ASK THE EXPERT

Transplantation in Eisenmenger Syndrome: Getting to the Heart of the Matter

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Pulmonary hypertension (PH) is a common complication of congenital heart disease (CHD), often developing as a result of vascular remodeling from long-standing left-to-right shunting and pulmonary overcirculation. The most severe form of CHD-associated PH is Eisenmenger's syndrome (ES), in which pulmonary vascular remodeling has led to irreversible changes, systemic pulmonary pressure, and shunt reversal, resulting in cyanosis. While the ever-increasing armamentarium of pulmonary vasodilators has given clinicians several effective treatment strategies, the disease can still progress to the point where advanced therapies such as lung transplantation, with or without heart transplantation, must be considered.

The optimal timing of transplantation in such patients is often difficult to ascertain, however, as ES patients often maintain clinical stability with favorable survival compared with pulmonary arterial hypertension (PAH) patients with similar hemodynamics. Furthermore, clinicians considering transplantation for these patients are faced with a difficult decision: to transplant the lungs only and concomitantly repair the cardiac defect, or to perform a technically less complicated heart and lung transplant.

The allure of a lung-transplant-and-repair strategy is clear: patients often have hearts that are relatively structurally healthy apart from the shunt lesion and its attendant cardiac remodeling, and should be expected to perform well after repair of the defect and relief of the afterload (high pulmonary vascular resistance) on the right ventricle (RV). Transplanting only the lungs avoids the significantly longer wait times for heart-lung blocks, obviates the long-term concern of coronary allograft vasculopathy, and allows the donor heart to be used for another patient in need of this scarce resource.

Heart-lung transplants (HLT) are associated with increased mortality and morbidity compared with lung transplants alone, and, not surprisingly, the use of HLT has declined dramatically over time, from over 200 HLTs performed in 1990 to just over 50 in 2016.[1] Despite all the aforementioned advantages, however, the reality of this decision is less than straightforward; the complexities of performing cardiac repair concomitantly with a lung transplant (LT) can lead to much longer bypass times and more major bleeding complications. In fact, in a 2002 analysis of ES patients in the United Network for Organ Sharing (UNOS)/International Society for Heart and Lung Transplantation (ISHLT) Joint Thoracic Registry who underwent either HLT or LT alone, LT was associated with *worse* survival than HLT, and most of this survival disadvantage occurred in the first month post-transplant, suggesting that technical and perioperative factors played an important role.[2] Other single-center studies have also highlighted the difficulties associated with an LT-and-repair strategy. Goerler and colleagues reported their experience with HLT or LT for ES,[3] with only 5 of 51 patients spanning 2 decades having undergone an LT-and-repair strategy, owing to the complexity of their CHD, while Ueno and colleagues reported that LT was associated with greater blood loss and worsened postoperative graft function compared with HLT, although mortality was not different by 2 years post-transplant.[4]

Clearly, a "one-size-fits-all" approach is inappropriate in this patient population; the question, then, is which patients should be treated with HLT, and which patients can be successfully managed with LT and repair of the cardiac defect? While this question is far from definitively answered, we do have some clues. In general, the more complex the cardiac repair, the less successful an LT-and-repair strategy is likely to be, as longer ischemic times associated with a complex repair are likely to lead to ventricular diastolic dysfunction; one group suggested that HLT be performed rather than LT in any patient in whom the cardiac repair is expected to take more than 60 minutes.[5] Curiously, in the above-mentioned UNOS analysis, while patients whose underlying cardiac defect was a ventricular septal defect (VSD) had better post-transplant outcomes than those with an atrial septal defect (ASD) or patent ductus arteriosus (PDA), the association between a lung (rather than heart-lung) transplant strategy and poorer outcomes was strongest among VSD patients. The reasons for this are

not entirely clear, as data concerning the specific anatomy of the VSDs or their repairs are not available; however, 5 deaths in the LT arm were due to ventricular failure, while no such deaths were reported in the HLT arm, suggesting that perhaps the recipient heart was not as healthy as expected in these cases. Toyama and colleagues reported 2 cases of ES treated with an LT-and-repair strategy[6]; in the first, the underlying cardiac lesion was an ASD and the postoperative course was complicated by significant left ventricular diastolic failure, manifested by elevated pulmonary capillary wedge pressure and severe pulmonary edema requiring prolonged extracorporeal membrane oxygenation (ECMO) and ventilator support. The second case involved both a VSD and an ASD, where no such difficulty was experienced. The left ventricle (LV) in the first case was extremely diminutive, squashed by the much larger, dilated RV, whereas the LV in the second case was normal in size, presumably attributable to the volume load initially imposed by the VSD. The authors postulate that the chronically underfilled LV in the first case was less able to accept the increase in preload after relief of RV afterload.

Clearly, making definitive conclusions regarding the optimal treatment strategies for these complex patients is not currently possible; ultimately, decision-making remains a highly individualized process that needs to incorporate the complexity of the congenital lesion and associated repair, patient comorbidities, and the experience of the transplant team.[7] Currently, the evidence and collective experience suggest that HLT is an excellent treatment strategy with acceptable outcomes and should probably be the strategy used for most CHD patients with ES. However, an LT-and-repair strategy could be considered for patients with lesions for which the repair is likely to be straightforward and relatively quick, such as simple ASDs, PDAs, and the most straightforward perimembranous VSDs. Patients with any evidence of structural or functional abnormalities of the LV should be approached with particular caution when considering an LT-and-repair strategy, as postoperative ventricular failure can be disastrous.

References

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