Advancing Hepatic Recompensation: Baveno VII Criteria and Therapeutic Innovations in Liver Cirrhosis Management.

Recompensation in Cirrhosis: Baveno VII Advances

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Abstract
The Baveno VII criteria redefine the management of decompensated liver cirrhosis, introducing the concept of hepatic recompensation marking a significant departure from the conventional view of irreversible decline. Central to this concept is addressing the underlying cause of cirrhosis through tailored therapies, including antivirals and lifestyle modifications. Studies on alcohol, Hepatitis C virus, and Hepatitis B virus-related cirrhosis demonstrate the efficacy of these interventions in improving liver function and patient outcomes. Transjugular intrahepatic portosystemic shunt (TIPS) emerges as a promising intervention, effectively resolving complications of portal hypertension and facilitating recompensation. However, optimal timing and patient selection for TIPS remain unresolved. Despite challenges, TIPS offers renewed hope for hepatic recompensation, marking a significant advancement in cirrhosis management. Further research is needed to refine its implementation and maximize its benefits. In conclusion, TIPS stands as a promising avenue for improving hepatic function and patient outcomes in decompensated liver cirrhosis within the framework of the Baveno VII criteria.

Key Words: Hepatic recompensation; Baveno VII; Transjugular intrahepatic portosystemic shunt; Portal hypertension; Cirrhosis; Decompensation.

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Core Tip: The manuscript explores the concept of hepatic recompensation outlined in the Baveno VII criteria, challenging the traditional view of decompensated liver cirrhosis as irreversible. It emphasizes the importance of addressing the underlying cause of cirrhosis, tailoring therapy accordingly, and achieving specific criteria for recompensation. Studies on alcohol, Hepatitis C Virus and Hepatitis B Virus-related
cirrhosis demonstrate how targeted interventions, including antiviral therapy and Transjugular intrahepatic portosystemic shunt (TIPS) procedures, promote hepatic compensation. While promising, optimal timing and therapy selection for TIPS remain unresolved. Nevertheless, TIPS emerges as a promising avenue for hepatic recompensation, offering renewed hope for patients previously deemed untreatable.

**INTRODUCTION**

The concept of hepatic recompensation, as outlined by the Baveno VII criteria, represents a significant advancement in the management of decompensated liver cirrhosis. Traditionally, decompensation has been viewed as a point of no return in the progression of liver disease. However, the Baveno VII guidelines propose a new paradigm by delineating specific criteria for hepatic recompensation, offering renewed hope for patients previously deemed ineligible for therapeutic intervention.

At the core of the Baveno VII concept of hepatic recompensation is the idea of addressing the underlying cause of cirrhosis. Whether through removal, suppression, or cure, targeting the primary etiology is essential to initiate the process of recompensation. Therapeutic modalities vary and are tailored to the specific etiology, including antiviral therapy for viral hepatitis, lifestyle modifications for alcohol-related liver disease or metabolic-associated fatty liver disease (MAFLD), or other targeted interventions as appropriate.

According to Baveno VII, liver recompensation is defined as the removal of the etiological factor of liver cirrhosis, resolution of ascites, hepatic encephalopathy, and absence of recurrent variceal hemorrhage for at least 12 months, along with stable improvement in liver function[1].

Regarding the alcoholic etiology, several studies have been conducted, such as that of Hofer et al[2], a retrospective study on 204 patients with alcohol-related liver cirrhosis, which analyzed the effect of alcohol abstinence on hepatic compensation. This research, based on the concept of hepatic compensation according to Baveno VII and through the
measurement of hepatic venous pressure gradient (HVPG), revealed that 18.1% of patients achieved compensation with a mean follow-up of 24 months. However, this compensation does not alter the risk of developing hepatocellular carcinoma (HCC), making adherence to screening programs still necessary. The study by Pose et al\textsuperscript{[3]}, a multicenter retrospective study conducted on 1001 Liver transplant-listed patients for alcohol-related liver cirrhosis, HCV-related, and non-alcoholic steatohepatitis-related cirrhosis, indicated that 8.7% were removed from the list due to improvement after a median follow-up of 29 months. The difference in results between the two aforementioned studies depends on both the different reference patient cohorts, which in the case of the Pose et al\textsuperscript{[3]} study is more selected, and on the diversity of the criteria chosen to define hepatic compensation, which only in the Hofer et al\textsuperscript{[2]} study faithfully follows the Baveno VII criteria.

Regarding HCV-related cirrhosis, the study by El-Sherif et al\textsuperscript{[4]} is a retrospective analysis of four clinical trials on the effects of direct-acting antiviral (DAA) therapy in patients with decompensated HCV-related liver cirrhosis. The primary outcome was improvement in liver function, defined as transition to Child-Pugh class A. Overall, 31.6% of Child-Pugh B patients and 12.3% of Child-Pugh C patients who achieved sustained virological response (SVR) after DAA therapy reverted to Child-Pugh class A. The study by Gentile et al\textsuperscript{[5]} is a multicenter prospective study involving 89 patients with Child-Pugh class B liver cirrhosis who received DAA therapy. Sustained virological response was achieved in 95.5% of patients; 61.8% of patients transitioned to Child-Pugh class A, 33.7% remained with Child-Pugh class B, and 4.5% worsened to Child-Pugh class C. This study demonstrated that DAA therapy is safe and has a high rate of sustained virological response and hepatic compensation. However, further research is needed to fully understand the long-term effects and impact on patient survival.

Regarding HBV-related liver cirrhosis, in cases of previous decompensation, therapy is based on nucleoside/nucleotide analogs (NUCs) that reduce circulating levels of HBV-DNA to undetectable levels in 80% of patients within a year\textsuperscript{[6-8]}. The study by Jang
et al\textsuperscript{[9]} is a prospective, multicenter study involving 707 patients who experienced their first episode of decompensation. The primary endpoint of the study was 5-year liver transplantation (LT)-free survival, while the secondary endpoint was virological response (VR), serological response, and improvement in liver function. Patients treated with antivirals showed significantly better survival without transplantation compared to untreated patients. The study by Yao et al\textsuperscript{[10]} recruited 23 patients with decompensated liver cirrhosis Child-Pugh B > 10 and treated them with Lamivudine. 60.9% of treated patients had a significant response, defined as a reduction in the Child-Pugh score of at least 3 points. Wang et al\textsuperscript{[11]} were the first to validate the Baveno VII criteria for liver compensation in patients with HBV-related liver cirrhosis treated with entecavir. In this multicenter study, 320 patients were enrolled, treated with Entecavir for 120 wk, and followed up for 6 months. 92.2% of the patients achieved a virological response with HBV DNA levels <20 IU/mL, and 56.2% of the patients achieved liver compensation according to the Baveno VII criteria. These studies demonstrate how antiviral therapy significantly modifies the natural history of decompensated cirrhosis, improving liver function and increasing survival.

All the studies mentioned so far indicate the importance of treating the underlying cause of cirrhosis to achieve liver compensation according to the criteria established by Baveno VII. In a specific subgroup of patients, an interventional radiology procedure can be added to improve the clinical outcome, which is transjugular intrahepatic portosystemic shunt (TIPS).

Traditionally, TIPS has been primarily indicated for specific complications of portal hypertension, such as acute variceal bleeding or refractory ascites. The rationale behind the use of TIPS lies in its ability to ameliorate the hemodynamic derangements characteristic of portal hypertension. By creating a shunt between the portal and systemic circulations, TIPS reduces portal pressure, thereby alleviating complications associated with portal hypertension (such as variceal bleeding and ascites), resolution of which is a prerequisite for hepatic recompensation according to the Baveno VII criteria.
As a consequence, it can be suggested that TIPS may play a broader role in promoting hepatic recompensation according to the criteria outlined in Baveno VII.

The retrospective evaluation by Gao et al\textsuperscript{[12]} highlighted the potential role of TIPS in achieving hepatic recompensation in a subset of patients with bleeding varices or refractory ascites, with approximately one-third of these patients meeting the criteria for recompensation after TIPS placement, underscoring its therapeutic efficacy in selected cases. In this retrospective study, 64 patients were enrolled, considering inclusion criteria and exclusion criteria. TIPS placement was successful in 100\% of cases, and no variceal bleeding occurred. The follow-up lasted for 12 months with patient reassessment at various intervals post-procedure. Several studies support the use of TIPS as a first-line treatment.

Regarding acute variceal bleeding, Liu et al\textsuperscript{[13]} conducted a retrospective study enrolling 50 patients with liver cirrhosis and portal pressure gradient (PPG) values $> 25$ mmHg. They divided the patients into two groups: one (35 out of 50 patients) treated with TIPS as first-line therapy in secondary prophylaxis of esophageal variceal bleeding, and the other (15 out of 50 patients) treated with TIPS as second-line therapy. The aim was to assess differences in survival and portal hypertension-related complications between the groups. During follow-up, a statistically significant difference in survival was observed between the first line and second-line groups (94.3\% vs. 66.7\%, log-rank $P = 0.01$), demonstrating the effectiveness of using TIPS as first-line therapy in improving survival.

Nicoară-Farcău et al\textsuperscript{[14]} conducted a meta-analysis of seven studies, including three randomized controlled trials and observational studies, comprising 1327 high-risk patients with liver cirrhosis and acute variceal bleeding (Child-Pugh B with active variceal bleeding or Child-Pugh C $< 14$). They compared the effects of preemptive TIPS, placed within 72 h of hospital admission for acute variceal bleeding, to endoscopy plus medical therapy with non-cardioselective beta-blockers. This meta-analysis clearly demonstrated beneficial effects in terms of survival, improved control of bleeding and ascites, and a lower rate of re-bleeding in this patient population.
Regarding the treatment of refractory ascites, Bureau et al. conducted a prospective study on 62 patients with liver cirrhosis complicated by decompensated ascites, requiring at least two large-volume paracenteses within a three-week period. Patients were randomized into two groups: one treated with TIPS placement (29 patients) and the other treated with large-volume paracentesis plus albumin (33 patients). All patients followed a low-salt diet and were evaluated at 1 month, 3 months, and after 1 year through blood tests and assessment of Child-Pugh and MELD scores. Additionally, Doppler ultrasound was performed at 6 and 12 months. The primary endpoint of the study was one-year transplant-free survival. The study demonstrated that the TIPS-treated group met the primary endpoint in 93% of cases, compared to 52% in the large-volume paracentesis plus albumin group. The latter experienced portal hypertension-related bleeding in 18% of cases (18% vs. 0%; \( P = 0.01 \)) and hernia-related complications in 18% of cases (18% vs. 0%; \( P = 0.01 \)). Hospitalization duration was higher in the large-volume paracentesis plus albumin group compared to the TIPS group (35 days vs. 17 days) \( (P = 0.04) \). In both groups, 65% of patients did not manifest hepatic encephalopathy in the first year. This study thus demonstrated the superiority of TIPS over large-volume paracentesis plus albumin in this patient population in terms of transplant-free survival and complications.

TIPS, however, is a technically complex procedure, with potentially fatal complications. These complications can be divided into intraprocedural, early, and late. Among the intraprocedural complications are those at the puncture site, during catheterization of the inferior vena cava or hepatic vein, during the puncture of the portal vein, hepatic artery injury, portal vein and/or mesenteric vein dissection. Early complications include hepatic encephalopathy, heart failure, bleeding, bile duct injury, STENT occlusion or migration. Late complications include TIPS dysfunction with persistence of signs of portal hypertension and endotipsitis. To reduce the rate of these complications and improve post-intervention survival, it is necessary to collaborate with a team of experts and perform adequate patient selection prior to the procedure. In this regard, the most commonly used score to predict outcome is the MELD score; for
example, a MELD > 18 at time zero is associated with an unfavorable outcome. Therefore, especially with elective procedures, a careful evaluation of the patient is necessary, taking into consideration various factors that correlate with the outcome as patient age, baseline liver function using CHILD-PUGH score, renal function, patient nutritional status, and cognitive status.

CONCLUSION
In conclusion, TIPS represents a promising therapeutic option for achieving hepatic recompensation in patients with decompensated liver cirrhosis, as it can address both the hemodynamic consequences of portal hypertension and the underlying etiology of cirrhosis, thereby improving hepatic function in this patient population. However, the concept of hepatic recompensation is still evolving, and several issues remain unresolved, such as the optimal timing for TIPS placement and therapy selection. Therefore, further studies are needed to maximize efficacy while minimizing risks.
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<td>1. Thomas Reiberger, Benedikt Silvester Hofer. &quot;The Baveno VII concept of cirrhosis recompensation&quot;, Digestive and Liver Disease, 2023</td>
<td>52 words — 2%</td>
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<tr>
<td>3. aasldpubs.onlinelibrary.wiley.com</td>
<td>19 words — 1%</td>
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<td>4. Portal Hypertension VI, 2016.</td>
<td>17 words — 1%</td>
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<td>5. <a href="http://www.ww.hivandhepatitis.com">www.ww.hivandhepatitis.com</a></td>
<td>17 words — 1%</td>
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<tr>
<td>6. Kadiyala Likitha Chowdary, Suneetha Manne, Yenduri Harshitha Lakshmi. &quot;Chapter 27 Detecting Retinopathy of Prematurity Disease Based on Fundus Image Dataset&quot;, Springer Science and Business Media LLC, 2024</td>
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