Management of Chronic Liver Disease in Patients with Hepatocellular Carcinoma

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KEYWORDS

• Hepatocellular carcinoma • Cirrhosis • Ascites • Esophageal varices • Viral hepatitis • MASLD

KEY POINTS

- Uncontrolled ascites and spontaneous bacterial peritonitis are contraindications to liver resection and catheter- and probe-based locoregional therapy.
- Variceal management is especially important in managing HCC with the systemic therapy combination atezolizumab/bevacizumab, which has an increased risk for bleeding complication.
- Nutrition is an underappreciated component of cirrhosis management, and correcting nutritional deficits is important in patients with hepatocellular carcinoma (HCC) who are awaiting various therapies to slow progression or undergo curative therapy such as resection or liver transplant.
- Treatment of hepatitis B virus (HBV) and hepatitis C virus infections improves overall survival for patients with HCC, and in some settings, it may help to reduce the risk of HCC recurrence.
- Incidence of HCC and its associated mortality are rising in patients with alcohol-related liver disease as well as metabolic syndrome-associated steatotic liver disease.

INTRODUCTION/BACKGROUND

Hepatocellular carcinoma (HCC) most often occurs in the setting of cirrhosis, thus the management of portal hypertension (PH) complications in the setting of pursuing treatment is a requisite consideration, particularly when decompensation is a frequent contraindication to undertaking any mode of therapy.[1] Maintaining hepatic compensation or using therapeutics to move a patient from a decompensated to a compensated state can be critical to keep all possible HCC treatment options available. Basic PH

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management is the cornerstone of compensation, but there are some liver disease-specific and HCC treatment-specific considerations regarding the management of these predictable clinical problems that occur frequently in patients with cirrhosis. Frequently, the most effective approach to accomplish hepatic compensation entails treating the underlying cause of liver disease or active PH complication and refining nutrition. Additionally, certain Model for End-Stage Liver Disease (MELD) score parameters represent contraindications to specific therapies for HCC, and medical therapy can help to mitigate those factors.

MANAGEMENT OF PORTAL HYPERTENSION AND CIRRHOSIS COMPLICATIONS IN HEPATOCELLULAR CARCINOMA

PH complications of cirrhosis are predictable impediments to undertaking most of the curative, bridging, and palliative therapies for HCC, which obviously affect a patient's prognosis and eligibility for definitive therapies like liver resection and transplant. Managing PH is a critical element to getting HCC patients with cirrhosis ready for therapy. These complications include ascites and fluid overload, hyponatremia, hepatic encephalopathy (HE), esophageal varices and gastric varices, and jaundice/hyperbilirubinemia.

Ascites

Management of ascites involves nutritional guidance and combination diuretic therapy with an aldosterone antagonist and loop diuretic.[2] A randomized controlled trial (RCT) comparing sequential versus combination therapy at the outset of ascites treatment concluded that combination therapy was more effective in resolving ascites (76% vs 56%) with fewer electrolyte disturbances.[3] Combination diuretic therapy is generally initiated with spironolactone and furosemide in a 100:40 ratio with titration of the medications per electrolytes and renal function. Diuretic therapy should be combined with dietary sodium restriction of 2000 mg/d under the supervision of a dietician, given that this naturally precludes many food options and thus may hamper patients' ability to reach protein and calorie goals.[2] Paracentesis is an effective temporizing measure to provide symptomatic relief while allowing assessment for spontaneous bacterial peritonitis (SBP), a high-risk condition with an estimated 3 month mortality of 22% even after appropriate treatment with third-generation cephalosporins and albumin[4] and with secondary antibiotic prophylaxis.[2] Uncontrolled ascites and SBP are contraindications to liver resection and catheter- and probe-based locoregional therapy (LRT). If serial paracentesis is required, consideration can be given to undertaking transjugular intrahepatic portosystemic shunt (TIPS) placement if liver function, clinical history, and MELD score are not prohibitive with a multidisciplinary, shared decision-making approach.[5] In a recent meta-analysis from RCTs, TIPS successfully decreases recurrent ascites versus standard combination diuretics (42% vs 89%) at the cost of increased HE episodes per year (0.6 vs 1.1).[6] Tumor location or degree of hepatic decompensation may preclude the safe placement of TIPS.

Hyponatremia

Reduced serum sodium (<135 mEq/L) is a common complication in decompensated cirrhosis, affecting 31% of a large national database of transplant candidates.[7] Hyponatremia management involves correcting volume depletion of any cause and actively managing diuretic therapy, sometimes resulting in temporary diuretic discontinuation and albumin infusions. Refectory severe hyponatremia (<125 mEq/L) is usually helped through fluid (especially water) restriction to less than 2000 mL/d.[2]

Esophageal and Gastric Varices

Much recent PH research has focused on refining therapy for varices given the short-term mortality of variceal bleeding has remained approximately 20%.[8] Carvedilol has emerged as the leading nonselective beta-blocker (NSBB) for most effective portal pressure reduction, theorized to be related to its effects in reducing intrahepatic resistance due to additive alpha-blocking effects.[9] Any patient with large, high risk-appearing varices or prior variceal bleeding should be prescribed NSBB.[10] Carvedilol at starting dose 3.125 or 6.25 mg twice daily per blood pressure is the preferred agent.[9] Carvedilol has been shown to reduce bleeding events more effectively than serial band ligation (10% vs 23%) when compared head-to-head over 20 months of follow-up in patients without prior bleeding.[11] NSBB also appears to reduce the risk of decompensation or death over a 3 year period compared to placebo (16% vs 27%) in patients with clinically significant PH.[12] Variceal management is especially important in the case of managing HCC with the systemic therapy combination atezolizumab/bevacizumab, which has an increased risk for bleeding complication[13,14]; therefore, it is standard of care for patients with HCC who are planned to undergo therapy with this combination to undergo pretreatment esophagogastroduodenoscopy (EGD) to assess for high-risk varices and esophageal variceal ligation and NSBB therapy. TIPS is a possible option for variceal management in selected patients with low traditional MELD score and a favorable HCC tumor location.[15]

Hepatic Encephalopathy

Typical triggers of overt HE ($\geq$ West Haven grade 2) include infection, gastrointestinal (GI) bleeding, intravascular volume depletion with electrolyte abnormalities, and sedating medications. Overt HE episodes should be treated with intravenous (IV) volume repletion and lactulose (oral $\pm$ rectal) until bowel movements begin and are maintained at a rate of 3-4 per day. Rifaximin is indicated as secondary prophylaxis to prevent rehospitalization (placebo 23% vs rifaximin 14%).[16] In a recent meta-analysis to assess lactulose benefit in cirrhosis and HE, lactulose reduced recurrent overt HE episodes compared to placebo (26% vs 47%) and was associated with overall survival benefit (93% vs 86%).[17]

Nutrition in Cirrhosis

Nutrition is frequently an underappreciated component of cirrhosis management, and this is particularly important in patients with HCC who are waiting for various therapies to slow progression or undergo curative therapy such as resection or liver transplant. Malnutrition is very common in cirrhosis—it occurs in 20% of compensated patients and up to 50% of decompensated patients—and contributes to loss of muscle mass and muscle contractive strength resulting in sarcopenia and frailty in 30% to 70% of patients with cirrhosis.[18]

Common tenets in nutrition management in cirrhosis include maintaining an evenly distributed daily target protein intake of 1.2 to 1.5 g/kg and calorie intake of 25 to 35 kcal/kg of dry body weight[19] while simultaneously following a sodium-restricted 2000 mg/d diet. With this era's obesity prevalence so high, many patients also face dietary limitations related to carbohydrates in following a diabetic diet. Clearly, guidance from a nutrition specialist/dietician can greatly benefit patients with these complex overlapping dietary restrictions. Screening for malnutrition and frailty should be a routine periodic assessment of all patients with cirrhosis. This applies especially to patients with HCC who are undergoing therapies where they may be none per oral (NPO) or suffer short-term or medium-term symptoms such as jaundice, nausea, loss of

appetite, or decompensation. Once malnutrition and/or frailty are identified, a structured plan designed by the nutrition and management team is critical to address deficits. This should include calorie and protein intake throughout the day including a day-end snack to avoid a long nighttime fasting period, which has been shown to lead to greater catabolism and muscle loss.[20] Cirrhosis complications such as ascites (early satiety) and HE (cognitive decline) present obstacles for many decompensated patients. Frailty should also be addressed via involvement of a certified physical therapist.[19] All of these components are important in preventing and treating any decline in functional status suffered by a patient with cirrhosis, regardless of the level of compensation.

COMPLICATIONS OF HEPATOCELLULAR CARCINOMA THERAPY

Catheter-based and probe-based locoregional therapies and systemic medical therapies all carry risks, especially in the impaired, cirrhotic liver. Maintaining or returning to a compensated state prior to therapy is important to avoid potential adverse events that can significantly worsen clinical status and jeopardize future therapies, transplant, or survival.

Locoregional Therapy

The predominant probe-based LRT utilized is microwave ablation (MWA). The therapeutic effects and complications of MWA are generally immediate with no delayed effects unlike catheter-based embolic therapies. MWA is also available to patients with a higher degree of decompensation because of its local, predictable, immediate effect. Despite these benefits, complications do occur. Major hemorrhage occurs in approximately 0.1% to 0.4% of cases; other vascular injuries including pseudoaneurysm and thrombosis (including portal vein thrombosis [PVT]) are less common. Biliary complications manifest as post-MWA biliary strictures, bile leak, biloma formation, or acute cholecystitis—all occur in less than 0.5% of cases. Diaphragmatic injury, perforation of the gallbladder, colon, and stomach and breeching the pleural space with the ablation needle causing pneumothorax or hemothorax are all rare complications.[21]

Transarterial chemoembolization (TACE) and radioembolization (TARE) are two of the most common catheter-based treatments for HCC. These are more regional therapies with somewhat delayed effects due to the release of embolics that contain either chemotherapeutic (TACE) or yttrium-90 (Y-90, TARE); thus, these therapies' adverse effects can be delayed and prolonged. Conventional TACE utilizes lipiodol to deliver a chemotherapeutic locally to the tumor, using the avidity of HCC for lipiodol. DEB-TACE versus TARE utilize chemotherapy versus Y-90 impregnated beads to deliver therapy to the tumor while also providing embolization of tumoral capillaries due to bead size.[21] Because of their embolic nature, both techniques carry similar complication risks. These include postembolization syndrome (PES), which includes symptoms of right upper quadrant pain, fever, nausea, vomiting, malaise, and jaundice in the most severe cases. PES occurs in 20% to 80% of TACE patients and slightly fewer TARE patients (40%–60%).[22] PES likely occurs due to systemic distribution of the therapeutic agent and also possibly from low-grade infarction of the treated territory. Liver infarction is more likely to occur with the treatment of a larger tumor or after repeat treatments. If infarction is large enough or PVT occurs, then liver failure may occur, but this is rare (0.5%–1%).[21] Liver abscess is rare but may occur in the setting of unrecognized smaller peripheral branch PVT. Biliary injury leading to biliary ischemia or fistulas are rare. Cholecystitis from reflux of beads into the cystic artery is also rare (1%–2% in older series).[23] Lung and skin injuries may occur with either

treatment, mainly related to shunting, but this is obviated in TARE by undertaking a "trial run" with radiotracer beads to quantify shunt fractions to lung and GI organs. TARE includes the additional complications related to radiation injury to nearby organs and skin.

Systemic therapeutics may be highly effective agents in patients with bilobar or multifocal disease; however, they carry side effects specific to each agent or combination of agents (**Table 1**). Sorafenib, a rapidly accelerated fibrosarcoma (RAF)-system and tyrosine kinase inhibitor (TKI), was the first agent with clinical trial data supporting efficacy in HCC,[24] but it carries a relatively limiting side effect profile that includes diarrhea, hypertension, bilirubin and liver enzyme elevation, and most notably hand–foot skin reaction. Lenvatinib is a second-generation TKI but has different side effects that include more vascular and renal problems along with hypertension. Atezolizumab is an immune checkpoint inhibitor (ICI), which is usually utilized in conjunction with bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor. This combination therapy has revolutionized HCC therapy. However, both agents convey a formidable list of side effects. Atezolizumab may cause musculoskeletal pain, electrolyte abnormalities, rash, cough, nausea, and diarrhea. Bevacizumab is associated with hypertension, fatigue, proteinuria, and most importantly GI bleeding and nosebleeds. Last, cabozantinib is an HCC salvage therapy from the TKI group with a similar side effect profile to sorafenib but with effectiveness as a rescue agent.[25]

DIAGNOSIS AND MANAGEMENT OF IMMUNE CHECKPOINT INHIBITOR HEPATITIS

ICI hepatitis is uncommon in monotherapy applications, but the condition occurs much more frequently with combination ICI-ICI or ICI-TKI therapy, occurring in approximately 25% of patients treated with ipilimumab–nivolumab combination.[26] More frequent hepatitis also occurs when ICI is utilized along with chemotherapy and other targeted agents. This raises the concern that ICIs sensitize the liver to injury by other agents. ICI hepatitis histologically resembles autoimmune hepatitis with lymphocytic-predominant inflammation but has much fewer plasma cells.

Table 1
Common systemic therapeutic agents versus advanced hepatocellular carcinoma and common side effects

Therapeutic Agent	Agent Class	Reported Side Effects
Sorafenib	TKI	Diarrhea, hand–foot syndrome, hypertension, fatigue, bilirubin elevation, thrombocytopenia, AST elevation, rash, anorexia, and alopecia
Lenvatinib	TKI	Hypertension, heart problems, hypercoagulability, liver enzyme elevations, proteinuria, and diarrhea
Atezolizumab	ICI	Musculoskeletal pain, decreased appetite, hyperglycemia, hyponatremia, hyperkalemia, hypermagnesemia, hypophosphatemia, pruritus, rash, cough, dyspnea, fatigue, fever, malaise, abdominal pain, diarrhea, constipation, and nausea
Bevacizumab	VEGF-I	Hypertension, fatigue, weakness, proteinuria, gastrointestinal bleeding, and nosebleeds
Cabozantinib	TKI	Diarrhea, fatigue, hypertension, hand–foot syndrome, weight loss, decreased appetite, stomatitis, nausea, dysgeusia, and dyspepsia

Abbreviations: ICI, immune checkpoint inhibitor; TKI, tyrosine kinase inhibitor; VEGF-I, vascular endothelial growth factor inhibitor.

Routine blood monitoring should include usual liver tests (AST, ALT, bilirubin, and alkaline phosphatase) along with serologic evaluation for hepatitis B, given the possibility of reactivation of the infection in the setting of ICI utilization with therapies recommended to combat ICI hepatitis. ICI hepatitis is frequently asymptomatic and diagnosed on periodic blood monitoring. Symptoms that patients may encounter include jaundice, fever, and malaise. Hepatologists are generally engaged to ensure a complete evaluation of other possible causes of hepatitis and to aid with the evaluation and management of more severe ICI hepatitis episodes. Given the immunomodulatory effects of oncology therapies and potential structural disease in the setting of solid metastases in the liver, complete evaluation for infectious, autoimmune, metabolic, and structural causes of hepatitis or jaundice should be performed with laboratories and imaging.

ICI hepatitis is generally categorized by 4 grades, stratified by the degree of elevation of AST, ALT, or bilirubin (**Table 2**). Grade I hepatitis (aspartate aminotransferase [AST] or alanine aminotransferase [ALT] 1–3× upper limit of normal [ULN] or total bilirubin [TBR] 1.5× ULN) generally requires closer monitoring but no dose adjustment or additional treatment is required, granted there is no progression. In grade II ICI hepatitis (AST or ALT 3–5× ULN or TBR 1.5–3× ULN), temporary hold of IC therapy is recommended with close attention to medication lists, as other possible hepatotoxic meds should be discontinued when feasible. Prednisone 0.5 to 1 mg/kd/d is reserved for symptomatic grade II patients or those without improvement with 1 to 2 weeks of delayed ICI dosing, and ICI may be resumed once the hepatitis has regressed to grade I with prednisone dose of 10 mg/d or less. In grade III patients (AST or ALT 5–20× ULN or TBR 3–10× ULN), the ICI agent should be discontinued. IV methylprednisolone 1 to 2 mg/kg/d is recommended with a multiweek taper. In patients who do not respond or who have flares following an initial improvement, second-line agents such as mycophenolate or tacrolimus should be considered. Grade IV patients (AST or ALT > 20× ULN or TBR > 10× ULN or presence of ascites or HE) should be hospitalized at a tertiary liver center. ICIs should be permanently discontinued with methylprednisolone 2 mg/kg/d treatment with similar multiweek taper with consideration of additional immunomodulatory agents as indicated by response. Liver biopsy should be considered in suspected grades III and IV ICI hepatitis.[26]

SPECIFIC LIVER CONDITIONS AND IMPACT IN HEPATOCELLULAR CARCINOMA

For some subsets of patients there may be disease-specific risks associated with the development of HCC, which may impact their outcomes. These include chronic hepatitis B virus (HBV) infection, chronic hepatitis C virus (HCV) infection, metabolic syndrome-associated steatotic liver disease (MASLD), metabolic syndrome in general, and alcohol abuse. In this section, we will discuss the ways in which these conditions impact HCC management.

Hepatitis B

Chronic HBV infection accounts for almost 50% of HCC cases worldwide, mostly in patients with HBV-related cirrhosis.[27,28] Common risk factors for developing HCC in the setting of chronic HBV infection include the presence of cirrhosis, older age, male sex, coinfection with hepatitis D or hepatitis C, metabolic syndrome, and family history of HCC. The most significant risk factors from this group appear to be the presence of cirrhosis and family history.[29] Studies suggest that the treatment of chronic HBV infection reduces the risk of de novo HCC development, and tenofovir or entecavir appear to be equal in this regard.[30,31] It is unclear, however, whether this evidence

Table 2
Management of immune checkpoint inhibitor hepatitis by grade of injury

	Grade I	Grade II	Grades III–IV
Degree of AST/ALT elevation	≤3× ULN	3–5× ULN	>5× ULN
Degree of bilirubin elevation	≤1.5× ULN	1.5–3× ULN	>3× ULN
Liver biopsy?	Not recommended	Consider liver biopsy	Perform liver biopsy
Hospitalization?	Not recommended	Not recommended	Consider hospitalization
Continue or hold ICI?	Continue ICI if no symptoms	Hold ICI	Discontinue ICI permanently
Corticosteroids?	Not recommended	Prednisone 0.5–1 mg/kg/d	Methylprednisolone 1–2 mg/kg/d
Alternative agent?	Not recommended	Not recommended	Consider mycophenolate, tacrolimus, or azathioprine if poor response by 3 d

All patients should undergo a serologic evaluation to exclude viral hepatitis and alternative etiologies of liver injury, be advised to avoid alcohol intake, supplement use, and hepatotoxic medications, and consider imaging to exclude biliary obstruction when indicated. All patients where ICI hepatitis is suspected should undergo close laboratory monitoring.

Abbreviations: ICI, immune checkpoint inhibitor; ULN, upper limit of normal.

can be extrapolated to patients with chronic HBV infection who have already developed HCC with regards to preventing recurrence and improving the response to HCC therapy.

Since most patients with HBV-related HCC will have underlying cirrhosis, treatment with nucleoside analog therapy per guidelines is standard of care.[32,33] Therefore, many patients with HBV cirrhosis may already be on therapy at the time of diagnosis of HCC or will otherwise have an obvious indication for therapy (presence of cirrhosis). Treatment is imperative in these patients as slowing progression of disease and maintaining a compensated state will keep open therapeutic options that may otherwise not be available in more advanced stages of cirrhosis.

Studies directly evaluating patients with noncirrhotic HBV-related HCC have shown long-term improvements in recurrence-free survival as well as overall mortality in patients who are on antiviral therapy prior to undergoing curative resection.[34–36] This is likely because one of the primary risk factors for HCC recurrence after surgical resection or liver transplantation is a high preoperative hepatitis B viral load.[37]

Beyond understanding the impact underlying liver disease has on the outcomes of the interventions for HCC, it is also important to understand how therapy for HCC may impact the underlying liver disease. This is most important for patients with HBV infection. There are data to suggest that patients undergoing TACE for HBV-related HCC have an increased risk of HBV reactivation, which can lead to severe acute hepatitis. Treatment with antiviral therapies can effectively mitigate this risk of reactivation.[38,39] Aside from TACE, viral reactivation has been reported in patients undergoing therapy with ablation, TKIs, and radiotherapy.[40–42] These risks all appear to be mitigated by antiviral therapy. In fact, in studies with ICI for HCC therapy, all patients with chronic HBV infection had to have viral suppression with antiviral therapy prior to enrollment. There have been very low rates of reactivation in these studies despite using medications that stimulate the immune system.[43–45] With adequate viral suppression, it appears that all HCC therapies are safe in patients with chronic HBV infection.

Hepatitis C

Since the advent of direct acting antiviral (DAA) therapies for the treatment of HCV infection, there have been debates on their effect regarding HCC, both in its initial development and recurrence following therapy.[46,47] However, subsequent analyses of DAA therapies have shown that eradicating HCV infection is associated with a decreased risk of developing de novo HCC; thus, treating HCV infection in patients who already carry a diagnosis of HCC would also help reduce the risk of recurrent disease.[48]

Early studies suggested the opposite result that DAA therapy may increase early recurrence risk, but a subsequent meta-analysis fortunately disproved this association noting significant heterogeneity and bias in the initial investigations.[49] Specifically, a study comparing patients who underwent DAA therapy after HCC treatment with those who did not undergo DAA therapy did not find a difference in HCC recurrence rates but did note a significantly improved overall survival in patients who underwent DAA therapy.[50] It is unclear based on this study if patients suffering recurrence were more likely to have underlying cirrhosis, as this study was not specifically controlled for the presence of cirrhosis.

In a multicenter cohort study evaluating patients with HCC secondary to chronic HCV infection, 95% of study patients had underlying cirrhosis. Only 26% of the entire cohort received HCV therapy during the study period, and subjects underwent a wide range of treatments including resection, transplantation, and loco-regional therapies, with a significant portion undergoing no therapy at all. HCV treatment was associated

with a significantly higher overall median survival (70 vs 21 months) and on multivariable analysis, HCV treatment remained a significant predictor of overall survival. For those patients who underwent curative therapy with surgical resection or liver transplantation, HCV treatment also significantly improved recurrence-free survival.[51] Two additional large multicenter studies from North America and Italy confirmed that, while eradication of HCV infection does have a significant overall impact on reducing risk of HCC recurrence, it does significantly improve the overall survival.[52,53]

Many of these studies suggested an improved overall survival with HCV therapy in the setting of HCC, most likely related to avoiding decompensation rather than secondary to direct HCC-related effects. A study from Japan supports this theory by using propensity score matching to compare Child–Pugh A patients with HCC who underwent DAA therapy with untreated patients. The authors found that while overall survival was significantly better in the group undergoing DAA therapy, the treatment group also maintained compensated Child–Pugh A status much more frequently over the 5 year follow-up period (96% vs 38%, respectively).[54]

Other Chronic Liver Diseases

Although there were previous suggestions that iron overload, and thus hereditary hemochromatosis (HH), may increase the risk of developing HCC, further clinical studies appear to disprove this.[55] In a large database study from the United States, there was an association between HH without cirrhosis and development of HCC.[56] However, a study comparing outcomes of patients with HH versus those without HH undergoing therapy for HCC did not show any significant difference in overall survival or recurrence rates between the groups.[57] In this study, the primary predictor of survival was Barcelona Clinic Liver Cancer (BCLC) stage at the time of diagnosis. Based on these reports, no special consideration is recommended for patients with HH who are undergoing therapy for HCC.

Alcohol-related liver disease (ALD) and MASLD are increasingly associated with both incidence of and mortality from HCC, with alcohol use itself potentially increasing HCC risk up to 5 fold.[58,59] More concerning, it has been postulated that up to one-third of HCC cases in patients with MASLD occur in the absence of cirrhosis, though it is unclear at this time which risk factors impact this enough to justify HCC screening/surveillance.[60,61] Beyond MASLD specifically, the presence of obesity increases the risk of HCC development. Additionally, the presence of type 2 diabetes mellitus also increases HCC risk, even in the absence of obesity.[62,63] These findings support a general increase in carcinogenesis in patients with underlying metabolic syndrome related diseases, irrespective of the presence of MASLD.

Despite these significant associations between metabolic syndrome and MASLD, there are no studies to support that weight loss, the primary treatment of these conditions, reduced the risk of HCC development or recurrence.[64] However, lifestyle interventions with a goal of weight loss should be pursued to slow the progression of liver disease and potentially preserve liver function to increase available therapy options for HCC. These must be done under careful supervision, especially in patients who already suffer from decompensated cirrhosis, as the combination of sarcopenia from chronic liver disease and underlying obesity may actually worsen with weight loss, thus negatively impacting these patients' physical functioning.[19]

SUMMARY

Most patients with HCC will present in the setting of cirrhosis, and underlying liver function has a significant impact on their ability to undergo and respond favorably

to specific HCC therapies. Managing patients with decompensated cirrhosis with the goal to improve their underlying liver function and portal hypertensive complications likely will improve their access to HCC therapy. Special attention should be paid to the importance of nutrition interventions in these patients. Management of comorbid, noncirrhotic liver disease in the setting of HCC also has implications for both risk of HCC recurrence and overall survival. Treating HBV and HCV infections prior to therapy can significantly improve patient outcomes and will help avoid acute reactivation of HBV. Managing lifestyle interventions in patients with ALD and MASLD may help improve access to various therapies for HCC though more investigation is needed in these areas to better understand the impact of these interventions.

CLINICS CARE POINTS

- Portal hypertensive complications, which include ascites, spontaneous bacterial peritonitis, esophageal varices, and hepatic encephalopathy, are common barriers to undertaking HCC treatment in cirrhosis patients.
- Most complications of HCC treatment are predictable and thus can be prevented or managed with acceptable outcomes.
- Effective treatment of viral hepatitis with currently available therapies clearly positively impacts prognosis in HCC.
- Management of the primary liver disease etiology positively impacts a patient's prognosis with HCC treatment through several possible mechanisms.

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