

34551-ANSWERING REVIEWERS

Reviewer 1

1. Because of relatively high incidence of CAD after LT, why didn't the authors consider cardiac angiogram under the situation of CKMB positives? Missing MI is critical, and some case might be reversible by stenting. Did they have a good reason?

Response: Authors agree that an aggressive approach in such cases as described here in this case series and doing coronary angiography may unveil coronary artery disease that may be stented. However such exercise should be undertaken only when there is a strong suspicion of coronary artery disease and other differential diagnosis are ruled out.

In the present case series, only two patients, case No.2 and 3, aged 53 and 55 years and possibly case no. 5 aged 40 in view of lifestyle were at risk of having CAD and these three patients were able to achieve target heart rates on DSE (Otherwise a limitation in patients with cirrhosis of Liver). DSE in these patients was negative for inducible ischemia. Considering this along with the presence of hemodynamic instability and presence of global and not regional wall motion abnormality specific to any coronary artery supplied region and the younger age of rest of the patients, decision was taken to not to do coronary angiogram in these patients. Explanation is now also incorporated in manuscript at Page 8 paragraph 3, and Page 9 lines 1-2 (Marked in Red).

2. Immuno-suppression (IS) has side effects on suppressing cardiac function. Did the authors consider changing IS regimens?

Response: Authors agree that immunosuppression especially in the long run can have adverse implication for cardiac function and would require changes and dose modification for immunosuppression.

However in the present case series, Heart failure presented by post operative day 2 when only immunosuppression that was given was the loading dose of Methylprednisolone, Authors did not suspect this as the cause for the observed Heart failure. However subsequent addition of Mycophenolate mofetil and Tacrolimus was deferred and Methylprednisolone doses were also gradually tapered.

3. The number of reference is too small for this type of article. The authors should increase more.

Response: The number of references has now been increased from 16 to 25.

Reviewer 2

1- A table summarizing pre-transplant cardiovascular work-up, clinical presentation and outcomes in the patients included would be helpful for the reader to understand the similarities and disparities among included clinical cases.

Response: A table summarizing the desired information is now incorporated in the manuscript as suggested and placed as Table 1. (Marked in Red)

2- In light of the clinical experience derived from these cases, How could cardiovascular pre-transplant assessment be improved in their clinical setting? There are some proposals in the literature for cardiovascular assessment in the transplant setting, which should be put into perspective here.

Response: The present case series highlights the limitation of the commonly used diagnostic tests at finding patients specifically at risk of developing heart failure after liver transplant. New diagnostic approaches may kindly be found mentioned in the manuscript under the heading '**New preoperative prognostic markers for heart failure after LT**' on page 9-10 (Marked in Red), and based on the reported utility, additional tests for preoperative workup has been suggested and may please be found under heading 'Conclusion' Lines 3-5 Page 12.

3- Aligning with the previous comment, What can be learned in terms of peri-operative cardiovascular management?

Response: Peri-operative cardiovascular management of Heart failure after Liver transplant confirms to management suggested by Heart failure guidelines, such as those adopted by the European Society of Cardiology or the American College of Cardiology/ American Heart Association. Management with Heart rate control, preload and after load reduction continues to form the mainstay of treatment. Further use of Left ventricle assist device, Extra-corporal membrane oxygenation and Intra-aortic balloon device may allow sufficient time for the recovery of the heart function. The same may kindly be found mentioned under heading 'Management' Page 10 Last Paragraph and Page 11, Paragraph 1.

4- The authors may consider including an algorithm proposal for patients showing cardiac failure in the early post-transplant phase.

Response: An algorithm has now been incorporated in the manuscript depicting suggested preoperative workup and postoperative management and has been labeled as Figure 1. (Marked in Red)