Changing Role of Heart Transplantation

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KEYWORDS

• Heart transplantation • Heart transplant allocation • Primary graft dysfunction • Sensitization • Rituximab • Bortezomib • Eculizumab

KEY POINTS

- Proposed changes to the heart transplant allocation policy may reduce waitlist mortality for the most critically ill candidates without a detrimental effect on posttransplant survival.
- Primary graft dysfunction is likely to increase as heart transplants are performed in older recipients with more comorbidities using older donors
- Advances to shorten ischemic time with an ex vivo perfusion platform may mitigate this risk.
- Identification of potentially cytotoxic donor-specific anti-HLA antibodies before transplantation offers hope of heart transplantation for highly sensitized candidates.

INTRODUCTION

Despite advances in pharmacologic and device treatment of chronic heart failure, long-term morbidity and mortality remain high and many patients progress to end-stage heart failure. The 5-year mortality for patients with symptomatic heart failure approaches 50%, and may be as high as 80% at 1 year for end-stage patients.[1–3] Over the last 4 decades, cardiac transplantation has become the preferred therapy for select patients with end-stage heart disease, with a 1-year survival post heart transplantation of almost 90% and a conditional half-life of 13 years (**Fig. 1**),[4] certainly far better than one could expect from end-stage heart failure.

Although heart transplantation has become standard of care for the management of end-stage heart failure, the role of heart transplantation in the United States is changing as the characteristics of heart transplant candidates continue to evolve. The number of patients with end-stage heart failure is increasing, and the number of donor organs remains constant and a limiting factor in transplantation.[5] Not only are there more potential heart transplant candidates, but heart transplant candidates today more complex. The proportion of candidates aged 65 years or older has increased: in 2013, 18.2% of candidates were aged 65 years or older, compared with 10.8% in 2003.[5] The proportion of candidates with mechanical circulatory support (most commonly ventricular assist devices [VADs]) at listing has also increased dramatically, from 7.5% in 2003% to 27.4% in 2013[5] and the proportion of patients transplanted from VADs has increased as well[4] (**Fig. 2**). Furthermore, the number of heart transplant candidates with antibodies to HLA, so-called sensitization is increasing over the past decade.[6]

Thus, the heart transplant candidates of the modern era are older, sensitized, with mechanical circulatory support, and at higher risk for poor outcomes, including primary graft dysfunction (PGD) and antibody-mediated rejection.[4,5,7] This article focuses on recent advances in heart transplantation that could address these challenges. These developments include (1) proposed changes in heart transplant allocation policy for more

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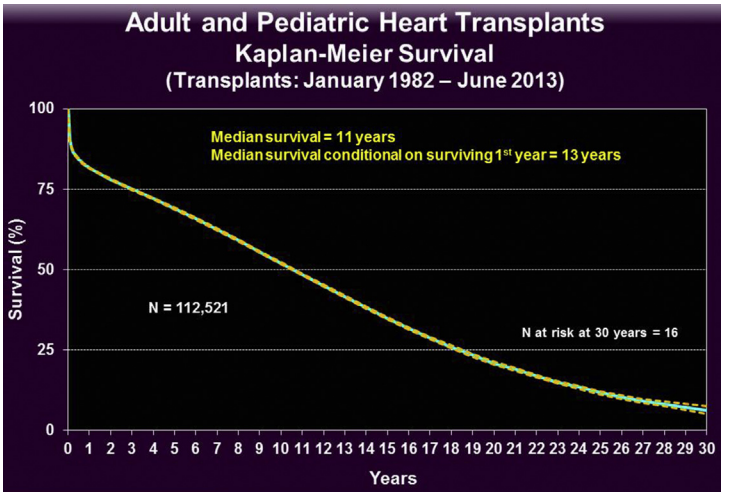

Fig. 1. Survival after heart transplantation. Actuarial survival for adult and pediatric heart transplants patients performed between January 1982 and June 2013. The half-life is the time at which 50% of those transplanted remain alive, and the conditional half-life is the time to 50% survival for recipients surviving the first year after transplantation. (*Data from* Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the international society for heart and lung transplantation: thirty-second official adult heart transplantation report—2015; focus theme: early graft failure. J Heart Lung Transplant 2015;34(10):1249.)

equitable organ distribution, (2) a better understanding of the definition and management of PGD, and (3) advances in the management of sensitized heart transplant candidates. Developments in these areas could result in more equitable distribution and expansion of the donor pool and improved quality of life and survival for heart transplant recipients.

HEART TRANSPLANT ALLOCATION POLICY

Current System

Allocation of thoracic organs in the United States is made according to the recipient's priority on the United Network for Organ Sharing waiting list and geographic distance from the donor. Priority on the recipient waiting list is determined by a recipient's assigned status code and time accrued within a status code. In general, patients with the highest medical urgency and lowest expected short-term survival are assigned a higher status code.[8] Donor hearts are first offered to local status 1 patients and then extended to status 1 patients within a 500-mile radius of the donor hospital (zone A). If no eligible recipients are identified, the organ is offered to local status 2 patients. This process repeats in a sequence of "zones" delineated by subsequent concentric circles of 1000- and 1500-mile radii from the donor hospital.

In the current system, there is marked regional variability in waitlist time.[9] As shown in **Fig. 3**, the median wait time for status 1A patients between 2006 and 2012 ranges from a low of 8 days in region 8, comprising the Great Plains states, to a high of 50 days in region 1, which includes the Northeastern states. Options to increase regional access to potential donors include offering hearts to status 1A candidates across a broader

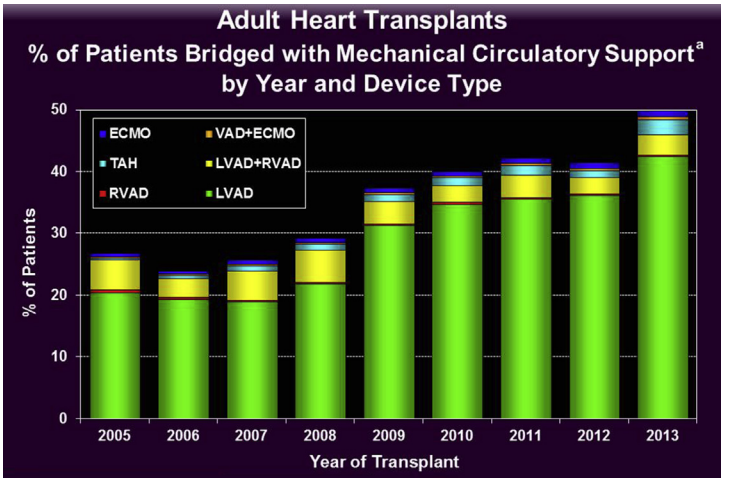

Fig. 2. Mechanical circulatory support as bridge to transplant. Use of mechanical circulatory support to bridge patients to transplant, predominantly in the form of left VAD (LVAD), is increasing over time with 42% transplanted from LVADs in 2013, and there was a resurgence in use of extracorporeal membrane oxygenation (ECMO), reaching 0.9% in 2013. RVAD, right VAD; TAH, total artificial heart. [a] LVAD, RVAD, TAH, ECMO. (*From* Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the international society for heart and lung transplantation: thirty-second official adult heart transplantation report—2015; focus theme: early graft failure. J Heart Lung Transplant 2015; 34(10):1249; with permission.)