Regenerative Medicine

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Executive Editor

Cardiac Muscle Tissue Scaffolding helps restore Heart Functions

Myocardial infarction (MI) refers to heart attack, which is a serious medical condition. MI corresponds to the irreversible death of heart muscle after a prolonged lack of oxygen supply (ischemia). A heart attack leads to the development of scar tissue that diminishes heart muscle function, which eventually results in catastrophic heart failure. Each year, an estimated 785,000 new heart attack cases occur in the United States with a high fatality rate. This is due to the fact that there is no established treatment currently available that can be employed for repairing the resulting damage to cardiac tissue.

Researchers have employed regenerative medicine to treat patients with MI and ischemic heart failure. In the regenerative medicine based approach, researchers investigated several growth factor and gene therapeutics. However, the vast majority of trials have employed different types of stem cells. Heart tissues are not only comprised of cells but they also include a distinct scaffolding framework, which is known as the extracellular matrix (ECM). The main challenge that the researchers have faced is replicating the native cardiac ECM. The ECM has many constituents that consist of numerous proteins and proteoglycans that has a unique tissue-specific composition. This provides cues that influence all aspects of cell behavior that is necessary for proper tissue function as well as repair. An MI not only causes cell death, but also results in an inflammatory response and up-regulation of matrix metalloproteinase that ultimately degrade the native cardiac ECM [1-3].

More recently, research has focused on developing innovative biomaterials that can increase cardiac muscle, reduce fibrosis, and eventually lead to significant improvements in both global and regional function after percutaneous, trans-endocardial delivery. It also includes preclinical safety standards that comprise adequate biocompatibility, hemo-compatibility, and lack of arrhythmias. The goal of the current research efforts is to replace the abnormal microenvironment in the native cardiac ECM with healthy myocardial ECM cues to facilitate cardiac repair after an MI [4].

Injectable ECM Hydrogel Scaffold Designed to Repair Damage and Restore Cardiac Function

In a research of major impact and significance, scientists recently evaluated the safety and feasibility of trans-endocardial injections of a novel cardiac ECM hydrogel, in early and late post MI patients with left ventricular dysfunction. They successfully conducted a first-in-human, FDA-approved Phase 1 clinical trial of an injectable ECM hydrogel that is made of cardiac muscle tissue. This injectable, catheter-deliverable hydrogel is derived from porcine decellularized myocardial ECM [4].

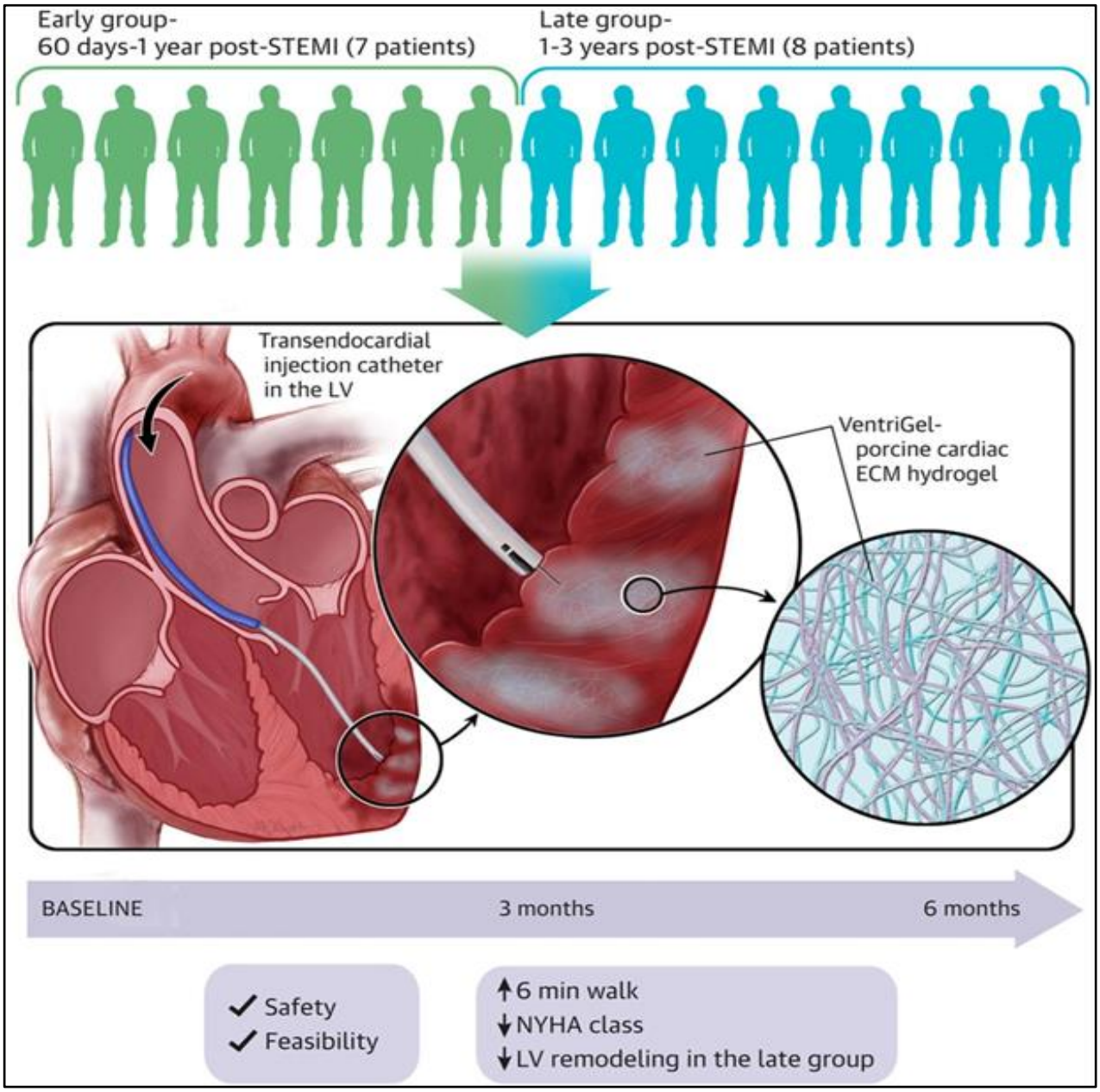

*Figure 1: The schematic process of injecting ECM hydrogel into the damaged region of heart and the phase 1 clinical trial [**Source:** JACC: Basic to Translational Science, 2019].*

This innovative hydrogel is designed to repair damage and restore cardiac function in heart failure patients who previously suffered a heart attack. The clinical trial conducted by the scientists is the first to test an ECM hydrogel designed to repair cardiac tissue in human. This research also demonstrates for the first time testing of a hydrogel made from the natural scaffolding of cardiac muscle tissue [4].

The hydrogel forms a scaffold that acts as a reparative environment where healthy cells migrate, once the gel is injected in damaged cardiac muscle. This phenomenon then leads to an increase in cardiac muscle, and less scar tissue that results in improvements in the heart function. The process of making the hydrogel involves taking cardiac connective tissue by stripping heart muscle cells through a cleansing process from pigs. It is subsequently freeze-dried and milled into powder form. The fluid which is generated can then be easily injected into heart muscle in a minimally invasive procedure that does not require surgery (Figure 1). Once it hits body temperature, the liquid turns into a semi-solid that forms a porous gel [4]. The Phase 1 trial of the hydrogel evaluated by the researchers involved 15 patients (Figure 1), who had sustained moderate damage in the left ventricle chamber of the heart following a heart attack. The trial showed that the hydrogel can be safely injected via catheter into patients who had suffered a heart attack in the past 2 to 36 months. Each patient was injected up to 18 doses of gel into the damaged region via catheter. Researchers then followed the patients for six months after this gel-based treatment [4].

This study is significant because of the fact that ECM hydrogels that have been shown in the preclinical studies have also the potential to be effective for other conditions. For example, such hydrogels could be beneficial in poor blood circulation that occurs due to peripheral artery disease.

Concluding Remarks

The field of regenerative medicine for the heart has evolved and grown from the earlier cell transplantation to increasingly preclinical studies on biomaterials or matrix-based approaches that help to recreate a more appropriate microenvironment for tissue repair. This transition of regenerative medicine in both cardiovascular and non-cardiovascular applications is further noticeable by the modern translational applications of biomaterial-alone therapies that can facilitate endogenous repair. In this regard, the latest advances in clinical trials to evaluate an injectable biomaterial hydrogel delivered via percutaneous trans-endocardial injections for cardiac repair are of immense value and interests. These new ECM technologies are expected to show significant advantages over the traditional regenerative medicine therapeutics.

References

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