Reviewer's report

Title: Uncontrolled donation after circulatory death: comparison of two kidney preservation protocols on graft outcomes.

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Reviewer: Sarah Osgood

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This manuscript compares in-situ cold perfusion and normothermic recirculation perfusion in uncontrolled DCD kidneys in two centres. In the first era 2006 - 2010 in-situ cold perfusion (ISP) was used and from 2010 - 2013 (n = 32) normothermic recirculation (NR) (n = 32). After retrieval all kidneys were preserved by cold machine perfusion.

The primary end point was graft function at 1 year. mGFR and eGFR was statistically higher in the NR group at 1 and 2 years. Protocol biopsies 3 and 12 month were also compared. Fibrosis, borderline changes and the Banff 07 score were assessed. Borderline changes and fibrosis were less in the NR group but these did not reach statistical significance.

This is an important manuscript and the only study to compare in-situ cold perfusion with normothermic regional perfusion in uncontrolled DCD donors. The differing protocols, differences in cold ischaemic times and post-transplant care during the two eras is a significant limitation of the study. However, a randomised controlled trial comparing the techniques is unable to be performed due to ethical reasons in France and Spain. Therefore, this likely to be the only study of its kind.

The results of both techniques are excellent with an extremely low rates of primary non function. Although the delayed graft function rate is high, graft function at 1 and 2 years is good. Kidneys undergoing normothermic perfusion had improved graft function at 1 and 2 years compared to cold perfusion.

Based on the biopsy information the authors speculate that normothermic perfusion may reduce activation of the innate immune system. I would be cautious in making such a conclusion with limited number of biopsies and without baseline samples.

The discussion could be improved by simply discussing the results of normothermic perfusion compared to the previous in-situ cold perfusion technique rather than making direct comparisons and speculating about the mechanisms.
Major comments

1: Baseline biopsies were not available. Therefore it is difficult to conclude any differences between the groups at 3 and 12 months. The change between 3 and 12 months would be more appropriate.

Minor comments

1: What do the authors mean in the discussion page 11 line 274 'duration of no flow or low flow'?

2: What temperature is ISP performed at?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

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