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Advances in Myocardial Infarction Treatment

INTRODUCTION

Myocardial infarction (MI) is defined as myocardial necrosis caused by myocardial ischemia (Kate Meier & Oyama, 2009). Myocardial infarction occurs as a result of either acute or chronic myocardial ischemia, which differs significantly from myocardial hypoxia in that ischemia leads in a stasis of metabolic waste products in addition to a lack of oxygen delivery, resulting in cellular damage (Reddy et al., 2015). Myocardial infarction is most frequently associated with ischemic myocardial necrosis. Coronary artery constriction or occlusion results in significantly diminished or interrupted coronary blood flow. The absence of blood flow and oxygen to the heart muscle results in persistent severe myocardial ischemia, which progresses to ischemic myocardial necrosis. Myocardial infarction is frequently associated with variable degrees of ventricular dysfunction. Myocardial infarction patients appear with systemic symptoms such as severe and persistent chest pain, tissue necrosis, acute circulatory failure, shock, heart failure, or severe cardiac arrhythmias that can result in rapid death (Peng et al., 2017). When a myocardial infarction occurs, it is classified according to the region of the heart that has been affected, which is ascertained by main coronary artery that has been obscured. As a result, the characterization contains the following:

(1) A condition in which the left anterior descending coronary artery is occluded, resulting in left ventricular anterior deformation;

(2) Left ventricular inferior and posterior enlargement, which is usually caused by occlusion of the right coronary artery or the circumflex coronary artery;

(3) Left ventricular lateral enlargement, which is usually caused by a clogged circumflex coronary artery;

(4) It is associated with involvement of a variety of coronary arteries, particularly the right ventricular (Bunag, 2007).

Current treatments for myocardial infarction are primarily focused on recanalization of the occluded coronary artery in order to regain bloodflow and inhibit myocardial necrosis from developing. Drug therapy, thrombolytic therapy, percutaneous coronary intervention (PCI), and coronary artery bypass graft

surgery (CABG) are some of the most commonly used methods for accomplishing this goal (Reddy et al., 2015). In recent years, integration of the two science disciplines, such as biotechnology and tissue engineering, has resulted in the development of new therapeutics, such as nanotechnology, stem cell therapy, robotic surgery, and other advances in medical technology (3-D printing and drugs). All of these treatment modalities have shown promising results in the management of myocardial infarctions of all types. Researchers in the field of stem cells are investigating the possibility of cardiac regeneration, while researchers in the field of nanotechnology are investigating nano-drug delivery and percutaneous coronary interventions such as stent modification and coating. The purpose of this article is to summarise the available literature (in vitro, translational, animal, and clinical) on these novel strategies and to explain the rationale for their potential use in the treatment of heart failure. These novel strategies have the potential to be effective alternatives to currently available treatment modalities in the future, owing to the extensive and ongoing efforts of researchers and clinicians worldwide (Kandaswamy & Zuo, 2018).

NEW STRATEGIC APPROACHES

Robotics

Robots have been used in mass production for a long period of time. Their use in medicine, on the other hand, is relatively recent, having begun with surgery and radiotherapy. Cardiology experience spanning more than a decade includes mitral valve repair, coronary bypass graft placement, and septal defect closure. The technology is rapidly evolving, with reports of PCI and AFib ablation applications. Robotics have the potential to improve ergonomics, precision, and intraoperative time. It has been demonstrated that robot-assisted surgery reduces hospital stay and increases patient satisfaction (Kandaswamy & Zuo, 2018). An extensive number of efforts have been made in the past to incorporate robotics into the surgical treatment of MI. Patient's cardiac arrest occurred three hours into the procedure of a robotic-assisted radical prostatectomy for cancer in a 52-year-old man with ASA physical status IV who was undergoing the procedure. All attempts at resuscitation were futile, and he was pronounced dead several hours after the initial incident. Comorbidity in the patient, as well as procedural errors, played a role in the patient's passing. Previously, the patient had a history of coronary artery disease that necessitated the placement of drug-eluting stents, which was the reason for this surgical procedure. A discussion is held on the preoperative cardiac evaluation and pharmacological management of patients who will be undergoing coronary angioplasty with drug-eluting stenting. For patients undergoing robotic surgical procedures, there are several positional and technical considerations to keep in mind, particularly when low-lithotomy and steep Trendelenburg positions are required. Heart and respiratory systems are particularly vulnerable to the effects of a prolonged head-down position. Because of the required positioning, as well as the complications associated with insufflation, this procedure presents a unique anaesthetic administration

challenge (Sharma & Berkeley, 2009). Minimally invasive surgical procedures have been developed in response to the growing recognition of the significant benefits of reducing surgical trauma. Endoscopic surgery provides patients with the benefits of minimally invasive surgery, and surgical robots have increased the capability and precision of surgeons in their operations. In recent years, technological advancements have made it possible to perform completely endoscopic robotic cardiac surgery, allowing surgeons to perform cardiac surgery endoscopically rather than through an incision in the middle of the chest (*Robotic Cardiac Surgery | Johns Hopkins Medicine*, n.d.). As a result, structural heart conditions, such as mitral valve plasty, atrial septal defect closure, multivessel minimally invasive direct coronary artery bypass grafting (MIDCAB), and completely endoscopic coronary artery bypass graft surgery, can be repaired entirely endoscopically (CABG). According to the article, robotic-assisted cardiac surgery can be considered a type of minimally invasive cardiac surgery (Ishikawa & Watanabe, 2015). Robotic surgery's current state of development in the treatment of MI is extremely encouraging. These systems are top-of-the-line in terms of quality and technology. Their proposed benefits, which include increased precision, visibility, ergonomics, and reduced radiation exposure, have been documented, resulting in improved patient recovery times and shorter hospital stays. This department stages procedures that are difficult to perform with endoscopy or catheters. However, due to the high cost of these procedures and the steep learning curve required to master them, they are not widely used in clinical practise. It remains to be seen whether this technology will be integrated into routine clinical practise and eventually replace more conventional technologies as technology advances (Schachner et al., 2009).

Nanotechnology

The current state of robotic surgery for MI is very encouraging. These systems are the best in quality and technology. A reduction in radiation exposure and improved patient recovery times have been documented as benefits of these new technologies. This department performs procedures that require endoscopy or catheters. However, due to their high cost and steep learning curve, these procedures are not widely used in clinical practise. It remains to be seen if this technology will eventually replace more conventional technologies as technology advances. Adult cardiac tissue, particularly cardiomyocytes, cannot be regenerated following ischemia or other catastrophic myocardial injuries. All of these methods have improved therapeutic delivery: small molecules, growth factors, exosomes, cells, and engineered tissues. Additionally, controlled release nanoparticle (NP) drug delivery systems may enhance the cardioprotective potential of drugs in patients with ischemic heart disease. Direct injection of NPs with active targets intramyocardially or intravenously can provide sustained exposure to the infarcted heart (Fan et al., 2020). Aikawa et al. used a cross-linked iron oxide fluorescent NP to simultaneously image macrophages in atherosclerotic plaques to determine the inflammatory response. Due to the absence of fluorine (19F) in the targeted tissue, the observed signals of 19F perfluorocarbon NPs from MRI provide spatial resolution and a high degree of specificity for demonstrating inflammation progression. Additionally, as described by

Yeager et al., the combined use of intravascular ultrasound and photoacoustic (IVUS/IVPA) imaging with gold nanoparticles as contrast agents to co-localize with active macrophages in plaques. Thus, the content, infiltration, and proliferation of macrophages can be used to assess the progression and fragility of atherosclerotic plaques. Apoptosis and oxLDL both contribute significantly to the initiation and promotion of plaque rupture(Chandarana et al., 2018). Numerous techniques, including agents labelled with radioisotopes (123I, 124I, 99mTc, and 18F) and superparamagnetic particles (iron oxide and gadolinium) for positron emission tomography (PET), single-photon emission computed tomography (SPECT), or magnetic resonance imaging (MRI), have been developed for imaging specific targets associated with apoptosis and oxLDL in plaques at risk of rupture. These findings suggest a role for neo-vessel generation in the growth, haemorrhage, and rupture of atherosclerotic plaques (Fan et al., 2020). A gadolinium-coated perfluorocarbon nanomaterial (containing 90,000 individual gadolinium chelates) derivatized with an arginine–glycine–aspartic acid peptidomimetic was used to target integrin v3. While this is going on, more research will combine diagnostic and therapeutic partners, allowing for more accurate diagnosis and treatment outcomes. The permeability of blood vessel walls and accumulation of liposomal NPs in atherosclerotic plaques were studied using multimodal imaging. There is a strong correlation between dynamic contrast-enhanced MRI permeability and NP plaque accumulation in the vessel wall. The accumulation of NPs may allow us to assess the degree of damage and inflammation to the blood vessel wall. Thus, nanotechnology-based cardiovascular imaging techniques can detect and differentiate fragile plaque, paving the way for early prevention and treatment of atherosclerotic plaque (DB, 2012).

Cardiomyocytes have historically been thought to be terminally differentiated cells. Once a cardiomyocyte has been damaged, it cannot regenerate. Myocardial infarction results in the replacement of dead myocardial cells by fibroblasts, which eventually results in ventricular remodelling and heart failure. The discovery of stem cells enables cardiomyocyte regeneration. Animal experiments demonstrated that stem cell transplantation can aid in cardiomyocyte regeneration and improve cardiac function. Cardiovascular disease research has focused on repairing myocardial damage and increasing blood supply to the heart during ischemic conditions, thereby reversing the effects of MI. Both vascular growth factors and stem cells have generated considerable interest as a mode of treatment for patients with MI in this regard. The rationale for this type of therapy is to increase blood supply to ischemic areas of the heart via stem cells while also promoting cardiac cell regeneration. This can be accomplished in one of two ways: directly by stem cells or indirectly through paracrine factors secreted by these stem cells. Hematopoietic stem cells, particularly mononuclear cells and endothelial progenitor cells, have been of particular interest in this regard. The results of studies using these cells in patients with various forms of ischemic heart disease (such as acute myocardial infarction (MI) and chronic ischemic heart disease) have been inconsistent, although some studies have demonstrated a beneficial effect in these patients. This has resulted in the inclusion of other types of stem cells in such studies, such as adipose derived stem cells. A novel approach

is to create induced pluripotent stem cells, in which adult cells are transformed into pluripotent stem cells in a manner similar to that of embryonic stem cells. Although it represents a promising alternative, concerns about the undifferentiated stem cells transforming into cancer must be addressed before they can be tested in human subjects (Reddy, 2015a). With the advancement of stem cell research, cardiac stem cells (CSCs) have been isolated and identified successfully. Cardiomyocyte stem cells are pluripotent stem cells found in the heart that can differentiate into a variety of cardiac cells, including myocytes, smooth muscle cells, and endothelial cells. In animal experiments, cardiac stem cells were injected into the hearts of mice with heart disease, where they migrated directly to the damaged heart tissue, promoting myocardial regeneration and improving the heart's ability to pump blood. Numerous types of CSCs, including Islet-1+ cells, Sca-1+ cells, cardiosphere-derived cells (CDCs), cardiac mesoangioblasts, cardiac specific side population, and epicardial progenitor cells, have been identified in both small and large animal models, indicating the potential for CSCs therapy in the treatment of MI. Following extensive research on CSCs in animal models, numerous clinical trials established CSCs as new promising therapies worthy of further investigation and application (Gershlick & More, 1998; Hong, 2012). Recently, it was discovered that a variety of stem cell types, including ESC, MSCs, and CSCs, secrete paracrine factors such as exosomes and exosome-like vesicles. Exosomes have been considered as a novel stem cell-derived strategy for MI treatment due to their high efficiency in transporting to donor cells, low toxicity, and high stability(HN et al., 2021). Exosomes derived from mouse embryonic stem cells were discovered to promote neovascularization and restore heart function in a mouse model of MI (W. Y, Z, et al., 2021). Additionally, exosomes derived from ESCs were abundant in miR-294, which has been shown to promote the survival and proliferation of CPCs (Gong et al., 2021; Reddy, 2015b; Shah & Hajouli, 2020). Exosomes secreted by mouse MSCs contained a high concentration of miR-22, which inhibited apoptosis in cardiomyocytes, restoring heart function and decreasing infarct size in a mouse MI model (Baron & Giugliano, 2011). Exosomes isolated from human CPCs were abundant in miR-210, miR-132, and miR-146a-3p, and their injection significantly increased angiogenesis, suppressed apoptosis, and improved heart function in a rat MI model (H et al., 2021). As a result, these findings provide compelling evidence that exosomes derived from stem cells are beneficial in the treatment of MI in animal models (Majumder & Nguyen, 2021; O. Y, LA, et al., 2021; Yang & Chen, 2016). And it is expected that stem cell-derived exosomes will be tested clinically in the near future as new strategies for heart regeneration therapy in patients with MI (AD et al., 2021).

OTHER TECHNIQUES-

(Hesari et al., 2021; Sivapathan et al., 2021; Wang et al., 2021; Wu et al., 2021; Yoshitomi & Nagasaki, 2021)

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