

Ex-vivo Hypothermic Oxygenated Perfusion and Cytokine Filtration (Cyto-HOPE) of human liver grafts: a Randomized Controlled Trial

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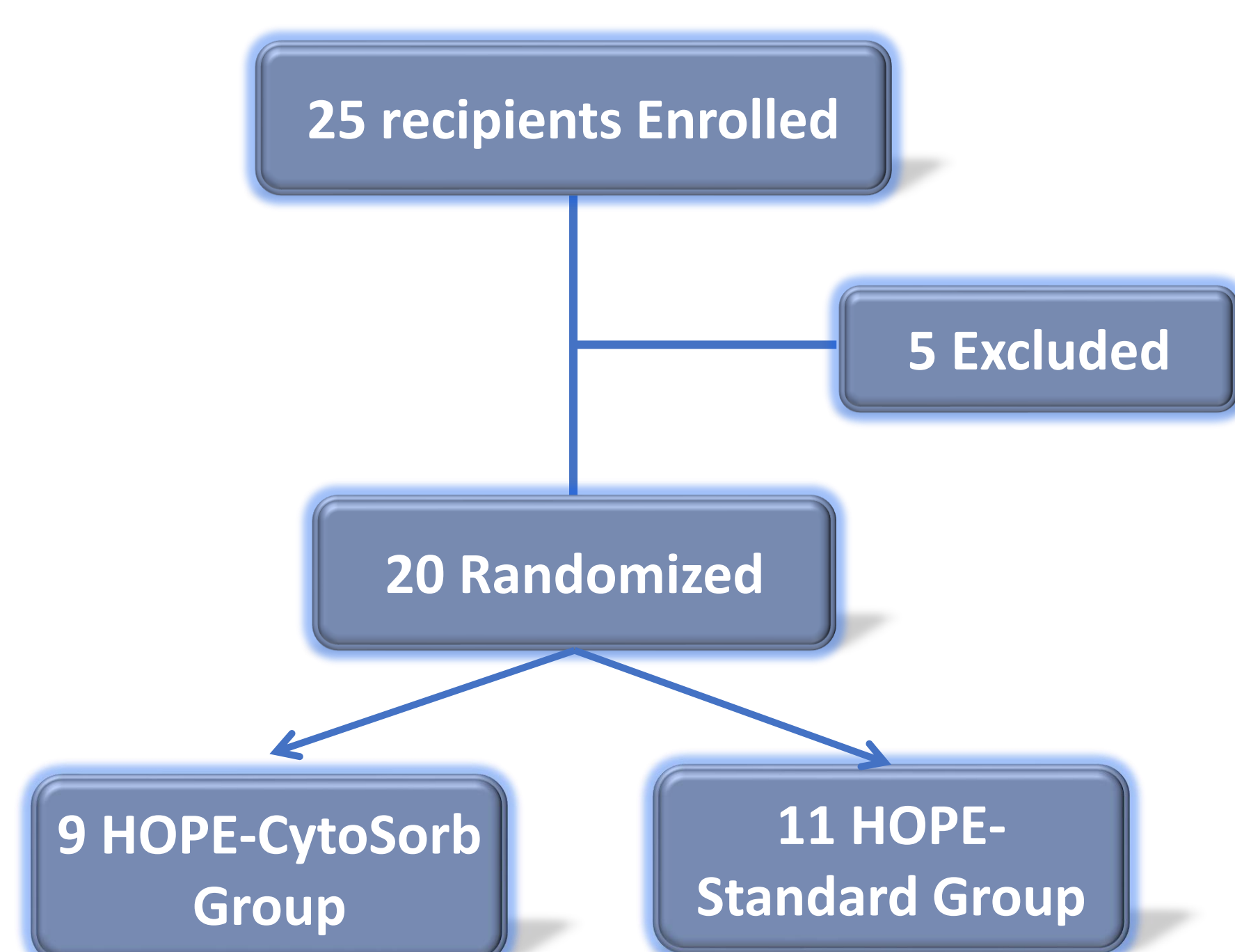
Introduction

Ischemia–reperfusion injury (IRI), a multifactorial pathological process largely mediated by cytokines, is the principal driver of post-reperfusion syndrome (PRS), early allograft dysfunction (EAD) and postoperative complications following liver transplantation. Graft procured from extended criteria donors (ECD) are especially sensitive to damage from IRI. Hypothermic oxygenated machine perfusion (HOPE) mitigates IRI by restoring mitochondrial function and modulating inflammation. We postulated that adjunctive cytokine adsorption during end-ischemic dual HOPE may further mitigate IRI and enhance LT outcomes.

Material and Methods

In this single-centre, open-label pilot randomized controlled trial (NCT04203004), adult recipients of whole ECD grafts were randomized 1:1 to dual HOPE with PerLife (Aferetica s.r.l, Bologna, Italy) device, with or without perfusate cytokine filtration using CytoSorb (CytoSorbents Inc., NJ 08852, USA) filter. The primary endpoint was incidence of PRS (Aggarwal et al. criteria); secondary endpoints were incidence of EAD (Olthoff et al. criteria) and histologically proven IRI (Modified Suzuki histopathological score). Perfusate and blood levels of TNF- α , IL-6, IL-8 and ET-1 were collected at different timepoints for correlation with outcomes. Post operative complications were assessed and recorded up to post-operative day 30 (POD 30).

Results



PRS occurred in 20% of recipients (3/9 HOPE-CytoSorb vs 1/11 HOPE-Standard; $p = 0.28$), and EAD in 30% (3/9 vs 3/11; $p = 1.00$). IRI was mild with no grade 3–4 injuries and did not significantly differ between the HOPE-CytoSorb and HOPE-Standard groups (grade 0 37.5% vs. 36.4%; grade 1 37.5% vs. 54.5%; grade 2 25.0% vs. 9.1%, respectively; $p = 0.55$ -1.00). No CytoSorb-related adverse events were observed. Cytokine assays remain under analysis.

Conclusion

Integrating CytoSorb™ into dHOPE is feasible and safe but did not significantly reduce PRS, EAD or IRI compared with standard dHOPE alone in this small pilot cohort. Ongoing cytokine profiling and larger, adequately powered trials with longer follow-up are required to determine whether targeted cytokine removal enhances the established protective effects of HOPE and improves graft function and survival.