Journal of Hepatology

Introduction to the Supplement: New Concepts and Perspectives in Decompensated Cirrhosis

--Manuscript Draft--

Manuscript Number:	JHEPAT-D-20-02889
Article Type:	Editorial
Section/Category:	Cirrhosis and Liver Failure
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Introduction to the Supplement: New Concepts and Perspectives in Decompensated Cirrhosis

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The recent description of acute on chronic liver failure (ACLF) has sparked a world-wide interest and an explosion of research into decompensated cirrhosis not only from the clinical perspective but also re-exploring 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 the Hepatologists, bringing large numbers of investigators from many different fields to start to address this problem. This intense research has led to a plethora of publications, which is starting to re-define cirrhosis in all its domains.

This Supplement organised by Journal of Hepatology is therefore very timely. Its main focus is therefore, to critically assess the current concepts and explain the state-of-the-art literature pertaining to decompensated cirrhosis illustrating how the syndrome is changing from the traditional concepts and how this implicates on clinical practice, development of biomarkers, devices and drugs. In keeping with the tradition of the Journal of Hepatology Supplements, each of the articles is written by multiple authors, who are some of the best 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 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. The article points out a problem with how the World Health Organisation views cirrhosis. They assign zero disability to compensated cirrhosis and consider decompensated cirrhosis as only mild disabling; this clearly needs to be

addressed. The second chapter attempts to find a consensus on trying to bring together the traditional multistate model of decompensated cirrhosis together with the new understanding of acute decompensation of cirrhosis in ***defining the trajectory of cirrhosis***. The third chapter focusses on evaluating the existing data in suggesting that a ***ACLF is a distinct clinical syndrome*** as opposed to a continuum of the same disease progression and 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.

The next four 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***. The next chapter evaluates the hugely important ***role of the microbiome in cirrhosis*** and points to this being an important therapeutic target. The final chapter focuses on the ***mechanisms underlying the pathogenesis of bacterial infections***, which has clearly been shown to be the most important precipitating factor for decompensation, complicates the course of the disease and its occurrence is an independent predictor of mortality.

The final six chapters address issues in relation to the diagnosis and treatment of the patients with decompensated cirrhosis. The first of these addresses the challenge of ***infection with multidrug resistant organisms***. The novel concept of ***disease modifying approaches to the treatment of cirrhosis*** as an unmet need is discussed in the next chapter. 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. 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 on all aspects of patients with cirrhosis. 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 and the second to the issues surrounding ***liver transplantation of patients with ACLF and multiorgan failure***. This is particularly challenging because of the risk of potential futility, lack of priority for patients at risk of imminent death as current allocation systems fail to identify these high risk ACLF patients.

Finally, we want to acknowledge the Journal of Hepatology Editorial Board for giving us the opportunity to edit this hugely important Supplement. 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 in producing the fantastic manuscripts that have contributed to the Supplement. We hope, you the readers enjoy this collection as much as we have done in bringing this together.