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# Post-ischemic normothermic machine perfusion and post-transplant cholangiopathy

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Dear Editor,

With interest we read the article by Fodor et al. on the use of normothermic machine perfusion (NMP) for post-ischemic preservation of donor livers<sup>1</sup>. In this study, the outcomes of 59 consecutive NMP procedures were compared with a historical, matched cohort of livers preserved using static cold storage (SCS) alone. The authors conclude that the use of NMP resulted in a lower rate of ischaemic-type biliary lesions (ITBL). However, there are several aspects of this study that need commenting.

First, the definition of the endpoint ITBL is unclear. The authors make a distinction between non-anastomotic biliary strictures (NAS) and ITBL. Authors report no significant difference in the occurrence of NAS between the NMP and SCS groups, but found a statistically significant difference in ITBL between both groups<sup>1</sup>. This is remarkable, because the terms NAS and ITBL have both been used for the same specific component of post-transplant cholangiopathy, namely biliary strictures at any other place than the anastomosis in the presence of a patent hepatic artery<sup>2</sup>. It is unclear how the authors distinguished between ITBL and NAS. Most previous studies on machine perfusion have used the combination of radiological biliary abnormalities and clinical symptoms, such as jaundice or cholangitis, as an endpoint, instead of the presence of radiological abnormalities alone<sup>3,4</sup>. Biliary abnormalities are frequently observed on post-transplant magnetic resonance cholangiography in the absence of clinical symptoms<sup>3,4</sup>.

Secondly, one of the most important risk factors for the development of ITBL after liver transplantation is cold ischemia time (CIT). As the difference in CIT was nearly significant between the two groups ( $P = 0.055$ ), it would have been interesting to see if the difference in ITBL remained significant after a correction for CIT. Overall, as no statistical corrections for any variable have been performed, residual confounding cannot be ruled out.

Thirdly, the authors state that 59 livers were transplanted of the 75 livers that underwent NMP (21 per cent discard rate). Surprisingly, the investigators found no significant difference in the EuroTransplant Donor Risk Index between livers that underwent NMP because of a high-risk donor profile and the control

cohort of SCS livers (Supplementary Table LXI). Based on these results, one could conclude that post-ischemic NMP results in higher discard rate of donor livers, yet that the outcomes in terms of graft survival are similar between NMP and SCS.

Several previous studies on post-ischemic NMP of high-risk donor livers, revealed high incidences of ITBL of up to 30 per cent<sup>4,5</sup>. In contrast to post-ischemic NMP, hypothermic oxygenated machine perfusion (HOPE) has been demonstrated to significantly reduce the incidence of ITBL after transplantation of donation after circulatory death livers<sup>3</sup>. A prospective, clinical trial was carried out to precede post-ischemic NMP by a short period of HOPE to avoid ischemia-reperfusion injury at the start of NMP and to help reduce the risk of ITBL after transplantation<sup>6</sup>. In conclusion, we disagree with the conclusion that post-ischemic NMP results in lower rates of ITBL. Moreover, as post-ischemic NMP resulted in a discard rate of 21 per cent, and similar graft survival was obtained in the control group of SCS livers with a comparable donor profile, we question the use of post-ischemic NMP for regular donor livers.

Disclosure. None to declare.

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