Sending our lungs to rehab: The future of ex vivo lung perfusion?

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Central Message

Ex vivo lung perfusion has opened the window to a future of potentially improving lung quality through intervention.

See Article page 910.

The development of ex vivo lung perfusion (EVLP) is centered on the evaluation of lungs of uncertain quality. In 2001, Steen and colleagues¹ reported the first case of ex vivo perfusion use. Lungs from a patient who died following myocardial infarction after failed cardiopulmonary resuscitation were evaluated ex vivo and transplanted into a patient with chronic obstructive pulmonary disease. Current experiences with donation after circulatory death, particularly under controlled conditions, have questioned the need for ex vivo lung perfusion reassessment.² The International Society of Heart and Lung Transplantation Donation after Circulatory Death registry reported that only 16% of the transplanted lungs were re-evaluated with ex vivo perfusion.³ In our experience, EVLP can aid lung transplant centers in starting their donation after circulatory determination of death (DCDD) programs. In addition, they can support experienced DCDD programs modify their current practices safely, ie, increase times to arrest.

The development of the Toronto method resulted in longer perfusion times. This led centers to consider EVLP as a platform for therapeutics.⁴ Extended EVLP provides a unique opportunity. Donated lungs can be targeted with therapies without concerns for systemic effects or logistic limitations. In addition, the physiological impact of these therapies can be evaluated in real time. Although these interventions have not been approved for clinical use, the era is coming.

The current report by Mehaffey and colleagues⁵ is an example of therapies delivered during EVLP with the goal to improve lung quality. The authors investigated the effects of increasing circulating levels of sphingosine-1-phosphate (S1P) during EVLP with the goal of attenuating lung injury. Their rationale was that S1P attenuates lung injury by preserving and promoting vascular integrity via cell-cell junction stabilization. They relied on a mice model of DCDD—1 hour of warm ischemia after euthanasia and 1 hour of cold

storage and ex vivo perfusion 1 hour. They increased S1P levels during lung perfusion by adding activated S1P and a SphK2 inhibitor, which in turn reduced S1P clearance.

The mice lungs that underwent EVLP with the addition of S1P+SphKi showed the greatest benefit. The pulmonary artery pressure and lung compliance during EVLP and endothelial integrity were all significantly better when compared with controls. Nevertheless, these results should be interpreted with caution. In this study, the lungs were not reperfused with blood either by adding it at the end of EVLP or by transplanting these organs. In addition, the short period of EVLP may not accurately reflect the quality of the organ or the full benefit of the therapy.

Several encouraging small animal and nonsurvival models testing therapies during EVLP have been published in the last 5 years. Large animal studies that include transplantation and potentially survival surgery should be the standard before these initial reports are translated to clinical trials. We wait with anticipated enthusiasm for these types of investigations to advance our field.

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