ACADEMICIA: An International Multidisciplinary Research Journal
ISSN: 2249-7137 Vol. 11, Issue 11, November 2021 SJIF 2021 = 7.492
A peer reviewed journal

A STUDY ON MYOCARDIAL TISSUE ENGINEERING

Dr Anil Kumar*

* Department of Medical,
Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, INDIA
Email id: dr.netin@gmail.com

DOI: 10.5958/2249-7137.2021.02549.0

ABSTRACT

Myocardial tissue engineering, a technique that helps to solve the barriers to extending patients' lives after a heart attack, is developing all the time. It consists of a biomaterial-based 'vehicle,' which may be either a porous scaffold or a thick patch composed of natural or synthetic polymeric materials, to facilitate cell movement into the sick area of the heart. For cell treatment and cardiac tissue engineering, a variety of cell types have been proposed. Those also include the autologous and embryonic stem cells, each with its own set of benefits and drawbacks. Biomaterials recommended for this tissue-engineering activity must be biocompatible with cardiac myocytes and have mechanical characteristics that are similar to native myocardium, allowing the supplied donor cells to integrate and stay intact in vivo. Despite the fact that considerable study is being done, many questions remain unsolved, necessitating more investigation. We address the different methods described in the area of cardiac tissue engineering in this review, concentrating on the successes of merging biomaterials and cells using various strategies to heal the infarcted region, as well as clinical trials and potential cell resources in cell therapy. Myocardial xenotransplantation, in situ engineering, and intraventricular devices are all considered as alternatives.

KEYWORDS: *Biomaterials, Cell therapy, Myocardial infarction, Scaffolds, Tissue Engineering.*

1. INTRODUCTION

Cardiovascular disease is a significant health issue in the Western world and the main cause of mortality. The damage to the heart suffered by the remaining patients who survive their first acute episode may ultimately evolve into heart failure. When one or more of the blood arteries feeding the heart abruptly occlude, it causes a heart attack, also known as a myocardial infarction (MI). The coronary arteries are these vessels, and when they are suddenly stopped, the supply of nutrients and oxygen to the part of heart muscle served by the artery is cut off(1–4).

If blood flow is not restored quickly, the damaged portion of the heart muscle will experience permanent cell death. The mature contracting cardiac cells, the cardio myocytes, are unable to divide, thus the adult heart cannot heal the injured tissue. Scar tissue forms as a consequence of a myocardial infarction, and it lacks the contractile, mechanical, and electrical characteristics of normal myocardium(5). The pounding performance of the ventricles, the heart's major pumping

chambers, is reduced when contractile myocardium is replaced by a non-contracting fibrous scar. In response to the decreased cardiac output, several compensation mechanisms are triggered.

These help to stabilize the injured heart and keep cardiac output at a reasonable level at first. In the end, these "compensatory mechanisms" put an additional strain on the weakening heart muscle. This causes a downward spiral in cardiac function and the development of the heart failure clinical condition. As heart failure develops, the decrease of cardiac function becomes more rapid. Mechanical ventricular support devices or heart transplantation are the sole alternatives in the end-stage of heart failure. Nevertheless, many people die while waiting on the waitlist owing to the exorbitant expense of VADs and the scarcity of donor organs. As a result, alternatives are needed, with cell therapy being one of them. It has been suggested that scarred tissue be replaced by skeletal muscle cells, bone marrow cells, or embryonic stem cells. Injection of cells in suspension, either into the circulating blood or directly into the dead myocardium, is now the preferred technique of delivering these cells into the dead myocardium. Both methods of cell administration are ineffective, resulting in significant cell loss. This has led researchers to look at other cell transport methods, such as tissue engineering (TE). The goal of cardiac tissue engineering is to restore or rejuvenate a portion of the heart that has been injured(6–9).

It's been suggested for heart valves and myocardial muscle, the latter of which is the focus of this study. CTE entails the creation of a scaffold or patch composed of a biomaterial and cells. The biomaterial's primary purpose is to serve as a vehicle for delivering cells to the injured region, i.e. scarred tissue(10). The aim is that once the cells are given to the appropriate location, they will integrate with the host tissue and create new myocardium. Engineers and material scientists are always searching for better candidates suited for use as scaffolds in TE, and biomaterials research is a wide topic field. Synthetic and natural polysaccharides, including that of collagen and alginate, have been suggested as CTE treatments to date. The current study is focused on worldwide research in the broad area of CTE.

1.1 Cardiac arrest

Cardiac failure is caused by the heart's inability to supply enough blood to satisfy the body's metabolic needs. It is a leading cause of mortality in developed countries, and it may be caused by any illness that destroys the myocardium, causing it to lose its capacity to pump blood. Coronary artery disease and hypertension (high blood pressure) are the most frequent causes, although injury to any portion of the heart's complex anatomy may impede cardiac function and lead to heart failure. This includes heart valve dysfunction, the heart's electrical conduction system, and external pressure surrounding the heart caused by constriction of the pericardial sac in which the heart is located. MI is caused by a prolonged decrease in coronary blood flow to a portion of the heart, resulting in non-contractile fibrous scar tissue with decreased or nonexistent contractile capacity relative to the remainder of the healthy heart. It is unable to compensate for the loss of cells that happens after a MI, resulting in maladaptive left ventricular remodeling and end-stage heart failure. As a result, there is a lot of interest in finding novel ways to repair and regenerate a myocardial infarct(11–14).

1.2 Heart failure therapy methods including cardiac regeneration or repair:

a. The heart's own cardiac stem cells can regenerate missing tissue:

Stem cells are cells that have the ability to self-renew and specialize along particular lineages. They are referred to as either embryonic stem cells (ESCs) or adult stem cells, depending on their origin. Pluripotent stem cells (ESCs) are generated from early embryos and have the potential to develop into any cell type in the body. Adult stem cells found in tissues and organs are called multipotent because they can only develop into a limited number of cell lineages. Adult stem cells comprise bone marrow hematopoietic and mesenchymal stem cells, liver and brain stem cells, and cardiac stem cells. However, their origin is unknown, and theories differ — these cells may migrate to the heart from the bone marrow, or they may have been present in the heart since fetal life. They may contribute to cell turnover and heart repair on a modest scale throughout normal life, but myocardial damage from acquired heart disorders, such as myocardial infarction, overwhelms this ability(15). Even though these cells have been demonstrated to be able to develop into cardiac myocytes and vascular cells when separated from human myocardium, their low population and lack of evidence for myocardial regeneration prevents their rapid application in clinical studies. Cells from a variety of sources, comprising bone marrow, skeletal muscle, and ESCs, as well as primary cardiac myocytes generated from newborn rat hearts, have been used to try to repair and regenerate myocardial tissue(16). Although primary myocytes implant successfully, constraints such as limited yield and poor proliferative capability have prompted tissue engineers to use stem cells as an alternate cell source to address this problem.

b. Regeneration by the bone marrow stem cells:

i. Bone marrow mobilization of progenitor cells:

Progenitor cell release from either the bone marrow is known to be stimulated by cytokines including granulocyte-colony stimulating factor and stem cell factor. This has been proposed that even these undifferentiated stem cells may relocate to the infarcted area of the heart after mobilization, which involves releasing a pool of stem cells into the peripheral circulation. There is much disagreement about whether this process happens in people, and if it does, whether the homing bone marrow cells have the ability to develop into cardiac myocytes, thus aiding myocardial regeneration. Some studies have shown an improvement in infarcted area and cardiac function, whereas others have reported that G-SCF and SCF had no impact on infarct size but promoted vessel development.

ii. Injection of bone marrow stem cells:

Bone marrow has received a lot of interest as a source of stem cells for cell therapy throughout the years. It is made up of two parts: stromal and hematopoietic, the former of which produces mesenchymal stem cells and the latter of which is involved in the creation of new blood cells. BMSCs have many advantages, including their ease of use and the fact that they are autologous, which means they will not be rejected. Mice that had hematopoietic stem cells infused into their bloodstream after a heart attack had a 26 percent survival rate(17). According to the findings, the transplanted stem cells reacted to signals in the infarcted region of the heart, prompting them to move to the injured area and develop into the cells needed for cardiac repair, resulting in neovascularization. selected Link-kit+ bone marrow cells from mice using a florescence-activated cell sorting technique; the cells were then injected directly into the infarcted area, creating new cardio myocytes, smooth muscle cells, and vascular endothelium, resulting in the formation of de novo myocardium with living tissue 9 days after cell transplantation.

iii. Myocardium repair with skeletal myoblasts:

After a muscular injury, a subset of skeletal muscle cells has the capacity to become active, self-renew, and differentiate, allowing for muscle regeneration. These autologous cells were injected into the heart to heal the infarcted region because of their capacity to contract and continually mend the injured muscle, as well as their ability to be readily grown, multiplied, and identified in vitro. The outcomes of experiments trying to restore cardiac function have been varied, with some being effective and showing some promise in clinical trials, while others showed no signs of physiological improvement or cardiac differentiation. The apparent inability of these cells to transdifferentiate into cardiac myocytes is a major roadblock to their application in myocardial regeneration. Because the impulse cannot travel uniformly throughout the heart and transplanted cells, this inhibits electrical connection with native cardiac myocytes, resulting in a pro-arrhythmic substrate(18). This is due to the lack of expression of the gap junctional protein connexin43 in skeletal myoblasts. Pacemakers or defibrillators are needed to guarantee synchronized heartbeats and to address any hazardous cardiac rhythms that may be caused(19–21). Connexin43 has not been successfully introduced into cells via genetic modification since it has been proven to impact cell life span. Despite these disadvantages, it has been proposed that injecting fibrin glue and skeletal myoblasts into a myocardial infarcted area may maintain heart function.

1.2 Biomaterials in the regeneration of cardiac tissue

i. Tissue engineering in the heart:

TE is a technique that includes mixing biomaterials and live cells to create tissue equivalents that may be utilized in the repair, maintenance, replacement, and augmentation of tissues or organs. CTE is still in its early stages. However, it is a new area that has great promise for improving heart disease therapy. CTE will help patients who may not need heart transplants; some patients may just require smaller tissues, such as muscle, valves, or even arteries, and they will enjoy the vast possibilities provided by CTE. Miller and colleagues in Philadelphia, USA, developed the heart–lung machine, which was one of the earliest methods to treating cardiac illness. Mitral valve replacement followed soon after, with the valve being surgically created using either cadavers or fascia lata. Initially, researchers focused on autologous tissues and cells, but recent advances in the utilization of synthetic materials and cells are paving the way for novel cardiac tissue engineering methods. CTE is a materials-based method that includes the growth of cells on prefabricated three-dimensional (3D) scaffolds in the form of mesh, patch, or foam, with several organizations focusing on the creation of replacement tissues for different regions of the heart. A material scientist's role is to design, manufacture, and characterize materials for scaffolds or patches that serve as supports for tissue development and, in certain instances, organ support. MTE is a new treatment idea that has a lot of potential. In order for tissue regeneration to be effective, sufficient numbers of cells must be generated in order to retain certain biological activities and develop to the proper phenotype. Producing extracellular matrix in the proper structure and secreting signaling molecules are two important cell activities when communicating with adjacent cells/tissue. Biomaterials are critical to the strategy's success.

ii. Biomaterials:

A biomaterial is a non-viable material that is utilized in medical devices to interact with biological systems. Most TE methods need the use of biomaterials. Enhancing cell adhesion, proliferation, and differentiation are the primary functions of an optimal biomaterial for TE. In order to start tissue regeneration, the biomaterial must promote in vivo revascularization as well as integration with the host tissue. At the same time, it should be able to be replaced with newly created tissue by deteriorating at a pace that is comparable to that of new tissue development and ultimately being eliminated from the body via normal metabolic pathways without generating harmful by-products. In TE, the fundamental criteria for cardiac bioengineered structures are strong but flexible mechanical qualities, the ability to contract, electrically physiologically stable, easily vascularized, and ideally autologous.

2. DISCUSSION

The results presented in this study contribute to a possible breakthrough in the area of MTE by emphasizing many key aspects. To begin, it is necessary to determine which cell type is appropriate for human usage in order to aid in the regeneration of the infarcted area. The absence of a viable human cell supply is still the biggest obstacle to regenerating the human myocardium, whether by cell injection or TE development. Adult cardio myocytes were formerly believed to be terminally differentiated and incapable of proliferating. As a result, studies have concentrated on alternate cell sources such skeletal myoblasts and bone marrow stem cells, which have demonstrated modest therapeutic benefits. Although progenitor cells have been found in the heart, there are several limitations, such as the contradictory findings that have been published, with various research groups claiming distinct subpopulations present in the heart. It will need further research to see whether these progenitor cells are present in sufficient quantities in human biopsies. Cells having higher ability to regenerate the heart and an endless supply, such as ESCMs, should be the focus of research. To maximize the potential of hESCs, further research is needed to address critical problems such as immunogenicity, tetratomic formation, animal product involvement, and, last but not least, ethical concerns. MTE is a rapidly growing area that includes a wide range of biomaterials, both synthetic and natural, whose contributions are presently being studied.

3. CONCLUSION

The significance of biomaterials in future heart regeneration has been shown in this review of the specialist literature. For MTE to succeed, a number of problems must be addressed. To guarantee that cells on the graft or patch beat in unison, electrical connection between them is needed first. Second, there is still a worry about electrical connection between the construct and the natural myocardial for synchronous beating. Cell sheeting has been claimed to solve this issue, with graft integration and no arrhythmias recorded. There is some debate over whether or not a thick ‘patch' is helpful. It may be claimed that the cells must be implanted in a 3D scaffold with pores in order to live and perform their full potential activities. In this case, the engineered construct's necessary functions must be considered. A patch may be appropriate if the construct's only purpose is to serve as a "vehicle" to carry the cells into the patient and subsequently disintegrate over time. If, on the other hand, the construct is intended to support the injured region for a long time, it is critical, among other things, that it has a porous structure to enable cell survival throughout the time they are in touch with the scaffold. The optimal cell density and

scaffold/patch composition, as well as the time of implantation, must yet be addressed. Which cell, if any, should you use? Finally, the ideal myocardial construct should have morphological, physiological, and functional characteristics that are similar to those of the original heart muscle it is intended to replace and be viable after implantation. As the damaged myocardium integrates with the heart, MTE should enhance its function, lowering the morbidity and mortality of individuals with heart failure.

REFERENCES:

1. Ketabat F, Khorshidi S, Karkhaneh A. Application of minimally invasive injectable conductive hydrogels as stimulating scaffolds for myocardial tissue engineering. Polymer International. 2018.

2. Mishra V, Singh N, Rai D V., Tiwari U, Poddar GC, Jain SC, et al. Fiber Bragg grating sensor for monitoring bone decalcification. Orthop Traumatol Surg Res. 2010;

3. Bhardwaj P, Rai DV, Garg ML. Zinc as a nutritional approach to bone loss prevention in an ovariectomized rat model. Menopause. 2013;

4. Goel S, Sinha AK. An improved modeling of mode-choice behavior in urban area using adaptive neural fuzzy inference system. In: 2014 International Conference on Computing for Sustainable Global Development, INDIACom 2014. 2014.

5. Akhyari P, Kamiya H, Haverich A, Karck M, Lichtenberg A. Myocardial tissue engineering: the extracellular matrix. European Journal of Cardio-thoracic Surgery. 2008.

6. Jawad H, Ali NN, Lyon AR, Chen QZ, Harding SE, Boccaccini AR. Myocardial tissue engineering: A review. Journal of Tissue Engineering and Regenerative Medicine. 2007.

7. Sharma PK, Srivastava R, Munshi A, Chomal M, Saini G, Garg M, et al. Comparison of the gross tumor volume in end-expiration/end-inspiration (2 Phase) and summated all phase volume captured in four-dimensional computed tomography in carcinoma lung patients. J Cancer Res Ther. 2016;

8. Iyer M, Tiwari S, Renu K, Pasha MY, Pandit S, Singh B, et al. Environmental survival of SARS-CoV-2 – A solid waste perspective. Environ Res. 2021;

9. Bhardwaj S, Singhal N, Gupta N. Adaptive neurofuzzy system for brain tumor. In: Proceedings of the International Conference on Innovative Applications of Computational Intelligence on Power, Energy and Controls with Their Impact on Humanity, CIPECH 2014. 2014.

10. Pecha S, Eschenhagen T, Reichenspurner H. Myocardial tissue engineering for cardiac repair. Journal of Heart and Lung Transplantation. 2016.

11. Chiono V, Mozetic P, Boffito M, Sartori S, Gioffredi E, Silvestri A, et al. Polyurethane-based scaffolds for myocardial tissue engineering. Interface Focus. 2014;

12. Agarwal D, Tripathi SP, Singh JB. TrFRA: A trust based fuzzy regression analysis. Int Rev Comput Softw. 2010;

13. Naaz R, Saxena AK, Ather D. A framework for implementing blockchain with enhanced e2e encryption on ethereum 2.0. Int J Adv Sci Technol. 2019;

14. Agarwal N, Rana A, Pandey JP. Proxy signatures for secured data sharing. In: Proceedings of the 2016 6th International Conference - Cloud System and Big Data Engineering, Confluence 2016. 2016.

15. Jawad H, Lyon AR, Harding SE, Ali NN, Boccaccini AR. Myocardial tissue engineering. British Medical Bulletin. 2008.

16. Barabadi Z, Azami M, Sharifi E, Karimi R, Lotfibakhshaiesh N, Roozafzoon R, et al. Fabrication of hydrogel based nanocomposite scaffold containing bioactive glass nanoparticles for myocardial tissue engineering. Mater Sci Eng C. 2016;

17. Sekine H, Shimizu T, Okano T. Myocardial tissue engineering: Toward a bioartificial pump. Cell and Tissue Research. 2012.

18. Fujita B, Zimmermann WH. Myocardial tissue engineering strategies for heart repair: current state of the art. Interactive cardiovascular and thoracic surgery. 2018.

19. Seif-Naraghi S, Singelyn J, de Quach J, Schup-Magoffin P, Christman K. Fabrication of biologically derived injectable materials for myocardial tissue engineering. J Vis Exp. 2010;

20. Srivastava R, Sharma PK, Das KJM, Manjhi J. A hybrid approach for head and neck cancer using online image guidance and offline adaptive radiotherapy planning. J Radiother Pract. 2019;

21. Mathur G, Ghai W, Singh RK. A totalitarian technique for wormhole detection using big data analytics in iot network. Int J Sci Technol Res. 2020;