



## Foreword

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Cirrhosis of the liver is a highly prevalent disease worldwide that can have a variety of causes, such as viral hepatitis B or C, alcohol consumption, non-alcoholic fatty liver disease (NAFLD), autoimmune diseases, cholestatic diseases, or iron or copper overload [1]. Cirrhosis is the 11th leading cause of death worldwide and the third leading cause of death in the population aged 45–64 years [2]. The disease progresses from an asymptomatic phase, or compensated cirrhosis, to a symptomatic phase, or decompensated cirrhosis, and its complications often lead to hospitalization, loss of quality of life and high mortality [1]. These complications are primarily the development of ascites, hepatic encephalopathy, esophageal variceal bleeding, infections and the development of hepatocellular carcinoma (HCC).

Of particular interest is the development of HCC. Liver cancer is a global health problem whose incidence and mortality have been increasing in recent years, it being the sixth most diagnosed cancer, the third leading cause of cancer deaths worldwide, and the foremost cause of death in cirrhotic patients [3]. Despite advances in surgical and locoregional treatment of HCC in recent years [4], it is estimated that 50–60% of HCC patients will require systemic treatment [5]. Its management is complex, since clinicians have to deal

with two complex and severe diseases, cancer and cirrhosis, and so, expertise in both is absolutely a must.

In this supplement, the focus is cirrhosis and its decompensations, as well as the adverse pharmacological effects and nutritional problems that can occur in these patients, building an updated review of the most frequent challenges in clinical practice for hepatologists. All the different chapters have been developed by well-known experts in their respective fields, who have aimed to display a practical approach helpful for daily clinics and to open eyes to future perspectives.

Hepatic encephalopathy (HE) is addressed in a chapter by Rita García and colleagues, with the discussion ranging from physiopathology and classification to a complete and adequate diagnosis and potential actual and future therapeutic approaches, emphasizing that prognosis and HE burden in patients and caregivers highlight the need for adequate clinical management [6].

Acute or chronic liver failure, renal impairment including hepatorenal syndrome, and cardiopulmonary complications of cirrhosis are summarized in the article by Luis Téllez and Antonio Guerrero. They give readers practical tools to recognize these diseases early to diagnose them, and recommend networking with reference centers, with a multidisciplinary approach the optimal way to give patients the best possible care [7].

Other relevant complications of cirrhosis such as ascites, hyponatremia, and gastroesophageal variceal bleeding are reviewed in this supplement by Anna Baiges and Virginia Hernández-Gea in a practical epitome of diagnostic and therapeutic approaches, from the basics in diagnosis, moving through pharmacological treatment, to more interventional approaches [8].

An overview of drug-related injury in patients with liver diseases has been redacted by Miren García and Alberto García, discussing not only why patients with cirrhosis are more susceptible to determined drugs but also the most recent data regarding immunomediated toxicity associated with immune check point inhibitors, an update that is a must

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for hepatologists today, given these agents' extended use in liver cancer and, in general, in the oncology setting [9].

Javier Ampuero discusses NAFLD, highlighting its growing involvement in the etiology of advanced liver disease and its relationship with metabolic syndrome, cardiovascular risk factors, and certain autoimmune processes, and outlining the tools currently available for its diagnosis and treatment. Unfortunately, we do not have specific drugs approved for the treatment of this disease. For the time being, we can only give recommendations for lifestyle modification through diet and physical exercise [10].

Joaquín Cabezas reviews alcohol-related liver disease, a condition that is still stigmatizing today. He highlights the importance of the use of alcohol consumption biomarkers to improve the diagnosis and follow-up of these patients, as well as the suboptimal results of the current available treatments, except liver transplantation. It is essential that the management of these patients, keeping an eye on potential treatment with liver transplantation, is conducted within multidisciplinary teams [11].

Rocío Aller de la Fuente addresses an aspect often forgotten in patients with chronic liver disease and in the sphere of liver transplantation, namely nutritional alterations. In this review, she emphasizes the hepatic causes and their risk factors, their importance in the prognosis of these patients, and the nutritional recommendations before and after liver transplantation and in hepatic steatosis [12].

We really hope that this easy-to-read overview of liver-related complications could be helpful in daily clinical practice, updating hepatologists on the latest knowledge and raising their interest in not-so-far future diagnostic and therapeutic tools.

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