ANSWERING REVIEWERS

Dear Editor,

Title: Cardiac surgery in patients with liver cirrhosis: Risk factors for predicting mortality

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer No. 02441180:

The manuscript entitled "Cardiac Surgery in Patients with Liver Cirrhosis: Risk Score for Predicting Mortality" has been reviewed, and I think that the article is acceptable for publication in World Journal of Gastroenterology. But, you can consider the title as "Cardiac Surgery in Patients with Liver Cirrhosis: Risk Factors for Predicting Mortality" instead of "Cardiac Surgery in Patients with Liver Cirrhosis: Risk Score for Predicting Mortality" Otherwise, not remarkable.

Answer:

The title was changed as the reviewer suggested. Thank you.

Reviewer No. 00069297:

This is an interesting retrospective observational study on the association between the operative results of cardiac surgery in cirrhotic patients and the predictors of early and late mortality. My major concerns are that the authors should give detailed standards for Child-Pugh grade and MELD score. And the authors also should give the web address of online EuroSCORE II calculator in the manuscript.

Answer:

The detailed standards of Child-Pugh grade and MELD score were not shown for the sake of the length of the article, but the original article was listed in the section of reference. And the web address of online

EuroSCORE II calculator was added in the manuscript.

Reviewer No. 00506608:

Overall, I think this manuscript contributes an important experience to the much needed literature on the difficulties on performing cardiac surgery in patients with advanced liver disease. There are a few small comments - like the redundant listing of the number of patients in each Child class in the abstract - to the obvious (and acknowledged) concern about the small number of patients in each group. Given the substantial differences (being sicker patients) between Child B and C patients, I am concerned that the lumping of both groups together might not completely convey the risks of operating on a patient with end-stage liver disease. Furthermore, the authors list the complications in very broad categories - such as neurologic, hepatic, renal, etc - but do not provide the specifics of the types of complications that these patient had. In addition, it appears that the INR - often a strong predictor of synthetic function of the liver - was relatively similar between groups and might suggest that these patients maybe did not have as advanced liver disease as suspected. Consequently, while the data/results suggest that liver disease should not preclude required cardiac surgery - the stance of it being safe in high-risk patients - particularly given the contradictory findings in other reports and the literature - might be a little strong. Given the experience of this Reviewer with these types of patients - 1 death out of 5 Child C patients (80% survival) does not convince me that cardiac surgery (other than emergent/urgent) procedures should be offered in this group unless there are no other medical/interventional options. I do find it interesting 5 patients with advanced liver disease (B or C) were offered heart transplantation. My understanding is that given this limitations of available hearts, that some types of liver disease are often a relative contra-indication for transplant. Do the authors have an information on how many of these patients were undergoing treatment for the viral hepatitis (acute/chronic/sub-acute) as again, maybe of these patients had untreated disease. In addition, given the small number of deaths in each group, maybe some further discussion regarding the relationships between the procedures (i.e. why was CABG a significant variable - but not other riskier procedures) and the significant variables. Obviously this group has studied this problem extensively over the years (and how is this manuscript better/newer/different than their previous manuscript(s) on the topic?) and maybe they can provide - in the discussion - some additional insight into how we should approach the cardiac surgical management of patients with various types and classes of advanced liver disease.

Answer:

1. The redundant listing of patient number was removed from the abstract as the reviewer suggested.
2. Taken the small case number of patients of Child class C in the current study into consideration, we need to put that of Child B and C together (as a group of advanced liver cirrhosis) to compare with the results of patients of Child A to draw a statistical significant conclusion.
3. Regarding the difference of INR between the groups of mild and advanced liver cirrhosis, although

it seemed small numerically, it is significant statistically. As clinician scientists, we shall never evaluate the difference by our subjective judgment, and that's why we need statistics beyond arithmatic.

4. In our opinions, the severity of liver cirrhosis is not a status that never changes. Instead, it would fluctuate with the general condition of the patient. A patient with Child class A liver cirrhosis might progress to class C with decompensated heart failure in a short period of time. That is what we learned from many patients of bacterial endocarditis and end-stage heart failure.
5. With limited capacity of publication, it is difficult to discuss in detail regarding specific procedures and postoperative complications. We think both of them shall be investigated as an isolated study.
6. With regard to the surgical approaches, all we could say are to shorten the duration of the procedures and to decrease the amount of blood transfusion, although the result of both were not shown statistically.
7. The point of our report is not that cardiac surgery is safe in high-risk patients, but rather that current tools for risk stratification, in terms of Child class and MELD score, are not compatible with our clinical findings, and that other patient-related, cardiac-related and procedure-related factors should be taken into consideration for risk stratification in this patient group, and, most important of all, that advanced liver cirrhosis alone should not preclude patients from cardiac surgery.

Reviewer No. 01215273:

I have read interest of this cardiac surgery for liver cirrhosis. The author found MELD score and Child classification had no influence on the patient survival; however, the strikingly, the mortality rate of this cohort was 16%. It is very high for the this age group of the patient. Several issues on the paper. Table 1 is too large and some of the category needs to be removed such as xx valve surgery etc.. Table 2 may not necessary since figures were well written. Fundamental issue: The author have to address high mortality rate 16% and morbidity rate or 60%. It is too high to conventional cardiac surgery for mean age of 60. It may be due to "cirrhosis" itself. But the discussion was vague. What is the selection criteria for cardiac surgery based on the preoperative informations. How the surgeons decide to take the patient to surgery even there is cirrhosis? I do not think all comer who has cirrhosis and surgically correctable lesions underwent surgery. What it the line surgeon draw to withdraw from surgery. What is the concern for cirrhosis intraop, or after surgery?

Answer:

1. In literature, the hospital mortality ranged from 8% to 33%, if not to include our previous report in 2005. Our result of 16% is just comparable to the published studies and far from "too high".
2. The design of the current study is retrospective and observational. We could only collect data from patients who had surgery, as most the other researchers have done so far. It is beyond the scope of our study to discriminate who can from who cannot undertake cardiac surgery in this patient

group, although we do want to know the answer.

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