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LETTER TO THE EDITORS

Machine perfusion versus static cold storage in expanded criteria donor kidney transplantation: 3-year follow-up data

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Sirs,

We recently reported the 1- and 3-year results of a large multicenter randomized trial showing that continuous hypothermic machine perfusion (MP) of kidneys from donors after brain death significantly reduces the risk of delayed graft function (DGF) and improves graft survival when compared with static cold storage (CS) [1,2]. We also reported the 1-year results of the subgroup analysis from expanded criteria donors (ECDs). In kidneys recovered from 91 donors after brain death, MP significantly reduced the risk of DGF [odds ratio (OR) 0.460, $P = 0.047$] and the incidence of primary nonfunction was lowered by 9% ($P = 0.04$) [3]. Graft survival at 1 year was significantly higher for machine-perfused kidneys than those preserved by CS (92.3% vs. 80.2%, $P = 0.02$) [3].

We believe that it is extremely important for clinical decision making, including aspects of cost-effectiveness and for future study designs, to provide longer follow-up data for the ECD subgroup. We therefore evaluated whether the graft survival advantage of MP seen at 1 year in ECD kidneys is maintained at 3 years. For this analysis, the 60 collaborating transplant centers provided graft survival data for 182 kidneys from 91 ECD donors via a secure online database hosted by Eurotransplant. Statistical analysis was undertaken using the same methods as those used in the original analysis [3].

Death-censored 1-, 2-, and 3-year graft survival are shown in Table 1. In a univariate analysis, no significant difference in 3-year graft survival rates between machine-perfused and cold-stored kidneys could be observed (83.0% vs. 74.5%, $P = 0.131$). However, when correcting for the most important confounding factors in a multivariate model, as shown in Table 2, we could show that MP is independently associated with an improved long-term renal graft survival ($P = 0.036$). Graft survival was significantly increased (35.8% absolute difference, $P = 0.0089$) in ECD kidneys that experienced DGF and were preserved by MP compared to those with DGF preserved by CS. We can conclude from these data that a graft survival advantage in favor of MP over CS persists at 3 years post transplant and that long-term survival of ECD kidneys that experienced DGF is dramatically worse when those grafts were not machine perfused.

There are some obvious limitations of this analysis: the number of patients included is relatively small, the data analysis was performed per protocol, and both kidneys had to be transplanted in two recipients to be included in the study.

Table 1. Univariate analysis of death-censored graft survival of kidneys recovered from ECD donors after brain death at 1, 2, and 3 years post transplant.

	Graft survival (%)			
	1 year ($n = 155$)	2 years ($n = 145$)	3 years ($n = 136$)	*P*-value (at 3 years)
Overall				
MP	91.2	87.7	83.0	0.131
CS	80.2	75.7	74.5	
DGF				
MP	85.0	74.4	68.7	0.0089
CS	40.7	37.0	32.9	
Non-DGF				
MP	93.0	91.5	87.0	0.36
CS	96.9	92.0	92.0	

CS, cold storage; ECD, expanded criteria donors; MP, hypothermic machine perfusion.

Table 2. Adjusted hazard ratios for graft failure at 3 years after transplantation of kidneys recovered from ECD donors after brain death.

	Hazard ratio (95% CI)	*P*-value
MP vs. CS	0.47 (0.23–0.95)	0.036
CIT	1.02 (0.94–1.11)	0.52
HLA MM	2.69 (0.40–17.93)	0.31
Recent PRA	1.56 (0.34–7.03)	0.56
Recipient age	0.97 (0.93–1.02)	0.27
Donor age	1.09 (1.00–1.19)	0.047
First/re-transplant	1.95 (0.43–2.09)	0.91
Duration of dialysis	1.05 (0.84–1.31)	0.65

CI, confidence interval; ECD, expanded criteria donors; MP, continuous hypothermic machine perfusion; CS, cold storage; CIT, cold ischemia time; HLA MM, no mismatch on HLA-B-DR; PRA, panel reactive antibodies.

Meanwhile, studies have suggested that end-ischemic (in house) reconditioning by MP, following a longer period of CS, might be equally effective as applying MP from procurement until transplantation [4–6]. So far, however, this approach has not been confirmed by large randomized clinical trials.

Anja Gallinat,[1] Cyril Moers,[2] Jacqueline M. Smits,[3] Agita Strelniece,[3] Jacques Pirenne,[4] Rutger J. Ploeg,[5] Andreas Paul[1] and Jürgen Treckmann[1]
1 Department of 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 Oxford Transplant Centre, John Radcliffe Hospital, Oxford, UK
e-mail: anja.gallinat@uk-essen.de

Conflict 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 MP 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.

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