Reply to: "Pre-retrieval reperfusion decreases cancer recurrence after rat ischemic liver graft transplantation"

OLDANI, Graziano, et al.
Pre-retrieval reperfusion decreases cancer recurrence after rat ischemic liver graft transplantation

To the Editor:
We read with great interest the article “Pre-retrieval reperfusion decreases cancer recurrence after rat ischemic liver graft transplantation” [1]. This elegant study assessed the impact of ischemic liver graft on the risk of cancer recurrence utilizing a rat liver transplantation model. Oldani et al. [1] demonstrated that ischemia/reperfusion lesions lead to an increased risk of post-transplant hepatocellular carcinoma (HCC) recurrence and growth, which can be reversed by graft reperfusion prior to retrieval. However, in this study, they clamped the vena porta and infra-hepatic vena cava during 10 or 30 min prior to flushing and retrieving the liver to simulate the ischemic donors, and the liver was reperfused for two hours after all clamps were removed at the end of the clamping to simulate ischemic/reperfused donors. Apparently, the quality of blood reperfused in this transplantation model is better than the perfusion solution used during normothermic extracorporeal membrane oxygenation (NECMO) after circulatory death in clinical situations to some extent [2]. Thus, we wonder if the risks of post-transplant cancer recurrence can be reduced by graft reperfusion with “perfusion solution” used in clinical prior to retrieval?

In addition in a further study, it is necessary to estimate the combined feasibility and availability of pre-retrieval reperfusion with different NECMO time with the aim to reduce the risk of cancer recurrence and to repair and resuscitate the liver grafts from donation after cardiac death (DCD) donors. This may help to increase the yield of transplantable livers from this source for HCC candidates awaiting liver transplantation.

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: “Pre-retrieval reperfusion decreases cancer recurrence after rat ischemic liver graft transplantation”

To the Editor:
We thank Drs Cheng and Lv [1] for their interest in our work suggesting an increased rate of hepatocellular carcinoma (HCC) recurrence/growth after transplantation of ischemic liver grafts, and the protective effect of in situ graft reperfusion prior to retrieval [2].

Our rat transplantation model only approximates clinical reality. It used liver grafts undergoing 10 or 30 min of ischemia prior to retrieval (clamping the porta hepatis and the infra-hepatic vena cava in the donor). HCC cells were injected intra-portalily, and liver HCC volumes were repeatedly assessed by magnetic resonance imaging. A two-hour donor liver reperfusion prior to retrieval was reversing the effects of ischemia/reperfusion and was associated to lower rates of post-transplant HCC growth.

Normothermic extracorporeal membrane oxygenation (NECMO) is the closest clinical procedure to reproduce the studied model, as it allows restoring the perfusion of the donor organs in case of donation after cardiac death (DCD). Apart from being primed with a perfusion solution, NECMO uses the donor’s own blood, with a maintained pH between 7.0 and 7.4 [3]. However, it is currently unknown whether NECMO can also have a protective impact on post-transplant HCC recurrence/growth, and this
field deserves further assessment. Similarly, ex situ machine perfusion, either normothermic, hypothermic or sub-normothermic has confirmed protective effects on liver ischemia/reperfusion lesions, but its impact on cancer has never been tested [4–8].

The minimal required time of liver graft reperfusion for preventing HCC growth is currently unknown. The used two-hour reperfusion matches international reports with NECMO or ex situ machine perfusion ranging between one and four hours [3,7,8]. It is also in agreement with the need for a minimal two-hour graft normothermic machine perfusion in order to restore the function of ischemic rat livers [4].

Overall, ischemia/reperfusion may be an added factor altering post-transplant cancer recurrence. This link is likely weaker than the one between pre-transplant HCC characteristics and recurrence, but it deserves further exploration both to better understand the underlying mechanisms and the ways to prevent it.

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References


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