Indian Society of Vascular and Interventional Radiology Expert Consensus Statements for Ablation in Hepatocellular Carcinoma: Part II

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Abstract

Keywords
► ablation
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► RFA

Locoregional therapies play an important role in the management of hepatocellular carcinoma (HCC). Percutaneous ablation is one of the most commonly employed nonsurgical methods for treating very early and early HCC. For small HCC, ablation is potentially curative and competes with surgical resection. The widespread availability and the spectrum of ablative techniques mandate uniform approach among interventional radiologists. Thus, it is desirable to have a consensus regarding various aspects of the liver ablation. This article represents a consensus document of the experts from the Indian Society of Vascular and Interventional Radiology involved in the care of patients with HCC. The statements are presented in two parts.

Guiding Principle and Objectives

Hepatocellular carcinoma (HCC) is the one of the most common cancers worldwide and is the leading cause of cancer-related mortality.[1] The majority of HCC occurs in the setting of cirrhosis and are diagnosed during surveillance.[2] The therapies of HCC have evolved over the past 20 years. Broadly, the therapeutic options for HCC are hepatic resection (HR), liver transplantation, locoregional therapies including percutaneous ablation, transarterial chemoembolization (TACE), transarterial radioembolization (TARE), stereotactic body radiation therapy, and systematic therapies including immunotherapies.[3] The treatment in an index patient is based on the tumor characteristics, including mainly the number and size of tumor nodules, the status of the portal vein, liver function, and performance status of the patient. Barcelona Clinic Liver

Cancer represents one of the most widely used approaches when assessing a patient for management.[3] Percutaneous ablation is a commonly utilized treatment for very early and early HCC.[4] There are several percutaneous ablation methods. The most commonly used is radio frequency ablation (RFA), followed by microwave ablation (MWA), and cryoablation. The other techniques are irreversible electroporation (IRE), high-intensity focused ultrasound, and laser ablation. As many tertiary care centers across India are offering liver tumor ablation, uniformity must be achieved. There is a lack of a document for the guidance of interventional radiologists involved in the ablation of HCC.

The present consensus aimed to generate statements about various aspects of ablation procedures for HCC to bridge a gap in the existing practice and the one supported by existing literature. The expert group comprising of interventional radiologists involved in the management of HCC performed multiple systematic reviews of the literature after selecting key questions. Grading of Recommendations Assessment, Development, and Evaluation system was used for grading evidence and strength of recommendation[5] (►**Table 1**).

Key Questions

The guideline developers identified key questions that the interventional radiologists are faced with while considering patients with HCC for percutaneous ablation. Following questions were included: -
1. What should be the aim of ablation?
2. Till what size, ablation may be performed?
3. What should be the target ablation margin?
4. Should adults with Child-Pugh class C cirrhosis or performance status>1 undergo ablation?
5. What is the pre-procedure platelet count and international normalized ratio below which ablation is contraindicated?
6. Which imaging modality should be preferred for the guidance of ablation procedure?
7. Is there a role of fusion imaging or navigation techniques during an ablation?
8. What is the role of prophylactic antibiotics before ablation?
9. What strategies should be adopted for ablation of lesions at high risk locations?
10. Should ascites be drained before ablation?
11. What is the role of transient vascular occlusion devices to prevent heat sink in lesions close to blood vessels?
12. Which is the preferred ablative method for perivascular tumors?
13. Should immediate postablation contrast imaging be routinely performed after ablation?
14. How should perihepatic hemorrhage postablation be managed?
15. What should be the protocol for postablation imaging?
16. What is the treatment of postablation residual or recurrent lesions?
17. What is the role of combination therapies with ablation? This part of the article deals with the questions 11 to 17.

Table 1 GRADE approach

Rating the quality of evidence	Definition	Type of evidence
High	Further research is very unlikely to change our confidence in the estimate of effect	RCT
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	RCT
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	Observational study
Very low	Any estimate of effect is very uncertain	Any other evidence
Rating the strength of recommendations	Implications	Determinants
Strong	Population: Most people in this situation would want the recommended course of action and only a small proportion would not. Health care workers: Most people should receive the recommended course of action. Policy makers: The recommendation can be adapted as policy in most situations	Quality of evidence Balance of benefit and harm Patient values and preferences Resources and costs
Conditional	Population: Most of the people in this situation would want the recommended course of action, but many would not. Health care workers: Be prepared to help patients make a decision that is consistent with their values using decision aids and shared decision making. Policy makers: There is a need for substantial debate and involvement of stakeholders	

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial.

What Is the Role of Transient Vascular Occlusion Devices to Prevent Heat Sink in Lesions Close to Blood Vessels?

Key Statement

Temporary percutaneous occlusion of the portal vein or hepatic vein during RFA is safe and increases the diameter of the ablation zone. No extensive studies are available to recommend occlusion of the hepatic artery during RFA.
Quality/certainty of evidence: low
Strength of recommendation: conditional

Evidence and rationale

Perivascular HCC is defined as a tumor having contact with first- or second-degree branches of portal vein or hepatic vein measuring 3 mm or greater in diameter.[6]

A series of 10 patients with perivascular tumors larger than 3.5cm treated with RFA by temporarily occluding hepatic or segmental portal vein showed it to be a safe procedure.[7] Later, a prospective study by the same group evaluated the role of percutaneous transient balloon occlusion of portal or hepatic vein during RFA of perivascular tumor. The rate of local tumor progression (LTP) was lower for perivascular tumors smaller than 3.5 cm. However, balloon occlusion did not affect the results for tumors larger than 3.5 cm.[8] The data regarding hepatic artery occlusion during RFA is limited. A study demonstrated that RFA with balloon occlusion of the common hepatic artery can achieve a significantly larger diameter of coagulation necrosis as compared with standard RFA.[9] However, the complications of hepatic artery balloon occlusion during RFA have not been studied. A study comprising four patients showed that balloon occlusion of both the hepatic artery and hepatic vein resulted in an ablation diameter of 50 to 60 mm using a single electrode with no major complications.[10]

Which Is the Preferred Ablative Method for Perivascular Tumors?

Key Statements

1. RFA with cluster electrodes or multibipolar electrodes are recommended for perivascular HCC ≤ 5 cm. MWA is an acceptable alternative.
2. IRE may be recommended for perivascular HCC ≤ 2 cm as an alternative for thermal ablation.
3. Cryoablation may be used as an alternative to RFA in perivascular HCC ≤ 3 cm in diameter.

Quality/certainty of Evidence: low
Strength of recommendation: conditional

Evidence and rationale

MWA has certain advantages when compared with RFA.[11] These include a higher tissue temperature, larger zone of ablation in shorter times, insensitivity to carbonization, and reduced susceptibility to heat sink effect.[12] In a study evaluating the efficacy of MWA for early HCC, 113 propensity matched pairs (perivascular tumors and tumors away from large vessels) were evaluated. There was no significant difference in LTP, overall survival (OS), and complications between the two groups.[13] A retrospective study comparing four different thermal ablative methods (monopolar RFA, MWA, cluster RFA, and multibipolar RFA) for the management of perivascular HCC ≤5 cm found that the overall LTP was significantly higher in nodules ablated by single-applicator techniques (monopolar RFA or MWA) when compared with nodules treated by multiapplicator techniques (multibipolar RFA or cluster RFA).[14] In another study by van Tilborg et al evaluating the efficacy of RFA versus MWA for colorectal metastases in proximity to a large vessel or bile duct, both RFA and MWA were found to be safe and equally effective for perivascular tumors.[15]

IRE is a nonthermal ablation method that involves a series of high voltage currents and achieves cell death by creating irreversible pores in cellular bilipid membranes.[16] As the predominant pathway for cell death is apoptosis, it has been demonstrated in experimental and clinical studies that the peritumoral connective tissue, vessels, and bile ducts are not damaged.[17] Hence, IRE seems to be an attractive alternative option for tumors near the porta hepatis or perivascular tumors.[18] IRE has been shown to be safe and effective alternative for inoperable HCC that may not be ideal candidates for thermal ablative techniques.[19] Although animal model-based studies have shown that an ablation zone of more than 6 cm may be achieved, clinical studies have shown that IRE has a poor efficacy with tumors > 3 cm.[20]

The advantage with cryoablation is the ability to precisely monitor the ablated area using ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI). RFA was shown to be superior to cryoablation in a meta-analysis, as it had lower complication rate and LTP although there was no significant difference in mortality.[21] However, a randomized controlled trial (RCT) reported that LTP was significantly lower in cryoablation than RFA.[22] The complications, tumor-free survival, and OS were not significantly different. Another recent study revealed that cryoablation was effective and did not result in vascular complications in patients with perivascular HCC.[23] A study comparing RFA with cryoablation in patients with perivascular HCC found that cryoablation is an effective alternative to RFA for HCC ≤3 cm.[24]

Should Immediate Postablation Contrast Imaging Be Routinely Performed after Ablation?

Key Statement

Postcontrast imaging plays an essential role in assessing the ablation zone and the presence of residual tumors so that ablation can be repeated in the same setting. Besides, imaging helps in the early detection of complications and timely management.
Quality/certainty of evidence: low
Strength of recommendation: conditional

Evidence and rationale

In a study by Yoon et al comprising 36 patients with 43 HCCs, multiphase CT was performed before and immediately after RFA.[25] Additionally, MRI was performed 1 to 3 days (mean, 1.25 days) after RFA. The conspicuity of the ablated tumor margin was significantly higher on MRI compared with CT. The ability to differentiate post-RFA hyperemia from the residual lesion was significantly higher for MRI. Moreover, there was a higher interobserver agreement for MRI than for CT. The authors concluded that contrast-enhanced MRI could be used as a surveillance imaging tool after RFA. In a study by Lekht et al, 64 patients underwent RFA of liver tumors.[26] Patients were divided into two groups based on whether postablation contrast-enhanced ultrasound (CEUS) was utilized. Thirty-six patients underwent standard RFA without postablation CEUS, while 28 patients underwent CEUS following ablation. At first follow-up imaging, six patients had residual tumors, and all these patients belonged to the group that underwent standard RFA. None of the patients who underwent CEUS following the procedure had a residual tumor. The utility of CEUS in predicting early therapeutic response to ablation was assessed by another study comprising 78 HCCs.[27] CEUS was performed 20 to 30 minutes after the RFA. Contrast-enhanced MRI was performed 1 month after RFA. CEUS had a concordance of 97.4% with MRI in the assessment of the therapeutic efficacy of RFA. In a study by Xu et al comprising 95 liver tumors in 76 patients who underwent RFA/MWA, postprocedure three-dimensional US-CEUS fusion assessment was performed to guide supplementary ablation in cases of residual lesions during the same session.[28] The success rate of fusion was 93.7%. Supplementary ablation was performed in 30 lesions. The authors concluded that three-dimensional US-CEUS fusion allows immediate assessment of response and guides additional ablation. Studies have reported the value of conventional US in assessing response to ablation. In a study by Minami et al, the utility of US-US overlay images whereby the preablation US images were superimposed on the postprocedure images to assess the ablative margin was investigated.[29] In this study, 68 HCC nodules in 35 patients were treated with RFA. The US-US overlay images accurately evaluated the response in 92.6% of the HCC when compared with an early dynamic CT scan. In a study by Rajesh et al, CEUS was utilized for guiding the ablation of HCC that were poorly defined on US and unenhanced CT.[30] Postablation CEUS was performed to document complete ablation. In this study comprising 19 HCCs in 14 patients, complete ablation was achieved in all patients. The authors concluded that CEUS is a useful tool for the ablation of early-stage HCC. Postablation color Doppler evaluation of the tract may identify active bleeding after the removal of the electrode.[31] Immediate postprocedure CT angiography may identify perihepatic hematoma or active contrast extravasation. However, presence of these findings has not been shown to predict unstable bleeding or need for angio-embolization.[32,33] Moreover, there are no recommendations on the routine use of postablation CT.

How Should Perihepatic Hemorrhage Postablation Be Managed?

Key Statement

The risk of significant bleeding with ablation of HCC is low (< 2%). Most venous bleeds are self-limited and can be managed conservatively. Endovascular embolization or surgery may be required for arterial bleeding.
Quality/certainty of evidence: low
Strength of recommendation: conditional

Evidence and rationale

The complication of intraperitoneal bleeding or subcapsular hematoma is of concern in patients undergoing ablation for HCC owing to two main reasons.[34] Most of the patients with cirrhosis have deranged coagulation parameters. Hemorrhagic complications though rare are considered as major complications and may lead to significant morbidity and mortality in these patients. Cases of hepatic artery rupture with the formation of pseudoaneurysms have been reported earlier and have been the cause of death in these patients.[35,36] Appropriate management of bleeding complications following the ablation of liver tumors is essential.[37] Venous bleeds in postablation settings are self-limiting, while arterial bleeds are best managed with transarterial embolization.[38]

What Should Be the Protocol for Postablation Imaging?

Key Statement

It is recommended to perform first follow-up scan at 1 month after ablation. Thereafter, imaging is recommended every 3 months for the first year.
Quality/certainty of evidence: low
Strength of recommendation: conditional

Evidence and rationale

Optimization of imaging modality, acquisition protocols, and consistency in the use of the same modality and protocol throughout follow-up examinations are vital for proper assessment of tumor response to ablation. Contrast-enhanced CT or contrast-enhanced dynamic MRI is the recommended imaging modality to follow patients after ablation.[39,40] The administration of intravenous contrast is recommended for all studies if not contraindicated. Mandatory arterial and portal venous phase imaging of the liver, with the equilibrium phase depending on the clinical practice and findings in the dual-phase acquisition, is suggested.[41] A review of contiguous thin slices with no interslice gap is mandatory not to miss the smaller lesions. The choice of imaging modality depends on the availability, institutional preference, and expertise. Following ablation, the first follow-up imaging is done at 1 month after treatment. For early detection of recurrence and clinical evaluation of decompensation, follow-up scans are suggested every 3 months during the first year and surveillance every

6 months after that.[41] However, Liu et al in their study on optimal monitoring divided the patients into high and low recurrence risk groups and followed up for rate of recurrence with short (less than four months) and long intervals (4–6 months interval).[42] Based on the recurrence rate and OS at 1, 3, and 5 years, they proposed the risk-based surveillance strategy to reduce the number of scans, radiation dose, and cost. Another study by Boas et al reported that the optimal schedule for surveillance after liver directed therapies is 2, 4, 6, 8, 11, 14, 18, and 24 months in the first 2 years.[43] Mikami et al showed that 4-month interval for CT surveillance of HCC after RFA detects majority of the recurrent nodules at a stage where repeat RFA (rRFA) is feasible.[44] Granata et al reported that hepatocyte specific contrast-enhanced MRI is more useful than multiphase CT in the assessment of HCC after RFA.[45]

Which Diagnostic Criteria Should Be Applied for the Detection of Residual or Recurrent Lesion after Ablation?

Key Statements

1. Ablation zone appears as a nonenhancing area with or without a smooth enhancing peripheral rim. The enhancing rim is relatively concentric, symmetric, and uniform with smooth inner margins.
2. Modified response evaluation criteria for solid tumors (mRECIST) or liver imaging reporting and data system (LI-RADS) locoregional treatment response (LR-TR) assessment criteria is recommended for the assessment of response/disease progression following locoregional therapies.

Quality/certainty of evidence: low
Strength of recommendation: conditional

Evidence and rationale

Residual tumor appears as a peripheral, nodular, or ill-defined area of arterial phase enhancement with washout on the venous phase.[41] On T2-weighted images, the residual tumor appears hyperintense compared with the hypointense signal of the coagulated area.[41] This shows enhancement on arterial phase and washout on delayed phase images. LTP is the appearance of tumor foci at the edge or within the ablation zone, after adequate ablation and an absence of viable tissue has been documented using imaging criteria at baseline follow up.[46,47]

For equivocal lesions, dynamic contrast-enhanced MRI with diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping act as useful adjunctive techniques and allow differentiation between tumor and post-treatment changes.[48] Low ADC value in the area of hyperintense signal on T2-weighted image is suggestive of viable tumor. Mohamed et al evaluated 56 patients with 74 HCCs treated with locoregional therapies (TACE or RFA) using DWI. DWI-MRI showed a sensitivity of 98.96% and specificity of 92.90%, for detecting residual tumors.[48] The dynamic contrast-enhanced MRI (with subtraction and perfusion maps) showed higher accuracy, sensitivity, and specificity. The combination of DWI and dynamic

contrast-enhanced MRI yielded 100% sensitivity, 100% specificity, and 99.09% accuracy. Mahmoud et al, in their study, documented significantly lower mean ADC values (0.91 ± 0.09) in the recurrent lesions as compared with ablation zone (1.36 ± 0.18) or postablation images (1.29 ± 0.12).[49] Positron emission tomography (PET)-CT can be used for early detection of recurrent disease in those patients where preablation PET-CT showed F-fluorodeoxyglucose-avid lesions.[18] Imaging appearance of remote intrahepatic distant recurrence and extrahepatic recurrence/metastasis is like that of a nonablated lesion.[50] Recent studies have evaluated the performance of LI-RADS for response assessment.[51,52] In a retrospective study by Chaudhry et al, LI-RADS v2018 was used to assess the response in patients who underwent ablation and histopathological evaluation of explant liver.[51] A total of 53 lesions in 36 patients were evaluated. Interreader agreement for treatment response category was high. The sensitivity and specificity of tumor necrosis were 40 to 77% and 85 to 97%, respectively, when LR-TR equivocal lesions were considered as nonviable. However, when these lesions were treated as viable, the sensitivity increased to 81 to 87%, and specificity reduced to 81 to 85%. Out of the six (11%) LR-TR equivocal lesions, five lesions showed incomplete necrosis at explant histopathological evaluation. A recent study by Seo et al comparing mRECIST with LI-RADS for treatment response assessment reported better performance of LI-RADS v2017 compared with mRECIST for CT-based assessment.[52] At the same time, there was no difference based on MRI assessment.

What Is the Treatment of Postablation Residual or Recurrent Lesions?

Key Statements

1. Residual lesions are managed with repeat ablation if <3cm and well defined or TACE/TARE if >3 cm and ill defined.
2. Recurrent lesions are managed with repeat ablation, resection, or salvage liver transplantation (SLT) based on the functional status of liver and macroscopic features of recurrent tumor.

Quality/certainty of evidence: low
Strength of recommendation: conditional

Evidence and rationale:

If the residual lesion is focal and well defined along the periphery or within the ablation zone and is less than 3 cm, then repeat ablation should be considered.[53] If the residual lesion is irregular, diffusely scattered along the margins of the ablated lesion, overall size more than 3 cm, and along the subcapsular region or in a difficult location, then transarterial therapies should be considered (TACE or TARE) based on portal vein status and Child-Pugh score.[53] There is no consensus on standardized treatment strategy for a recurrent lesion at present. The choice of treatment depends on two critical factors: the functional status of the liver and macroscopic

features of the recurrent tumor. Options are rRFA and SLT.[54] Aggressive treatment strategy should be employed in cases of recurrence as they signify the aggressive nature of the tumor, preferably with resection or SLT whenever feasible.[54]

In the study by Chan et al, rRFA in recurrent HCC was associated with early re-recurrence and reduced median disease-free survival as compared with resection and SLT group.[54] In this study, 87 patients with recurrent HCC were treated with SLT, resection, and rRFA. The 1-, 3-, and 5- year disease-free survival rates were significantly lower after rRFA.

What Is the Role of Combination Therapies with Ablation?

Key Statements

1. A combination of ablation procedure with TACE offers survival benefit compared with ablation alone; the benefit is more in HCC greater than 3 cm in size.
2. Irrespective of the timing of combination, that is, sequential or simultaneous, within 4 weeks, the outcomes of combination therapy are better than monotherapy.

Quality/certainty of evidence: Moderate
Strength of recommendation: Strong

Evidence and rationale

RFA or MWA are equivalent therapeutic options to surgical resection for small, early-stage HCC.[55] Heat sink restricts their efficacy in large lesions. A combination of RFA/MWA with TACE potentiates necrosis, increases the clearance of micrometastasis, leading to reduced recurrence, improved OS and progression-free survival (PFS) with no significant difference in major complications.[56]

In a meta-analysis by Ni et al comprising eight RCTs, 306 patients underwent RFA plus TACE, while 292 patients underwent RFA alone.[56] The former group showed significantly higher 1, 2, and 3 years OS. This benefit was seen for intermediate and large-sized HCC and not the small-sized HCC. Additionally, patients in the combination groups had a lower LTP rate and higher PFS, with no significant difference in the major complications. In an RCT by Peng et al, TACE–RFA treatment was found to be superior to RFA alone in OS and recurrence-free survival.[57] In a study by Abdelaziz et al, TACE was followed by MWA (n = 45) or RFA (n = 22) within 2 weeks later. TACE–MWA was found to give higher complete response rates than TACE–RFA for lesion 3 to 5 cm.[58] However, there was no survival benefit.

Different investigators have adopted different protocols for the combination of RFA with TACE. In the study by Song et al, 201 patients with single HCC ≤ 5.0 cm or up to three HCC ≤ 3.0 cm were treated with TACE+RFA (performed 4 weeks after TACE) (n = 87), TACE (n = 71), and RFA alone (n = 43).[59] The TACE + RFA group showed significantly lower local recurrence than the RFA (p = 0.008) or TACE alone (p = 0.011). The OS at 1, 3, and 5 years was significantly better in the TACE + RFA group compared with the RFA group. However, the OS was not significantly different compared with the TACE group

(97.2%; p = 0.1). Subgroup analysis revealed better long-term survival in tumors < 3 cm treated with TACE + RFA than those treated with TACE or RFA alone. In the study by Chen et al, MWA was performed within two weeks of TACE.[60] After initial treatments, significantly greater number of patients in the TACE–MWA group (92.1%) had complete necrosis when compared with the TACE group (46.3%). At 6 months, the TACE–MWA group had better tumor responses compared with TACE alone group.

In the RCT by Kamal et al, evaluating TACE vs TACE-RFA, RFA was performed within 5 days of the TACE.[61] Complete response rates at 1 month were 100 and 84% for combined RFA–TACE therapy and TACE only, respectively. One-year disease-free survival rate was 56 and 24% in RFA–TACE and TACE groups, respectively. The OS rate was also significantly higher in the combination group (88 vs. 80%). Xu et al performed TACE immediately after RFA in the same session in 93 patients with solitary massive intermediate stage HCC. One, 3-, 5-, and 7-year survival rate was 94.4, 52.3, 26.1, and 14.1%, respectively.[62]

In another study, patients with solitary intermediate sized HCC were randomized to receive either RFA alone or RFA+TACE (on the same day).[63] Fewer sessions of RFA were required when combination therapy was utilized. LTP at 3 years was significantly higher in the RFA group compared with the TACE–RFA groups (39 vs. 6%, p = 0.012). However, the OS at 3 years was not significantly different between the two groups. In the meta-analysis by Dong et al comprising five RCTs, RFA was compared with RFA plus TACE for small HCC.[64] There were no significant differences in the 1-year (p = 0.27) or 3-year (p = 0.183) OS. However, the 5-year OS was significantly higher in patients treated with RFA+TACE than those treated with RFA alone. In the study by Chen et al, tumors < 5 cm subjected to TACE were compared with those undergoing TACE+MWA.[60] Subgroup analysis showed that for tumors < 3 cm, TACE–MWA showed longer time to progression and better OS than TACE alone. For tumors < 5 cm, TACE–MWA led to longer time to progression, but there was no significant difference in the OS.

In the study by Song et al, patients with a tumor size < 3 cm who underwent TACE + RFA had significantly better long-term survival than those who underwent only TACE or RFA.[59]

Other adjuvant therapies in the combination regimen are being investigated. An ongoing trial is investigating simultaneous TAE and ablation versus sequential TACE followed by ablation for large HCC.[65]

In the propensity-matched cohort study of 228 patients of HBV-related HCC, patients were divided into two groups: those that underwent RFA (n = 103) and those who received RFA + antivirals (n = 125, mean duration of antiviral treatment 60.1 months).[66] At 5 years, the probability of HCC recurrence was significantly lower for the patients receiving antiviral treatment. Similarly, the probability of OS at 5 years was significantly higher in the combination group. Several studies and meta-analysis on the role of antiviral therapy following surgical resection have shown mixed results.[67-70] There is a need for a well-designed prospective

study to evaluate the benefit of antiviral therapy in patients undergoing ablation.[71]

In an RCT by Cui et al, 62 patients were randomized to receive RFA alone ($n = 32$) or RFA+ cellular immunotherapy (CIT, $n = 30$). The PFS was significantly higher in the combination group than the monotherapy group.[72] No significant adverse effects were reported in patients receiving CIT. In another multicenter open-labeled RCT, 230 patients were randomized to two groups, one receiving definitive treatment (HR, ablation, or percutaneous ethanol injection) plus immunotherapy with cytokine-induced killer cells ($n = 115$) and other group not receiving immunotherapy.[73] The median recurrence-free survival was significantly greater in the combination group (44 vs. 30 months). No serious adverse events were reported. In a double-blind, placebo-controlled trial, surgical resection ($n = 900$) or local ablation ($n = 214$) was followed by sorafenib ($n = 556$) or placebo ($n = 558$).[74] There was no significant difference in the recurrence-free survival between the two groups.

In conclusion, the guidelines presented in two parts cover the most important areas related to ablation of HCC. These guidelines are expected to be useful for the practicing interventional radiologists in their day-to-day practice.

Financial Disclosures
None.

Conflict of Interest
None.

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