

January 2, 2015

Dear Editor.

Thank-you for giving us the opportunity to revise our manuscript. Please find enclosed the edited manuscript in Word format We provide a point-by-point response to each reviewer below.

Title: Hepatosplanchnic circulation in cirrhosis and sepsis

Authors: Meghan Prin, Jan Bakker, Gebhard Wagener

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 14443

Reviewed by 00068912

The manuscript "Hepatosplanchnic circulation in cirrhosis and sepsis" by Meghan Prin et al. is a review. Liver cirrhosis and sepsis remains one of the most important problems in reanimatology. This review presents the physiological and pathophysiological mechanisms of hepatosplanchnic circulatory disorders in patients with cirrhosis and sepsis. The review is well written. The authors should give the full name of C. difficile. The review will be useful for clinicians working in intensive care units

Thank you for the kind comments. We have updated the manuscript to include the full name of *Clostridium difficile*.

Reviewed by 00004936

This review is overall very well-written and worth for publishing in World Journal of Gastroenterology after minor revision as listed below. Comments 1. Although the authors use "stellate ganglion cell", it is not a common name for "hepatic stellate cell". stellate ganglion usually means ganglia cell of the sympathetic nervous system. The authors are advised to reconsider about this point. 2. The authors mentioned about the role of renin-angiotensin-aldosterone system (RAAS) on splanchnic hemodynamics. RAAS is also well-known to play an important role on liver fibrosis development as they referred on #49. The authors are advised to discuss RAAS in more detail.

Thank you for the kind comments. We agree with your comment regarding hepatic stellate cells versus stellate ganglion cells and have updated the manuscript to reflect this. Your suggestion to discuss RAAS in more detail is timely, and we have updated our discussion to reflect more recent research.

Reviewed by 00762087

Comments to the Authors The manuscript "Hepatosplanchnic circulation in cirrhosis and sepsis" by Meghan Prin et al. is a review on Hepatosplanchnic circulation abnormalities in sepsis and cirrhosis leading to MOF. This review provides an overview of the hepatosplanchnic circulation in the healthy state and in cirrhosis, examines the signaling pathways, the physiology of cirrhosis and sepsis, and reviews important issues in the management of this disease. It is interesting, well written and up to date. Revise the references style.

Thank you for the kind comments. References and typesetting were corrected to reflect the standards of *World Journal of Gastroenterology*.

Reviewed by 00054683

A well conducted review. Please report the full name of C. difficile

Thank you for the kind comments. We have updated the manuscript to include the full name of *Clostridium difficile*.

Sincerely yours,

Gebhard Wagener, MD

Thank you for your comments. We made the following changes as suggested:

- We added a paragraph describing the use of the transient elastography in septic patients and added the following reference:
 - Koch A1, Horn A, Dückers H, Yagmur E, Sanson E, Bruensing J, Buendgens L, Voigt S, Trautwein C, Tacke F. Increased liver stiffness denotes hepatic dysfunction and mortality risk in critically ill non-cirrhotic patients at a medical ICU. Crit Care. 2011;15(6):R266. 2.

Page 13: *"Recently a novel method of transient elastography has been used to measure liver stiffness, a metric associated with hepatic fibrosis. In a prospective study of ICU patients, liver stiffness was highest in patients with decompensated cirrhosis (compared to other critical illnesses or comorbidities), and was associated with increased ICU- and post-discharge-mortality¹²². Transient elastography may serve as a useful triage tool for critically ill patients with liver disease."*

- We also added a paragraph detailing a score to assess mortality and added the following reference:
 - López-Velázquez J1, Chávez-Tapia NC, Ponciano-Rodríguez G, Sánchez-Valle V, Caldwell SH, Uribe M, Méndez-Sánchez N. Bilirubin alone as a biomarker for short-term mortality in acute-on-chronic liver failure: an important prognostic indicator. Ann Hepatol. 2013 Jan-2014 Feb;13(1):98-104.

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Page 12: "Furthermore, in an effort to identify patients at risk for imminent decompensation, Lopez-Velazquez et al found that bilirubin concentration alone was an independent predictor of 7-day mortality^[121]."

Best regards,

Gebhard Wagener