

ANSWER TO REVIEWER

Reviewer's code: 02650654

Dear Reviewer,

Thank you very much for reviewing our manuscript. Please find below our explanations about changes in the manuscript as a response to your remarks.

Remark 1. It would be interesting to discuss more in details the proposed correlations between LV diastolic dysfunction and liver cirrhosis.

Answer:

Thank you for your valuable suggestions. We have made changes in the discussion section according to your comments. The paragraph about correlations between ascites and LVDD has been included in the discussion.

Remark 2. Besides, the contra-indications to beta-blocker medication have to be considered in the discussion.

Answer:

This is a very important point that we totally agree with. The data about impact of beta-blockers to liver cirrhosis patients and contraindications have also been added.

ANSWER TO REVIEWER

Reviewer's code: 00036801

Dear Reviewer,

Thank you very much for the evaluation of our manuscript. Please find below our explanations about changes in the manuscript.

Remark 1. Data in general are well described but in order to provide all the information to the reader tables 5, 7 and 9 should show the average data or the percentages in addition to the p values.

Answer:

Thank you for the suggestion. We have changed the tables 5, 7, 8 and included the mean Child-Pugh score in patients with and without LVDD in table 5, Number of patients and percentages of patients with ascites and LVDD in table 7 and mean age of patients with and without LVDD in table 8.

Remark 2. An important part of the discussion is devoted to comparing the results of a retrospective study carried out by the authors with several of the prospective studies included in the review. It seems excessive to devote so much discussion to a study that according to the exclusion criteria of the authors does not enter into the review. All this paragraph should be reduced to a brief paragraph indicating the agreement between the results of this study and what was observed in the review.

Answer:

Thank you for your suggestion and we agree with the reviewer's comment. We have shortened the paragraph about the retrospective study.

ANSWER TO REVIEWER

Reviewer's code: 02540171

Dear Reviewer,

Thank you very much for the evaluation of our manuscript and for the very good appreciation.

ANSWER TO REVIEWER

Reviewer's code: 02998360

Dear Reviewer,

We are grateful for the comprehensive and thoughtful evaluation of our manuscript which let us to improve it significantly. Please, find below our explanations and elaborations as a response to your remarks.

Remark 1: the algorithm for the literature search is not very clear and seems that it could be improved by including more variations and key-words. Also there is no mention of searching through references of reviewed articles for further papers.

Answer:

We appreciate the Reviewer's helpful comment. The algorithm for the literature searching used was added to the manuscript as supplement.

Since left ventricle diastolic dysfunction occurs most often due to other disorders, the search words variations would result in a bulk of literature sources not related to the liver cirrhosis. That is why we were extremely accurate in the verification of the main key-words and subheadings to avoid unnecessary sources inclusion in our analysis.

Limited amount of papers included as references in analysed sources were included in our study when they fulfilled inclusion criteria, but it worth to stress that there is still lack of well-done studies on that topic.

Remark 2: The presence of ascites seems to be a much more powerful predictor of LVDD and this has been previously documented and make sense from a pathogenetic point of view. It also might explain why there is a statistical difference according to Child but not MELD scores. Are the MELD scores reported classic MELD or adjusted MELD?

Answer:

We have performed additional statistical analysis of reviewed literature and it revealed a greater prevalence of LVDD in patients with ascites exactly as reviewer assumed. The Results section was supplemented with those findings and they were talked over in Discussion.

Although it was not stressed in the publications usually classic MELD is used for the evaluation of cirrhosis severity unless adjusted was clearly defined, for example MELD-Na score.

Remark 3: A more nuanced conclusion seems appropriate.

Answer:

Thank you for highlighting this imperfection in our manuscript. The Conclusions section was redone completely according to the reviewer's remarks.

ANSWER TO REVIEWER

Reviewer's code: 01490498

Dear Reviewer,

Thank you very much for reviewing our manuscript. Please find below our explanations as a response to your remarks.

Remark 1. The criteria to assess LVDD is mostly 2009 ASE but two papers use the 2016 ASE/EACVI guidelines. I would like to see a separate analysis excluding these two studies using the newer guidance.

Answer:

There are no big differences in 2009 and 2016 issued LVDD guidelines. Moreover, two studies, that used 2016 guidelines found contradictory results. Hammami observed 80 patients and did not identify any association between severity of liver disease and cardiac dysfunction. In Rimbas study (46 patients) Child–Pugh scores were significantly higher in liver cirrhosis patients with LVDD grade II than in those with grades I and 0 LVDD.

Remark 2. There is some debate about the role of LVDD on clinical outcomes. This should be discussed more, with particular relevance to recent studies showing that diastolic dysfunction had not effect on outcomes following TIPSS (Armstrong et al, 2019).

Answer:

The aim of this systematic review is to analyse the correlation between the severity of liver cirrhosis and LVDD and we have not included the data about TIPSS.

Please direct all correspondences to

Julija Sarnelyte, MD

Vilnius University, Institute of Clinical Medicine, Clinic of Gastroenterology,
Nephrourology and Surgery

sarnelyte.julija@gmail.com

+37062602666

Lithuania