

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 27958

Title: Systemic-to-pulmonary artery pressure ratio as a predictor of patient outcome following liver transplantation

Reviewer's code: 00504591

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2016-06-28 18:34

Date reviewed: 2016-07-09 13:50

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | <input type="checkbox"/> No | <input type="checkbox"/> Major revision |
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| | | <input type="checkbox"/> The same title | |
| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | <input type="checkbox"/> No | |

COMMENTS TO AUTHORS

Rebel et al described that the systemic to pulmonary artery pressure ratio can be a predictor of survival after liver transplantation. I have some comments. (Major) (P7, L1) The definition of groups are unclear. The author described that MAP/mPAP ratio by ≥ 1 from baseline to anhepatic phase were categorized into Group 1. Please define the MAP/mPAP ratio of the baseline. Is it the MAP/mPAP ratio before the operation? Next point is as to the MAP/mPAP ratio of the anhepatic phase. Anhepatic phase is not a pin point time but is a term which has a duration usually more than one hour. During the duration, the MAP/mPAP ratio should be fluctuate. How do the authors define the MAP/mPAP ratio of the anhepatic phase? (P21, Table) Also please explain how the measure point of the MAP/mPAP ratio during the pre-anhepatic, neo-hepatic phases. (P15, L3 from the bottom) The author refer the manuscript number 3 in which the preoperative MAP/mPAP ratio was significantly higher in survivors of the cardiac surgery. However not referring the paper on the cardiac surgery, previous paper (Bushyhead D et al. Liver Transpl. 2016 Mar;22(3):316-23) has already disclosed that the preoperative MAP/mPAP ratio was a prognostic factor of liver transplantation.



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The author should consider referring the paper. (Minor) (P22) The legend of the table is too much, which should be short or explain in the results section. (P23) The legends of x axis in Figure 1 cannot be seen which should be replaced with clearer and larger letters.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 27958

Title: Systemic-to-pulmonary artery pressure ratio as a predictor of patient outcome following liver transplantation

Reviewer's code: 00054120

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2016-06-28 18:34

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| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | Google Search: | <input type="checkbox"/> Accept |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection |
| <input checked="" type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade D: Rejected | <input checked="" type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E: Poor | | [Y] No | <input type="checkbox"/> Major revision |
| | | BPG Search: | |
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| | | <input type="checkbox"/> Duplicate publication | |
| | | <input type="checkbox"/> Plagiarism | |
| | | [Y] No | |

COMMENTS TO AUTHORS

Title: THE SYSTEMIC-TO-PULMONARY ARTERY PRESSURE RATIO AS A PREDICTOR OF PATIENT OUTCOME FOLLOWING LIVER TRANSPLANTATION The aim of this retrospective study was to assess the value of the MAP/mPAP ratio for predicting outcomes following OLT. The investigators used the changes MAP/MPAP ratio during the anhepatic phase relative to the pre-anhepatic as a factor that impacted the patient outcomes. The outcome criteria that they used were: duration of ICU and hospital stay, duration of post-transplant intubation and mechanical ventilation. Here are my comments: 1- The paper needs some minor language editing and correction of some grammatical errors. 2- The extubation time should be changed to duration of post-operative intubation and/or mechanical ventilation; it makes more sense that than term (extubation time). 3- Not sure why the investigators selected the anhepatic phase, it would be better if they selected the post-re-perfusion phase which is the most stressful phase during OLT. They could compare the post-reperfusion phase to the baseline and/or to the neohepatic phase. 4- It seems that the preferred surgical technique that they used is cross-clamp the IVC without veno-venous bypass



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and without piggy-back technique, this will lead to cut-off 50% of venous return and 50% decrease in the pre-load which explained the use of high vasopressors during this phase. The changes in the MAP/MPAP ratios may be due to use of the vasoconstrictors and not changes in the cardiac condition which is different from the patients undergoing cardiac surgery where the primary etiology is pump dysfunction. The dose and the type of the pressors they used may affect the SVR and PVR, for instance vasopressin has little or no effect on the PVR while strongly affects the SVR which will be reflected by positive changes in the MABP/MPAP. Although, I do not doubt their findings but in my opinion during such tremendous variations in the SVR/PVR and use of pressors and IV fluid administration, it is very difficult to make such a conclusion. 5- I am not sure that their speculation that the outcomes are truly related to the variations in the intraoperative ratios of MABP/MPAP! They did not explain what was the etiology of such post-operative courses (prolonged hospital/ICU stay, prolonged intubation), surely they cannot be due to changes in these ratios! 6- It may be an interesting and new finding in these patients, but it requires further validation!. I suggest that they should check the ratios during the ICU stay and if it correlates to post-operative course, check the ratios during the reperfusion phase and try to find the real cause of the complicated post-operative course in group-2. 7- Any consideration for the graft function, sepsis, AKI all can be the reasons for postoperative complications in group-2.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 27958

Title: Systemic-to-pulmonary artery pressure ratio as a predictor of patient outcome following liver transplantation

Reviewer's code: 00049727

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2016-06-28 18:34

Date reviewed: 2016-08-02 17:19

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| | | <input type="checkbox"/> Plagiarism | |
| | | <input type="checkbox"/> No | |

COMMENTS TO AUTHORS

In this paper, Rebel et al. evaluated the MAP/mPAP ratio as a potential indicator for poor outcome after OLT. This paper may raise awareness to MAP/mPAP ratio. I think the following points will further improve the quality of your paper. 1. Is it possible to modulate MAP/mPAP ratio by therapeutic intervention? Please discuss this insight in more detail. 2. Figure 1: The text is too small. Please increase the letter size. 3. Could you perform prospective validation study? Your hospital had many OLT cases.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 27958

Title: Systemic-to-pulmonary artery pressure ratio as a predictor of patient outcome following liver transplantation

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| | | <input type="checkbox"/> No | |

COMMENTS TO AUTHORS

The authors attempt to assess the usefulness of mean AP/mean PP in cases of OLTx. This is not an entirely new idea as pulmonary hypertension is a known adverse risk factor and a predictor of bad outcomes in cases of cardiac surgery. ? De Pietri L1, Montalti R, Begliomini B, Reggiani A, Lancellotti L, Giovannini S, Di Benedetto F, Guerrini G, Serra V, Rompianesi G, Pasetto A, Gerunda GE. ? Pulmonary hypertension as a predictor of postoperative complications and mortality after liver transplantation. *Transplant Proc.* 2010 May;42(4):1188-90. doi: 10.1016/j.transproceed.2010.03.068. ? Zhen-Dong Xu,1,* Hai-Tao Xu,2,* Wei-Wei Li,2 Zui Zou,2 and Xue-Yin Shi2 Influence of preoperative diastolic dysfunction on hemodynamics and outcomes of patients undergoing orthotopic liver transplantation. *Int J Clin Exp Med.* 2013; 6(5): 351-357. PMID: PMC3664002 ? Cristina Ripoll1, Raquel Yotti2, Javier Bermejo2, Rafael Ba?ares1, The heart in liver transplantation. *J Hepatol* 2011, 54 (4); 810-822. doi:10.1016/j.jhep.2010.11.003 ? Gautam Ramakrishna, MD?; Juraj Sprung, MD, PhD?; Barugur S. Ravi, MD?; Krishnaswamy Chandrasekaran, MD?; Michael D. McGoon, MD? . Impact of Pulmonary Hypertension on the Outcomes of Noncardiac Surgery Predictors of



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Perioperative Morbidity and Mortality. J Am Coll Cardiol. 2005;45(10):1691-1699. doi:10.1016/j.jacc.2005.02.055 ? However, the strong point is that the measurements included different time points in the course of the preoperative and operative phases. The conclusion that the anhepatic phase is the valid predictor of outcome is novel. However, this is a unique study in the sense that it has related pulmonary hypertension ie decreased or stable mean arterial pressure to mean pulmonary pressure ratio in cases of OLTx. The use of vasoactive agents has to be clarified in greater detail. This does not affect the final outcome of the study. That an elevated mean AP/PP ration is a good prognostic parameter. However, it does lend weight to the fact that use of vasoactive substances in cases of OLTx may have a favorable effect on the AP/PP ratio during the anhepatic phase and therefore should be advocated .