Management of the ACC/AHA Stage D Patient
Cardiac Transplantation

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KEYWORDS

- Cardiac transplantation • End-stage heart failure • Rejection • Immunosuppression

KEY POINTS

- Heart transplantation is indicated in patients with heart failure despite optimal medical and device therapy, manifesting as intractable angina, refractory heart failure, or intractable ventricular arrhythmias.
- The evaluation for heart transplantation focuses on assessment of the presence of optimal medical management, the stability of extracardiac function, and adequate compliance and caregiver support.
- Standard immunosuppression after transplantation consists of triple-drug therapy with corticosteroids, calcineurin inhibitors (most commonly tacrolimus), and antiproliferative agents (most commonly mycophenolate mofetil).
- Treatment of rejection is progressively more aggressive as the patient's clinical status worsens, and ranges from an oral corticosteroid bolus and taper to intravenous pulse corticosteroids, cytolytic therapy with antithymocyte globulin, intravenous immune globulin, plasmapheresis, and circulatory support with inotropic therapy, intra-aortic balloon counterpulsation, and extracorporeal membrane oxygenation.
- The major long-term complications of heart transplantation are cardiac allograft vasculopathy, infections, and malignancy.

INTRODUCTION

Despite advances in pharmacologic and device treatment of chronic heart failure, long-term morbidity and mortality remain unacceptably high, with many patients progressing 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 the end-stage patients.[1] Over the last 4 decades, cardiac transplantation has become the preferred therapy for select patients with end-stage heart disease. Approximately 2400 heart transplants are performed annually in the United States. According to the registry of the International Society of Heart and Lung Transplantation, the median survival of patients after transplantation is currently 10 years, and up to 14 years for those surviving the first year (Fig. 1), a significant improvement over that of medical therapy for heart failure.[2]

The purpose of this article is to provide an overview of heart transplantation in the current era, focusing on the evaluation process for heart transplantation, the physiology of the transplanted heart, immunosuppressive regimens, and early and long-term complications.
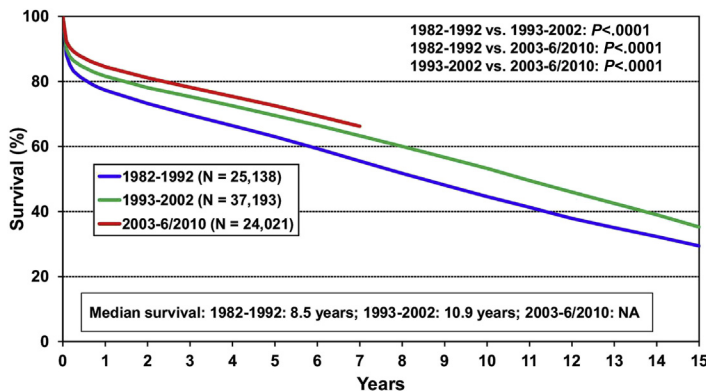
Fig. 1. Survival by era from the International Society of Heart and Lung Transplantation Registry. The median survival for the cohort of 96,273 adult and pediatric heart recipients who completed at least 1 year of follow-up is 10 years. For patients who survive the first year, the half-life is 14 years. When survival is stratified by the era of transplant, there has been a continued improvement in survival over the past 3 decades. (*From* Stehlik J, Edwards LB, Kucheryavaya AY, et al. The Registry of the International Society for Heart and Lung Transplantation: 29th official adult heart transplant report—2012. J Heart Lung Transplant 2012;31(10):1056; with permission.)

EVALUATION FOR HEART TRANSPLANTATION
Indications

The 3 major indications for heart transplantation are heart failure, angina, and ventricular arrhythmias refractory to maximal medical therapy. The most common indication for heart transplantation is refractory heart failure. Angina alone is often not considered an indication for transplantation in the absence of heart failure, as it is not clear if the survival of such patients is improved with heart transplantation. Intractable ventricular arrhythmias, commonly referred to as "VT storm," may merit heart transplant evaluation, and often urgent listing, given the association with hemodynamic compromise. The relative scarcity of donor organs makes it essential to determine whether patients are truly refractory to maximal medical therapy and require heart transplantation (**Fig. 2**).

Objective measurements that may help stratify the severity of illness include cardiopulmonary exercise stress testing and right heart catheterization. The cardiopulmonary exercise stress test measures maximal oxygen consumption (Vo_2max), which is proportional to cardiac output. A compensated patient with a Vo_2max of 12 to 14 mL/kg/min with adequate effort indicates poor survival over the next year and is an indication to proceed with evaluation.[3] Adequate effort is defined as the patient's achievement of anaerobic threshold, at which point CO_2 production exceeds O_2 consumption (indicated by respiratory exchange ratio [RER] >1).

Performing right heart catheterization once the patient is euvolemic is helpful in assessing the degree of fixed postcapillary pulmonary hypertension and cardiac output at rest. A cardiac index value of less than 2.5 L/min/m^2 suggests poor reserve and the need for transplant evaluation.[4]

Contraindications

The 2 major contraindications for heart transplantation are medical and social/psychological. The standard testing for the heart transplant evaluation is outlined in **Box 1**, and the potential contraindications are described in detail in **Table 1**. Many of these factors are not absolute, and need to be considered in the context of the severity of the patient's heart disease and associated comorbidities.

PHYSIOLOGY OF THE TRANSPLANTED HEART
Lack of Innervation to the Transplantation Heart

When the donor heart is placed into the recipient, both afferent (from the heart to the central nervous system) and efferent (from the central nervous system to the heart) nerve supply is lost. The loss of afferent nerve supply means that the recipient will not experience angina. Therefore, chest discomfort in a heart transplant recipient, especially early after transplant, is likely not caused by coronary ischemia, and coronary ischemia will likely not present with chest discomfort. The standard practice of annual angiograms for surveillance of transplant coronary artery disease is a direct consequence of the lack of afferent nerves supplying the transplanted heart.