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The rescue of DCD rodent livers grafts: Is there HOPE?

To the Editor:

It is with great interest that we have read the article of Schlegel *et al.* [1] on normothermic machine perfusion (NMP) *vs.* hypothermic oxygenated perfusion (HOPE) to rescue rodent liver grafts, suffering from extended warm ischemia. In this study, a comparison was made between the ability of NMP and HOPE to rescue DCD rodent liver grafts with prolonged warm ischemia of 30 and 60 min. Grafts were subjected to *ex vivo* reperfusion using an isolated perfused rat liver model (IPRL) and orthotopic liver transplantation (OLT). The authors claim superiority of HOPE to rescue rat liver grafts with extended warm ischemia time.

This is an interesting finding, which is explained by the authors as the result of downregulation of several physiological processes, which protect grafts from oxidative stress following transplantation. However, these differences in outcome could very well be affected by different methods in both groups, which, to our opinion, the authors do not address in their publication.

1. In NMP, the perfusate composition of Brockmann *et al.* [2] was chosen, instead of the composition described by Op den Dries *et al.* The aim of NMP is to preserve a metabolically fully active liver and to resemble physiological circumstances [3]. Unpublished data from our institution show metabolic dysfunction as key mechanism underlying graft failure upon kidney transplantation. Energy supply during NMP might not be sufficient to correspond to the physiological setting, and specific demands for liver grafts are not studied yet. Regarding metabolic dysfunction, NMP might not be optimal in this experiment.
2. The authors show that DCD grafts are more subject to ischemic damage, encountered during the first warm ischemic period. We assume that graft oxygenation was sufficient, however, since the perfusate contained only a haematocrit of 14–16%, are the authors certain that the right amount of oxygen was added to the perfusate, since Op den Dries *et al.* previously chose supernormal oxygen levels [3]. The oxygen level was targeted at 40–50 kPa in the NMP group and at 50–60 kPa in the HOPE group. No pH and lactate measurement levels were reported in this publication.
3. HOPE was performed only through the portal vein and NMP through both the portal vein and hepatic artery, when OLT was performed with only portal anastomosis. May the arterial flow during NMP have injured the liver graft? Could it be that the difference in outcome is caused by this method?

We have to be careful to extrapolate rodent transplantation experiment results into clinical transplantation in humans; no UW solution flush was performed in these experiments. We would like to congratulate the authors on their achievements, but HOPE these questions could be addressed by the authors and are looking forward to discuss these promising techniques.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

References

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Reply to: "The rescue of DCD rodent livers grafts: Is there HOPE?"

To the Editor:

We read with great interest the letter by Kopp *et al.* regarding our study on machine perfusion of rat livers, donated after cardiac death (DCD). Our goal was to compare the two main liver perfusion techniques, normothermic (NMP) and hypothermic oxygenated perfusion (HOPE) in terms of liver function and injury in a transplant model, closely adapted to the clinical situation [1].

We are pleased to discuss the points raised by the letter from the Leiden's group. The first question targets on the perfusate composition used in the normothermic experiments. We have carefully chosen a perfusate for NMP experiments that is closely adapted to