Chapter 12
Surgical Stem Cell Therapy for the Treatment of Heart Failure

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Abstract Congestive heart failure (CHF) is a complex clinical syndrome resulting from myocardial dysfunction that impairs the cardiovascular system’s function. Both medical and surgical therapy still results in a large number of patients with very few options and persistent ventricular dysfunction. The major process to reverse ventricular remodeling would be the enhancement of regeneration of cardiac myocytes, as well as the stimulation of neovascularization within the affected area of the myocardium. This can be achieved by introducing progenitor cells that are capable of differentiating into cardiac myocytes or that promote neovascularization and restore the normal characteristics of myocardium environment. However a number of issues remain as to the type of cells, delivery, timing, and mechanisms involved. There have been a number of clinical trials based on very early small and large animal experiments that investigate stem cell therapy for heart failure, most of which have employed bone marrow stem cells or myoblasts. The majority of studies demonstrate an improvement in ventricular function, reduction in scar, or improvement in symptoms. There are a few trials that show no improvement at all. Here we present our surgical experience over the past 4 years with autologous and fetal liver stem cells in patients with heart failure.

Keywords Stem cell, heart failure, regeneration

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12.1 Introduction

Congestive heart failure (CHF) is a complex clinical syndrome that results from myocardial dysfunction that impairs the heart’s ability to circulate blood at a rate sufficient to maintain the metabolic needs of peripheral tissues and various organs. Heart failure is a relatively common clinical disorder, estimated to affect more than 5 million patients in the United States, and it remains the predominant cause of mortality in the western world. About 400,000 new patients are diagnosed with CHF each year. Morbidity and mortality rates are high; annually, approximately 900,000 patients require hospitalization for CHF, and up to 200,000 patients die from this condition. The average annual mortality rate is 40–50% in patients with severe (New York Heart Association [NYHA] class IV) heart failure. In the United States CHF treatment is estimated to cost more than 25 billion dollars for 2004 [1]. CHF has multiple etiologies including ischemic myocardial disease, the main cause of heart failure, and infective agents such as bacteria, viruses and protozoa. The protozoa Trypanosome cruzi is the causative agent of Chagas disease. Chagas disease may also be transmitted through blood transfusion and to the newborn from infected mothers. Trypanosome cruzi infects 10–18 million people in the Americas [2] and infection leads to a myocarditis with immunological pathogenesis that results in CHF. CHF is the natural evolution of a good part of Chagas patients. A progressive destruction of the myocardium occurs in approximately 30% of infected persons [3].

CHF is a systemic disease that affects many different organs including activation of the immune system with release of proinflammatory cytokines, activation of the complement system, and production of antibodies [4]. Animals with CHF after a prior myocardial infarction show a reduced immune response to an inflammatory challenge [5]. Inflammatory mediators are important in the pathogenesis and maintenance of CHF, contributing to cardiac remodeling and peripheral vascular disturbances. An imbalance in favor of inflammatory cytokines, such as tumor necrosis factor alpha (TNF-alpha), interleukin (IL)-1beta and IL-6 is present in both plasma and circulating leukocytes and the myocardium itself [6]. Considering the natural release of proinflammatory cytokines in infectious myocarditis that progress to CHF, it is very important in that the potential direct or indirect immunomudulatory effects of transplanted cells may have on progression of the disease [3].

The initial stages of heart failure are managed with medical therapy, and end-stage heart failure is managed with surgical procedures in addition to medical therapy. Some of the proven surgical procedures include myocardial revascularization, ventricular assist devices, and heart transplantation [7]. Although surgical and catheter-based revascularization of ischemic myocardium can treat angina, reduce the risk of myocardial infarction, and improve function of viable myocardium, the viability of severely ischemic myocardium, necrotic myocardium, or both cannot be restored. The major process to reverse the left ventricular remodeling would be the enhancement of regeneration of cardiac myocytes, as well as the stimulation of neovascularization within the affected area of the myocardium [8]. Thus the aim of