

LETTER TO THE EDITORS

Machine perfusion in clinical trials: "machine vs. solution effects"

doi:10.1111/j.1432-2277.2012.01460.x

Dear Sirs,

In their letter Chatauret *et al.* [1] address an interesting issue: in hypothermic machine perfusion for kidney preservation we should have a better understanding of the machine effects versus solution effects.

During the discussions concerning the study design the scientific steering committee also discussed which preservation solutions should be used.

For more than 40 years, KPS-1 is the standard solution for clinical machine perfusion. An increasing number of animal experimental studies demonstrate that machine perfusion with either HTK [2] or UW [3] leads to good results. Nevertheless clinical data are missing so we decided to use the standard solution.

For static cold storage use of HTK or UW is clinical reality in the Eurotransplant region. Therefore both solutions were accepted for cold storage in the trial.

Vaziri [3] performed an experimental study in a porcine autotransplantation model with 60 min warm ischemia and 24 h hypothermic preservation. Four Groups were compared: Machine perfusion was with either KPS1 or UW and Cold storage with either KPS1 or UW.

Since no animal in the group with cold storage and UW survived, the authors concluded that UW is bad for kidney preservation because of its potassium content. In a similar autotransplantation model with 60 min warm ischemia but 4 h hypothermic treatment [4] we found different results: four of seven animals survived with cold storage in UW. Somehow dissociated the Chatauret *et al.* interprete the group with machine perfusion and UW. This group has the highest survival whereas the differences between MP with KPS1 and CS with KPS1 were not so "obvious." You would expect the deleterious effect of a preservation solution to be aggravated by MP that permanently exposes kidney parenchyma to the preservation solution.

Chatauret *et al.* expect "extrapolating from their results that UW solution in the CS arm of the multicenter trial pulls down the survival curve." This is pure speculation.

Of all the experimental and clinical trials up to now at least no inferior results have been shown for UW compared with HTK [5,6].

We actually analyzed the results in the ECD subgroup of the multicenter trial comparing UW and HTK preserved kidneys. There were no significant differences for DGF rates (25% UW vs. 33% HTK), PNF rates (10% UW vs. 13, 9% HTK) and 1 year graft survival (90% UW vs. 78% HTK).

Chatauret *et al.* remind us that in experiments designed to compare two conditions only one parameter must change between the two conditions. An experimental animal DCD model with long, warm ischemia times and preservation times seems to change more than one parameter, compared with our clinical study.

The authors also see a "clear superiority of MP over CS in their study independent of the solution used."

We do not see a reason to question our conclusions concerning MP.

Although new solutions belong to the most interesting developments in transplantation, from our point of view multicenter trials comparing different solutions in machine perfusion are not realizable in the next few years without additional data.

Jürgen Treckmann,¹ Cyril Moers,² Jacqueline M. Smits,³
Anja Gallinat,¹ Ina Jochmans,⁴
Jean-Paul Squifflet,⁵ Jacques Pirenne,⁴
Rutger J. Ploeg,^{2,6} and Andreas Paul¹

1 Clinic for General, Visceral and Transplantation Surgery, University Hospital Essen, Essen, Germany

> 2 Department of Surgery, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

3 Eurotransplant International Foundation, Leiden, The Netherlands

4 Department of Abdominal Transplant Surgery – Transplant Coordination, University Hospital Leuven, Leuven, Belgium

5 Department of Abdominal Surgery and Transplantation, CHU Sart Tilman, University of Liège,

Liège, Belgium

6 Oxford Transplant Centre, John Radcliffe Hospital, Oxford, UK

e-mail: j.treckmann@gmx.net

Funding

Deutsche Forschungsgemeinschaft DFG TR 811/1-1. Organ Recovery Systems (Des Plaines, IL, USA).

Conflicts of interest

Drs. Moers and Paul report receiving one congress travel grant from Organ Recovery Systems; Dr. Pirenne,receiving a research grant from the government of Flanders, Belgium,in cooperation with Organ Recovery Systems to study machine perfusion of liver grafts, for which he receives no salary; Dr. Ploeg, receiving consulting fees from Bristol-Myers Squibb and grant support from Nuts Ohra Trust; Dr. Moers, receiving grant support from the Dutch Kidney Foundation; and Dr. Ploeg having a patent on a portable preservation apparatus for donor organs. No other potential conflict of interest relevant to this letter was reported.

References

 Chatauret N, Thuillier R, Barrou B, Hauet T, Eugene M. Machine perfusion in clinical trials: the preservation

- solution bias. *Transpl Int* 2011; **24**: e81 doi: 10.1111/j.1432-2277.2011.01300.x. Epub 2011 Jul 12. PubMed. PMID: 21749482
- Manekeller S, Leuvenink H, Sitzia M, Minor T. Oxygenated machine perfusion preservation of predamaged kidneys with HTK and Belzer machine perfusion solution: an experimental study in pigs. *Transplant Proc* 2005; 37: 3274.
- 3. Vaziri N, Thuillier R, Favreau FD, *et al.* Analysis of machine perfusion benefits in kidney grafts: a preclinical study. *J Transl Med* 2011; **25**: 9.
- 4. Treckmann J, Nagelschmidt M, Minor T, Saner F, Saad S, Paul A. Function and quality of kidneys after cold storage, machine perfusion, or retrograde oxygen persufflation: results from a porcine autotransplantation model. *Cryobiology* 2009; **59**: 19.
- de Boer J, De Meester J, Smits JM, et al. Eurotransplant randomized multicenter kidney graft preservation study comparing HTK with UW and Euro-Collins. Transpl Int 1999; 12: 447.
- Roels L, Coosemans W, Donck J, et al. Inferior outcome of cadaveric kidneys preserved for more than 24 hr in histidine-tryptophan-ketoglutarate solution. Leuven Collaborative Group for Transplantation. *Transplantation* 1998; 12: 1660.