Post–Heart Transplant Complications

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KEYWORDS

• Heart transplant • Complications • Immunosuppression • Rejection

KEY POINTS

- Managing patients after heart transplantation is challenging.
- After heart transplantation, patients have unique clinical complications (associated with the immunosuppressive therapy and cardiac allograft rejection) together with atypical clinical presentations for infection and systemic inflammatory response syndrome.
- High vigilance, early diagnosis, and appropriate intervention for allograft-related and non–allograft-related syndromes with significant morbidity and mortality are the keys to long-term survival of patients after transplantation.

INTRODUCTION

Heart transplantation remains the only definitive therapy for advanced heart failure. Approximately 2000 heart transplantations are performed annually in the United States.[1] The survival rates have improved with the use of new immunosuppressive drugs, with median survival of approximately 11 years.[1]

Soon after the transplantation, all patients should receive 3 classes of immunosuppressive drugs: glucocorticoids, calcineurin inhibitors (cyclosporine, tacrolimus), and antiproliferative agents (azathioprine, mycophenolate mofetil).[2] Glucocorticoids are gradually weaned 6 months after the transplantation. It is beyond the scope of this article to discuss the detailed mechanism and side effects of the immunosuppressive drugs.

INDICATIONS FOR HEART TRANSPLANTATION

Heart transplantation is recommended in various cardiac diseases. The most important indication is end-stage heart failure. These patients are American Heart Association stage D, New York Heart Association class III or IV with objective evidence of impaired functional capacity (peak oxygen consumption <14 mL/kg/min) despite optimal medical therapy.[1]

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Infrequent medical conditions requiring cardiac transplantation include (1) recurrent life-threatening ventricular arrhythmias, despite medical therapy and electrophysiologic interventions; (2) intractable angina despite maximal medical therapy and not amenable to revascularization; (3) primary cardiac tumors; (4) severe hypertrophic or restrictive cardiomyopathy.[1]

Current contraindications for heart transplantation include (1) severe irreversible pulmonary hypertension (pulmonary artery systemic pressure >60 mm Hg, mean transpulmonary gradient >15 mm Hg, and/or peripheral vascular resistance [PVR] >5 Wood units on maximal vasodilator therapy. When these patients are transplantable, they usually have right ventricle allograft failure); (2) significant peripheral vascular disease; (3) severe diabetes mellitus with end-organ damage; (4) severe irreversible hepatic, renal, or pulmonary disease (unless dual-organ transplantation is planed); (5) active infection; (6) ongoing tobacco use; (7) high or low body mass index (>30 or <20); (8) age (in most centers the age limit is 70 years, although some centers use alternative listing for elderly patients).[1]

GRAFT REJECTION

Graft rejection can be classified according to its acuity (hyperacute, acute, and chronic rejection) and to the mechanism of the rejection (cell-mediated rejection vs antibody-mediated rejection). Hyperacute rejection is mediated by preexisting antibodies to allogenic antigens and occurs within minutes to hours after the transplantation, causing rapid occlusion of graft vasculature with rapid graft failure. It rarely occurs with the current blood and human leukocyte antigen (HLA) typing techniques. Acute rejection can be subdivided into cell-mediated and humoral-mediated rejection. Acute cellular rejection may occur in the first week to several years after the transplantation. The inflammatory response of cell-mediated rejection consists mainly of T-cell lymphocytes.[3–5] To date, there are no sensitive serologic markers for acute rejection and myocardial biopsy remains the gold standard for this diagnosis.[3] In most institutions myocardial biopsies are done on a regular basis at least during the first year after the transplantation. It is essential to perform the biopsy on a routine basis regardless of symptoms, because patients can be asymptomatic during the rejection. Low compliance with immunosuppressive drugs remains the major risk factor for the occurrence of acute rejection. Humoral-mediated (or antibody-mediated) rejection consists mainly of antibodies directed against the donor HLA, and may occur during the first days to years after the implantation.[3,4] Chronic rejection may occur months to years after the implantation. It causes an irreversible graft dysfunction.[6]

As stated earlier, the diagnosis of acute cellular rejection is based on the biopsy results. Thus, endomyocardial biopsy should be performed as early as possible in any clinical suspicion of rejection. Every biopsy is graded according to the revised nomenclature of the International Society for Heart and Lung Transplantation (ISHLT)[5]:

- Grade 0: no rejection
- Grade 1 R, mild: interstitial and/or perivascular infiltrate with up to 1 focus of myocyte damage
- Grade 2 R, moderate: 2 or more foci of infiltrate with associated myocyte damage
- Grade 3 R, severe: diffuse infiltrate with multifocal myocyte damage, with or without edema, hemorrhage, or vasculitis[5]

All patients with acute cellular or antibody rejection should be admitted and undergo basic evaluation, including echocardiogram and blood tests. Those who have acute heart failure or hemodynamic compromise should be admitted to the intensive care