See Article page XXX.

Commentary: If the first time is the best time, should there ever be a next time?

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Orthotopic heart transplantation (OHT) is a highly successful treatment option for patients with advanced heart failure symptoms refractory to optimal medical management with ongoing symptoms and a poor prognosis.¹ Survival after OHT is acceptable, with 1-year survival exceeding 85% and 3-year survival around 80%.² Nevertheless, this treatment option is severely limited in its scope of use due to limited numbers of suitable donor organs being available: fewer than 6000 OHTs are carried out each year, with approximately 1% to 2% of eligible patients receiving a transplant.^{2,3} This places a responsibility on all members of the heart transplantation community to ensure that this limited resource is optimally distributed, ensuring that patients undergoing OHT are in the best position to make use of the donor organ. Patients with unacceptably high peri- and postoperative risks are precluded from being listed for OHT for this reason.¹ Therefore, the concept of performing a second OHT after failure of the first transplanted organ remains controversial.

In this issue of the *Journal*, Hess and colleagues⁴ report an analysis of outcomes after redo OHT from data collected as part of the United Network for Organ Sharing registry between 2000 and 2020. Only 2.6% of recorded procedures were redo transplants, the majority being for chronic rejection and cardiac allograft vasculopathy. These patients more

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CENTRAL MESSAGE

Redo orthotopic heart transplantation has a reduced 5-year adjusted survival compared with primary transplantation. These results have ethical implications for equitable donor organ allocation.

likely to be on temporary mechanical circulatory support and inotropes beforehand. Unadjusted survival was inferior for redo procedures compared with primary transplantation (1 year: 83.4% vs 90.0%; 5 years: 68.6% vs 77.6%). Despite the comparison of 2 propensity-matched cohorts, redo transplantation continued to have inferior survival outcomes, although the patient groups still differed in terms of greater mechanical ventilation and less durable mechanical circulatory support beforehand in the redo cohort. Risks for poorer outcomes in the redo cohort included female sex, preoperative mechanical ventilation, donor history of hypertension, and left ventricular ejection fraction less than 50%.

These analyses confirm previously reported outcomes that redo OHT confers inferior survival compared with primary OHT. The differences are not adequately explained by the risk factors assessed. Previous studies have shown that redo sternotomy increases risk associated with OHT, but in this study, the survival deficit was greater than expected due to this alone.^{4,5} This suggests that important risk factors were not considered or that there is an intrinsic disadvantage associated with redo OHT. Important determinants of post-OHT outcomes, such as degree of sensitization, were not considered in this study; additionally, there was no reporting of whether donor-specific antibodies were more likely to be crossed in redo OHT, a factor associated with poorer outcomes.⁶ Donor factors such as hypertension and

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reduced cardiac function are known to result in poorer outcomes in all OHT, as are prolonged ischemic times and pre-operative mechanical ventilation.⁷

What is not adequately captured in this study is to what degree individual centers were willing to accept suboptimal donor organs to facilitate OHT at a time of high recipient instability; accepting that a suboptimal organ would be better than no organ at all. This remains the Achilles heel of all registry-based observational data and will never be adequately addressed. The other overarching question that remains unanswered is whether after a median survival of 9.1 years (interquartile range, 3.9-14.2 years) after OHT, it is fair and equitable to offer patients another transplant when all reports suggest organ survival would be better in a patient who had never previously been transplanted. This difficult consideration is something that the heart transplantation community as a whole need to address.

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