Hitting the target with lung perfusion

Jason M. Gauthier, MD,^a Varun Puri, MD,^a and Daniel Kreisel, MD, PhD^{a,b}

From the ^aDivision of Cardiothoracic Surgery, Department of Surgery, and ^bDepartment of Pathology and Immunology, Washington University in St Louis School of Medicine, St Louis, Mo.

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Address for reprints: Daniel Kreisel, MD, PhD, Department of Pathology and Immunology, Washington University School of Medicine, Campus Box 8234, 660 S Euclid Ave, St Louis, MO 63110 (E-mail: kreiseld@wustl.edu).

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Expansion of the donor lung pool may reduce the waitlist mortality for prospective pulmonary transplant recipients. At the present time, most lungs that are transplanted worldwide are obtained via donation after brain death. In an effort to expand the donor pool, some programs have developed algorithms to use lungs donated after circulatory death (DCD). Controlled DCD is defined as the planned withdrawal of life support in donors who do not meet criteria for brain death, whereas uncontrolled DCD involves urgent procurement following unplanned cardiac arrest. Recent studies have shown that short- and long-term outcomes after transplantation of controlled DCD lungs are not inferior to those after transplantation of donation after brain death lungs.¹ Nevertheless, such organs are only infrequently used due to concerns over organ quality given the warm ischemia inherent to the process. Moreover, only a few centers have reported successful transplantation of lungs that were recovered after uncontrolled DCD.² Over the past decade, ex vivo lung perfusion (EVLP) has been used to assess lungs deemed marginal for transplantation and some have advocated the routine use of this technology for DCD lungs.

In this issue, Charles and colleagues³ from The University of Virginia report the results of an elegant preclinical study examining the short-term influence of EVLP on lung graft function in a porcine model of uncontrolled DCD with prolonged warm ischemia. The authors demonstrate that EVLP alone yields superior results compared with cold preservation. Furthermore, the addition of an adenosine A2B receptor antagonist to the ex vivo lung perfusate improves dynamic lung compliance, decreases expression of interleukin-12 and reduces neutrophilic graft infiltration when compared with EVLP alone. These observations extend this group's previous findings regarding the effects of targeting adenosine receptors in attenuating pulmonary ischemia reperfusion injury.⁴ Moreover, others have demonstrated that EVLP can be used as a platform to administer pharmacologic

Jason M. Gauthier, MD (left), Varun Puri, MD (middle), and Daniel Kreisel, MD, PhD (right).

Central Message

Targeted therapy during ex vivo lung perfusion is a promising technique to improve donor lung function before transplantation, thus expanding the donor pool.

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agents to donor lungs. Finally, the study by Charles and colleagues³ supports the notion that targeting the local microenvironment of the pulmonary graft provides a rational approach to improving outcomes after lung transplantation, as we and others have shown that the lung provides a suitable environment for the interaction of immune cells.⁵

Preliminary reports have demonstrated the value of using EVLP in the evaluation of human lungs from uncontrolled DCD.⁶ The study by Charles and colleagues³ may provide further impetus to consider transplanting lungs obtained from uncontrolled DCD. It is important to point out that controlled DCD lungs should not be regarded as marginal organs, and, therefore, should not be routinely subjected to EVLP.⁷ More importantly, EVLP will allow for targeted pharmacologic treatments that improve graft function, as demonstrated by Charles and colleagues.³ As we gain a better understanding of the cellular and molecular pathways that contribute to failure of lung grafts, we will be able to administer therapeutic agents during EVLP. One can envision that targeted therapy during EVLP will lead to improved function even in lungs that are not considered marginal based on current criteria.

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