

Review Article

Management of small hepatocellular carcinoma in cirrhotic patients: resection versus ablative therapies

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ABSTRACT

Hepatocellular carcinoma (HCC), the most prevalent liver cancer type, has a heterogeneous molecular and physiological basis with several contributing factors. Cirrhosis is the number one underlying factor for HCC, accounting for approximately 80% of cases. The recent advances in diagnostics and screening have led to a substantial increase in the number of patients diagnosed at an early stage with small HCC. The gold-standard curative treatments for early-stage HCC are thermal ablation or resection. HCC treatment is particularly challenging in cirrhotic patients due to liver dysfunction and their being prone to portal hypertension. Thus, choosing between thermal ablation and resection remains an unresolved debate that requires balancing radical removal of the tumor with preserving adequate functioning liver tissue. This review aims to explore the distinct etiology of HCC in cirrhotic patients and how it contributes to the development of malignancy. It also seeks to explore how cirrhosis affects the response to available treatment approaches by comparing the gold-standard methods used, ablation vs resection, taking into account recent evidence on liver cell preservation, portal hypertension consequences, and microvascular invasion, along with novel radiomics tools. To provide evidence-based recommendations for enhancing small HCC management in cirrhotic patients.

Keywords: Hepatocellular carcinoma, Management, Resection, Liver cirrhosis, Ablation, Radiomics

INTRODUCTION

The burden of cancer continues to pose a global challenge. According to the world health organization (WHO), 1 in 5 people develop cancer during their lifetime, with approximately 11% of men and 8.3% of women dying from the disease.¹ Being the 6th most common cancer type, liver cancer accounted for

approximately 866,136 new cases and 758,725 related deaths recorded worldwide in 2022, according to the WHO. Liver cancer is classified based on the type of cells involved. Among them is HCC, which arises from the hepatocytes. It is the predominant type, accounting for 75% of all liver cancer cases. The management of HCC remains a persistent challenge with poor prognosis and adverse patient outcomes. This can be attributed to its heterogeneous etiology.²

HCC has a heterogeneous molecular basis with a broad spectrum of morphological and phenotypic characteristics. In an attempt to understand its complex pathogenesis, the WHO, in the 5th edition classification in 2019, categorized HCC into eight subtypes based on molecular and histopathological characteristics, including steatohepatitis, clear cell, macrotrabecular-massive (MTM), scirrhous, chromophobe, fibrolamellar, neutrophil-rich, and lymphocyte-rich. Hepatitis B and C infections are among the main factors contributing to the pathogenesis of HCC.³ Recent research reported a substantial increase in the incidence of HCC in those struggling with obesity or metabolic syndrome in some high-income countries.⁴ Being in association with alcohol-induced cirrhosis, chronic alcohol abuse is a significant contributor to the malignant transformation of hepatocytes.⁵

Among all risk factors, cirrhosis is an underlying comorbidity in 80-90% of HCC patients.⁶ However, HCC may occur in non-cirrhotic patients with chronic viral infection or metabolic disorders. The risk for HCC increases in cirrhotic patients caused by viral infection or those struggling with non-alcoholic fatty liver disease.⁵ Treatment for cirrhotic patients with HCC requires a multidisciplinary approach owing to its multifaceted nature. Those at high risk of developing HCC are recommended to undergo regular surveillance with ultrasound and alpha-fetoprotein blood tests every 6 months.⁷ Given the recent advances in screening and diagnostic techniques, a massive number of HCC patients are being discovered at an early stage and have the opportunity for various curative treatment options, including surgery, liver transplantation, and other systemic therapies.⁸

HCC treatment is complex, and multiple options may be available for the same patient. The management of HCCs measuring 3 cm or less in patients with underlying cirrhosis remains controversial.⁶ Microwave ablation (MWA) and radiofrequency ablation (RFA) are the gold-standard treatments for very early (BCLC 0) and early (BCLC A) HCC based on the Barcelona Clinic Liver Cancer (BCLC) staging system.⁹ However, global guidelines contradict in balancing between the effectiveness of surgical resection in the radical removal of the tumor and the advantage of thermal ablation, preserving liver cells.¹⁰ Given the multifactorial etiology of HCC with factors of portal hypertension, microvascular invasion risk, and anatomical constraints, along with technological improvements in MWA and laparoscopic resection, the future of therapies continues to be reshaped. This emphasizes the need for specific guidelines and treatment approaches for cirrhotic patients with small HCC.¹¹

This review aims to explore the distinct etiology of HCC in cirrhotic patients and how it contributes to the development of malignancy. It also seeks to explore how cirrhosis affects the response to available treatment

approaches by comparing the gold-standard methods used, ablation vs resection, taking into account recent evidence on liver cell reserve, portal hypertension, and microvascular invasion, along with emerging radiomics tools. To provide evidence-based recommendations to enhance small HCC management in cirrhotic patients.

LITERATURE SEARCH

This review is based on a comprehensive literature search performed on November 6th, 2025, in the PubMed and ClinicalKey databases, as well as Google Scholar. Utilizing MeSH (Medical Subject Headings) and relevant keywords such as “hepatocellular carcinoma”, “management”, “resection”, “liver cirrhosis”, “ablation”, and “radiomics”. This review aims to explore the distinct etiology of HCC in cirrhotic patients and how it contributes to the development of malignancy. It also seeks to explore how cirrhosis affects the response to available treatment approaches by comparing the gold-standard methods used, ablation vs resection, taking into account recent evidence on liver cell preservation, portal hypertension consequences, and microvascular invasion, along with novel radiomics tools. The search was not restricted by date, language, or type of publication to ensure a broad exploration of the available literature.

DISCUSSION

Pathogenesis of HCC in cirrhotic patients

Cirrhosis is characterized by the progressive fibrosis of liver tissue and replacement of healthy tissue with regenerative nodules. It often occurs in association with chronic liver conditions, including hepatitis B and C viral infections, chronic alcohol abuse, autoimmune liver diseases, or metabolic disorders like hemochromatosis and non-alcoholic fatty liver disease.¹² Portal hypertension is the most substantial consequence of liver cirrhosis, underlying most of the adverse outcomes of the disease. Portal hypertension results from an increased resistance in the intrahepatic arteries combined with increased blood flow of portal (and hepatic arterial) blood flow. This can be attributed to structural alterations in liver tissue resulting from persistent fibrosis and angiogenesis.¹²

Such structural alterations impair the fundamental process of toxic substance detoxification by the liver. This triggers a pro-inflammatory response, which further enhances disease progression. Inflammation is the basis of the link between cirrhosis and HCC, as the vicious cycle between persistent inflammation and chronic liver injury creates a biological environment that fosters malignant transformation. While the exact role of inflammation in carcinogenesis is complex and not fully established, it is suggested that reactive oxygen species (ROS) resulting from inflammation-induced DNA damage in hepatocytes can lead to genetic alterations that can initiate malignant transformation.¹³

A constant stimulus for hepatocellular regeneration in the liver microenvironment characterizes cirrhosis. This is attributed to chronic inflammation and tissue fibrosis, leading to the formation of regenerative nodules. On the molecular level, ROS produced causes DNA damage in hepatocytes, which may induce gene mutations that can initiate malignant transformation. Moreover, hepatocytes exhibit a rapid turnover rate and an accelerated cell cycle, increasing the likelihood of replication errors and further contributing to genetic instability and oncogenesis.¹⁴

Cirrhosis fosters oncogenesis through persistent inflammation, increased hepatocyte cell proliferation, genetic mutations, and alterations in the liver microenvironment. These underlying mechanisms together contribute to the risk of HCC.¹² Being at a high risk of developing increased portal pressures, thrombocytopenia, poor clotting function, and stiff liver parenchyma due to fibrosis.¹⁰ Surveillance and treatment approaches for HCC patients with underlying cirrhosis should be more targeted to address this complex, multifaceted nature. Currently, there is a contradiction in balancing between the effectiveness of radical removal of the tumor via surgical resection and the advantage of preserving liver cells by using thermal ablation.

Current guidelines for clinical management of small HCC

The BCLC staging system, which is the most widely used HCC staging system, indicates that liver resection (LR) and local ablation (LA) are gold-standard curative treatments for very early (BCLC 0) and early (BCLC A) HCC. The Child-Pugh assessment is used to identify the appropriate treatment approach. According to these guidelines, LR should be performed in HCC patients with Child-Pugh A liver function and good liver reserve, no portal hypertension, and normal serum bilirubin. However, these guidelines do account for impact of underlying cirrhosis on surgical outcomes for patients with HCC.¹⁵

To address this issue, the American Association for the Study of Liver Diseases (AASLD) established an algorithm to select the appropriate surgical treatment for early-stage HCC based on tumor burden and liver function. However, surgical resection has been shown to help achieve tumor control and improve overall survival. In the most recent published AASLD algorithm for surgical treatment, resection was recommended for patients with a single lesion measuring 2 to 5 cm, Child-Turcotte-Pugh (CTP) class A, and no clinically significant portal hypertension (CSPH). This algorithm was reported to have superior patient outcomes compared to other selection approaches.¹⁶

Hepatic resection in small HCC management

Surgical resection has been recommended as the gold standard intervention for suitable candidates with very

early (BCLC) stage 0 and early (BCLC A) stage HCC with a single lesion. In 2022, an update to the BCLC prognosis and treatment strategy considered resection appropriate for patients with BCLC 0 disease who are liver transplant (LT) candidates and for those with BCLC A disease and a single HCC lesion. Identifying surgical candidacy depends on liver function, the absence of clinically significant portal hypertension, lesion location, and the patient's health status. Surgical resection has been shown to yield several beneficial outcomes in patients with small HCC.¹⁵

Surgical resection has been frequently reported to have high 5-year overall survival rates of 50-70% in small HCC patients with preserved liver function.^{17,18} However, the presence of microvascular invasion (MVI) increases the risk of recurrence. A systematic review of 11 non-randomized studies, including 1,576 patients, reported that anatomic resection significantly reduced the risk of local recurrence and improved 5-year overall survival. Anatomic resection was also effective in reducing early intrahepatic recurrence. However, it showed no effectiveness over non-anatomic resection in preventing late intrahepatic recurrence. Similarly, no significant differences were observed between anatomic and non-anatomic resections regarding postoperative morbidity, mortality, and hospitalization.¹⁹

The recent introduction of laparoscopic and robotic resection techniques has significantly reduced perioperative morbidity and shortened hospitalization duration without compromising recovery outcomes. However, careful assessment of liver function and portal hypertension is essential for cirrhotic patients to avoid postoperative liver failure.²⁰

Thermal ablation in small HCC management

Another widely used method is thermal ablation, particularly RFA and MWA, which have emerged as the fundamental treatment for very early (≤ 2 cm) and early (≤ 3 cm) HCC in non-candidate patients for surgical intervention. It is a minimally invasive image-guided method that uses heat to destroy tumor tissue, allowing the preservation of functional liver parenchyma and the opportunity of repeated treatments in case of tumor recurrence. A recent study by Gaia et al compared the efficacy of RFA and MWA in achieving a complete response in cirrhotic patients with early and very early HCC. The study included 251 HCC patients; 81 were treated with MWA and 170 with RFA. The complete response rate was similar between the MWA and RFA groups ($p=0.504$). However, a sub-analysis demonstrated that the probability of achieving a complete response using MWA for 21-35 mm nodules was almost 5 times higher than for RFA ($p=0.014$). Furthermore, the recurrence rate in 21-35 mm nodules was higher with RFA than with MWA ($p=0.019$). The survival rate was also significantly higher in the MWA than in the RFA group ($p=0.027$). No significant difference was observed

between the two treatments in the 15-20 mm nodules group. Thus, indicating that MWA is superior to RFA in achieving a complete response in HCC nodules measuring 21 to 35 mm in cirrhotic patients.⁹

Several technical considerations should be considered when applying thermal ablation, including the precise placement of image-guided probes and adherence to tumor size limitations. For instance, thermal ablation is not applicable for tumors larger than 3 cm in size, those located near bile ducts or major vessels, or those with underlying disease. Nevertheless, recent advancements, such as the implementation of image-guided fusion and the use of multi-probe MWA, are enhancing the precision and overall efficacy of thermal ablation for HCC. Despite having a slightly higher recurrence rate than surgical resection, it is still favorable for HCC patients with underlying cirrhosis.²¹

Ablation vs resection in cirrhotic patients with small HCC

In HCC patients with underlying cirrhosis, deciding between surgical resection and thermal ablation requires careful balancing between the need to radically remove the tumor and preserving enough functioning liver tissue, taking into account that cirrhotic patients suffer from impaired liver function and portal hypertension.

Current research supports the effectiveness of surgical resection over thermal ablation, with better long-term outcomes in the management of small HCC. For instance, a systematic review by Hu et al found that resection is associated with better long-term survival than ablation in early-stage HCC.²² Similarly, in patients with cirrhosis, Zhang et al reported, in a systematic review involving 16 comparative studies and a total of 3760 patients, that resection was associated with a significantly higher overall survival rate and significantly lower mortality and recurrence rates than RFA. The RFA group demonstrated fewer postoperative complications and shorter operative times than the resection group.²³ This suggests that ablation offers a better alternative for patients with compromised liver function or higher surgical risk.

Moreover, a study comparing MWA to laparoscopic resection in cirrhotic patients with portal hypertension found that MWA resulted in a significantly lower rate of postoperative liver decompensation (15.5% vs 32.8%), fewer complications, and a shorter period of hospitalization, while the two groups showed no significant difference regarding overall survival.²⁴ Given that ablation preserves liver function while maintaining overall survival, it may be a better option in patients with cirrhosis and portal hypertension.

Future prospects

Recent advances in radiomics and imaging-based biomarkers could help in early diagnosis of HCC, predict

treatment outcomes, and refine the decision between ablation and resection through risk stratification.²⁵ For instance, Guo et al developed and validated the ALARM model, the first clinical decision tool, which accurately provides early warning of HCC development in patients with cirrhosis 3-12 months before clinical diagnosis. The study included a large multicenter cohort of 1858 patients. The ALARM could identify the majority of individuals at risk of HCC in advance by integrating radiomics and deep learning scores with an aMAP HCC risk score.²⁶ Moreover, a systematic review and meta-analysis by Maung et al assessed the predictive performance of MRI radiomics models for HCC recurrence after curative treatments. They reported that radiomics models achieved high sensitivity and specificity and could potentially serve as non-invasive tools for treatment planning.²⁷

CONCLUSION

Management of early-stage small HCC is particularly challenging in cirrhotic patients and requires a multidisciplinary approach. Choosing between radically removing the tumor via surgical resection or preserving more functioning liver tissue by using thermal ablation remains an unresolved debate. Extensive research is required to further assess the safety and efficacy of both approaches and to establish specific guidelines for the management of small HCC in cirrhotic patients. With recent advances in technology, radiomics models can identify cirrhotic patients at risk of developing HCC earlier, before clinical diagnosis, and stratify them based on the prediction of treatment outcomes. Integrating clinical data, molecular findings, and radiomics can improve treatment outcomes and provide a personalized approach.

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