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Trends in Heart Transplantation

G Ramasubramanyam*

Department of Cardiothoracic Surgery, Care Hospital, Road number 1, Banjara Hills, Hyderabad, India.

***Corresponding author**: Dr. G Ramasubramanyam, MS, MCh. Department of Cardiothoracic Surgery, OPD Room no 6, Care Hospital, Banjara hills, Road no 1, Hyderabad – 500034, India. E-mail: d_gutti@rediffmail.com

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The first heart transplant was performed in 1966 by Christian Bernard in South Africa, remained relatively unknown until the development of more effective anti-rejection drug regimens in 1970s and 1980s. The current indications for heart transplantation are patients with severely impaired left ventricular function, intractable angina, unmanageable arrhythmias and severe diastolic failure [1].

In the year 2013, 3526 patients underwent heart transplantation of which 45.5% of patients were of the age group 50-64 years and 20.5% were of 35-49 years. The male to female ratio was 75.1% to 24.9% respectively. The leading causes for transplantation was cardiomyopathy (57.7%) followed by coronary artery disease (17.9%). The 1st year survival rates are 85%, whereas the 3 year survival rates are 80%. In Asia, in 2013, 143 patients underwent cardiac transplant of which 84.6% were male and 15.4% were female. 40.6% were of the age group 50-64 years and 22.4% were of 35-49 year old [2].

Heart transplantation is an established treatment for refractory cardiac failure in children. The survival of infants and 1 to 5 year old children after heart transplantation is 78% and 85% at 1 year and 70% and 75% at 1 year respectively. Adverse neuro-developmental outcomes in survivors of heart transplant before the age of 6 years were common particularly in those with congenital heart disease [3].

Indication for heart transplant are 1) cardiogenic shock requiring mechanical support or high dose inotropic or vasopressor drugs, 2) chronic, progressive, refractory or stage D heart failure symptoms despite optimal therapy, 3) recurrent life threatening arrhythmias despite maximal interventions including implanted defibrillators and 4) refractory angina without potential for revascularization. The most potent predictor of outcomes in ambulatory patients with heart failure is a symptom limited metabolic stress test to calculate the peak oxygen consumption of peak VO2. A peak VO2 of less than 12 ml/kg/min indicates a poor prognosis, with a survival that is less than that of a transplant [4].

Ventricular assist devices are commonly used to bridge the patient with end-stage heart failure to cardiac transplantation. Early device removal and transplantation was associated with significantly reduced 1 year post transplant survival. Multivariate analysis suggests that outcomes after heart transplantation are particularly poor in 2 to 4 weeks of VAD support and that the window of optimum rehabilitation-resuscitation are measured on the basis of post transplantation survival that occurs 1 and 3 months after VAD implantation [5].

Ischemia and reperfusion injury with graft preservation may impair ventricular contractility during the transplantation procedure which leads to right ventricular failure. Shahrokthagvi et al. showed that ECMO seems to be a better option as a mechanical circulatory support for right ventricular failure in heart transplantation [6]. In cases of severe left ventricular failure, a minimally invasive technique for decompression of the left ventricle in this setting, using a novel pulsatile paracorporeal assist device, the iVAC 3L (pulse cath, Groningen, The Netherlands). It is implanted through the right axillary artery and provides hemodynamic support while directly off loading the left ventricle [7].

Hemodynamic and biochemical parameters measured at the time of procurement could serve as predictive indicators of contractile recovery. Evaluation of graft suitability is feasible prior to transplantation with donation after circulatory declaration of death (DCDD) [8].

The early (<3months) and late (>3months) known causes of death after heart transplantation identified from a large scale single centre experience (Cleveland clinic foundation 1984-1995) were rejection, infection, graft failure, cerebrovascular hemorrhage, malignancy and other causes in the decreasing order of their incidence [9].

It was revealed that combination of different acting immunosuppressive drugs with adjusted dosage enhance their effectiveness and reduce toxicity. Induction therapy includes the use of polyclonal antibodies (20%), use of IL2 receptor antibodies (30%). Most centres avoid the use calcineurinin inhibitors for their nephrotoxic side effects and to achieve high immunosuppression. Maintenance phase comprises of triple drug immunosuppression (combining cyclosporine A, azathioprine and corticosteroids) which showed improved survival for short medium and long term follow up. The triple drug protocol even if modified i9s used around the globe and it increases the survival after a heart transplant from 60% to 80%. Today's standard immunosuppression may be replaced by immunosuppression individualized for each patient on basis of genomic profile, baseline risks for rejection and infection, and perhaps serial assessments of immune response after transplantation. After heart transplantation, rejection episodes and immune reactivity is highest within the first 3-6 months. Corner stone of treating graft rejection are corticosteroids, both oral and intravenous, anti thymocyte globulin (ATG), IL2 receptor blockers and murine monoclonal antibodies [10]. Induction therapy

in paediatric age group includes anti-thymocyte globulin (45%) and interleukin 2 receptor (27%) antagonists made up the majority. In the maintenance phase Tacrolimus remained the calcineurin inhibitor (CNI) of choice in 78% of patients at the time of discharge from the transplant hospitalization vs cyclosporine in 20%. Mycophenolate Mofetil (MMF) and Mycophenolic acid use increased to 87% of patients at the time of hospital discharge. Prednisolone use was 70%. Long term survival can now be reported at 22 years post transplant. Median survival continues to increase and was 20.6 years for infants, 17.3 years for children between ages 1 and 5 years, 14.6 years for children transplanted between 6 and 10 years and 12.9 years for adolescents. The long term survival in pediatric heart transplant recipients is better compared to adult heart transplant recipients [11].

Median time for cardiac transplantation has declined from 359 days in 1999 to 113 days in 2007. With decline in waiting time, the absolute mortality rate for status 1A has declined from 21.7% in 1999 to 8.6 in 2007 [12].

As per the United network of organ sharing data base registry, as on 10th October 2014, the total number of candidates waiting for cardiac transplantation are 4016.

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