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PERCUTANEOUS RADIOFREQUENCY VERSUS MICROWAVE ABLATION FOR MANAGEMENT OF HEPATOCELLULAR CARCINOMA

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ABSTRACT **BACKGROUND:** Cirrhotic patients with small HCC lesions may be treated with ablative techniques like RFA and MWA. This study aims to compare these two techniques in management of HCC based on local tumour recurrence, association of complications and duration for complete tumour ablation.

METHODS: Study population included 88 cirrhotic patients meeting the inclusion criteria posted for RFA or MWA treatment between October 2019 - 2021. Patient demographic, laboratory investigations, radiological characteristics of tumor (based on a triphasic preablative(4 weeks before ablation) CECT / MRI) and mean duration of follow up were recorded. Outcome was analysed based on technical success, tumour free survival and local tumour progression. Categorical variables were expressed using frequency and percentage; continuous variables using mean, standard deviation, median(25^{th} and 75^{th} percentile). Chi square test, student t test, Mann Whitney u test, Kaplan Meier analysis and log rank test were used for analysis. A p value of <0.05 was considered statistically significant.

RESULTS: Technical success in both groups were comparable with no statistical significance. The mean tumor free survival in RFA group(8.1+/-0.55 months) was significantly longer compared to MWA group(5.8+/-0.59 months) ($p = 0.01$). There was higher rate of LTP in MWA group with borderline statistical significance ($p = 0.056$).

CONCLUSION: Higher rate of LTP was noted in MWA group compared to RFA group with borderline statistical significance. Tumour free survival was longer in RFA group than MWA group. Post procedure complications in both groups were comparable.

KEYWORDS : Radiofrequency ablation(RFA), Microwave ablation(MWA), Hepatocellular carcinoma(HCC), Liver cirrhosis.

INTRODUCTION:

Various treatment options have been explored for the treatment of hepatocellular carcinoma among which ablative techniques are considered as an effective means with curative outcomes especially in patients with pre-existing cirrhosis and small HCC lesions (<3cm in diameter)(1). Among the ablative techniques, radiofrequency ablation is based on heating of tissue due to circulation of alternating electric current in target tissues. This is related to the water content of tissues and hence for temperatures above 100^{0}C, dehydration and carbonisation of tissues prevents further heating. In addition, the heat sinking effects of RFA renders it less effective(2). In contrast, microwave ablation is based on the dielectric effect that overcomes all these barriers to complete tissue ablation(3). However, sufficient data is not available in current literature to compare the efficacy of both these modalities in terms of tumor ablation time, survival rate and tumor recurrence. In this study, we are comparing the efficacy of RFA and MWA in management of HCC using a prospective study.

METHODS:

Selection And Description Of Study Participants:

Study setting : Department of Radiology, Amrita Institute of Medical Sciences

Duration of study : For two years duration starting from October 2019 to 2021 after obtaining approval from the thesis protocol review committee (Scientific, Ethical & Financial), Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala.

Study Design : Observational study - Cohort

Study population: Patients with cirrhosis posted to undergo either RFA or MWA treatment at Amrita Institute of Medical Sciences during the study period.

Inclusion Criteria :

- Patients with chronic liver disease with Child-Pugh score A or B.
- Hepatocellular carcinoma with lesions of 4 cm or smaller with up to three nodules.
- A diagnosis of hepatocellular carcinoma as per the AASLD criteria with LIRADS 5 score.

Exclusion Criteria :

- Patients with chronic liver disease with Child-Pugh score C.
- Evidence of extrahepatic disease or vascular invasion.
- Liver decompensation (particularly in presence of ascites).
- Lesions > 4 cm and more than three lesions.
- Severe pulmonary or cardiac disease. Refractory coagulopathy.

Sample size: Based on the proportion comparison of the efficacy of radiofrequency ablation (70%)and microwave ablation (40%) in management of hepatocellular carcinoma based on local tumour recurrence observed from the pilot study conducted in 10 samples in each group and with 80% power and 95% confidence the minimum sample sizes comes to 42 in each group, totalling to 84.

Technical Information:

OBJECTIVES:

Primary Objective:

To compare the efficacy of radiofrequency ablation and microwave ablation in management of hepatocellular carcinoma based on local tumor recurrence.

Secondary Objective:

To study the association of complications and duration for complete tumor ablation in patients with hepatocellular carcinoma treated with radiofrequency ablation and microwave ablation.

Technique:

The liver protocol included an abdominal MDCT with unenhanced and contrast-enhanced phases (arterial phase 25s after contrast administration and venous phase 70s after contrast administration) or a contrast enhanced MRI. The quantity of contrast was based on the patient's body weight. The following characteristics of the lesions were reported from the pre-intervention CT/MRI : lesion size (defined as the largest lesion diameter), location (lobar or segmental, nearness to capsule or viscera).Counselling of patients was done before the procedure regarding the advantages and disadvantages of both ablative techniques. Consensus about the ablative technique was arrived after

discussion with the patient and clinician. In accordance with standard procedure guidelines, both RFA and MWA were done percutaneously under ultrasound guidance (when the lesion was visible by ultrasound) or MDCT guidance. All the procedures were performed by experienced radiologists under conscious sedation and local anaesthesia (vitals were monitored during the procedure). Under USG guidance, ablation zone was closely monitored. Adequate ablation was defined as the echogenic cloud completely covering the tumor area along with a rim of 5-10mm of adjacent normal liver parenchyma. In case the ablation was considered incomplete, repositioning of needle and re ablation was done. While needle removal, the tract was ablated to avoid complications such as bleeding from hepatic capsular surface and seeding of tumor. The duration for complete tumor ablation was also noted. Screening of the patients was done immediately after the procedure with ultrasound to rule out complications. Post procedure the patients' vitals were monitored for approximately two hours.

Details of data to be collected:

Radiological assessment of the ablation procedure was done by USG and a CECT taken immediately post procedure and by triphasic CT/MRI abdomen with contrast done at 4 weeks to 3 months, at 6 months and upto 1year after ablation. Complete tumor ablation/ response to treatment was denoted by complete absence of any enhancing tumor residue adjacent to the ablation zone. In case of any residual unablated tumor, an additional ablation procedure was done with the same technique. For these patients, follow-up started only when the lesion was considered completely ablated. Additional radiological assessments were done at 1 month after the additional procedure to identify local tumor. The date of tumor progression was recorded to ascertain local tumor free survival.

Statistics:

Statistical analysis was performed using IBM SPSS version 20.0 software. Categorical variables were expressed using frequency and percentage. Continuous variables were presented using mean, standard deviation, median(25^{th} and 75^{th} percentile). To test the statistical significance of the difference in the proportion of categorical variables between two groups, Chi square test was used. To test the statistical significance of the difference in the mean and median of continuous variables between two groups, student t test was used for normal data and Mann Whitney u test was used for skewed data. To find the tumor free survival time, Kaplan Meier analysis was used and log rank test for multiple comparison. A p value of <0.05 was considered to be statistically significant.

RESULTS :

In our study 44 patients with 50 nodules (48.5%) were treated with RFA and 44 patients with 53 nodules (51.5%) were treated with MWA.

The baseline characteristics(age, sex, Child score, MELD score, blood parameters, Diabetic status) between both groups showed no significant statistical significance. The mean age of the patients in RFA group was 67.5+/-9.6 and in MWA group was 66.5+/-9.4 ($p = 0.632$). 9 out of 44 patients in RFA group were females (20.45%) and 4 out of 44 patients were females in MWA group(9.09%) ($p = 0.229$). 5 out of 44 patients in RFA group fell under Child category B(11.4%) and 7 out of 44 patients in MWA group fell under Child category B(15.9%) ($p = 0.756$). The median(IQR) MELD score of the patients in RFA group was 10.0(9-16.25) and in MWA group was 12.0(8.3-21.25) ($p = 0.517$). 27 out of 44 patients in RFA group were diabetic(61.4%) and 31 out of 44 patients were diabetic in MWA group(70.5%) ($p = 0.368$).

The comparison of the distribution of serum alphafetoprotein levels, INR, creatinine, transaminases, platelets and total bilirubin levels in patients between the 2 groups was not found to be statistically significant.

The location of tumor location based on depth from surface (exophytic lesions and capsular involvement) and proximity to major organs were studied. Enhancement and washout pattern of the tumors were also compared across the groups. These parameters showed no statistically significant differences. The median(IQR) tumor size of the patients in RFA group was 2.10(1.80-2.60) cm and in MWA group was 2.80(1.95-3.10)cm ($p = 0.063$).

The comparison of the median complete tumor ablation time in both groups was found to be statistically significant ($p = 0.002$) with lesser duration in microwave ablation group (8.0(5.0-10.0)minutes) compared to RFA group(10.0(6.0-12.0) minutes).

There was no statistically significant difference in development of complications in both the groups($p = 0.456$).

Technical success of 96% was obtained in RFA group and 96.3% in MWA group. Among the 53 nodules in MWA group and 50 nodules in RFA group, residue along the margins suggestive of technical failure was noted in 2 nodules in RFA and 2 nodules in MWA groups

Both groups were followed up for a period of one year. The overall tumor free survival was 6.9 +/-0.42 months. The mean tumor free survival was 8.1+/-0.55 months in RFA group and 5.8+/-0.59 months in MWA group with statistically significant difference ($p = 0.01$).

Out of the 48 tumors that were treated with RFA, LTP was seen in 27 tumors(56.3%) and in 38 out of 51 tumors(74.5%) in MWA group(table 5.15). There was higher rate of local tumor progression in MWA group with borderline statistical significance ($p = 0.056$).

DISCUSSION:

Among the non surgical modes of treatment for HCC, percutaneous ablation of tumor is an important technique. In practice, RFA and MWA are the most common modes of ablation with advantages and disadvantages unique to each. RF ablation makes use of alternating electrical current in the radiofrequency range that is conducted to the tumor via electrodes. The electrical current oscillates between the electrodes through the ion channels in tissues, which are imperfect conductors of electricity and as a result, flow of current leads to friction and agitation at ionic level and heat generation(2). This produces heating effects that leads to coagulative necrosis and thus therapeutic effect. However the heat sink effects and carbonization of tissue limit the effectiveness of RF ablation. As against this, MWA has emerged as a superior modality of ablation that overcomes these disadvantages of RFA. MWA makes use of dielectric effect that produces a homogenous field of ablation with larger volume of ablation and shorter time for ablation(3). Demerit of MWA includes quick heating of tissues which can result in injury to critical structures in close proximity to the ablated zone. Microwave ablation in general was considered superior with decreased duration of procedure that translates to more patient comfort.

Usually it is hypothesized that MWA is superior to RFA with reduced ablation time, larger zones of ablation with lesser heat sink effects. However, contradictory outcomes have been described in literature. Potretzke et al in their study concluded that lower rates of LTP was observed after MW ablation compared to RFA whereas Qian et al have found no significant difference in local tumor progression in lesions treated with MWA and RFA in HCC lesions less than 3 cm diameter(4,5).

The study by Bouda et al showed lower LTP after MWA compared to RFA regardless of tumor size and vascular contact(6). In contrast Violi et al in their study concluded that MWA was not superior to RFA and that proportion of lesions with local tumor progression at 2 years of follow-up was low with both percutaneous methods(7).

In our study, we have compared the technical success of RFA and MWA, local tumor progression and tumor free survival in tumors less than 4 cm in size.

Both the groups in our study were comparable in terms of age, gender, tumor size, Child Pugh score, MELD score and lab parameters with no statistically significant differences.

Technical success in both groups were comparable with 96.2% in MWA and 96% in RFA groups($p = 1.00$). A meta-analysis by Tan et al revealed that RFA and MWA have comparable technical success(8). The findings in our study are in agreement with this study.

The comparison of the median tumor ablation time in both groups was found to be statistically significant ($p = 0.002$) with lesser duration in microwave ablation group(8.0(5.0-10.0)minutes) compared to RFA group(10.0(6.0-12.0) minutes). This is concordant with the study by Kamal et al which reported shorter ablation time with MWA(4.41 minutes) compared to RFA(14.21 minutes) with statistically significant difference($p < 0.001$)(9). Since MWA uses electromagnetic field to create a rapid and homogenous zone of ablation and does not rely on electrical current flow, it requires lesser time for ablation.

Both groups were followed up for a time period of at least one year.

LTP was noted in 27 out of 48 tumors(56.3%) in RFA group and 38 out of 51 tumors (74.5%) in microwave ablation group with borderline statistical significance (p = 0.056). Glassberg et al in their systematic review and meta-analysis demonstrated significant reduction in LTP by 30% with MWA versus RFA (RR=0.70; P=0.02) in tumors more than or equal to 2.5 cm(10). The contradictory results maybe explained by the fact that in their study, lower LTP was observed in MWA compared with RFA when tumor sizes were more than or equal to 2.5cm. When the tumor size was smaller, there was no demonstrable difference in the local tumor progression. Higher LTP in MWA can be attributed to larger median(IQR) size of tumor in MWA (2.80(1.95-3.10)cm) compared to RFA(2.10(1.80-2.60)cm) group.

Mean tumor free survival in RFA group(8.1+/-0.55 months) was observed to be more than microwave ablation(5.8+/-0.59 months). This was found to be statistically significant (p = 0.01). Lower TFS could be attributed to the under ablation of lesion by various MW systems used in our study, larger tumor size compared to RFA and initial learning curve required for the performing radiologist.

Two major complications were observed in the overall population as per the criteria dictated by the society of interventional radiology. One patient in RFA group developed contained perforation of the hepatic flexure and one patient in MWA group developed pneumothorax(SIR class D)(11).

Minor complications such as mild transaminitis, fever and mild hypotension(SIR class B) were observed in three patients in RFA group that were managed conservatively. In patients who underwent MWA, five patients developed mild transaminitis(SIR class B), one patient developed mild renal dysfunction(SIR class B) and another developed abdominal pain and distension(SIR class B). All these patients were conservatively managed.

There were no statistically significant differences in the development of complications in MWA(17%) and RFA(10%) groups(p = 0.456).

Though the large volume of tissue ablated in microwave ablation is thought to be associated with injury to adjacent structures such as vessels and bile ducts, our study demonstrated no such complications.

Limitations:

There are some limitations in our study principally due to small sample size, single centre data and due to shorter time period of study. Overall survival was also not analysed owing to short duration of study. Further studies with larger study population and longer period of follow up are required to better validate the outcomes.

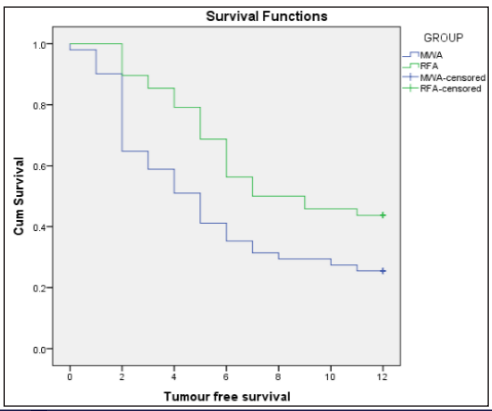
CONCLUSION:

In conclusion, there was higher rate of local tumor progression in MWA group compared to RFA group with borderline statistical significance. The tumor free survival was significantly longer in patients who underwent RFA compared to those in MWA. Post procedure complications in RFA group and MWA group had no statistically significant difference.

Tables & Figures:

Table 1 & Figure 1: Impact of RFA and MWA groups on tumor free survival

Variable	RFA n=48 (months)	MWA n=51 (months)	p value
TFS	8.1+/-0.55	5.8+/-0.59	0.010



The mean tumor free survival was 8.1+/-0.55 months in RFA group and 5.8+/-0.59 months in MWA group with statistically significant difference (p = 0.01)

Table 2 : Comparison Of Local Tumor Progression In Both Groups

Groups	LTP		p value
	Positive	Negative	
RFA n=48 (%)	27 (56.3)	21 (43.8)	0.056
MWA n=51 (%)	38 (74.5)	13 (25.5)	

Out of the 48 tumors that were treated with RFA, LTP was seen in 27 tumors(56.3%) and in 38 out of 51 tumors(74.5%) in MWA group. There was higher rate of local tumor progression in MWA group with borderline statistical significance (p = 0.056).

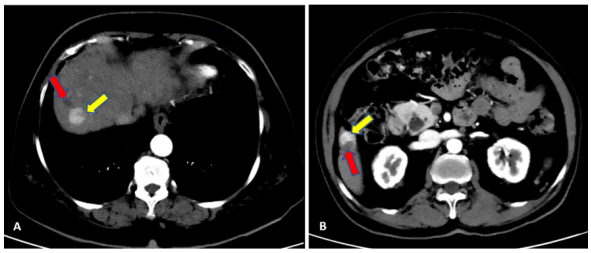


Figure 2:
(A)Post RFA CECT at two months after ablation showing a recurrent lesion(yellow arrow) at the margins of the post RFA ablated lesion (seen as a hypodense area(red arrow)) in segment VII/VIII of liver and (B)Post MWA CECT at two months after ablation showing a recurrent lesion(yellow arrow) at the margins of the post RFA ablated lesion (seen as a hypodense area(red arrow)) in segment VI of liver.

REFERENCES:

1. Chen MS, Li JQ, Zheng Y, Guo RP, Liang HH, Zhang YQ, Lin XJ, Lau WY. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Annals of surgery. 2006 Mar;243(3):321.
2. Lencioni R, Crocetti L. Radiofrequency ablation of liver cancer. Techniques in vascular and interventional radiology. 2007 Mar 1;10(1):38-46.
3. Gala KB, Shetty NS, Patel P, Kulkarni SS. Microwave ablation: How we do it?. The Indian Journal of Radiology & Imaging. 2020 Apr;30(2):206.
4. Potretzke TA, Ziemlewicz TJ, Hinshaw JL, Lubner MG, Wells SA, Brace CL. Microwave versus radiofrequency ablation treatment for hepatocellular carcinoma: A comparison of efficacy at a single center. J Vasc Interv Radiol. 2016;27:631–8. doi: 10.1016/j.jvir.2016.01.136. et al.
5. Qian GJ, Wang N, Shen Q, Sheng YH, Zhao JQ, Kuang M, Liu GJ, Wu MC. Efficacy of microwave versus radiofrequency ablation for treatment of small hepatocellular carcinoma: experimental and clinical studies. Eur Radiol. 2012;22:1983–1990.
6. Bouda D, Barrau V, Raynaud L, et al. Factors associated with tumor progression after percutaneous ablation of hepatocellular carcinoma: comparison between monopolar radiofrequency and microwaves. Results of a propensity score matching analysis. Cardiovasc Intervent Radiol. 2020.
7. 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. 10.1016/S2468-1253(18)30029-3.
8. Tan W, Deng Q, Lin S, Wang Y, Xu G. Comparison of microwave ablation and radiofrequency ablation for hepatocellular carcinoma: a systematic review and meta-analysis. Int J Hyperthermia 2019;36(1):264–272.
9. Kamal A, Elmoety AAA, Rostom YAM, Shater MS, Lashen SA. Percutaneous radiofrequency versus microwave ablation for management of hepatocellular carcinoma: a randomized controlled trial. J Gastrointest Oncol. 2019;10:562–71. doi: 10.21037/jgo.2019.01.34.
10. B. Glassberg, S. Ghosh, J.W. Clymer, R.A. Qadeer, N.C. Ferko, B. Sadeghirad, et al. Microwave ablation compared with radiofrequency ablation for treatment of hepatocellular carcinoma and liver metastases: a systematic review and meta-analysis. Onco Targets Ther, 12 (2019), pp. 6407-6438.
11. Bruix J, Sherman M on behalf of the American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. Hepatology. 2011;53:1020–2.