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<p>Patients with compensated advanced chronic liver disease have different prognoses depending on the presence of portal hypertension. Current non-invasive diagnostic methods allow identification of clinically significant portal hypertension. Portosystemic collaterals on imaging or liver stiffness of more than 20 to 25 kPa by using transient elastography identifies patients with clinically significant portal hypertension. Patients with liver stiffness of less than 20 kPa and platelet count of greater than 150 g/L can avoid endoscopy. This rule could be expanded using spleen stiffness. Methods to risk stratify for portal hypertension in compensated advanced chronic liver disease and successfully treated chronic hepatitis C and B are subject of research.</p>	
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<p>The first occurrence of decompensation constitutes a watershed moment in the natural history of chronic liver disease; it denotes a point of no return in a relevant proportion of patients. Preventive strategies may profoundly decrease cirrhosis-related morbidity and mortality. Removing the primary etiologic factor and cofactors, is key; however, a considerable proportion of patients require additional etiology-independent treatment strategies that target important pathomechanisms promoting decompensation (ie, portal hypertension and systemic inflammation). This article explains the importance of preventing first decompensation and summarizes the evidence for etiologic and etiology-independent (most important, nonselective beta-blockers and statins) therapies.</p>	
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<p>Nonselective beta-blockers represent the mainstay of medical therapy in the prophylaxis of variceal bleeding and rebleeding in patients with portal hypertension. Their efficacy has been demonstrated by numerous trials; however, there exist safety concerns in advanced disease, such as in patients with refractory ascites. Importantly, nonselective beta-blockers also exert nonhemodynamic beneficial effects that may contribute to a prolonged decompensation-free survival, as recently shown in the PREDESCI trial. This review summarizes the current evidence on nonselective beta-blocker therapy and proposes a tailored, patient-centered approach for the use of nonselective beta-blockers in patients with portal hypertension.</p>	

- The Role of Hepatic Venous Pressure Gradient in the Management of Cirrhosis** 327
Daniel Veldhuijzen van Zanten, Elizabeth Buganza, and Juan G. Abraldes
- Quantifying the degree of portal hypertension provides useful information to estimate prognosis and to evaluate new therapies for portal hypertension. This quantification is done in clinical practice with the measurement of the hepatic venous pressure gradient. This article addresses the applications of measuring portal pressure in cirrhosis, including the differential diagnosis of portal hypertension; estimation of prognosis in cirrhosis, including preoperative evaluation before hepatic and extrahepatic surgery; assessment of the response to drug therapy (mainly in the context of drug development); and assessing the regression of portal hypertension syndrome.
- Treatment of Acute Variceal Bleeding in 2021—When to Use Transjugular Intrahepatic Portosystemic Shunts?** 345
Anna Baiges, Marta Magaz, Fanny Turon, Virginia Hernández-Gea, and Juan Carlos García-Pagán
- Variceal bleeding in patients with cirrhosis is associated with high mortality if not adequately managed. Treatment of acute variceal bleeding with adequate resuscitation maneuvers, restrictive transfusion policy, antibiotic prophylaxis, pharmacologic therapy, and endoscopic therapy is highly effective at controlling bleeding and preventing death. There is a subgroup of high-risk cirrhotic patients in whom this strategy fails, however, and who have a high-mortality rate. Placing a preemptive transjugular intrahepatic portosystemic shunt in these high-risk patients, as soon as possible after admission, to achieve early control of bleeding has proved not only to control bleeding but also to improve survival.
- Bacterial Infections in Cirrhosis as a Cause or Consequence of Decompensation?** 357
Salvatore Piano and Paolo Angeli
- Bacterial infections are ominous events in liver cirrhosis. Cirrhosis-associated immune dysfunction and pathologic bacterial translocation are responsible for the increased risk of infections. Bacteria induce systemic inflammation, which worsens circulatory dysfunction and induces oxidative stress and mitochondrial dysfunction. Bacterial infections, frequently associated with decompensation, are the most common precipitating event of acute-on-chronic liver failure (ACLF). After decompensation, patients with cirrhosis have an increased risk of developing infections. Bacterial infections should be ruled out in these patients and strategies to prevent infections should be implemented to prevent further decompensation. We review infections as a cause and consequence of decompensation in cirrhosis.
- Nutritional Evaluation and Treatment of the Cirrhotic Patient** 373
Shira Zelber-Sagi, Dana Ivancovsky-Wajcman, Liane Rabinowich, Itay Bentov, and Liat Deutsch
- Malnutrition and sarcopenia that lead to functional deterioration, frailty, and increased risk for complications and mortality are common in cirrhosis. Sarcopenic obesity, which is associated with worse outcomes

than either condition alone, may be overlooked. Lifestyle intervention aiming for moderate weight reduction can be offered to obese compensated cirrhotic patients, with diet consisting of reduced caloric intake, achieved by reduction of carbohydrate and fat intake, while maintaining high protein intake. Dietary and moderate exercise interventions in patients with cirrhosis are beneficial. Cirrhotic patients with malnutrition should have nutritional counseling, and all patients should be encouraged to avoid a sedentary lifestyle.

Diagnosis and Management of Hepatic Encephalopathy **393**

Marika Rudler, Nicolas Weiss, Charlotte Bouzbib, and Dominique Thabut

Hepatic encephalopathy (HE) is a severe complication of cirrhosis. The prevalence of overt HE (OHE) ranges from 30% to 45%, whereas the prevalence of minimal HE (MHE) is as high as 85% in some case series. Widespread use of transjugular intrahepatic portosystemic shunt to control complications related to portal hypertension is associated with an increase in HE incidence. If the diagnosis of OHE remains simple in most cases, then the diagnosis of MHE is less codified because of many differential diagnoses with different therapeutic implications. This review analyzes current knowledge about the pathophysiology, diagnosis, and different therapeutic options of HE.

Acute Decompensation and Acute-on-Chronic Liver Failure **419**

Philip Ferstl and Jonel Trebicka

Liver cirrhosis is a major healthcare problem. Acute decompensation, and in particular its interplay with dysfunction of other organs, is responsible for the majority of deaths in patients with cirrhosis. Acute decompensation has different courses, from stable decompensated cirrhosis over unstable decompensated cirrhosis to pre-acute-on-chronic liver failure and finally acute-on-chronic liver failure, a syndrome with high short-term mortality. This review focuses on the recent developments in the field of acute decompensation and acute-on-chronic liver failure.

Management of Severe and Refractory Ascites **431**

Hélène Larrue, Jean Pierre Vinel, and Christophe Bureau

Considering the poor prognosis, severe and refractory ascites is a milestone in cirrhotic patients. Liver transplantation must be considered first. In the case of contraindication to liver transplantation or when the waiting period is estimated to be more than 6 months, transjugular intrahepatic portosystemic shunt should be discussed in eligible patients. Regardless of the type of treatment, a careful selection of patients is crucial to avoid further decompensation and specific complications of each treatment.

Monitoring Renal Function and Therapy of Hepatorenal Syndrome Patients with Cirrhosis **441**

Adrià Juanola, Cristina Solé, David Toapanta, Pere Ginès, and Elsa Solà

Acute kidney injury (AKI) is a frequent complication in patients with cirrhosis. Patients with cirrhosis can develop AKI due to different causes.

Hepatorenal syndrome (HRS) is a unique cause of AKI occurring in patients with advanced cirrhosis and is associated with high short-term mortality. The differential diagnosis between different causes of AKI may be challenging. In this regard, new urine biomarkers may be helpful. Liver transplantation is the definitive treatment of patients with HRS-AKI. Vasoconstrictors and albumin represent the first-line pharmacologic treatment of HRS-AKI. This review summarizes current knowledge for the diagnosis and management of HRS in cirrhosis.

Invasive Procedures in Patients with Cirrhosis: A Clinical Approach Based on Current Evidence

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Annabel Blasi and Andres Cardenas

The aim on of this article is to provide an update on the coagulation disturbances of patients with cirrhosis. It summarizes basic concepts of coagulation in cirrhosis, available tests used to predict bleeding, procedures and risk of bleeding, and the rationale and expert-based recommendations of prophylactic measures for patients with cirrhosis who undergo invasive procedures.

Current Concepts of Cirrhotic Cardiomyopathy

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Manhal J. Izzy and Lisa B. VanWagner



Video content accompanies this article at <http://www.liver.theclinics.com>.

Cirrhotic cardiomyopathy (CCM) connotes systolic and/or diastolic dysfunction in patients with end-stage liver disease in the absence of prior heart disease. Its prevalence is variable across different studies but recent data suggest that CCM may affect up to one third of liver transplant candidates. The etiology of CCM is multifactorial. CCM defining features were recently revised to improve the diagnostic and prognostic yield of CCM criteria and inform candidate selection for liver transplantation. CCM appears to increase the risk for unfavorable outcomes pre- and post-transplant. Close clinical and echocardiographic follow-up of patients with CCM may mitigate adverse cardiac outcomes.