Extracorporeal lung perfusion may be used to improve metabolic support, extend perfusion times, and potentially optimize organ repair. Hozain and colleagues recently reported improved perfusion times and enhanced lung recovery using a model of xenogeneic cross-circulation. Human lungs were, in this manner, perfused using swine circulation and regained function. Nevertheless, the findings highlight the metabolic and hormonal limitations of contemporary ex vivo techniques. They also demonstrate the need for improvements in organ support capabilities that will eliminate the need for xenogeneic cross-circulation.

In this article, Takahashi and colleagues catalog their use of modified ex vivo lung perfusate in a porcine model to achieve stable homeostasis in a bid to extend perfusion time. The contribution is timely and relevant and reflects the efforts of an experienced group of transplant surgeons. The authors used 4 groups of 5 Yorkshire male domestic pigs in keeping with the convention endorsed within previously published works. However, the small sample size engenders the threat of a type 2 error that remains prevalent throughout the article. The authors used a mixed-effects linear regression and predicated the analysis on alterations in dynamic compliance and airway pressure. They selected, somewhat arbitrarily, the value of 15 mL/cm H2O as a cutoff for futility with a rationale that caters perhaps more to convenience than strict pathophysiologic construct.

For this determination, the authors refer to previously published works in which they investigated the kinetics of lactate metabolism, highlighting the fact that lungs with high lactate/pyruvate ratios demonstrated higher peak airway pressures, lower glucose levels, and higher lactate levels. There was a significant increase in dynamic compliance in the treatment groups, together with reductions in peak airway pressure and pulmonary vascular resistance, the latter of which distinguishes it from previous reports. Nevertheless, multiple questions abound. How best can one interpret the observations, considering the use of lungs that had no significant inflammatory injury? Could the difference potentially be the result of a type 1 error?

By their own admission, the authors admit this effect to be an incompletely understood phenomenon, and so it remains unclear how nutritional augmentation contributes to lung preservation. Unmitigated, the ambiguity tempers the enthusiasm and confidence with which the study is received. Furthermore, despite the decrease in cytokine levels within the small sample, it remains unclear which circulating biomarkers best reflect airway inflammation and lung function. As a result, authoritative conclusions must be attenuated somewhat. Nevertheless, the total parenteral nutrition group achieved significantly longer stable perfusion times. Likewise, inflammatory cytokine production was also notably reduced in the continuous replacement group.

Having achieved intravascular delivery of mesenchymal stem cells during ex vivo lung perfusion in an earlier exploration, establishing homeostasis that might extend the duration of perfusion is truly of considerable clinical importance. Success in this regard may pave the way for the routine use of augmenting mediators in ex vivo perfusion. The rationale, nonetheless, remains equivocal in

CENTRAL MESSAGE
Extending perfusion times in ex vivo techniques.
structure, process, and outcome but serves as fertile sub-
strate to generate hypotheses and broaden the search for
even more ways to extend perfusion in a quest, ultimately
to increase the number of available organs for donation—
the ultimate gift.

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parenteral nutrition in ex vivo lung perfusion: addressing metabolism improves

Commentary: Maintaining the pHysiological equilibrium

Alberto Benazzo, MD, and Konrad Hoetzenecker, MD, PhD

A great potential of ex vivo lung perfusion (EVLP) lies in
reconditioning grafts of an unacceptable quality so that
they can be used for transplantation. In this regard, several
approaches have been described in experimental studies,
including the treatment of infected donor lungs with
high-dose antibiotics, increasing endogenous interleukin-
10 production by gene therapy, and clearing a graft from
hepatitis C virus. However, the clinical applicability of
most of these approaches is limited by the inability of
perfusing human allograft for a prolonged period of time.
In the clinical routine, a 4- to 6-hour EVLP run can be per-
formed safely, which usually allows a thorough quality
assessment of marginal organs; however, it is often too short
to correct severe derangements of allografts.

In the article “Strategies to Prolong Homeostasis of
Ex Vivo Perfused Lungs,” Takahashi and colleagues explored 3 different modifications of the Toronto perfusion
protocol in a pig EVLP model of 24 hours: (1) a continuous
replacement of EVLP perfusate, (2) adding glucose and
sodium to maintain perfusate osmolality, and (3) adding
parenteral nutrition supplemented with amino acids and vi-
tamins. The authors showed that all 3 protocols resulted in
stable perfusion conditions for 24 hours, improved func-
tional parameters of the grafts, and reduced inflammatory
burden.

This paper highlights the necessity to develop more phys-
iological EVLP protocols to be able to safely prolong