structure, process, and outcome but serves as fertile substrate 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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Commentary: Maintaining the pHysiological equilibrium

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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,¹ increasing endogenous interleukin-10 production by gene therapy,² and clearing a graft from hepatitis C virus.³ 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 performed safely, which usually allows a thorough quality

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CENTRAL MESSAGE

Adaptions of current EVLP protocols are needed to be able to perfuse donor lungs for 24 hours and longer.

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 colleagues⁴ 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 vitamins. The authors showed that all 3 protocols resulted in stable perfusion conditions for 24 hours, improved functional parameters of the grafts, and reduced inflammatory burden.

This paper highlights the necessity to develop more physiological EVLP protocols to be able to safely prolong

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perfusion times. In particular, the fact that pH could be maintained above 7.0 in most of the lungs is noteworthy. pH homeostasis plays a fundamental role in physiology. During most EVLPs, a slow decrease of pH can be observed, and deteriorating lungs usually have a faster decay of pH.⁵ An acidic pH can destabilize proteins and ultimately leads to their denaturation, with consequent destruction of cell membranes and apoptosis. A low pH during EVLP is the result of an increased anaerobic glycolysis and lactate accumulation.⁵⁻⁷ The reasons for this remain elusive; however, mitochondrial dysfunction in damaged grafts seems likely.⁸

Current EVLP protocols do not consider an acid–base compensatory or electrolyte-stabilizing mechanisms as physiologically provided by the kidney. Keshavjee and colleagues chose to substitute large volumes of perfusate during EVLP to maintain a physiological equilibrium. It is tempting to speculate whether the addition of a hemodialysis membrane to the EVLP setup would lead to similar results and allow a stable long-time perfusion, maybe even beyond 24 hours. In conclusion, this study performed by the Toronto Extended pig EVLP research group is highly

relevant and represents the next step toward 24-hour organ preservation.

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