Development of a machine perfusion device for cold-to-warm machine perfusion

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LETTER TO THE EDITOR

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To the editor,

With interest we read the article by Goumard et al. on the development of a novel circuit for combined hypo- and normothermic machine perfusion.[1] The authors are to be commended for their work, and the attempt to make an inexpensive perfusion machine available to a broader public.

Cold-to-warm perfusion, even with two different perfusion solutions, has been successfully performed in various studies with a widely used and CE-marked perfusion device (Liver Assist [Organ Assist, Groningen, Netherlands]).[2,3]

There are several potential issues that are not clarified in this article. First, it appears the same perfusion pressures are used during hypothermia and normothermia. We would like to stress the importance of using lower pressures during hypothermic machine perfusion (HMP) to prevent undesired shear stress due to increased vascular resistance.[4] Most centers that have used HMP clinically over the last years, have been using pressure-guided systems at portal pressures $\leq$5 mmHg and arterial pressures $\leq$25 mmHg.[5,6]

Secondly, it remains unclear what perfusion solution is used during HMP. To the best of our knowledge, the safety of using the only CE-certified perfusion solution (Pump Protect®, Carnamedica, Poland) for HMP has not been studied nor been approved for temperatures up to 20 °C.

Lastly, in a recent study combining hypo- and normothermic machine perfusion (NMP) to assess viability of initially declined human donor livers, all grafts cleared lactate and maintained a physiological perfusate pH.[7] We hope that the authors of the present study can validate their results by showing that livers perfused with this new system can meet the viability criteria for transplantation previously described by our own group[7] and others[8] (Table 1).

Table 1 Viability criteria for liver transplantation during normothermic machine perfusion. Modified from van Leeuwen et al.[7] and Watson et al.[8]

Viability criteria after 150 min of NMP	
Perfusate lactate	<1.7 mmol/L
Perfusate pH	7.35–7.45
Bile production (cumulative)	>10 mL
Bile pH[a]	>7.45[a]
Difference between perfusate glucose and bile glucose	>10 mmol/L

[a] Especially the difference between perfusate pH and bile pH should be positive, as described earlier.[7]

Conflict of interest

None declared.

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References

1. C Goumard, E Savier, J Danion, J Pelissie, C Legallais, O Scatton. (2020) Cold-to-warm machine perfusion of the liver: a novel circuit for an uninterrupted combined perfusion protocol. *HPB* 22:927–933.
2. Westerkamp AC, Karimian N, Matton APM, Mahboub P, van Rijn R, Wiersema-Buist J *et al*. (2016) Oxygenated hypothermic machine perfusion after static cold storage improves hepatobiliary function of extended criteria donor livers. *Transplantation* 100:825–835.
3. Boteon YL, Laing RW, Schlegel A, Wallace L, Smith A, Attard J *et al*. (2019) The impact on the bioenergetic status and oxidative-mediated

tissue injury of a combined protocol of hypothermic and normothermic machine perfusion using an acellular haemoglobin-based oxygen carrier: the cold-to-warm machine perfusion of the liver. *PloS One* 14.

4. Schlegel A, de Rougemont O, Graf R, Clavien P-A, Dutkowski P. (2013) Protective mechanisms of end-ischemic cold machine perfusion in DCD liver grafts. *J Hepatol* 58:278–286.
5. van Rijn R, van den Berg AP, Erdmann JI, Heaton N, van Hoek B, de Jonge J *et al*. (2019) Study protocol for a multicenter randomized controlled trial to compare the efficacy of end-ischemic dual hypothermic oxygenated machine perfusion with static cold storage in preventing non-anastomotic biliary strictures after transplantation of liver grafts donated after circulatory death: DHOPE-DCD trial. *BMC Gastroenterol* 19:40.
6. Dutkowski P, Schlegel A, de Oliveira M, Müllhaupt B, Neff F, Clavien P-A. (2014) HOPE for human liver grafts obtained from donors after cardiac death. *J Hepatol* 60:765–772.
7. van Leeuwen OB, de Vries Y, Fujiyoshi M, Nijsten MWN, Ubbink R, Pelgrim GJ *et al*. (2019) Transplantation of high-risk donor livers after ex situ resuscitation and assessment using combined hypo- and normothermic machine perfusion: a prospective trial. *Ann Surg* 270:906–914.
8. Watson CJE, Kosmoliaptsis V, Pley C, Randle L, Fear C, Crick K *et al*. (2018) Observations on the ex situ perfusion of livers for transplantation. *Am J Transplant* 18:2005–2020.