

Role of Interventional Radiology in Management of Hepatocellular Carcinoma: Systematic Review

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Abstract

The purpose of this study is to analyse and evaluate the function of interventional radiology in such instances by evaluating several elements of each procedure, such as its influence on survival rates, recurrence, tumour response, and complications. The following databases were searched: PubMed, Web of Science, Science Direct, EBSCO, and the Cochrane Library. Using Rayyan QCRI, study papers were screened by title and abstract before being subjected to a full-text evaluation. This review included 13 studies with participants of varying ages and genders; more than half were males. All included studies discussing the role of interventional radiology in hepatoma cases in diagnosis and treatment. We included Sex studies that were systematic reviews; two were randomized controlled, one was a case-control study, one was a prospective study, two were retrospective studies, and one was a pilot study. In the ablation therapy of hepatocellular carcinoma nodules, we determined that microwave ablation had greater complete ablation and lower local tumour growth than radiofrequency ablation. In large tumors (up to 6 cm), mwa is preferred, and cryoablation is preferred in recurrent disease. Because of a lesser heat-sink effect, mwa and cryoablation are preferred to RFA in perivascular disease. Chemoablation can be used in smaller lesions (<3 cm). In intermediate-stage, multifocal lesions (>3), tace, debs, and tare are to be used.

Keywords: Interventional radiology, Hepatocellular carcinoma, Radiofrequency ablation, Microwave ablation, Ultrasound-guided.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the second leading cause of cancer mortality in men and the sixth leading cause in women [1]. However, there were many options for its management and treatment, like liver transplantation, surgical resection, and locoregional therapies are the treatment options for HCC. Still, only a small proportion of patients are suitable for the first two options [2]. Various helping tools, such as image-guided interventions, now play a vital role in managing HCC. A multidisciplinary approach to those cases involving interventional radiologists became the main component in treatment success for patients with HCC. Cirrhotic patients with unresectable HCC have been treated with percutaneous local ablative methods such as percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), microwave (MV), and cryoablation (CRYO) [3]. Because of its superior local tumour control, tolerable morbidity³, and tumour seeding risk, percutaneous RFA is presently the most extensively used ablation treatment for HCC [4]. Through various methods, including thermal coagulation, fast freezing, and chemical cell dehydration, ablative treatments cause the necrotization of tumor tissue, with varying post-ablative effects [5-7].

These two techniques are mentioned in international standards for HCC treatment [8]. Other alternative ablative procedures, with modest modifications, have been found to

provide a satisfactory therapeutic response [7]. As a result, doctors considering local ablation for HCC must choose among many ablative techniques [9]. Every case has a specific profile upon which the physician selects the suitable ablative technique. Local ablation, such as radiofrequency ablation (RFA) and microwave ablation, is frequently used as a therapeutic option for small HCC or hepatic resection in patients with reduced liver function [10, 11]. Several recent studies have demonstrated that microwave ablation is a successful therapy for HCC, with 5-year overall survival rates ranging from 43-60% [11]. However, to the best of the authors' knowledge, little information exists about the real safety and efficacy of each interventional approach.

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Objectives

This study seeks to examine and evaluate the function of interventional radiology in managing HCC patients using various techniques and approaches, including the influence on survival rates, recurrence, tumour response, and complications.

MATERIALS AND METHODS

This systematic review was carried out in accordance with the specified principles (Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA).

Study Design

This was a systematic Review.

Study Duration

The research was carried out between November and December of 2022.

Study Condition

This review looks at new research on the function of interventional radiology in identifying and treating various stages of hepatocellular carcinoma.

Strategy for Search

A complete literature search was conducted in five major databases, including PubMed, Web of Science, Science Direct, EBSCO, and Cochrane Library, to locate relevant material. Our search was limited to English and was tailored to each database. To discover the right studies, the following keywords were transformed into Mesh terms in PubMed: "Interventional radiology," "hepatocellular carcinoma, the role of interventional radiology in the management of HCC, techniques of interventional radiology in HCC, rates of survival after interventional radiology in HCC, recurrence after interventional radiology in HCC, tumor response after interventional radiology in HCC, complications after interventional radiology in HCC" The relevant keywords were combined with the "OR" and "AND" Boolean operators. The search results included full-text publications in English, freely available papers, and human trials.

Criteria for Selection

Criteria for Inclusion

The participants will be chosen for inclusion based on their relevance to the research, which includes the following criteria: patients with hepatocellular carcinoma who have been studied. There were no age restrictions.

Criteria for Exclusion

All further publications, recurrent research, and research reviews that did not have one of these topics as their major goal were ignored.

Extraction of Data

Rayyan (QCRI) [8] was used to identify redundant search strategies results. The relevance of the abstracts and titles was determined by sifting through the aggregated search results according to a set criterion for inclusion/exclusion. The reviewers evaluated the total texts of the papers that met the inclusion criteria. The writers discussed any disagreements that needed to be resolved. The qualifying study was included in a data extraction form. The writers gathered information on the research titles, authors, study year, study design, study aims, number of HCC participants, kind of intervention utilised, diagnosis, management, and key findings.

Assessment of the Risk of Bias

The qualitative data synthesis used the non-randomized studies ROBINS-I approach [11] to assess the quality of the included research. The reviewers investigated and addressed any flaws in the quality assessment.

Data Synthesis Strategy

To provide a qualitative overview of the included research components and findings, summary tables containing information acquired from eligible studies were created. After the data extraction procedure for the systematic review was completed, decisions about how to make the most of the data from the included study articles were made. Studies that satisfied the full-text inclusion criteria but did not offer clinical data on HCC patients were disqualified.

RESULTS AND DISCUSSION

Results of a Search

The systematic search yielded 540 study papers, after removing 57 duplicates. 483 papers were screened for title and abstract, with 390 being rejected. Only ten items were not retrieved out of the 93 reports that were searched. Finally, 83 papers were screened for full-text evaluation; 52 were removed due to incorrect research results, 5 due to insufficient data, and 13 due to the incorrect population type. This systematic review comprised thirteen study papers (**Table 1**). **Figure 1** depicts an overview of the study selection procedure.

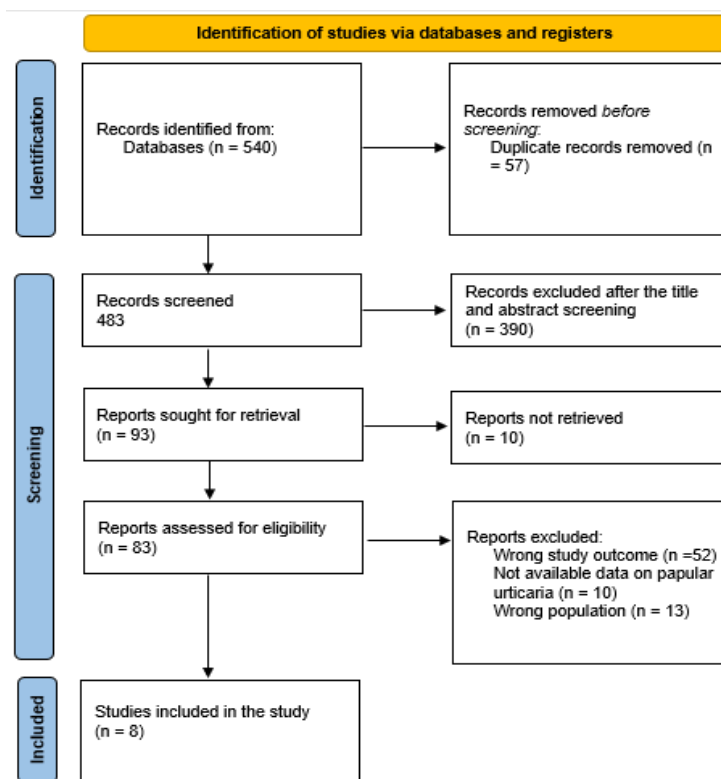


Figure 1. Depicts a flowchart of the PRISMA research selection process

Characteristics of the Studies Included

This study comprised 13 papers with a significant number of patients with hepatoma who were diagnosed and treated using various interventional radiology techniques. In terms of the

study designs, Sex studies were systematic reviews [12-17], two were randomized controlled [18, 19], one was a case-control study [20], one was a prospective study [7], two were retrospective studies [21, 22] and one pilot study [23].

Table 1. Summarises the features of the collected research publications.

Study	Study design	patients	Objectives	Intervention	Key findings and management
Gupta <i>et al.</i> 2021 [12]	systematic review	3043	The purpose of this study was to assess overall survival (OS) and local recurrence (LR) after radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation (CA) for very early and early hepatocellular carcinoma (HCC).	Radiofrequency ablation Cryoablation Microwave ablation	For the locoregional treatment of very early and early HCC, RFA, MWA, and CA are all equally effective.
Yeow <i>et al.</i> 2022 [13]	A Systematic Review and Meta-Analysis	1317	To assess the efficacy of radiofrequency ablation (RFA) against repeat hepatectomy (RH) in patients with recurrent hepatocellular carcinoma (rHCC) following prior liver resection.	Radiofrequency Ablation Repeat Hepatectomy	RH may be related with improved DFS for rHCC at the tradeoff of increased morbidity and a longer LOHS. However, the OS of both techniques is comparable. As a result, depending on the particular patient and illness characteristics, these approaches may be used as complimentary strategies. To confirm these findings, large-scale, randomised, prospective investigations are needed.
Dou <i>et al.</i> 2022 [14]	A systematic review and meta-analysis	4589	The purpose of this study was to examine the effectiveness and safety of radiofrequency and microwave ablation in the treatment of HCC.	Ablation using radiofrequency Ablation by microwave	In the ablation therapy of HCC nodules, microwave ablation yields higher total ablation and lower local tumour growth than radiofrequency ablation. There was no statistically significant difference in overall survival between the two treatment modalities.

Lu <i>et al.</i> 2022 [15]	a systematic review and meta-analysis	854	To compare radiofrequency ablation with percutaneous ethanol injection for hepatocellular cancer to radiofrequency ablation alone.	Percutaneous ethanol injection with radiofrequency ablation radiofrequency ablation alone	Despite the fact that RFA-PEI appeared to be superior in terms of OS for HCC patients with compensated livers, current evidence contained moderate to significant heterogeneity, making it difficult to draw a firm conclusion regarding LRF and CTN therapeutic management.
Radosevic <i>et al.</i> 2022 [18]	a randomized controlled phase 2 trial	Total: 82, subdivided into two equal groups	To compare microwave ablation to radiofrequency ablation for the treatment of liver cancer.	Microwave radiofrequency ablation	In this randomised trial, MWA produced bigger ablation zones than RFA. However, with identical ablation zone morphologies (reported as a short to big diameter ratio), technical success, and local tumour development rate in liver tumours measuring 1.5 to 4 cm. We found no significant difference in the rate of complications, median time to progression, or overall survival after a mean 2-year follow-up, despite the fact that both modalities might be a potential therapeutic choice for this tumour size group.
Schullian <i>et al.</i> 2019 [20]	a case-control study	435	to assess the efficacy and safety of stereotactic radiofrequency ablation (SRFA) in the treatment of subcardiac hepatocellular carcinoma (HCC).	Stereotactic radiofrequency ablation	Subcardiac tumour SRFA is as safe and effective as tumours distant from the heart.
Peng <i>et al.</i> 2021 [23]	A pilot clinical study	32	to assess the effectiveness, feasibility, and tolerability of ultrasound-guided percutaneous microwave ablation (MWA) for the treatment of caudate lobe hepatocellular carcinoma (HCC).	ultrasound (US)-guided percutaneous microwave ablation	Percutaneous MWA with US guidance was a safe and effective treatment. It is a promising alternative therapy for caudate lobe-originating HCC.
Paul <i>et al.</i> 2020 [19]	A randomized controlled trial	55	A randomised study was used to assess the effectiveness of percutaneous acetic acid (PAAI) with radiofrequency ablation (RFA) in the treatment of small (5cm) hepatocellular carcinoma (HCC).	percutaneous acetic acid of radiofrequency ablation	PAAI and RFA show comparable effectiveness in the treatment of minor HCC. In cases when RFA is unavailable or prohibitive, PAAI might be a cost-effective alternative.
Ryu <i>et al.</i> 2019 [21]	retrospective study	459	to evaluate real 10-year survival and to define the clinicopathological characteristics of patients who survived 10 years following surgical microwave ablation	Microwave Ablation	Ten-year survival following surgical microwave ablation for HCC is projected in roughly 24% of patients, despite the fact that nearly two-thirds of our 10-year surviving patients had recurrence. Close postoperative surveillance and further curative therapy for recurrence are critical for enhancing long-term survival.
Zheng <i>et al.</i> 2018 [22]	retrospective study	62	The purpose of this study was to look at the impact of interventional treatment on HIV-1 Tat interactive protein 2/Tat interactive protein 30 (HTATIP2/TIP30), B7-H4, and the short-term curative effect in primary hepatocellular cancer.	interventional therapy	Interventional treatment for primary hepatocellular carcinoma has a good short-term curative outcome. It can lower serum HTATIP2/TIP30 and B7-H4 levels while improving liver function and patient quality of life, extending survival time. It has a high research value and merits further investigation.
Luo <i>et al.</i> [16]	a systematic review and meta-analysis		The purpose of this study was to compare the therapeutic effects of radiofrequency ablation (RFA) and other ablative techniques on HCCs.	radiofrequency ablation	MWA and CRA groups had equal results when compared to RFA. The PEI and LSA groups had less difficulties. PEI with RFA proved to be more successful, although it was associated with a greater risk of problems. To corroborate the foregoing findings, well-designed randomised controlled studies are required.
Wang <i>et al.</i> 2015 [7]	a prospective, multicenter study	2,426	To compare percutaneous cryoablation versus radiofrequency ablation in hepatocellular carcinoma	percutaneous cryoablation radiofrequency ablation	Although both cryoablation and RFA were similarly safe and effective, with identical 5-year survival rates, cryoablation resulted in much reduced local tumour progression than RFA.
Molla <i>et al.</i> 2014 [17]	a systematic review		To analyse and appraise the role of interventional radiology in the management of such cases by evaluating several elements of each approach, such as the influence on survival rates, recurrence, tumour response, and complications.		Existing statistics suggest the value of a multidisciplinary approach to HCC treatment. To offer unambiguous indication recommendations for each approach, large randomised controlled trials are required.

Radiofrequency ablation (RFA) and cryoablation are considered successful curative treatment options for hepatocellular carcinoma (HCC). In order to compare the two techniques, Wang *et al.* This research evaluated the therapeutic effectiveness of percutaneous cryoablation to RFA in cirrhotic individuals with HCC measuring 4 cm and no more than two tumours [7]. The primary technique efficacy rate, LTP, distant intrahepatic recurrence, comorbidities, overall survival, and tumor-free survival did not differ significantly between the two groups. To our knowledge, this is the biggest prospective, multicenter randomised trial comparing these two HCC therapy approaches. Another nonrandomized trial compared the results of cryoablation versus RFA for hepatic malignancies such as HCC and metastatic liver cancers [24, 25]. A meta-analysis based on these studies revealed that RFA was considerably superior to cryoablation in terms of complications and LTP [26], however it had been observed that problems following cryoablation were related to the total ablation or freeze volume [27, 28].

Luo *et al.* also compared the therapeutic effects of multiple ablative techniques in their systematic review and meta-analysis [16]. They discovered that the effects of MWA and CRA looked to be similar to those of RFA, however there were lower rates of LTR and greater rates of CTA in big tumours compared to RFA (P 0.05). CTA rates were lower in PEI patients (odds ratio [OR] 0.16, 95% confidence interval [CI] 0.06-0.42) and higher in PEI + RFA patients (OR 2.28, 95% CI 1.19-3.60), with an increased incidence of fever (P 0.05). LSA was associated with decreased CTA rates (OR 0.32, 95% CI 0.13-0.81) and overall survival (hazard ratio 1.47, 95% CI 1.01-2.15), as well as less comorbidities. Kazutaka and colleagues [29]. The PEI-RFA group had bigger regions of coagulated necrosis (34 29.3 cm³) than the RFA group (6.5 3.6 cm³; P 0.0001). The volume of coagulated necrosis was substantially and positively associated with the amount of ethanol injected into the tumour, but not with the energy need. As a result, when using PEI-RFA in high-risk regions, such as near arteries or other vital organs, ethanol infusion reduces RFA energy, sparing the surrounding tissues. However, according to Luo *et al.* Fever was observed to be more common following PEI-RFA than after RFA in one research [16]. In a Japanese research [30], however, the tumour in CRA patients was adjacent to the hollow viscera, such as the gallbladder, or an essential structure, such as the hepatic hilum, was not mentioned in the thermal ablation group. Furthermore, lesser LTR in the CRA group was recorded in the RFA/MWA group for tumours with a diameter higher than 2 cm in the same research. In terms of complications, myoglobinemia was not reported during RFA but occurred in 3 of 33 CRA operations [31].

In the treatment of hepatocellular cancer, Paul *et al.* compared the effectiveness of percutaneous acetic acid (PAAI) to that of radiofrequency ablation (RFA) (HCC) [19]. They discovered that PAAI and RFA had comparable cumulative overall survival. Furthermore, the tumour response rate to

PAAI was comparable to that of RFA. However, they discovered that employing PAAI required more sessions than RFA to cure HCC. Lin *et al.* also reported the need for further PAAI therapy sessions [32]. Paul *et al.*'s tumour response rate after PAAI [19]. The research was 75% complete. There are no studies on the use of PAAI only on similar-sized HCCs in the literature. A combination of TACE and PAAI yielded response rates of 100% and 95% in HCCs 5 cm [33, 34].

Peng *et al.* found that percutaneous MWA showed satisfactory therapeutic efficacy for local cancer control [23]. Nevertheless, the percutaneous MWA treatment was found to be inadequate in four patients. CEUS, CT, or MRI indicated that percutaneous MWA produced complete necrosis of tumors on the other 28 (87.5%) patients and thus successfully prevented LTP. Studies have shown that tumor ablation in the caudate lobe would be more affected by the heat-sink effect because of the proximity of the lobe to the hepatic veins and the IVC [35]. It is challenging to increase the ablative margin for tumors in the caudate lobe because of the complex surrounding tissues. Portal vein tumor thrombus was treated by TACE combined with sorafenib, and during follow-up, the tumor thrombus was reduced significantly. Some scholars have already reported that TACE and sorafenib could improve OS for HCC patients with tumor thrombus [36].

Schullian *et al.* conducted a prior case-control research to assess the safety and efficacy of stereotactic radiofrequency ablation (SRFA) for the treatment of subcardiac hepatocellular carcinoma (HCC) [20]. They discovered no statistically significant difference in terms of significant complications (p = 0.76), primary and secondary efficacy (p = 0.93 and 0.23, respectively), local recurrence (p = 0.25), OS (p = 0.28, in terms of singular HCC), and DFS (p = 0.89, in terms of singular HCC) between cases and controls. These findings are significant because they demonstrate that patients with subcardiac tumours should still be offered the operation and that the consent process for tumours located far from the heart should be identical. They also found a low complication rate, which might be attributed to higher tumour sizes and the treatment of many tumours in a single session. The surgical literature, on the other hand, reveals higher levels of postoperative morbidity ranging from 5 to 45% [37]. They treated tumours in 95.6% of instances with complete removal of tumour enhancement in the first session and 99.1% following retreatment, with a 7% local recurrence rate and no significant difference compared to the control group.

It was reported previously that hyperosmotic saline-enhanced radiofrequency and microwave ablation had the same results in treating hepatocellular carcinoma and colorectal liver metastasis [38]. These results were obtained by Radosevic *et al.* [18]. They also discovered that MWA produced bigger ablation zones than RFA, while having identical ablation zone morphologies (reported as a short to large diameter ratio) and a similar technical success and local tumour growth rate in liver tumours ranging in size from 1.5 to 4 cm. However, even with traditional RFA devices, local tumour

progression is less than 1% in tumours under 2 cm [39, 40], and in liver tumours larger than 4 or 5 cm may result in an unacceptable incidence of local tumour progression, occasionally exceeding 60% in classical references [39, 40].

Tilborg *et al.* [41] discovered that biliary complications (biloma/biliary leakage, biliary blockage, and bilio-pleural fistula) were more common following peribiliary-MWA (57%) vs. peribiliary-RFA (3%), in a retrospective investigation of 774 colorectal metastases treated with MWA or RFA in 243 patients. These large disparities did not diminish with operator experience, suggesting that MWA was initially regarded as less safe than RFA due to the less predicted ablation zone shape [42].

In contrast to Radosevic *et al.* [18], Zhimin *et al.* [14] conducted a prior systematic study on the efficacy and safety of radiofrequency and microwave ablation in the treatment of HCC. In cohort studies, microwave ablation exhibited a lower rate of local tumour development than radiofrequency ablation (OR = 0.78, 95% CI 0.64-0.96, P =.02). In cohort studies, the complete ablation rate of microwave ablation was greater than that of radiofrequency ablation (OR = 1.54, 95% CI 1.05-2.25, P =.03). There was no statistically significant difference between the two groups in terms of overall survival or disease-free survival. A meta-analysis revealed no statistically significant difference in the primary problems of microwave and radiofrequency ablation.

CONCLUSION

Following a thorough assessment of the literature, we determined that in the ablation therapy of hepatocellular carcinoma nodules, microwave ablation had greater complete ablation and lower local tumour growth than radiofrequency ablation. Mwa is preferable in big tumours (up to 6 cm), while cryoablation is recommended in recurring disease. MWA and cryoablation are recommended to RFA in perivascular disease due to a lower heat-sink effect. Chemoablation can be performed on lesions as small as 3 cm. Multifocal lesions (>3), tace, debs, and tare are to be employed in the intermediate stage.

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