

**ARTICLE OF THE MONTH**

Nickkholgh A, Nikdad M, Shafie S, et al. Ex Situ Liver Machine Perfusion as an Emerging Graft Protective Strategy in Clinical Liver Transplantation: the Dawn of a New Era. *Transplantation*. 2019;103(10):2003-2011.

**Abstract:**

The disparity between the number of available donor livers and patients awaiting a liver transplant has led transplant centers to accept suboptimal livers. There has been no universally accepted tool to predict the posttransplant function of these organs to safely increase the donor pool, protect these livers against ischemia-reperfusion injury, or improve their quality before implantation. Ex situ liver machine preservation has emerged as a promising novel graft protective strategy in the field of liver transplantation, with remarkable ongoing research and evolving clinical trials within Europe and the United States. This technology has been shown to be safe and feasible in the clinical liver transplantation field, has shown to reduce liver ischemia-reperfusion injury, and has shown to decrease the graft discard rate compared with conventional static cold storage. This review focuses on the current status of ex situ machine preservation in clinical liver transplantation, describing the most important technical aspects with the emphasis on the findings of the most recent clinical studies.

COMMENTS MADE BY SCHLICHTING, NICOLETTE MD

**Summary:**

This review article from the October issue of Transplantation discusses the newest literature on the exciting field of ex situ machine perfusion. Due to the ongoing discrepancy between the number of patients awaiting transplantation and the number of available donor organs, transplant centers are often willing to transplant allografts from extended criteria donors (ECDs), meaning that the allografts may be suboptimal. Ex situ machine perfusion may decrease ischemic-reperfusion injury and increase the utilization of these suboptimal grafts.

Early attempts at ex situ machine perfusion began almost a century ago, however they were largely set aside in favor of the simpler static cold storage (SCS) techniques. SCS utilizes hypothermia to decrease cellular metabolism and specific preservation fluid for cryoprotection. The continued need for liver allografts and resultant increase in use of ECDs has revived interest in machine perfusion. Ex situ machine perfusion techniques are most commonly classified by temperature. Normothermic machine perfusion (NMP) is performed at body temperature (37°C) and hypothermic machine perfusion (HMP) and subnormothermic machine perfusion (SNMP) are performed below body temperature, usually at 4-6°C and 20°C, respectively. Different methods utilize varying flows, pressures, perfusion routes (hepatic artery vs portal vein vs both), oxygenation, and perfusates.

Nickkholgh et al have written an excellent review describing the different protocols and summarizing both the published and ongoing studies assessing feasibility and outcomes. The overall goal of NMP is to maintain a normal physiologic environment thereby decreasing ischemia and promoting metabolic activity. This technique permits evaluation of organ viability prior to transplantation. Conversely, HMP does not preserve a normal physiologic environment and does not allow for allograft assessment due to decreased cellular metabolism. HMP causes time-dependent vasoconstriction and increased levels of reactive oxygen species. HMP can easily be converted to SCS in the setting of pump failure. Some studies demonstrate that utilization of machine perfusion may decrease organ discard rates and increase preservation times without negatively impacting allograft and patient survival. Others suggest that rates of early allograft dysfunction may be decreased with machine perfusion. There are no randomized controlled trials comparing NMP and HMP. The authors believe that advancements are needed in both protocols as they each offer benefits and the ideal method may be a combined approach.

The continued advancement of ex situ machine perfusion is exciting for the field of liver transplantation. While further studies are needed to better elucidate the most appropriate indications and uses for machine perfusion, these protocols have the potential to decrease discard rates of marginal allografts thereby increasing the donor pool and allowing more of our patients to receive life-saving transplantations.

**References:**

1. Nickkholgh A, Nikdad M, Shafie S, et al. Ex Situ Liver Machine Perfusion as an Emerging Graft Protective Strategy in Clinical Liver Transplantation: the Dawn of a New Era. *Transplantation*. 2019;103(10):2003-2011.

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