

# The Authors' Reply to Letter to the Editor, Re

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**The Authors' Reply to Letter to the Editor,**

**Re: Biliary Bicarbonate, pH and Glucose Are Suitable Biomarkers of Biliary Viability During Ex Situ Normothermic Machine Perfusion of Human Donor Livers**

Alix P.M. Matton, MD[1,2], Vincent E. de Meijer, MD, PhD[1], Ton Lisman, PhD[2], Robert J. Porte, MD, PhD[1]

[1] Section of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery,

[2] Surgical Research Laboratory, Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands.

*Re: Biliary Bicarbonate, pH and Glucose Are Suitable Biomarkers of Biliary Viability During Ex Situ Normothermic Machine Perfusion of Human Donor Livers*

*Raphael P.H. Meier, Shareef Syed, John P. Roberts*

*Transplant Surgery, University of California San Francisco, San Francisco, CA, USA*

**Corresponding author**: Robert J. Porte, MD, PhD, Department of Surgery, Division of HPB Surgery and Liver Transplantation, University Medical Center Groningen, P.O. Box 30.001 9700 RB Groningen, The Netherlands. E-mail: r.j.porte@umcg.nl, Telephone: +31 50 361 2896, Fax: +31 50 361 4873

**AUTHORSHIP**

*Writing of the first version of the reply:* APMM, VEdM, RP

*Critically revised the manuscript:* APMM, VEdM, TL, RP

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To the editor:

We thank Meier and colleagues for their interest in our recent article.[1,2] The authors comment that in our previous paper the histological parameters (i.e., the presence of stroma necrosis, injury of the extramural peribiliary glands and injury of the perivascular plexus) in pretransplant bile duct biopsies were only individually correlated with the post-transplant development of nonanastomotic strictures.[3] In the present work, we assessed the degree of bile duct injury per histological item and combined the scores into a composite outcome to separate the group into livers with a low and high degree of bile duct injury. The identified biomarkers of bile duct injury (i.e., biliary bicarbonate, biliary pH, biliary glucose, the bile/perfusate glucose ratio and biliary LDH) were subsequently used and validated as cholangiocellular viability criteria, in addition to hepatocellular viability criteria, in a subset of patients from a prospective clinical trial (Figure 5 of our manuscript).[2] By using the identified biomarkers from the present preclinical work, we were able to safely select and transplant previously nationwide declined donor livers. The current follow-up time is 16.5 (interquartile range 15.8 – 18.4) months with a 100% patient and graft survival. Histology of bile duct biopsies obtained in this study will provide a definite answer to the predictive ability of the combined bile duct injury score.

The reasons why the research livers were declined for transplantation have been published previously.[4] We would like to clarify that the intention of this preclinical study was to investigate cholangiocellular viability criteria to assess livers that were declined for transplantation, to potentially allow safe transplantation. The characteristics of the livers used in the present preclinical study were, therefore, very similar to the cohort of declined livers assessed in the prospective clinical trial.[5]

The author's call for a large randomized controlled trial using a combination of biliary viability criteria and bile duct histology on frozen sections as a preimplantation diagnostic tool compared to standard of care seems unfounded. Histological quality of frozen sections from bile duct biopsies is inferior to paraffin-embedded sections.

## References


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