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Ruo-Yu Ma, MD
Science Editor, World Journal of Hepatology

Manuscript no: 51192
Manuscript Title: A Concise Review of Machine Perfusion in Liver Transplantation

Dear Professor Ma,

Thank you for the kind critique and comments from the reviewers who have taken the time to review our manuscript submission. We have edited the manuscript to include the comments that we have received and the following is a specific summary of the changes in our manuscript.

Reviewer 03737603—We have added the following language that outlines our search strategy. *“A systematic search of Embase, PubMed, Cumulative Index for Nursing and Allied Health Literature (CINAHL), ClinicalTrials.gov, and EU Clinical Trials Register, Scopus was conducted from January 1, 2000 to April 30, 2019. Search strategies for the concepts of machine perfusion and liver transplant were created appropriately. Database-supplied limits for English language and journal article publication types were used. Both authors performed title and abstract screening, and all irrelevant articles were omitted. Of the remaining articles, a full text screening was performed, and articles describing machine perfusion and liver transplant were selected. Articles were excluded for having wrong patient population and letters/ commentary. Included articles were evaluated for the concept. Intention was not to do a qualitative systematic review, but to perform a contemporary -concept review so readers to could become aware of the progress in the field.”*

Reviewer 03727922—We are sorry that you feel that this concise review is not valuable to the literature. We have intentionally focused on clinical trials so that clinicians in the liver field would be able to get a summary of ex vivo machine perfusion as a clinical entity in liver transplantation.

Reviewer 03293832—Thank you for your review and we have incorporated the majority of your suggestions regarding syntax and structure of the manuscript. In addition we have used the revision to continue to improve the readability of the review.

Reviewer 03317080—Thank you for the comments and suggestions that you have shared with us. We have added the following paragraphs with their references:

“Hypothermic machine perfusion conditions influence plasma membrane fluidity, leading to a marked difference between fatty and normal livers. Additional studies involving MP and expanding the use of macrosteatotic livers has focused on MP at 20°C, defined as subnormothermic machine perfusion. It is felt that this strategy reduces fatty liver susceptibility associated with organ preservation, when compared with conventional cold storage. Steatotic livers preserved by subnormothermic MP exhibit a marked reduction in damage based on

enzyme and cytokine release, excretory function, and energy recovery when compared with preservation at 4°C (HMP). Most of the work using subnormothermic MP has occurred in animal models, but it demonstrates a benefit by reducing the degree of mitochondrial damage with associated improvements based on microscopic and ultrastructural analysis when compared to HMP. Subnormothermic machine perfusion has also been shown to have a benefit with DCD donors further expanding the donor pool. Further analysis will need to be performed in clinical trials to confirm that the cellular improvements with subnormothermic strategies persist in human livers.”

Reviewer 03475120- This paper is well written. For journal readers, please add some schemas of machine perfusion. It is difficult to understand this by only sentences. We have added Figure 1 in the manuscript.

Thank you again for everyone's reviews.

Respectfully,

A handwritten signature in black ink, appearing to read 'D. Gerber', with a long, sweeping horizontal flourish underneath.

David A. Gerber, MD