Editorial

JOURNAL OF HEPATOLOGY

New concepts and perspectives in decompensated cirrhosis

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The recent description of acute-on-chronic liver failure (ACLF) has sparked worldwide interest in decompensated cirrhosis, leading to an explosion of both clinical research and research into the pathophysiologic basis of its manifestations. The hypothesis that systemic inflammation may underlie the pathophysiology of decompensated cirrhosis coupled with portal hypertension and metabolic dysfunction has democratised cirrhosis, which up until recently was the domain of hepatologists, with investigators from many different fields starting to address this problem. This intense research has led to a plethora of publications that are beginning to re-define cirrhosis in all its domains.

Therefore, this supplement – organised by *Journal of Hepatology* – is very timely. Its main focus is to critically assess the latest concepts and literature in the field of decompensated cirrhosis, illustrating how our understanding of the syndrome is changing from traditional concepts and discussing the implications of these changes on clinical practice, and the development of biomarkers, devices and drugs.

In keeping with the tradition of the *Journal of Hepatology*'s special issues and supplements, each article is written by multiple authors, all of whom are experts in the field, often with differing views on the subject being discussed. Each of the chapters will also describe areas of unmet need and important future research questions.

The first chapter describes the ***changing epidemiology and global burden of decompensated cirrhosis*** and introduces in detail the importance of disability-adjusted life years lost.[1] The article points out a problem with how the World Health Organization views cirrhosis. They assign zero disability to compensated cirrhosis and consider decompensated cirrhosis as only mildly disabling; this clearly needs to be addressed. The second chapter attempts to bring together the traditional multistate model of decompensated cirrhosis with the new understanding of acute decompensation of cirrhosis to ***define the trajectory of cirrhosis***.[2] Based on an evaluation of existing data, the third chapter suggests that ***ACLF is a distinct clinical syndrome*** as opposed to a continuum of the same disease progression,[3] while chapter four evaluates the ***role of predisposing factors and precipitating events*** in the transition of patients from stable cirrhosis to a state of acute decompensation.[4]

The next three chapters focus on the pathophysiological basis of decompensated cirrhosis. This series starts with an elegant fusion of traditional and new concepts underlying the development of decompensation, describing the ***relative roles of portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction***.[5] The next chapter evaluates the hugely important ***role of the microbiome in cirrhosis*** and points to this being an important therapeutic target.[6] The final chapter focuses on the ***mechanisms underlying the pathogenesis of bacterial infections***, which have clearly been shown to be the most important precipitating factor for decompensation, complicating the disease course, while being an independent predictor of mortality.[7]

The final six chapters address issues relating to the diagnosis and treatment of patients with decompensated cirrhosis. The first of these addresses the challenge of ***infection with multidrug resistant organisms***.[8] The novel concept of ***disease modifying approaches to the treatment of cirrhosis*** as an unmet need is discussed in the next chapter.[9] The following chapter deals with the very common scenario where the clinical team is working ***beyond clinical guidelines*** to try and save the lives of the patients with decompensated cirrhosis.[10] This is a particularly difficult situation as the team is open to criticism and potential litigation. This is followed by a chapter detailing new concepts in the pathogenesis, assessment and management of ***sarcopenia and frailty,*** which have been shown to impact heavily on patients with cirrhosis.[11] The final two chapters focus on the sickest patients with decompensated cirrhosis. The first of these is devoted to ***intensive care management*** of these patients with extremely high attendant risk of death[12] and the second to the issues surrounding ***liver transplantation of patients with ACLF and multiorgan failure***.[13] This is particularly challenging because of the risk of potential futility and the lack of priority for patients at risk of imminent death, as current allocation systems fail to identify these high-risk patients.

Finally, we want to acknowledge the *Journal of Hepatology* Editorial Board for giving us the opportunity to edit this hugely important publication. We want to thank the Journal office for their splendid support in helping to execute this project. Most importantly, we want to acknowledge the authors who have so generously given their time and energy to producing the fantastic manuscripts that have contributed to this special issue. We hope you enjoy reading this collection as much as we have enjoyed bringing it together.

Received 9 December 2020; accepted 9 December 2020;
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https://doi.org/10.1016/j.jhep.2020.12.008

Conflict of interest

Dr. Jalan has research collaborations with Yaqrit and Takeda. Dr. Jalan is the inventor of OPA, which has been patented by UCL and licensed to Mallinckrodt Pharma. He is also the founder of Yaqrit limited, a spin out company from University College London. Dr. Szabo has declared no conflict of interest.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2020.12.008.

Transparency declaration

This editorial is published as part of a supplement entitled New Concepts and Perspectives in Decompensated Cirrhosis. Publication of the supplement was supported financially by CSL Behring. The sponsor had no involvement in content development, the decision to submit the manuscript or in the acceptance of the manuscript for publication.

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