

Markmann JF, et al. Impact of Portable Normothermic Blood-Based Machine Perfusion on Outcomes of Liver Transplant: The OCS Liver PROTECT Randomized Clinical Trial. *JAMA Surg.* 2022 Mar 1;157(3):189-198.

Abstract

“Importance: Ischemic cold storage (ICS) of livers for transplant is associated with serious posttransplant complications and underuse of liver allografts.

Objective: To determine whether portable normothermic machine perfusion preservation of livers obtained from deceased donors using the Organ Care System (OCS) Liver ameliorates early allograft dysfunction (EAD) and ischemic biliary complications (IBCs).

Design, setting, and participants: This multicenter randomized clinical trial (International Randomized Trial to Evaluate the Effectiveness of the Portable Organ Care System Liver for Preserving and Assessing Donor Livers for Transplantation) was conducted between November 2016 and October 2019 at 20 US liver transplant programs. The trial compared outcomes for 300 recipients of livers preserved using either OCS (n = 153) or ICS (n = 147). Participants were actively listed for liver transplant on the United Network of Organ Sharing national waiting list.

Interventions: Transplants were performed for recipients randomly assigned to receive donor livers preserved by either conventional ICS or the OCS Liver initiated at the donor hospital.

Main outcomes and measures: The primary effectiveness end point was incidence of EAD. Secondary end points included OCS Liver ex vivo assessment capability of donor allografts, extent of reperfusion syndrome, incidence of IBC at 6 and 12 months, and overall recipient survival after transplant. The primary safety end point was the number of liver graft-related severe adverse events within 30 days after transplant.

Results: Of 293 patients in the per-protocol population, the primary analysis population for effectiveness, 151 were in the OCS Liver group (mean [SD] age, 57.1 [10.3] years; 102 [67%] men), and 142 were in the ICS group (mean SD age, 58.6 [10.0] years; 100 [68%] men). The primary effectiveness end point was met by a significant decrease in EAD (27 of 150 [18%] vs 44 of 141 [31%]; $P = .01$). The OCS Liver preserved livers had significant reduction in histopathologic evidence of ischemia-reperfusion injury after reperfusion (eg, less moderate to severe lobular inflammation: 9 of 150 [6%] for OCS Liver vs 18 of 141 [13%] for ICS; $P = .004$). The OCS Liver resulted in significantly higher use of livers from donors after cardiac death (28 of 55 [51%] for the OCS Liver vs 13 of 51 [26%] for ICS; $P = .007$). The OCS Liver was also associated with significant reduction in incidence of IBC 6 months (1.3% vs 8.5%; $P = .02$) and 12 months (2.6% vs 9.9%; $P = .02$) after transplant.

Conclusions and relevance: This multicenter randomized clinical trial provides the first indication, to our knowledge, that normothermic machine perfusion preservation of deceased donor livers reduces both posttransplant EAD and IBC. Use of the OCS Liver also resulted in increased use of livers from donors after cardiac death. Together these findings indicate that OCS Liver preservation is associated with superior posttransplant outcomes and increased donor liver use.”

Comments by Scott Byram M.D.

Summary:

Normothermic machine perfusion (NMP) is a relatively novel liver preservation strategy as an alternative to the standard, ischemic cold storage (ICS). In NMP, the donor liver is harvested, the hepatic artery, portal vein, and supra-hepatic cava are cannulated. Using type specific blood, the portable machine delivers oxygenated blood flow to both the portal and arterial circulations. The machine and donor organ are then transported to the recipient location for transplantation after several hours of perfusion. During the perfusion time, oxygenation, arterial and portal pressures, and lactate levels are measured. NMP may be a viable or even superior method for preservation compared to ICS. NMP may have the potential to both expand the pool of acceptable organs for transplant, as well as lower the incidence of post-transplant, ischemia-induced cholangiopathy and early allograft dysfunction (EAD).

The PROTECT trial¹ is a multi-center, randomized clinical trial comparing these two different liver preservation strategies, NMP and ICS. NMP was accomplished using the Organ Care System (OCS). The donor inclusion criteria were preselected to capture organs particularly vulnerable to ICS induced damage. These risk factors included DBD > 40 years old, DCD, macrosteatosis, and expected prolonged ischemic time. After organ allocation, the donor liver was randomly assigned to either OCS or ICS. Ultimately, 293 recipients were included in the analysis (151 OCS, 142 ICS). The groups were similar with the exception of significantly more DCD donors existed in the OCS group. This potentially reflects that certain marginal grafts were placed on the OCS, which would have been discarded had they been assigned to ICS. In fact, more than twice as many organs were discarded during procurement in the ICS group due to “clinical judgement” of the surgeon. The organs in the OCS group were perfused a mean of 276 minutes. The primary endpoint (EAD) was significantly reduced in the OCS group (18% vs. 31%, $p=0.01$). Additionally, ischemic biliary complications were lower in the OCS group compared with the ICS group at 6 months (1.3% vs 8.5%; $P = .02$) and 12 months (2.6% vs 9.9%; $P = .02$). Finally, the authors state that reperfusion syndrome was more severe in the ICS group. However, this claim was based on post reperfusion lactate levels rather than any hemodynamic parameters.

The PROTECT trial is the first trial assessing the superiority of NMP over the standard ICS. In this study, the authors found that NMP was associated with a lower incidence in early allograft dysfunction and ischemic biliary complications at 6 and 12 months. Additionally, the use of NMP was associated with an increased number of DCD organs acceptable for transplant. More studies are warranted; however, NMP appears to be a promising liver graft preservation strategy.

References

1. Markmann JF, Abouljoud MS, Ghobrial RM, Bhati CS, Pelletier SJ, Lu AD, Ottmann S, Klair T, Eymard C, Roll GR, Magliocca J, Pruett TL, Reyes J, Black SM, Marsh CL, Schnickel G, Kinkhabwala M, Florman SS, Merani S, Demetris AJ, Kimura S, Rizzari M, Saharia A, Levy M, Agarwal A, Cigarroa FG, Eason JD, Syed S, Washburn WK, Parekh J, Moon J, Maskin A, Yeh H, Vagefi PA, MacConmara MP. Impact of Portable Normothermic Blood-Based Machine Perfusion on Outcomes of Liver Transplant: The OCS Liver PROTECT Randomized Clinical Trial. *JAMA Surg.* 2022 Mar 1;157(3):189-198. doi: 10.1001/jamasurg.2021.6781. PMID: 34985503; PMCID: PMC8733869.