

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 84150

Title: Liver replacement therapy with extracorporeal blood purification techniques
current knowledge and future directions

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03755068

Position: Peer Reviewer

Academic degree: MD

Professional title: Consultant Physician-Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: Greece

Manuscript submission date: 2023-02-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-03-16 06:45

Reviewer performed review: 2023-03-18 16:48

Review time: 2 Days and 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

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

SPECIFIC COMMENTS TO AUTHORS

This is a nice narrative review on extracorporeal devices in the setting of acute liver failure and acute on chronic liver failure. The paper is of interest and is well written. Table 1 is informative. Major comments. - A main issue, in my opinion, is the actual applicability of such devices in clinical practice. In my opinion, only few patients with ALF and ACLF may receive a great benefit from these devices. This point should be discussed. - Side effects / complications / contraindications are not properly discussed. For instance, patients with ACLF may suffer from hypotension, volume overload. - Inflammation is one of the main drivers of ACLF, therefore removal of some inflammatory molecules as interleukines may be clinically relevant. However, it is not clear if the (temporary) removal of some of these molecules may change the underlying pathways, thus modifying prognosis. In other words, it is not clear if these devices could serve as game changers in patients with ALF/ACLF. - It would be interesting to see if Authors consider extracorporeal devices only as bridge to transplantation, thus reserving their applicability only in patients having this option. - The Authors said that applicability of LRT is often underused due to lack of comparative trials. What can be



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the right setting, according to the Authors' view? Who should be enrolled (ACLF, ALF, both?). What should be the primary endpoints of these trials (overall survival, transplant-free survival, reduction of ACLF-grades, others)? Minor comments. - I think that a brief explanation about differences in pathophysiology between ALF and ACLF should be added, also for non-expert Readers. - The point about CRRT for isolated hyperammonemia without AKI should be discussed more in depth. - I think that some data about emerging techniques (DIALIVE, and perhaps CARBALIVE) should be mentioned. - In my opinion, the Authors rightly discussed about costs. Nevertheless, also indirect costs (e.g., patients must be treated in ICU, albumin supplementation is costly if protracted for long-time...) should be considered.

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Author's Country/Territory: Greece

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

It is a well written review on a topic where the research is ongoing. The following are suggested to enhance the manuscript: 1. The available data on modalities like Plasma exchange should be depicted in a tabular form. Similarly summary of available guidelines and any systematic review or meta analysis should be mentioned 2. The discussion maybe enhanced by addition of the following : a. Chen, Y., Han, T., Duan, Z. et al. Clinical application of artificial liver and blood purification: expert consensus recommendations. Hepatol Int 17, 4-17 (2023). <https://doi.org/10.1007/s12072-022-10430-8>