocellular carcinoma.

Table 5 Comparison between the two studied groups according to negative impacts after HCC ablation procedure

Negative impacts	RFA (n=28)		MWA (n=28)		χ^2	P
	No.	%	No.	%		
Pain at the site of intervention	12	42.9	12	42.9	0.00	1.000
Right shoulder pain	2	7.1	4	14.3	0.747	FEp=0.669
Low grade fever	6	21.4	8	28.6	0.381	0.537
Bleeding requiring embolization	0	0.0	1	3.6	1.018	FEp=1.000
Hematemesis within 24 hours after the procedure	0	0.0	1	3.6	1.018	FEp=1.000

χ^2, Chi square test; FE, Fisher Exact; P, P value for comparing between the studied groups. HCC, hepatocellular carcinoma; RFA, radiofrequency ablation; MWA, microwave ablation.

survival at 1-year follow up was 90.9% of subjects for the RFA group and 92.3% for the MWA group which was not statistically significant difference (*Figure 2*). The estimated mean local recurrence free time was 11.7 months in the RFA group and 11.3 months in the MWA group.

Till the end of 1-year follow up, there were no statistically significant differences between both groups regarding the development of *de novo* lesions or macrovascular tumor invasion (*Table 6*). In addition, there was no statistically significant difference between both groups regarding Child-Pugh score over time (*Table 7*).

Two patients died within 30 days after MWA while no one died after RFA during the same period, but this was not statistically significant difference. By the end of 1-year follow up, four patients died in each group (*Table 8*). Two patients in the RFA group died with unrelated causes (one with pulmonary embolism and the other due to intracerebral hemorrhage). The other two died with *de novo* aggressive HCC. The two early mortalities in MWA group were due to liver decompensation, one of them died few days after successfully stopped bleeding from the tumor occurred on the same day of the procedure. Another patient died with recurrent HCC while the fourth one died with *de novo* HCC.

Discussion

Although the theoretical advantages of MWA over RFA, results of clinical studies are different. Most of these studies are retrospective.

Our study was a randomized controlled trial. This is similar to Shibata *et al.* (14) and Violi *et al.* (15). On the other hand, Lu *et al.* (16), Ohmoto *et al.* (17), Ding *et al.* (18), Zhang *et al.* (19), Abdelaziz *et al.* (20), Potretzke *et al.* (21) and Lee *et al.* (22) were retrospective studies. Lee *et al.* (22) compared both techniques using surgical approach instead of percutaneous approach.

In the current study, we included patients with HCCs up

Table 6 Comparison between the two studied groups according to local tumor recurrence, development of *de novo* lesions and malignant vascular invasion

Time	RFA		MWA		χ^2	FEp
	No.	%	No.	%		
Local HCC recurrence						
3 months	0/28	0.0	2/26	7.7	2.237	0.227
6 months	0/26	0.0	2/24	8.3	2.257	0.225
12 months	2/22	9.1	2/22	9.1	0.00	1.000
De novo lesions						
3 months	4/28	14.3	2/26	7.7	0.593	0.670
6 months	2/26	7.7	2/24	8.3	0.007	1.000
12 months	4/22	18.2	4/22	18.2	0.000	1.000
Malignant vascular invasion						
3 months	2/28	7.1	0/26	0.0	1.929	0.491
6 months	0/26	0.0	1/24	4.2	1.105	0.480
12 months	2/22	9.1	0/22	0.0	2.095	0.488

χ^2, Chi square test; FE, Fisher Exact; P, P value for comparing between the studied groups. RFA, radiofrequency ablation; MWA, microwave ablation; HCC, hepatocellular carcinoma.

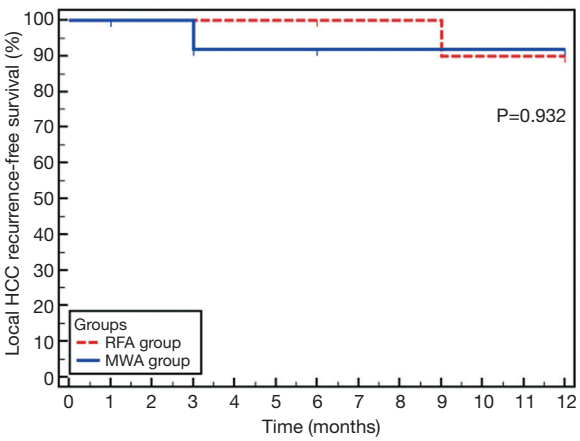

Figure 2 Kaplan-Meier curve of local HCC recurrence-free survival. HCC, hepatocellular carcinoma.

Table 7 Comparison between the two studied groups according to Child Pugh score over time

Child Pugh score	RFA	MWA	t	P
3 months	(n=28)	(n=26)	1.175	0.246
Range	5.0–9.0	5.0–8.0		
Mean ± SD	6.07±1.25	5.73±0.83		
Median	6.0	6.0		
6 months	(n=26)	(n=24)	1.116	0.270
Range	5.0–7.0	5.0–9.0		
Mean ± SD	5.54±0.65	5.83±1.17		
Median	5.0	5.50		
12 months	(n=22)	(n=22)	1.389	0.174
Range	5.0–9.0	5.0–7.0		
Mean ± SD	6.0±1.31	5.55±0.80		
Median	5.0	5.0		

t, Student *t*-test; P, P value for comparing between the studied groups. RFA, radiofrequency ablation; MWA, microwave ablation.

to three lesions with no lesion more than 5 cm in diameter. There were no statistically significant differences between both groups regarding number and sizes of lesions. Shibata *et al*. (14), Xu *et al*. (23) and Violi *et al*. (15) included subjects with lesions up to 4 cm while Ohmoto *et al*. (17) included subjects with lesions up to 2 cm. Potretzke *et al*. (21) included lesions up to 4.5 cm. Similar to our study, Ding *et al*. (18), Zhang *et al*. (19) and Abdelaziz *et al*. (20) included subjects with HCCs up to 5 cm. On the other hand, Lee *et al*. (22) included lesions up to 6 cm while the largest lesion that were included by Lu *et al*. (16) was 7.2 cm.

Table 8 Comparison between the two studied groups according to mortality during 1-year follow up

Parameter	RFA (n=28)		MWA (n=28)		χ^2	P
	No.	%	No.	%		
Mortality (1 month)					2.074	FEp=0.491
Survived	28	100.0	26	92.9		
Died	0	0.0	2	7.1		
Mortality (12 month)					0.496	MCp=1.000
Survived	22	78.6	23	82.1		
Died	4	14.3	4	14.3		
Lost to follow-up	2	7.1	1	3.6		

χ^2, Chi square test; MC, Monte Carlo; FE, Fisher Exact; P, P value for comparing between the studied groups. RFA, radiofrequency ablation; MWA, microwave ablation.

In our study, a follow up triphasic CT was done 4 weeks after the procedure to ensure complete ablation. If there was residual activity another session was done and follow up triphasic CT was performed after another 4 weeks. Thirty lesions from a total 34 lesions (88.2%) in the RFA group were completely ablated after single session, while 32 lesions from a total 34 lesions (94.1%) in the MWA were completely ablated after single session, but this was not statistically significant difference (P=0.673). These results are similar to that were reported by Lu *et al*. (16), Qian *et al*. (24), Zhang *et al*. (19), Ding *et al*. (18), Abdelaziz *et al*. (20), Vogl *et al*. (25), Lee *et al*. (22) and Violi *et al*. (15) who reported no statistically significant differences between RFA and MWA regarding achievement of complete tumor ablation, ranging from 83.4% to 98.5%. On the other hand, the number of sessions per nodule was significantly smaller in the RFA group than MWA group in Shibata *et al*. (14) study, but this study was performed on 1999 and 2000 using the old version of microwave apparatus. On contrary, Xu *et al*. (23) reported significantly higher complete ablation in the MWA group.

In current study, local tumor recurrence didn't differ statistically between both groups. At the 6th month follow up, local recurrence was 0% (0/26) at the RFA group while it was 8% (2/24) at the MWA group (P=0.225). At 1-year follow up, local recurrence was 9% (2/22) in both groups. The Kaplan-Meier estimate for local tumor recurrence free survival at 1-year was 90.9% at RFA group and was 92.3% at MWA group with no statistically significant difference (P=0.932).

These results regarding local tumor recurrence were in concordance to that reported by Xu *et al*. (23), Lu *et al*. (16), Qian *et al*. (24), Zhang *et al*. (19), Vogl *et al*. (25), Lee *et al*. (22) and Violi *et al*. (15) who also found no statistically significant differences between both procedures. On the other hand, Abelaziz *et al*. (20) and Potretzke *et al*. (21) reported significantly lower local tumor recurrence with usage of MWA for HCC treatment. On the contrary, the study performed by Shibata *et al*. (14) which was done using the old generation of MWA apparatus showed significantly higher local tumor recurrence. Also, Ding *et al*. (18) reported higher local recurrence after MWA in their study, but they explained this by the larger sizes of lesions in the MWA group compared to the RFA group. A meta-analysis done by Facciorusso *et al*. (26) which included seven studies didn't find any significant difference between both techniques regarding local tumor recurrence rates.

There was no statistically significant difference regarding development of *de novo* HCC lesions in both groups. This was in concordance with results published by Lu *et al*. (16), Abdelaziz *et al*. (20), Lee *et al*. (22) and Violi *et al*. (15).

In our study, there were no significant differences between both groups regarding Child-Pugh score at 3, 6 and 12 months of follow up. To our knowledge, no other authors compared the two techniques regarding these parameters.

Regarding negative impacts, there were no statistically significant differences between both techniques in our study. One subject in the MWA group experienced bleeding from the tumor that needed embolization. Another patient in the MWA group experienced an attack of hematemesis from esophageal varices the day after the procedure. Regarding 30-day mortality, 2 patients died within 30 days after MWA versus no one died within the same period after

RFA, but this was also statistically insignificant. This was in concordance with the results of the meta-analysis done by Facciorusso *et al*. (26) that showed higher rate of major complications after MWA, like hemothorax, intrahepatic hematoma and intraperitoneal hemorrhage requiring blood transfusion, but was also not statistically significant finding. This comes against the early fears of higher complications after MWA due to broader ablation zones.

The mortality rate at 1 year was 15.3% in the RFA group (4 out of 26) *vs.* 14.8% in the MWA group (4 out of 27). This was in concordance with previous studies which showed generally comparable survival rates after both techniques.

Limitations of our study include the small sample size but we had decided to consider all patients referred to our unit during a whole period of 6 months to be included in this study. We randomized study subjects using simple randomization. Tumor size as a covariate that can influence the recurrent rate makes stratified randomization to be theoretically more appropriate, but this was not possible in our study as subjects were enrolled one at a time and so the baseline tumor sizes were not available before assignment. Although we used the simple method of randomization, there was no statistically significant difference between both groups regarding number of subjects with tumors less than 3 cm and those with tumors that measure 3 cm or more. Another limitation is that we didn't analyze anatomical characteristics of tumors like location and proximity to blood vessels due to small sample size. No previous clinical study analyzed this issue in particular. This should be a point for future research.

Strengths of our study include that it is a randomized controlled trial unlike most of other studies that were retrospective. Shibata *et al*. (14) study was a randomized controlled one but this was done using the first generation MWA generator. Qian *et al*. (24) was also a randomized controlled trial but it was for a short period of follow up (5.5 months). Our study is the most recent randomized controlled trial comparing. To our knowledge, we are the only study that compared the changes in Child-Pugh score over time after both techniques.

In conclusion, RFA and MWA are comparable techniques for HCC treatment. Our group couldn't prove the superiority of MWA over RFA.

Acknowledgements

Authors acknowledge Dr. Mona H. Ashry, Assistant professor of Public Health, Alexandria University and Dr. Dalia K. El Deeb, lecturer of Public health, Alexandria University for their assistance in statistical analysis of the data. In addition, we acknowledge Ahmed Smman, MBBCh. for his technical support.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was conducted in accordance with the provisions of the Declaration of Helsinki, as revised in 2013, and Good Clinical Practice guidelines. It was approved by the Ethics Committee of Faculty of Medicine, Alexandria University (IRB No. 00007555). An informed consent was obtained from all subjects included in the study.

References

1. Galle PR. Management of Liver Cancer. Dig Dis 2016;34:438-9.
2. Kudo M. Recent Trends in the Management of Hepatocellular Carcinoma with Special Emphasis on Treatment with Regorafenib and Immune Checkpoint Inhibitors. Dig Dis 2016;34:714-30.
3. Han K, Kim JH, Ko GY, et al. Treatment of hepatocellular carcinoma with portal venous tumor thrombosis: A comprehensive review. World J Gastroenterol 2016;22:407-16.
4. Yu SJ. A concise review of updated guidelines regarding the management of hepatocellular carcinoma around the world: 2010-2016. Clin Mol Hepatol 2016;22:7-17.
5. Shi Y, Zhai B. A Recent Advance in Image-Guided Locoregional Therapy for Hepatocellular Carcinoma. Gastrointest Tumors 2016;3:90-102.
6. Facciorusso A, Serviddio G, Muscatiello N. Local ablative treatments for hepatocellular carcinoma: An updated review. World J Gastrointest Pharmacol Ther 2016;7:477-89.
7. Best J, Schotten C, Theysohn JM, et al. Novel implications in the treatment of hepatocellular carcinoma. Ann Gastroenterol 2017;30:23-32.
8. Poulou LS, Botsa E, Thanou I, et al. Percutaneous microwave ablation vs radiofrequency ablation in the treatment of hepatocellular carcinoma. World J Hepatol 2015;7:1054-63.
9. Lu DSK, Raman SS, Limanond P, et al. Influence of

Large Peritumoral Vessels on Outcome of Radiofrequency Ablation of Liver Tumors. J Vasc Interv Radiol 2003;14:1267-74.
10. Brace CL. Radiofrequency and Microwave Ablation of the Liver, Lung, Kidney, and Bone: What Are the Differences? Curr Probl Diagn Radiol 2009;38:135-43.
11. Poggi G, Tosoratti N, Montagna B, et al. Microwave ablation of hepatocellular carcinoma. World J Hepatol 2015;7:2578-89.
12. Mitchell DG, Bruix J, Sherman M, et al. LI-RADS (Liver Imaging Reporting and Data System): summary, discussion, and consensus of the LI-RADS Management Working Group and future directions. Hepatology 2015;61:1056-65.
13. Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis 2010;30:52-60.
14. Shibata T, Iimuro Y, Yamamoto Y, et al. Small hepatocellular carcinoma: comparison of radio-frequency ablation and percutaneous microwave coagulation therapy. Radiology 2002;223:331-7.
15. Vietti Violi N, Duran R, Guiu B, et al. Efficacy of microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma in patients with chronic liver disease: a randomised controlled phase 2 trial. Lancet Gastroenterol Hepatol 2018;3:317-25.
16. Lu MD, Xu HX, Xie XY, et al. Percutaneous microwave and radiofrequency ablation for hepatocellular carcinoma: a retrospective comparative study. J Gastroenterol 2005;40:1054-60.
17. Ohmoto K, Yoshioka N, Tomiyama Y, et al. Radiofrequency ablation versus percutaneous microwave coagulation therapy for small hepatocellular carcinomas: a retrospective comparative study. Hepatogastroenterology 2007;54:985-9.
18. Ding J, Jing X, Liu J, et al. Comparison of two different thermal techniques for the treatment of hepatocellular carcinoma. Eur J Radiol 2013;82:1379-84.
19. Zhang L, Wang N, Shen Q, et al. Therapeutic efficacy of percutaneous radiofrequency ablation versus microwave ablation for hepatocellular carcinoma. PLoS One 2013;8:e76119.
20. Abdelaziz A, Elbaz T, Shousha HI, et al. Efficacy and survival analysis of percutaneous radiofrequency versus microwave ablation for hepatocellular carcinoma: an Egyptian multidisciplinary clinic experience. Surg Endosc 2014;28:3429-34.
21. Potretzke TA, Ziemlewicz TJ, Hinshaw JL, et al. Microwave versus radiofrequency ablation treatment for hepatocellular carcinoma: a comparison of efficacy at a single center. J Vasc Interv Radiol 2016;27:631-8.
22. Lee KF, Wong J, Hui JW, et al. Long-term outcomes of microwave versus radiofrequency ablation for hepatocellular carcinoma by surgical approach: A retrospective comparative study. Asian J Surg 2017;40:301-8.
23. Xu HX, Xie XY, Lu MD, et al. Ultrasound-guided percutaneous thermal ablation of hepatocellular carcinoma using microwave and radiofrequency ablation. Clin Radiol 2004;59:53-61.
24. Qian GJ, Wang N, Shen Q, et al. Efficacy of microwave versus radiofrequency ablation for treatment of small hepatocellular carcinoma: experimental and clinical studies. Eur Radiol 2012;22:1983-90.
25. Vogl TJ, Farshid P, Naguib NN, et al. Ablation therapy of hepatocellular carcinoma: a comparative study between radiofrequency and microwave ablation. Abdom Imaging 2015;40:1829-37.
26. Facciorusso A, Di Maso M, Muscatiello N. Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: A systematic review and meta-analysis. Int J Hyperthermia 2016;32:339-44.

Cite this article as: Kamal A, Elmoety AA, Rostom YA, Shater MS, Lashen SA. Percutaneous radiofrequency versus microwave ablation for management of hepatocellular carcinoma: a randomized controlled trial. J Gastrointest Oncol 2019;10(3):562-571. doi: 10.21037/jgo.2019.01.34

