TRANSPLANT TRIAL WATCH

Edited by Reshma Rana Magar and Liset Pengel

To keep the transplantation community informed about recently published level 1 evidence in organ transplantation ESOT and the Centre for Evidence in Transplantation have developed the Transplant Trial Watch. The Transplant Trial Watch is a monthly overview of 10 new randomised controlled trials (RCTs) and systematic reviews. This page of Transplant International offers commentaries on methodological issues and clinical implications on 2 articles of particular interest from the CET Transplant Trial Watch monthly selection. For all high quality evidence in solid organ transplantation, visit the Transplant Library: www.transplantlibrary.com

Randomized controlled trial 1

Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomised, double-blind, paired, phase 3 trial. Jochmans, I., et al. *Lancet 2020; 396(10263): 1653–1662*. https://doi.org/10.1016/S0140-6736(20)32411-9

Aims

This study aimed to determine whether supplemental oxygen during hypothermic machine perfusion (HMP) led to improvements in the outcome of kidneys donated following circulatory death.

Interventions

One kidney from each donor was randomized to either oxygenated hypothermic machine perfusion (HMPO2) or HMP without oxygenation.

Participants

197 kidney pairs were randomized.

Outcomes

The primary endpoint was the estimated glomerular filtration rate (eGFR) at 12 months post-transplant. The secondary endpoints included patient survival and graft survival up at 12 months, primary nonfunction, delayed graft function, renal function according to CKD-EPI and MDRD equations, acute rejection and safety outcomes.

Follow-up

12 months.

CET conclusions

The well-designed, multicentre, double-blind, randomized controlled trial compared oxygenated hypothermic machine perfusion (HMP) with standard (nonoxygenated) HMP in kidney pairs from DCD donors aged 50 and over with sites in Belgium, The Netherlands and the United Kingdom. Kidneys from each pair were randomized according to a computer-generated sequence. Blinding was ensured by using empty dummy oxygen bottles in the standard HMP arm, and all healthcare professionals and transplant recipients were blinded to the allocation. The sample size calculation showed that 81 pairs were needed to provide 90% power to show an 8 ml/min/1.73 m^2 difference in the primary outcome estimated GFR. The primary analysis, based on intention-to-treat analysis and including only kidney pairs for which both grafts were functioning at 12 months, showed no significant difference in eGFR. A sensitivity analysis that accounted for failed grafts and patient death showed a significantly higher eGFR in the oxygenated group. Graft failure was significantly lower in the oxygenated HMP group as was the number of biopsy-proven rejection episodes. The authors conclude that oxygenated HMP has the potential to improve clinical outcomes and reduce healthcare costs.

Jadad score

5.

Data analysis

Strict intention-to-treat analysis.

Allocation concealment

Yes.

Trial registration

ISRCTN – 32967929.

Funding source

This study was non-industry-funded.

Clinical impact summary

By John Matthew O'Callaghan, Consultant Transplant Surgeon, University Hospitals Coventry & Warwickshire, and Deputy Director, Centre for Evidence in Transplantation, University of Oxford, UK.

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The publication of this recent paper revisits the addition of oxygen to hypothermic machine perfusion (HMP). The trial was conducted across 19 European transplant centres in three countries (Belgium, the Netherlands and the United Kingdom). The trial was of a robust design, with double-blinding, effective randomization and intention-to-treat analysis. In order to maximize the potential benefit, only donors over the age of 50 from Donation after Circulatory Death were included, and initially, they were analysed in paired fashion, one being allocated to receive oxygen and the other without. Possibly because of this analysis method, there was not significant evidence of improved GFR at 12 months after transplantation; kidney pairs where one kidney was lost or not transplanted could not be included in this analysis. However, graft failure at 12 months was significantly higher in the group without oxygen (10% vs. 3%) and severe complications were also significantly higher (11% vs. 8%). When including in the analysis kidneys from pairs where one kidney failed, GFR at 12 months was also significantly better for the group receiving oxygen. One standout, and unexpected result, was the significant reduction in acute rejection seen in the oxygenated group as well (14% vs. 26%). It is speculated that this may be related to the improved GFR at 12 months.

This study demonstrates potential important clinical benefits of oxygenated HMP over standard HMP in this study cohort. The device used for perfusion was the Kidney Assist Transporter (Organ Assist BV, Groningen, the Netherlands), and no changes to perfusion settings were made once started. Machine perfusion was not possible in only 5% of kidneys retrieved and deemed suitable for transplantation at that point. The process of oxygenated perfusion is therefore straightforward and suitable for the majority of kidneys. Perfusion was maintained from retrieval to implantation, which may prove to be a logistical challenge for some centres or programmes, when transport of the machine has to be considered. The median cold ischaemic time was 10–11 h. It is unclear whether the potential benefit would be present with a shorter period of oxygenated perfusion after a period of either static cold storage or nonoxygenated cold perfusion. However, the addition of supplemental oxygen to HMP can be a simple process with the right equipment, is safe, feasible for many kidneys and may have significant clinical benefits.

John O'Callaghan is a member of the Consortium for Organ Preservation in Europe and the COMPARE Trial Collaboration.

Randomized controlled trial 2

Life satisfaction and happiness in patients shielding from the COVID-19 global pandemic: a randomised controlled study of the 'mood as information' theory. O'Donnell, A., et al. *PLoS One 2020; 15(12): e0243278*. https://doi.org/10.1371/journal.pone.0243278

Aims

This study aimed to examine the effects of the COVID-19 pandemic on the life satisfaction and happiness of kidney transplant patients undertaking mandatory shielding.

Interventions

Participants were randomized to those who were to be primed with a question regarding the COVID-19 pandemic and those who were not.

Participants

200 kidney transplant recipients.

Outcomes

The outcomes of interest were overall life satisfaction, momentary happiness, overall lifetime happiness and desire to change.

Follow-up

N/A.

CET conclusions

This is a very interesting and well-conducted RCT in renal transplantation during the COVID-19 pandemic in the UK. The study is predicated on the basis that humans desire explanations for behaviours and feelings. Telephone interviews were conducted to assess patients' life satisfaction and happiness. 200 renal transplant recipients, who were shielding during the period of the study (1–29 May 2020), were randomized to one of the two groups. The first group received a 'priming' introduction whereby they were asked 'By the way, how's the COVID-19 pandemic making you feel at the moment?' Both groups had the same introductory conversation apart from this one sentence and then were asked the same four questions about their life satisfaction. Patients who had the priming introduction gave significantly better scores for lifetime happiness, life satisfaction and momentary happiness, and desire for change. It seems that asking a question about the COVID-19 pandemic, which brings this negative event into the frame, resulted in a discounting effect, whereby positive changes in both momentary happiness and other components of global life satisfaction were given higher scores. This has strong implications for how and when measures of life satisfaction should be gathered.

Jadad score
3.
Data analysis
Per-protocol analysis.
Allocation concealment
None.
Trial registration
Exempt from trial registration.

Funding source
This study was non-industry-funded.

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