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Commentary: Colder may be better in ex vivo lung preservation

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Ex vivo lung perfusion (EVLP) has emerged over the last decade as a method of expanding the donor pool for lung transplantation.¹ The current clinical use of EVLP occurs with normothermic perfusion of the donor allograft, which has resulted in similar short-term¹ and long-term² outcomes compared with non-EVLP lung transplants. However, other solid organs have used hypothermic machine perfusion with good outcomes,³ leading to a current clinical trial to determine whether normothermic or hypothermic machine perfusion results in improved outcomes for liver transplantation.

To determine whether subnormothermic perfusion for EVLP can be beneficial, the authors used a rat model to evaluate damage-associated molecular patterns (DAMPs) at different temperatures while on EVLP.⁴ Clinical studies have previously demonstrated that increased ischemia-reperfusion injury, as measured by increased cell death signals, in EVLP perfusate has been associated with grade 3 primary graft dysfunction (PGD), as well as higher mortality.⁵ Thus, the authors evaluated cell death signals and DAMPs in the perfusate at normothermic (37°C) and subnormothermic (30°C and 25°C) temperatures. The 25°C EVLP was associated with a lower increase in certain

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CENTRAL MESSAGE

Ex vivo lung perfusion (EVLP) at 25°C appears to be associated with decreased histologic injury and cell death signals compared to normothermic EVLP in an animal model. Further studies are needed to evaluate clinical efficacy.

cytokines and DAMPs compared with normothermic EVLP, suggesting decreased inflammation with subnormothermic EVLP. Transplanted lungs from the 3 EVLP groups (37°C, 30°C, and 25°C) and from static cold storage (SCS) were also compared at 2 hours posttransplantation. Although there was no significant difference in the ratio of arterial oxygen concentration to the fraction of inspired oxygen (P/F ratio), there was a greater histologic injury in the 37°C and 30°C groups compared with SCS, with no difference between 25°C and SCS. Although this rat model demonstrates the potential decreased inflammation and posttransplantation graft injury in subnormothermic EVLP, the posttransplantation measurement of DAMPs and cytokines still favor SCS even over subnormothermic EVLP.

The results from this article are overall promising in demonstrating possible decreased injury in subnormothermic EVLP. However, there are additional models that

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should be assessed. The posttransplantation P/F ratio and histologic injury were assessed only at 2 hours posttransplantation, whereas primary graft dysfunction presents within 72 hours after transplantation and often progresses over this time period. Use of a longer posttransplantation rat model would further elucidate the different effects of normothermic EVLP, subnormothermic EVLP, and SCS. Additional work in large animal models also may help determine the efficacy of subnormothermic EVLP. Overall, this study suggests that perhaps 25°C perfusate in EVLP may result in less inflammation compared with normothermic EVLP, laying the groundwork for future studies with potential clinical applications.

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