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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 82814

Title: Emerging concepts in the care of patients with cirrhosis and septic shock

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06151472
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2022-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-28 08:17

Reviewer performed review: 2022-12-29 08:10

Review time: 23 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I read with interest the paper by Dr. Jimenez and collaborators regarding the emerging concepts on septic shock in patients with cirrhosis. The paper overviews on many aspects of the topic, including pathophysiology, diagnosis and management. The manuscript is well written and easy to read. Figures are informative. I have only few comments for the Authors. - I appreciate the comment about the poor reliability of hypoperfusion according to a fixed MAP value in patients with cirrhosis. This is a good point for the everyday clinical practice, in my opinion - Impairment of mental status can be another important sign in patients with cirrhosis and sepsis. Very often, altered mental status has been considered an unreliable tool in cirrhosis because of hepatic encephalopathy. Nevertheless, I think that acute alteration of mental status, especially in a hospitalized patient with negative blood ammonia levels, should be taken into account as a tool for sepsis - Lactate is a very useful tool, in my opinion, to diagnose septic shock in patients with cirrhosis, where other signs of sepsis are often poorly represented. Therefore, I would encourage the Authors to give the Reader more precise indication about lactate. For instance, would the Authors prefer arterial vs venous lactate levels? Is

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there a concordance between levels in cirrhosis? Is there a fixed diagnostic threshold of lactate serum levels for diagnosis of sepsis? Have lactates been incorporated in any diagnostic or prognostic score for patients with cirrhosis? - What is the role of terlipressin in noradrenaline-refractory septic shock in cirrhosis. Any available evidence in such a setting? - I appreciate the section about antibiotics, and the need of a rapid broad-spectrum coverage, in order to decrease mortality. However, I think that rapid diagnosis of strains responsible for infection is of paramount importance, too, in order to de-escalate antibiotic therapy and/or to shift empiric therapy to targeted therapy. I suggest to briefly discuss emerging diagnostic tools (e.g., array panels) that should improve the diagnostic process in patients with cirrhosis. I think that, given the peculiarities of sepsis in patients with cirrhosis and CSPH, these arrays should be made available once sepsis is suspected, not only in the ICUs but also in the regular ward. - Culture negative infections represent 40-50% infection in hospitalized patients with cirrhosis (pneumonia, SBP). This should be briefly discussed, in my opinion. - Emerging concepts about the pharmacokinetics of antibiotics have been developed in cirrhosis, for instance, in patients with spontaneous bacterial peritonitis, where penetration of molecules into ascites has been questioned. I think that a brief comment would be valuable

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Reviewer's code: 06187298
Position: Peer Reviewer
Academic degree: MD, PhD

Professional title: Associate Professor, Chief Physician, Doctor

Reviewer's Country/Territory: Romania

Author's Country/Territory: United States

Manuscript submission date: 2022-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-29 10:20

Reviewer performed review: 2023-01-01 10:13

Review time: 2 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
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Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

- Although this is a review, the authors are encouraged to add a Materials and Method section to better and clearly explain the type of review (descriptive, systematic, etc.), how many RCTs were considered, timespan, what databases were used for interrogation, inclusion and exclusion criteria of RCTs, etc. For a systematic review the PRISMA checklist must be followed. For a descriptive review, a more relaxed structuring can be followed, such as classical IMRAD construction; - After clarifying the type of review, the title should be modified to better reflect the study; - A section dedicated to the limitations of the study is also recommended.