

MYOCARDIAL INFARCTION/HEART FAILURE

INTRODUCTION

Myocardial infarctions (MIs, also known as heart attacks) are the number one cause of death in the world. MIs occur when blood flow to the heart muscle is interrupted by coronary artery disease, leading to death of heart muscle fed by that vascular branch. The heart has minimal ability to regenerate, so the lost muscle is replaced by scar tissue. This leaves patients with reduced cardiac pump function, and in many cases, this progresses to heart failure, where the heart cannot meet the body's demand for blood flow. Current treatments for heart failure focus on managing symptoms (like reducing blood pressure) but do not address the root problem of muscle deficiency. New treatment strategies are needed to cure, rather than manage, this chronic disease.

RATIONALE AND EXPERIMENTAL EVIDENCE FOR CELL-BASED THERAPIES FOR MI

Since heart failure after MI results from a deficiency of cardiac muscle cells, researchers have been developing strategies to “remuscularize” the damaged heart wall, and thereby improve its function. Preliminary work with adult stem cells from bone marrow, adipose tissue (fat), and the heart itself showed that these cells die shortly after transplantation but may still improve cardiac function. This led to the idea that these cells have “paracrine” benefits, where short-term signals from transplanted cells can improve healing and function without replacing the lost muscle (Mayourian et al, 2018). In contrast, research in animal models has demonstrated that pluripotent stem cell-derived cardiac cells can form beating human heart muscle that has paracrine benefits and replaces muscle lost to MI. These cells have substantial benefits to cardiac function in animals ranging from mice to macaque monkeys (Liu et al, 2018).

WHAT IS THE CLINICAL STATUS OF CELL-BASED THERAPIES FOR MI AND HEART FAILURE?

Clinical trials began in the early 2000s with transplantation of bone marrow stem cells, followed by cells derived from adult hearts. These trials demonstrated that cell therapy for acute MI or chronic heart failure is feasible and generally safe for patients. Early trials with small numbers of patients suggested the possibility of improved cardiac function but as the field moved into larger trials that were randomized, blinded, and placebo-controlled, there were fewer indications of improved function. Taken together, the consensus now is that adult cells have only modest, if any, benefit to cardiac function (Eschenhagen et al, 2017). The first trials of human pluripotent stem cell derivatives were recently performed, with “patches” of human cardiac cells placed onto the surface of the failing heart (Menasché et al, 2018). Early results suggest that this approach is feasible and safe, but it is too early to know whether there are functional benefits.

WHAT DOES THE NEAR FUTURE HOLD?

Clinical trials with cells derived from bone marrow and the heart will continue, with some investigators suggesting that mixing the two together or performing repeated dosing will provide greater benefit. Work is accelerating markedly with transplantation of cardiac muscle cells derived from pluripotent stem cells. Groups in France, Germany and Japan are pursuing muscle patches that can be applied to the heart's surface. Groups in the US, Canada and Japan are transplanting heart muscle cells directly into the damaged region to remuscularize the wall. These studies are currently targeted to begin in ~2020.

Unfortunately, many unscrupulous clinics are offering stem cell therapies for heart failure. These clinics require direct cash payments for unproven therapy, and we urge patients to avoid them.

REFERENCES

Eschenhagen et al, Circulation. 2017 Aug 15;136(7):680-686
Liu et al, Nat Biotechnol. 2018 Aug;36(7):597-605
Mayourian et al. Circ Res. 2018 Jan 5;122(1):167-183
Menasché et al, J Am Coll Cardiol. 2018 Jan 30;71(4):429-438

USEFUL WEBSITE

<https://www.eurostemcell.org/>

<http://www.closerlookatstemcells.org/>

Charles E Murry, MD, PhD, University of Washington Institute for Stem Cell and Regenerative Medicine, and the [ISSCR Clinical Translation Committee](#)

September 2018