Author’s response to reviews

Title: Validity of Mini-Fluid Challenge for Predicting Fluid Responsiveness Following Liver Transplantation

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Version: 1 Date: 21 Feb 2019

Author’s response to reviews:

Dear prof. Bezinover

I am grateful for your sincere and meticulous help and advice you made to improve the quality of the current manuscript. In the new draft form; you will find all changes that had been required from you and from the other reviewers.

Point by point response to the reviewer’s comments:
Editor Comments:

- Your evaluation need much more information about study population (as was pointed by reviewer). Considering inclusion of Child B and C patients please describe preoperative (cardiac situation, ICU stay, need in CVVH/HD and catecholamine and others ) as well as intropesrve situation )hemodynamic instability, PRS and others)

  o Response: additional details added to p 10 line 23 and table 1

- I am wondering that Child C patients were allegeable for LDLD: this is not usual approach. Can you please describe acceptance criteria for LDLT

  o Response: We do not have cadaveric program in our country and all patients indicated for liver transplant undergo LDLT. The indications for LDLT in our center include; patients with decompensated liver cirrhosis, liver cirrhosis with MELD score more than 15, and patients with hepatocellular carcinoma within transplant criteria. P7 line 3

- Was TTE performed blindly?

  o Response: The assessor was blinded to Child-Pugh class of the patients. P8 line 16

- Were any other cardiac parameter evaluated for example diastolic dysfunction?

  o Response: Only the overall contractility was assessed but not any other parameter like diastolic dysfunction as the objective of the study is to assess fluid responsiveness only

- Can mini-challenge approach be used for prediction of cirrhotic cardiomyopathy with combination of other factors such as BNP levels, diastolic dysfunction and QT prolongation?

  o Response: all our patients had excellent cardiac function during the early. postoperative period, so we cannot extrapolate our findings to patients with poor cardiac function or patients with cirrhotic cardiomyopathy. This is one of limitations in our study P14 line 11

Reviewer reports:

Reviewer 1

- I would suggest to clearly identify hypothesis of this study. Your study would benefit from having a control group.
Response: Our hypothesis was that mini-fluid challenge would not be a valid tool to predict fluid responsiveness in cirrhotic patients after liver transplant (page 6. Line 7)

Your study would benefit from having a control group

Response: This is really a good idea but we thought that including only cirrhotic patients following liver transplant may minimize many confounders that may occur if we enroll other types of patients and/or surgery which affects the interpretation of our results.

The study would benefit from the more detailed description of the patients enrolled: age, gender, EF pre-operatively, hemodynamic parameters by the end of the surgery and first hour in ICU, urine output, fluids received, etc..

Response: some details are added on P10 line 7 and other details (age, gender, and amount of fluid received, use of vasopressor) included in table 1

Responsiveness to the fluid challenge could’ve been the function of the volume status of participant before the enrollment into the study. There is no clarity why this specific type of the bolus was chosen.

Response: Albumin 5% infusion was chosen to test fluid responsiveness instead of hydroxyethyl starch because we have previously shown that this solution is as effective for volume expansion.[14] Moreover, the safety of hydroxyethyl starch has been questioned and we have abandoned its use in the postoperative period. P14 line 7

An idea that the fluid responsiveness could’ve been multi-factorial was not discussed.

Response: Other factors that affect fluid responsiveness was added in discussion section P13 line 18

Reviewer 2:

- Why the authors chose SV of 15% instead of 10%. Probably 15% will be to insensitive. Please give a comment on this topic

Response: This cut of value was chosen as described previously in Mini Fluid challenge study P8 line 22. Another paragraph was added in the discussion section describes the variability of fluid responsiveness in the literature P 14 line 1
• Did the patients had a right-heart catheter or a PICCO system in order to assess the cardiac index, which is the gold standard for fluid response?

  o Response: We did not use PICCO to assess fluid responsiveness. We used transthoracic echo cardiography which is validated tool for CO assessment.