Chapter 12

Immunosuppressive Therapy in Heart Transplantation

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ABSTRACT

Heart transplantation is a surgical procedure performed on patients with end-stage heart failure or other irreversible heart disease. Heart transplant prolongs the life of severe heart disease patients. Most of the receipts could survive more than 2-3 years, five-year survival rate could reach 70-80% with immunosuppressive therapy, rejection still an important problem after transplantation. Currently, traditional calcineurin inhibitors, antimetabolite agents, and steroids, wildly used after transplantation, the new generation of immunosuppressive medicines have been developed, and cell-based immunotherapy, as mesenchymal stem cell, myeloid-derived suppressor cells, dendritic cells, pluripotent cells and Treg cells are promising to be used in cellular immunotherapy in organ transplantation.

INTRODUCTION

The chapter focused on heart transplantation indication, prognosis, traditional and new generation immunosuppressive medicine, cell immunotherapy in adult and pediatric heart transplantation.

DOI: 10.4018/978-1-5225-2092-4.ch012
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Transplantation Opportunity and Clinical Prognosis

Indications

Congestive heart failure (CHF) affects 7.5 million people in North America and 23 million people worldwide (Alraies & Eckman, 2014). 550,000 patients develop heart failure (HF) each year, and the incidence is increasing, doubling with each decade after 45 years of age (Mozaffarian et al., 2015).

It has been reported that about 20% lifetime risk after midage for heart failure and while more patients are surviving the early stages of cardiac disease 10% of patients with HF are in the advanced stage (Deng, 2002). Based on 2011 mortality data from the American Heart Association, CHF contributes more than 30% of any-mention deaths attributable to cardiovascular disease (Mozaffarian et al., 2015). Cardiac transplantation has become the primary course of treatment for those in the last phases of this disease (Jung et al., 2011).

Heart failure is a complex syndrome defined by elevated cardiac filling pressure at rest or when under stress, also characterized by inadequate peripheral oxygen delivery, caused by cardiac dysfunction (Tse, 2011). HF is normally characterized by cardiac muscle dilation (dilated cardiomyopathy) or hypertrophy (Leclercq, 2007). There are two types of heart failure, reduced ejection fraction (systolic dysfunction), and preserved ejection fraction (diastolic dysfunction) (Lilly, 2012). Ejection fraction (EF) is a measurement of how well the heart is pumping each time it contracts. If this is low, it is an indication that the heart is not contracting during systole as well as it should be and, therefore, cannot pump blood to the periphery effectively. When EF is "preserved", it means that while the fraction of blood being pumped is the same, there is an overall decrease in the amount of blood being pumped, even though the percentage of blood being ejected from the ventricles is the same (Lilly, 2012).

Some conditions that can lead to a reduced EF include coronary artery disease, chronic volume overload as is seen in aortic or mitral valve regurgitation, dilated cardiomyopathies, advanced aortic stenosis, and uncontrolled severe hypertension. Conditions that can lead to preserved EF are all as a result of impaired filling of the ventricles during diastole. These can include left ventricular hypertrophy, restrictive cardiomyopathy, myocardial fibrosis, transient myocardial ischemia, and pericardial constriction or tamponade (Lilly, 2012). According to research studies, the most common diagnoses associated with heart transplantation were dilated cardiomyopathy, ischemic cardiomyopathy, and hypertrophic cardiomyopathy (Jung et al., 2011).

Systolic dysfunction heart failure comprises 50% of all heart failure patients (Alraies & Eckman, 2014). Congestive heart failure (CHF) is a form of systolic dysfunction, and its prevalence has increased over the years as a result of improved longevity of the population and better-quality management of acute coronary syndromes (Deng, 2002).

The first heart transplant was successfully done in 1967 in Groote-Schuur-Hospital, Kapstadt, South Africa. The U.S. accomplished its first successful heart transplant at Stanford University in 1968 (Deng, 2002). Currently, tens of thousands of heart transplants are being performed worldwide and due to major advancements in immunosuppression, rejection control, and infection control, the results of the procedures have improved dramatically since its inception (Deng, 2002; Jung et al., 2011) (Table 1).

The indications for heart transplantation are many and varied. Common indications such as having advanced heart disease unaltered by optimal medical therapy or failure of cardiac resynchronization therapy to improve symptoms of the underlying pathology are often considered in the stratification of patients on extensive waiting lists. There are criteria, however, in the determination of eligible patients.