PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 86968

Title: Corrected QT interval in cirrhosis: A systematic review and meta-analysis

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06140863

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Research, Assistant Professor, Research Scientist

Reviewer's Country/Territory: Spain

Author's Country/Territory: Greece

Manuscript submission date: 2023-07-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-07-20 16:36

Reviewer performed review: 2023-07-23 16:53

Review time: 3 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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	[Y] Grade A: Excellent [ ] 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

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	[ ] Grade A: Priority publishing [Y] 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

The authors have developed an interesting and novel work in the context of liver cirrhosis. A systematic review and meta-analysis of the relationship between QT interval and disease status has been designed for the first time in the literature. The manuscript is coherent, and the structure is adequate. The risk of bias analysis includes different correct studies. However, to improve the quality of the manuscript, I propose the following suggestions and comments: Material and methods: How many authors conducted the systematic review? Please indicate the initials of the names. In addition, the literature review is usually performed by 2 or 3 authors, and a different coauthor is included to resolve discrepancies once the results have been agreed upon. I suggest that this be included as a methodological limitation in the discussion. The phrase "KM was responsible for resolving any discordance" is duplicated. The search strategy only contemplates the term "QTc", but terms such as "QT interval, QT-interval, Q-T syndrome or QT syndrome" can be found in the literature. Please confirm that the strategy includes all available scholarly articles or, if not, add the missing ones. Results: I suggest including quantitative results in the figures to facilitate understanding of the manuscript.

How do you explain the high heterogeneity of the results described in Figure 3? Why is the pre-specified upper normal limit for QTc different in the studies analyzed? Figure 11: Please develop the methodology of the regressions in the figure. Also, please include the line equation and the statistical significance level. Figure 12 only includes three studies, which could be considered a limitation. I suggest discussing

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Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07759418

Position: Editorial Board

Academic degree: MD, MSc, PhD

Professional title: Full Professor, Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: Greece

Manuscript submission date: 2023-07-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-07-24 10:46

Reviewer performed review: 2023-08-02 11:45

Review time: 9 Days

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 [ ] Grade B: Good [Y] 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

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] 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	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The author(s) had put great effort and hard work in this manuscript. The present manuscript is a meta-analysis of the value/utility of QTc interval prolongation in patients with liver cirrhosis. The subject is not original and is well known, however, to my knowledge no meta-analysis studied this issue. It should be mentioned that the QTc interval is known to be affected by many factors some of them are characteristically present in cirrhosis: the presence or absence of hyperdynamic circulation (which is the case in most patients with cirrhosis specially Child B and C), the intake of drugs such as B blockers, recent attack of bleeding OV, electrolyte imbalance due to diuretic treatment (very common in Child B and C).   All the above factors should be put in mind when conducting a research like that and when drawing a conclusion. To increase the impact of this work it should have been including studies in cirrhosis patients at first diagnosis and/or non hospitalized cirrhosis patients and should state the absence of any comorbid condition that might affect the QTc interval. COMMENTS: The abstract is too long and contains many unneeded details for an abstract. Should be summarized. The aim: What exactly is the aim of this work. Is it: assessing if QTc is prolonged in liver

cirrhosis(compared to control subjects), OR OR defining a cutoff value of QTc predicting disease severity OR studying its utility in assessing severity of cirrhosis (CTP and MELD scores)? I think the study is totally concerned with last question (and that what was also written PROSPERO). So, the aim should be clearly stated. Also in the aim of work: studying the "Factors" mean all the factors including the effect of drugs, the presence or absence of bleeding, hospitalization, other comorbid conditions....etc. The present manuscript only studied the effect of age, sex, and severity of liver disease as predicted from CTP and MELD scores. So, the aim should be corrected.   Methods: Google scholars are not a usual source or search database included in meta-analysis, sometimes it contains unpublished data. A meta-analysis and systematic review should include only published peer reviewed studies. Why including those few studies from Google scholar? There is a contradiction between PROPSERO data and the manuscript. In PROSPER; the publication date were from Jan 2003, while in the manuscript says it is since 1998! should be revised and should be as mentioned in POSPERO. Conclusion: Should be the same in the abstract as in the end of the manuscript. It should just answer the question in the aim of work (and in PROSPERO). At the end, due to the many factors affecting the QTc interval (as mentioned above); the manuscript should not draw a final solid conclusion like (Therefore, QTc is an easy-to-perform, inexpensive, and efficient tool for assessing liver cirrhosis)!   Research background/motivation/perspectives and objectives should be modified according to the above comments. Exclusion: again there were a contradiction between PROSPERO data and the manuscript. Were studies published as abstracts included or excluded? Kindly revise the PROSPERO, the study selection section and fig.1 Discussion: Kindly explain the sentence (Therefore, this compensatory mechanism might be compromised in patients with cirrhosis of alcohol etiology in case that decline from alcohol abstinence occurs). Also, what is meant by (inextricably intertwined). Limitations should be mentioned under a separate subtitle,

and should be clearly explained. The last paragraph of the last section (limitations) is not understood, may be the sentence was too long! Should be revised. Again, limitations are many as mentioned before. Explaining the limitations and not underscoring them is important for the integrity of any research. This part is the one that other researchers/readers will improve in further studies to add more and more to our knowledge. Forest plot figures are not clearly showing data. May it is Zoomed in more than needed, the part of the legend "with and against" is not properly put in its exact place.