

Format for ANSWERING REVIEWERS

April 2, 2015

Dear Editor,



Title: Influence of perfusate on liver viability during hypothermic machine perfusion

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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 (the red ones are our response)

The aim of this study was clear and relevant. It was relatively hard to evaluate the results because formation of UW and HTK were not explained. Comparison of UW and HTK would provide basis for the future experiments. The common reagents between UW and HTK would be necessary formula. Different reagents between UW and HLT would be a clue to the difference of storage performance. Investigation of the difference might pave the way to a better storage solution.

Thank you for your comment; we will work hard on it further.

One of the limitations of this study was short period of experiment as the authors stated. Were there any reason of the experiments were completed within 6 hours?

As state in my manuscript, the time period is based on the experience of our center in clinical. The limitation of time period is no more than 6h which based on our 1500+ cases of liver transplantation, especially for the extend criteria donors. Besides, many others articles also choose 6h as research time period: Cobert et al.using a heart model for 6h perfusion[1];Post et al. using a kidney model for optimal flow and pressure management during 6h preservation[2]; Izamis et al.resuscitation of ischemic donor Livers by machine perfusion for 6h[3]; Gringeri et al. non-heart-beating donor liver grafts preservation for 6h[4].

[1] M.L. Cobert, M. Peltz, L.M. West, M.E. Merritt, M.E. Jessen, Glucose is an ineffective substrate for preservation of machine perfused donor hearts, *J Surg Res* 173 (2012) 198-205.

[2] I.C. Post, M.C. Dirkes, M. Heger, R. Bezemer, J. van 't Leven, T.M. van Gulik, Optimal flow and pressure management in machine perfusion systems for organ preservation, *Ann Biomed Eng* 40 (2012) 2698-2707.

[3] M.L. Izamis, H. Tolboom, B. Uygun, F. Berthiaume, M.L. Yarmush, K. Uygun, Resuscitation of ischemic donor livers with normothermic machine perfusion: a metabolic flux analysis of treatment in rats, *PLoS One* 8 e69758.

[4] E. Gringeri, P. Bonsignore, D. Bassi, F.E. D'Amico, C. Mescoli, M. Polacco, M. Buggio, R. Luisetto, R. Boetto, G. Noaro, A. Ferrigno, E. Boncompagni, I. Freitas, M.P. Vairetti, A. Carraro, D. Neri, U. Cillo, Subnormothermic machine perfusion for non-heart-beating donor liver grafts preservation in a Swine model: a new strategy to increase the donor pool?, *Transplant Proc* 44 (2012) 2026-2028.

Brief introduction of malondialdehyde would be desirable in "Introduction".

Firstly, we introduce malondialdehyde in the material and method part (Levels of lipid peroxidation and wet/dry weight ratio). Then, we added brief introduction of MDA in "Introduction" according to your suggestion.

Figures. Abbreviations should be spelled out. Figure 3, 4. ALT, AST and others should be in Y-axis. Unit of X-axis should be inserted in X-axis.

Thank you for your suggestions. Abbreviations were spelled out in the figure legends. The AST, ALT and LDH added in Y-axis and unit of X-axis were also added.

Figure 7. The results are interesting that portal vein pressures are different among perfusion reagents. Are there any speculation regarding these results? Portal hypertension is a major problem after liver transplantation. These results might be a potential solution

Our speculation about the different portal vein pressures were as follows: HTK solution contains lower sodium, lower potassium concentrations, no HES and with 1/3 viscosity of UW to allow safely releasing into the circulation. The low viscosity and no HES of HTK partially contribute to low VR and less ATP consumption.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,
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