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Exercise and Stem Cell Therapeutics for the Infarcted Heart

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Heart failure afflicts 5.1 million individuals in the United States and its prevalence is expected to increase 25% by 2030. It is associated with a poor quality of life, increased mortality, and is extremely expensive to health care systems [1-4]. The progressive loss of cardiomyocytes is a central feature of heart failure from multiple etiologies. Thus there is a dire need for interventions that can preserve or even increase the number of well-functioning cardiac myocytes in patients with heart failure [5].

In this regard, the field of stem cell therapeutics has provided some very significant findings over the last fifteen or so years [5]. The field was initiated by attempts to utilize skeletal myoblasts to repopulate the damaged heart [6]. Since that time, numerous preclinical and clinical studies have been conducted (For Review See 5). Numerous studies have injected or infused a wide variety of stem cell sub-types in the heart [5]. While there is great controversy regarding the physiological mechanisms of improvement and the best stem cell type/number to use; the general findings of these studies suggest that stem cell therapy can benefit myocardial function and attenuate infarct size in both experimental animals and patients [5].

Still, despite these promising results, further advances are needed to more fully realize the benefits of stem cell therapy. One intervention that might prove to be a beneficial adjuvant is aerobic exercise. Beyond being safe and low cost, aerobic exercise changes the overall metabolic milieu of the heart and may trigger reparative mechanisms integral for success in stem cell therapeutics. For example, low engraftment and long term retention of stem cells have limited the overall efficacy of cell therapy [5]. By increasing cardiac output and stimulating a host of inflammatory and cell adhesion processes, aerobic exercise may increase stem cell homing and retention in the heart [7].

Studies have shown that the heart contains a population of progenitor cells that can form new cardiac tissue, albeit at very low rates [8]. Thus, while most cardiac myocytes in the adult heart are terminally differentiated, some new cardiac myocytes and endothelial cells can be formed from endogenous sources [8]. It is well accepted that stem cells initiate growth factor paracrine signaling to host myocardium, and it is feasible that stem cell paracrine signaling is altered by exercise, which in its own right, activates insulin-like growth factor signaling and is seminal in the development of physiologic-induced cardiac hypertrophy following exercise training [9]. Moreover aerobic exercise training may alter this dynamic, as training has been reported to increase the myocardial abundance of endogenous stem cells (c-Kit+ cells), increase the rate of cardiac myocyte proliferation, and attenuate cardiomyocyte cell death [10-12]. Additionally, other studies have shown that aerobic exercise stimulates the mobilization and circulation of endogenous progenitors [13,14].

To date only one small study has examined the effect of bone marrow mononuclear cells transplantation in a rat model of myocardial infarction following thirty days of low level swimming exercise (15 min/day; 3 days/wk). The authors found an improvement in left ventricular ejection fraction and more favorable post infarction remodeling following swim training compared to sedentary animals receiving cell injections alone [15]. Thus while stem cell therapeutics holds great promise for treating heart failure, novel adjuvant therapies like aerobic exercise may potentially optimize treatment efficacy. While understanding how exercise alters stem cell biology is in its infant stages, the use of therapies like cardiac rehabilitation may have utility far beyond what was previously understood. While accessing funding for such studies is challenging, the preliminary biology is enticing for a call to action in understanding whether exercise may improve the efficacy of stem cell therapeutics.

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