Section: Radiology

Original Research Article

THE ROLE OF IMAGE-GUIDED RADIOFREQUENCY ABLATION IN PRIMARY AND METASTATIC LIVER TUMORS AND ITS EARLY TREATMENT RESPONSE ASSESSMENT

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Abstract

Background: Radiofrequency ablation (RFA) has shown superior anticancer effects and greater survival benefits. Thus, in the present study, we have assessed the role of image-guided RFA in primary and metastatic liver tumors and its early treatment response. **Materials and Methods:** We have included 25 patients in this study. Baseline imaging (diagnostics USG, contrast-enhanced CT (CECT) or MRI) was performed before RFA is essential to assess tumor size and location and the relationship of the tumor to adjacent structures. For the RFA procedure, we have used USG, CT, Maxio-assisted CT guidance, and intraoperative RFA depending on the tumor size and location. **Result:** Out of 25, 16 were primary, and nine were secondary. Among 25 patients, seven were treated under USG guidance, seven under CT guidance, six under the Maxio-guided robotic needle placement system, and five with the open RFA technique. Among the size criteria, 16 patients had at least one lesion over 3 cm, and nine had lesions less than 3cm. Among nine patients with lesions more than 3 cm, one patient had unsuccessful ablation, and eight patients were successful ablation. One patient had unsuccessful ablation because the lesion was near (5mm) the major vessels. In this study, size criteria showed significant statistical difference with less than 3 cm lesion showed complete ablation. **Conclusion:** RFA is the better locoregional treatment option for small primary and secondary liver tumours. RFA can compete with open surgical resection as a first-line treatment.

INTRODUCTION

Hepatic resection and transplantation are the only curative options for patients with liver metastases or primary liver tumors. Unfortunately, resection is possible in only about 20% of patients. Most hepatic malignancies are surgically inaccessible or are associated with a large tumor burden or inadequate hepatic reserve. A shortage of donor organs limits liver transplantation for hepatocellular carcinoma (HCC). Patients with unresectable diseases may be candidates for systemic therapy, local ablative techniques, or chemoembolization.[1-4]

The Food and Drug Administration (FDA) approved radiofrequency ablation (RFA) for generic tissue ablation in 1996 and for ablation of unresectable hepatic metastases in 2000. RFA destroys tumors by generating heat within a lesion using a high-frequency alternating current. As tissue temperature increases above 45° C, loss of cellular structure and protein denaturation result in tumor cell death.[5,6] Long-term survival data have been reported in HCC and colorectal, hepatic metastases. A recently published position statement by the Society of Interventional Radiology describes four categories of patients who are candidates for RFA those with inadequate liver function, comorbid conditions, anatomic distribution, and local tumor control as a bridge to transplantation.[5-7] Therefore, in the present study, we have assessed the role of image-guided radiofrequency ablation in primary and metastatic liver tumors and its early treatment response.

MATERIALS AND METHODS

We have enrolled 30 patients for this study. Among 30 patients, two patients did not come for follow-up after RFA, 1 Patient was not willing to further procedure, and one patient died before the RFA

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procedure because of cardiac complications. So, this study proceeded with 25 patients.

Inclusion Criteria

Patients aged between 20 and 80 years with liver tumors who will fit the following criteria, HCC at an early stage, Inoperable primary liver tumor, a patient who cannot undergo general anaesthesia, liver metastasis, recurrent and progressive lesions, and patients with liver tumors who are waiting for transplantation were included.

Exclusion Criteria

Patients who are not willing to the procedure, patients who do not fulfil the above-said criteria, patients with Significant extrahepatic disease, patients with Child class C cirrhosis or active infection, patients with Decompensated liver disease, patients with liver Tumors that occupy more than 40% of liver volume, patient with Primary liver lesion larger than 5cm, patients with Metastatic liver lesions larger than 3cm, and patients with several liver lesions of more than three were excluded.

Baseline imaging performed before RFA is essential to assess tumor size and location and the relationship of the tumor to adjacent structures. Diagnostic USG (ALOKA CO LTD, Mure, Mitaka-shi, TOKYO, JAPAN.), contrast-enhanced CT (CECT) or MRI (SIEMENS Shanghai Medical EQUIPMENT Ltd, Shanghai, CHINA) were used for treatment planning.

For the RFA procedure, we have used various image guidance such as USG, CT, Maxio-assisted CT guidance (stereotactic navigation), and intraoperative RFA, depending on the tumor size and location. Imaging after RFA with multiphase CECT, dynamic contrast-enhanced MRI, and occasionally F-FDG (FDG) PET/CT is integral to post-ablation surveillance, depending on the patient's need and availability of the resources.

RFA was done using the COVIDIEN Cool tip RF Ablation system. It consists of an RFA generator (RFA GEN), RF ablation pump (RFA PUMP), and RFA electrode (COOL TIP RF Ablation system electrode E series) Covidien Ireland Limited, IDA, business & technology Park, Tullamore, USA. We have used RFA probe RFA1530 15 CM length and 3cm tip exposure single electrode kit.

We enrolled five patients for intraoperative RFA as per the reference from gastroenterologists. All the lesions are bi-lobar, larger than the size criteria for percutaneous RFA. IRFA was done under USG guidance using Aloka Machine (Aloka CO LTD. Mure mitaka-shi, Tokyo, Japan) by directly keeping the probe over the liver under strict aseptic precaution.

Post RFA Imaging

Imaging Modalities

Imaging after RFA with multiphase CECT, dynamic contrast-enhanced MRI, and occasionally F-FDG (FDG) PET/CT (SIEMENS Shanghai Medical Equipment Ltd, Shanghai, CHINA) forms an integral part of post-ablation surveillance post-ablation follow-up will be done 1,3,6 month after RFA.

Assessments of parameters:

Detailed evaluations of post-RFA images were done on the following basis calculating tumor index volume. The largest diameter of the tumor in 3 orthogonal planes was measured. The formula measures the volume of the tumor; 1/6xaxbxc. Ablation zone=include a 1cm margin surrounding the tumor. Ablative marginal volume (AMV)= Ablation Zone –Tumor Volume.

Statistical analysis was done using SPSS software (V.19 IBM USA). Since data was qualitative, it was denoted in frequency and percentage. The chi-square test was used for comparison between the groups. A p-value was less than 0.05 was considered to be statistically significant.

RESULTS

Total of twenty-five patients enrolled for Radio Frequency ablation. Out of 25, 16 were primary tumours, and 9 were Secondary Tumours. Among 25 patients, seven were treated under USG guidance, seven under CT guidance, six under the MAXIO-guided robotic needle placement system, and five with the open RFA technique. Among the size criteria, 16 patients had at least one lesion over 3 cm, and nine had lesions less than 3cm. The final result for the ablation was obtained by imaging at 1,3, and 6 months. Complete ablation was considered if the ablation site developed total necrosis without any residual or new enhancing lesion at the ablation site. All the patients were followed up for a median period of 8 months.

Among nine patients with lesions more than 3 cm, one patient had unsuccessful ablation, and eight patients were successful ablation. Even if the size is more than three cm, the lesion was successfully ablated because the procedure was done under MAXIO-guided needle positioning and OPEN RFA technique. One patient had unsuccessful ablation because the lesion was near (5mm) the major vessels. In this study, size criteria showed significant statistical difference with less than 3 cm lesion showed complete ablation [Table 1].

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Table 1: Descriptive analysis of the type of lesion, size, and image modalities in the study population

Type of lesion	Outcome [N (%)]			p-value
	SA	UA	Total	
Primary	14 (87.50%)	2 (12.50%)	16 (100%)	0.073
Secondary	5 (55.60%)	4 (44.40%)	9 (100%)	
Type of lesion	Death (Mets)	Survived	Total	
1	1 (6.30%)	15 (93.80%)	16 (100%)	0.022
2	4 (44.40%)	5 (55.60%)	9 (100%)	
Size	SA	UA	Total	
<3 cm	8 (88.90%)	1 (11.10%)	9 (100%)	0.258
>3cm	11 (68.80%)	5 (31.30%)	16 (100%)	
	Death (Mets)	Survived	Total	
<3 cm	2 (22.20%)	7 (77.80%)	9 (100%)	0.835
>3cm	3 (18.80%)	13 (81.30%)	16 (100%)	
Image modality	SA	UA	Total	
USG	4 (57.10%)	3 (42.90%)	7 (100%)	0.583
CT	6 (85.70%)	1 (14.30%)	7 (100%)	
SRFA	5 (83.30%)	1 (16.70%)	6 (100%)	
IRFA	4 (80.00%)	1 (20.00%)	5 (100%)	
Image modality	Death (Mets)	Survived	Total	
USG	1 (14.30%)	6 (85.70%)	7 (100%)	0.6654
CT	1 (14.30%)	6 (85.70%)	7 (100%)	
SRFA	1 (16.70%)	5 (83.30%)	6 (100%)	
IRFA	2 (40.00%)	3 (60.00%)	5 (100%)	

Seven patients were treated under USG guidance; among the 7, 4 were successfully ablated, and three were unsuccessful. The difficulty we found in USG Guidance was patient motion after needle positioning, lesions in the difficult location (Close to the diaphragm, bowel loops, and blood vessels), and Echo genericity (Iso echoic lesions difficult to locate in USG). Among the three unsuccessful, one was near a blood vessel, one was near the dome of the diaphragm, and all three patients had sizes of more than 3 cm of the lesion. We encountered one patient with hemothorax.

Under CT guidance, we did seven ablations; among 7, 6 were successful one unsuccessful. Among six successful ablations, we ablated one lesion with more than 5 cm by overlapping ablation. One lesion was unsuccessful because the lesion was more than 3 in number. Among the three, one is more than 3 cm in size. We encountered one patient with pneumothorax.

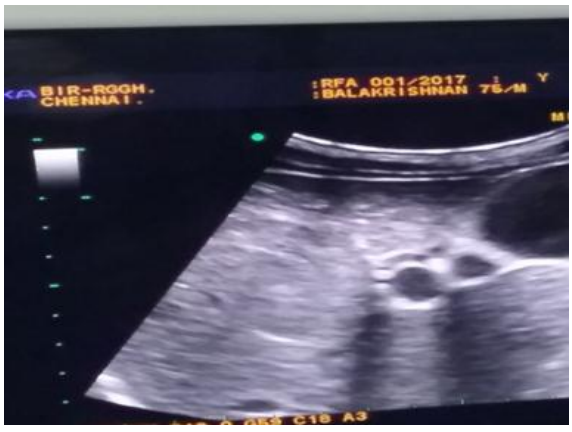
We did six patients under MAXIO robotic guided needle positioning system. Among the six, five were successful; one was unsuccessful because the lesion was very close to the major blood vessel. Hence it showed HEAT SINK EFFECT. Among the five successful ablations, four lesions were more than 3 cm. Because of the exact needle positioning and respiratory control under MAXIO guidance, we ablated successfully with an ablative margin of 0.5 cm. No complications were encountered.

We did five patients under the intraoperative RFA technique. Among the 5,4 were successful, one was unsuccessful, and that patient showed a recurrent lesion at the ablation site. Among the four successful in 3 patients were lesions near the major blood vessel. But they were ablated completely during laparotomy by clamping the portal triad (pringle's maneuver). No major complications were observed in the open technique.

Among 25 patients, 16 were primary lesions 9 were secondary lesions. Among 16 primaries, 14 were successfully ablated, two were unsuccessful, and two lesions were sized more than 3 cm under USG guidance. Both lesions showed enhancing residual lesions. Among nine secondary lesions, five were successfully ablated, and four were unsuccessful because 2 were more than 3 cm in size, and 2 were less than 5mm close to the blood vessel.

RFA under various image guidance and primary and secondary lesions shows no statistical difference. Only size criteria showed statistical difference (lesion less than 3 cm successfully ablated). So, of 25 patients, 19 were successful, and 6 were unsuccessful ablation. Among six unsuccessful ablations, four patients showed residual lesions after one-month follow-up, and two patients showed a recurrent lesions at the site of RFA. In an overall 8-month median follow-up of my patients, five patients died because of the residual lesion at the site of RFA, remote recurrence, and distant metastasis, and 20 patients survived (Table 1).

Representative Images



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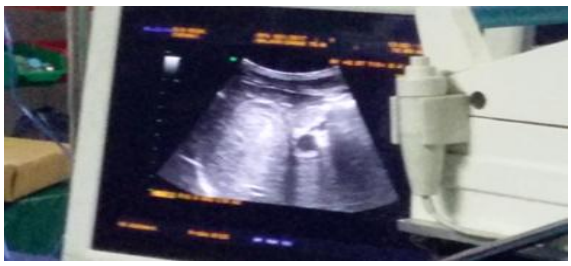

Figure 1: 76-Year-old male who underwent RFA of Hepatocellular carcinoma in the rt lobe of the liver under USG guidance a) USG appearances in this case (isoechoic). b) during RFA, there is an echogenic focus in the ablation zone.

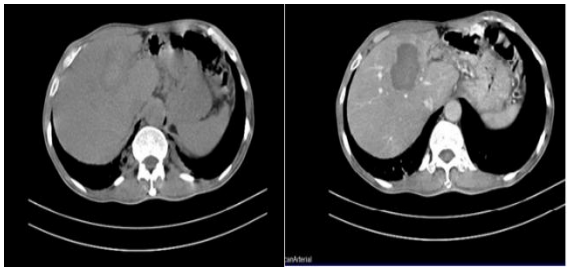

Figure 2: Post RFA follow-up image in the same patient in fig 1 a) unenhanced CT axial section shows heterogeneously hyperattenuating ablation zone due to coagulative necrosis and hemorrhagic products. b) one month later, in the same patient, CECT axial sections show non enhancing oval ablation zone. This suggests adequate treatment without residual disease.

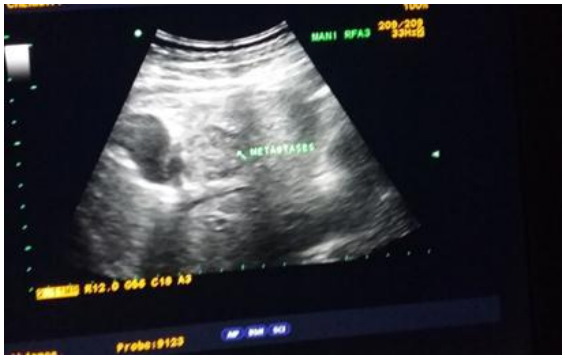

Fig 3. 60-year male patient with nasopharyngeal carcinoma USG shows a heteroechoic lesion in segment four who underwent USG GUIDED RFA

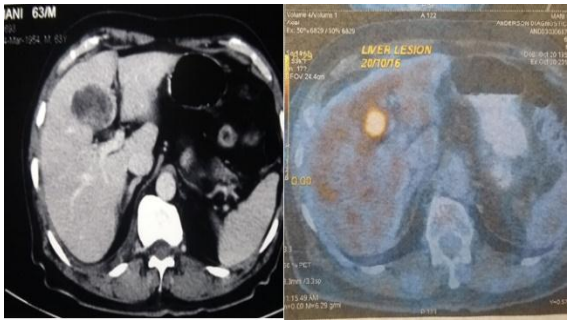

Fig 4. The same patient in Fig 3 1 month post-RFA a) CECT b) Fused FDG PET axial images show nodular enhancement in CECT and nodular avid uptake in the posterior aspect of the ablation zone in segment 4 representing residual lesion. This suggests unsuccessful ablation.

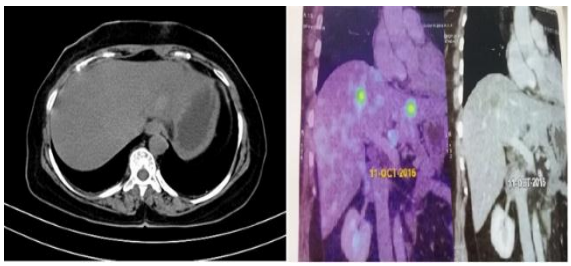

Figure 5: 59-year female patient colo rectal carcinoma with multiple liver mets post RFA 6 months back a) axial unenhanced CT revealed hyperdense mets in seg, 2. b)Fused FDG PET CT coronal section in the same patient shows another area of FDG uptake in seg. 8 suggestive of mets.

CASE 4:

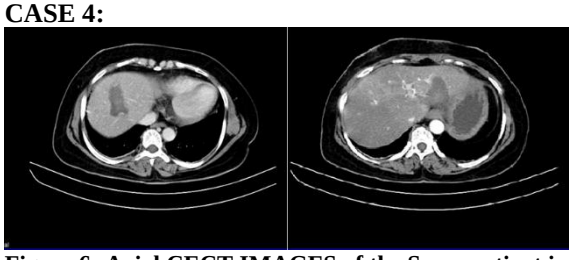

Figure 6: Axial CECT IMAGES of the Same patient in fig.5. who underwent CT-guided RFA for both lesions a) lesion in seg 8, b) lesion in seg.2. Both lesions show oval-shaped non-enhancing foci after one month, suggesting successful ablation.

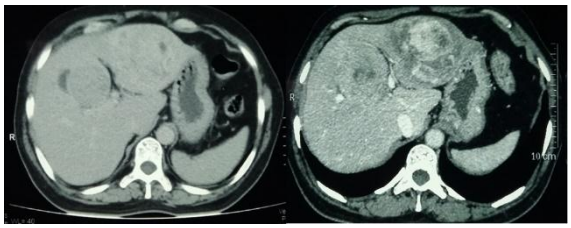

Figure 7: Axial plain and contrast images of 58 Year male patient with multifocal HCC in seg 2/3 and seg 4. one lesion is very close to the major portal vein branches

CASE 5

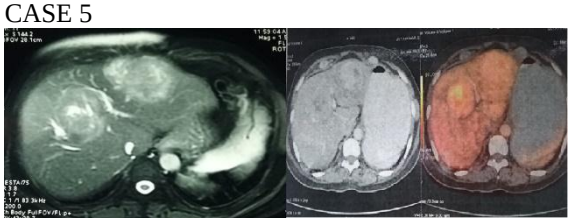

Figure 8: a) same patient of fig 7 MRI, T2WI. b) Fused FDG PET Axial images both lesions are FDG avid, and the lesion in seg.4 is very close to major vessels.

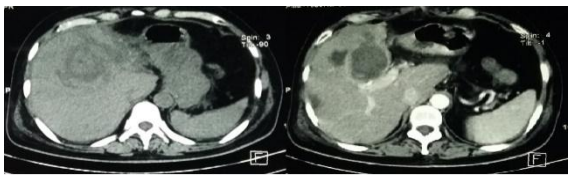

Figure 9: The same patient in fig 7&8, plain and contrast CT axial images two days after left lateral segmentectomy for a lesion in seg 2/3 and Intraoperative RFA for a lesion in seg 4, shows absent left lateral segment and post RFA Ablation zone in seg 4.

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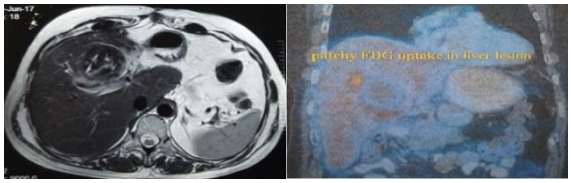

Fig 10, a) Same patients in Fig 9 Axial MRI T2WI, After 1-month post-RFA, show hemorrhagic products of varying age in the ablation zone. b) coronal FDG PET CT shows nodular peripheral uptake suggestive of the residual lesion because of HEAT SINK EFFECT caused by the nearest major vessel.

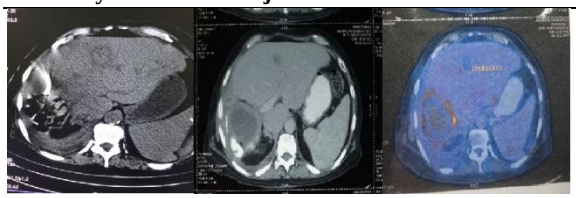

Figure 11: 61-Year male with multiple mets in the right lobe of the liver and another lesion in seg, 4, right hepatectomy and Intraoperative RFA done a) Axial CT plain image 24 hrs post-op. Showing post-operative changes in the region of the right lobe and ablation zone in seg 4 b) & c) 1-month post-op, axial CECT image(b) and FDG PET axial image (c) showing no enhancement and FDG uptake in ablation zone suggestive of successful ablation, and peripherally enhancing collection in post-operative site suggestive of abscess formation.

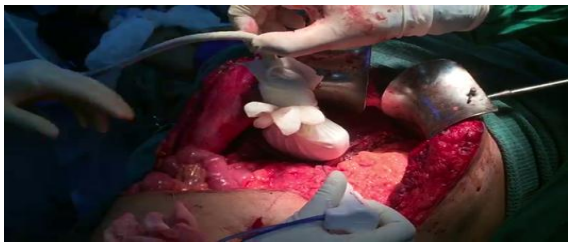

Figure 12: shows Intra operative RFA. The sterile USG probe is kept over the liver surface; bowel loops and diaphragm are retracted from the RFA electrode inserted under USG GUIDANCE.

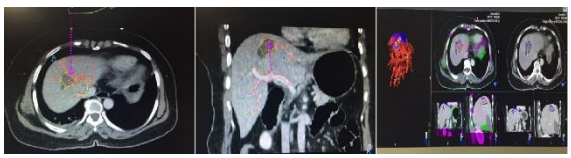

Fig. 13. Treatment planning and simulation on Maxio's workstation. a) & b) Identifying and segmenting the lesion in seg 8. The CT images are displayed in axial, coronal planes. The straight pink line indicates the trajectory of the ablation probe from the skin surface (entry point) to the centre of the target volume (target point). c) 3D simulated diagram is shown. The Tumor volume is calculated automatically by the software and indicated in the treatment plan (shown as green spheres covering the tumour).

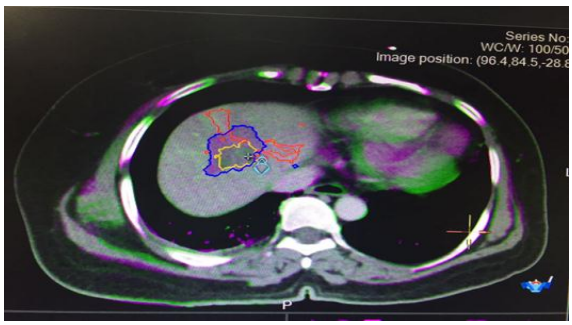

Figure 14: Comparison image. After the RFA procedure under MAXIO guidance, the calculated tumor volume before the procedure and ablation volume after the procedure will be automatically matched by the software in the machine and clearly show the Ablation zone, Ablated tumor volume, and Ablative marginal volume. These findings suggest successive ablation.

DISCUSSION

Locoregional treatments play a key role in managing hepatocellular carcinoma (HCC). Image-guided tumor ablation is recommended in patients with early-stage HCC when surgical options are precluded. Radiofrequency ablation has shown superior anticancer effects, and greater survival benefits concerning the seminal percutaneous technique, ethanol injection, in meta-analyses of randomized controlled trials and is currently established as the standard method for local tumor treatment. Novel thermal and nonthermal tumor ablation techniques include microwave ablation, irreversible electroporation, and light-activated drug therapy. Seem to have the potential to overcome the limitations of radiofrequency ablation and warrant further clinical investigation.[8-11]

Despite the advances and refinements in locoregional approaches, the long-term survival outcomes of patients managed with interventional techniques are not fully satisfactory, mainly because of the high tumour recurrence rates. The recent addition of molecular-targeted drugs with antiangiogenic and antiproliferative properties to the therapeutic armamentarium for HCC has prompted the design of clinical trials to investigate the synergies between locoregional and systemic treatments. The outcomes of these trials are eagerly awaited because they have the potential to revolutionize the treatment of HCC.[11-14]

MWA is emerging as a valuable alternative to RFA for the thermal ablation of HCC. However, only one RCT has compared the effectiveness of MWA with that of RFA so far. Although no statistically significant differences were observed concerning the efficacy of the two procedures, a tendency favouring RFA was recognized in that study concerning local recurrences and complication rates. To date, few data are available concerning the clinical efficacy of laser ablation because the treatment has been adopted by a few centres worldwide. In particular,

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no RCTs to compare laser ablation with any other treatment have been published thus far.[12,14,15]

For studies that reported major complications, however, the incidence in RFA-treated patients was 4.1% (95% confidence interval [CI], 1.8%-6.4%), compared to 2.7% (95% CI, 0.4%-5.1%) observed in PEI-treated patients. This difference was not statistically significant; nevertheless, this safety profile should be considered part of the overall risk/benefit profile.[16]

Recent reports on long-term outcomes of RFA-treated patients have shown that in patients with Child-Pugh class A and early-stage HCC, 5-year survival rates are as high as 51%-64% and may reach 76% in patients who meet the BCLC criteria for surgical resection.[16]

Five RCTs have compared RFA versus PEI for the treatment of early-stage HCC. These investigations consistently showed that RFA has a higher anticancer effect than PEI, leading to better local disease control. The assessment of the impact of RFA on survival has been more controversial. Although a survival benefit was identified in the three RCTs performed in Asia, the two European RCTs failed to show statistically significant differences in overall survival between patients who received RFA and those treated with PEI, despite the trend favouring RFA.[17-19]

Even with high efficacy in managing early HCC, different modalities, such as US or CT in the guidance of RFA, might produce discrepant clinical outcomes. Their equivalence in efficacy needs further confirmation. In previous studies, either US or CT was used in the guidance of RFA, but investigations of comparing clinical outcomes between different guidance methods were limited. In this study, no significant difference could be made in the outcome of RFA using USG and CT guidance.

CONCLUSION

RFA is the better locoregional treatment option for small primary and secondary liver tumours. RFA can compete with open surgical resection as a first-line treatment for patients with a small solitary HCC of less than 3 cm. RFA is done under USG, CT, MAXIO robotic guided needle positioning, and intraoperative technique. Only 20% will be the surgical candidate; only size criteria show statistically significant differences among the groups. Comparison using various image guidance shows that primary and secondary tumours do not show any statistically significant difference because of the small sample volume.

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