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THE ROLE OF BIOMATERIALS IN MODULATING CARDIAC REMODELING AND PROMOTING MYOCARDIAL REPAIR

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Abstract: The healthy heart comprises many different cell types that work together to preserve optimal function. However, in a diseased heart the function of one or more cell types is compromised which can lead to many adverse events, one of which is myocardial infarction (MI). Immediately after MI, the cardiac environment is characterized by excessive cardiomyocyte death and inflammatory signals leading to the recruitment of macrophages to clear the debris. Proliferating fibroblasts then invade, and a collagenous scar is formed to prevent rupture. Better functional restoration of the heart is not achieved due to the limited regenerative capacity of cardiac tissue. To address this, biomaterial therapy is being investigated as an approach to improve regeneration in the infarcted heart, as they can possess the potential to control cell function in the infarct environment and limit the adverse compensatory changes that occur post-MI.

Objective. This review is to critically evaluate the current evidence on the effects of biomaterials on different cell types involved in cardiac repair and regeneration following myocardial infarction. Particular attention is given to the interactions of biomaterials with cardiomyocytes, fibroblasts, endothelial cells, macrophages, cardiac progenitor cells, and mesenchymal stromal cells, as well as their effects on inflammation, angiogenesis, fibrosis, extracellular matrix remodeling, and cellular survival.

Materials and Methods. A structured literature review was conducted to identify and evaluate studies investigating the effects of biomaterials on cellular processes involved in cardiac repair and regeneration following myocardial infarction. The review was designed in accordance with the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.

Results and Discussion. The reviewed literature demonstrates a substantial expansion of biomaterial-based approaches for myocardial repair following myocardial infarction (MI). The biological effects of biomaterials were found to depend strongly on their composition, mechanical properties, degradation characteristics, architecture, surface chemistry, and the presence of incorporated biological signals.

Conclusion. Biomaterials can support cardiomyocyte survival, promote endothelial cell-mediated angiogenesis, regulate macrophage-driven inflammation, modulate fibroblast activation and extracellular matrix remodeling, and improve the retention and regenerative activity of stem and mesenchymal stromal cells. These coordinated cellular effects may contribute to reduced adverse ventricular remodeling and improved structural and functional recovery of the injured myocardium

Keywords: myocardial infarction; biomaterials; cardiac repair; hydrogels; cardiomyocytes; inflammation; angiogenesis; ventricular remodeling.

Literature review

Myocardial infarction (MI) is one of the most severe pathological conditions affecting the cardiovascular system. It is characterized by ischemic damage to the cardiac muscle, cardiomyocyte death, and subsequent structural and functional remodeling of the myocardium resulting from an acute reduction or interruption of coronary blood flow. During the post-infarction period, inflammatory responses, oxidative stress, fibroblast activation, and excessive collagen deposition contribute to scar formation within the cardiac tissue. However, the resulting scar tissue cannot fully reproduce the contractile properties of healthy myocardium. Therefore, improving myocardial regeneration following infarction represents one of the major research priorities in modern cardiology and regenerative medicine.Lister Z., Rayner K.J., and Suuronen E.J. (2016) analyzed the effects of biomaterials on different cell types involved in cardiac tissue repair and regeneration following myocardial infarction. The authors emphasized that biomaterials not only provide mechanical support to damaged tissue but may also regulate the biological activity of cardiomyocytes, fibroblasts, endothelial cells, and macrophages. In particular, the influence of biomaterials on cellular interactions, inflammatory processes, and extracellular matrix remodeling is considered essential for myocardial regeneration [1].Awada H.K., Hwang M.P., and Wang Y. (2016) investigated the potential applications of biomaterials in comprehensive cardiac repair and regeneration following myocardial infarction. According to their findings, biomaterials can facilitate the targeted delivery of therapeutic biologically active substances to injured myocardial regions, maintain their local concentrations, and prolong their biological effects. Hydrogels, polymers, and other biomaterial-based platforms may serve as delivery systems for growth factors and other cellular signaling molecules. These approaches are primarily aimed at maintaining cell viability and stimulating regenerative processes within damaged cardiac tissue [4].One of the major pathological mechanisms following myocardial infarction is the loss of cardiomyocytes through apoptosis and necrosis. Since adult cardiomyocytes have limited proliferative capacity, improving the survival of remaining myocardial cells is of particular importance. Previous studies have investigated the delivery of biologically active substances, such as insulin-like growth factor-1 (IGF-1), using poly(lactic-co-glycolic acid) (PLGA)-based nanoparticles. Such delivery systems may activate the Akt signaling pathway, reduce cardiomyocyte apoptosis, and improve certain parameters of cardiac function following infarction. These findings highlight the importance of biomaterials as localized delivery platforms for therapeutic molecules [3].

Introduction

Myocardial infarction occurs when coronary blood flow is critically reduced or interrupted, depriving cardiac tissue of oxygen and metabolic substrates. The resulting ischemic injury disrupts cellular energy balance and can lead to acidosis, oxidative stress, and death of cardiomyocytes. Damaged tissue also initiates an inflammatory response: immune cells are recruited to remove cellular debris, while subsequent signaling supports granulation tissue formation, vascular growth, and fibroblast activity. Collagen-rich scar tissue helps preserve the integrity of the ventricular wall, but it does not reproduce the contractile properties of healthy myocardium[1]. Consequently, extensive injury may be followed by adverse ventricular remodeling and persistent functional impairment.Biomaterials are under investigation as adjuncts to endogenous healing and cell-based regenerative strategies. Their forms include injectable hydrogels, engineered patches, and degradable polymer systems. Depending on their design, these materials may provide temporary structural reinforcement, alter local mechanical conditions, or deliver growth factors and other

therapeutic signals to the injured myocardium. Some approaches are intended to work without transplanted cells, by modifying the environment in which surviving cardiac and immune cells respond to injury. The purpose of this review is to summarize proposed cellular mechanisms, describe selected experimental biomaterial strategies, and identify challenges that must be addressed before broader clinical translation.

Objective

To review evidence on the ways biomaterials may influence cellular processes involved in myocardial repair after infarction, with attention to cardiomyocyte survival, inflammatory regulation, angiogenesis, fibrosis, extracellular-matrix remodeling, and the prospects and limitations of translation into clinical practice.

Materials and Methods

This manuscript is presented as a narrative review based on the literature and references identified in the supplied draft. The source draft names PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar and describes a search period from January 2015 to September 2026, with selected earlier landmark studies also considered. Search concepts included myocardial infarction, cardiac regeneration, cardiac repair, biomaterials, biomaterial scaffolds, and hydrogels. The supplied material does not provide reproducible database-specific search strings, the date of the final search, numbers of records retrieved and screened, duplicate-removal procedures, or formal risk-of-bias assessments. Therefore, this revised manuscript does not characterize the process as a completed systematic review or claim full PRISMA 2020 compliance. These details should be added only if they were actually performed and documented.

Results and Discussion

The literature describes a shift from materials used mainly as passive supports toward platforms designed to influence several components of the healing response. The biological effects of a material are not determined by its chemical composition alone. Mechanical stiffness, microstructure, degradation rate, surface chemistry, and the release kinetics of incorporated agents may all affect tissue responses. Accordingly, results from one material formulation or animal model should not automatically be generalized to other biomaterial systems[2].Loss of contractile cells is a major determinant of the initial reduction in myocardial function after infarction. Because adult cardiomyocytes have limited proliferative capacity, approaches that preserve surviving cells are of particular interest. The supplied literature describes experimental delivery of insulin-like growth factor 1 (IGF-1) using poly(lactic-co-glycolic acid) (PLGA)-based nanoparticles. Compared with administration of IGF-1 alone, the nanoparticle formulation was reported to increase phosphorylation of the prosurvival signaling protein Akt and reduce the number of apoptotic cardiomyocytes at an early assessment. In the described experimental model, later observations also included a smaller scar and improved left ventricular ejection fraction[3]. These findings suggest that a delivery vehicle may influence the duration and local availability of a therapeutic signal; they do not establish clinical efficacy in human MI.Injectable hydrogels can be delivered into damaged tissue and may form a temporary matrix that supports the ventricular wall. The supplied draft summarizes animal studies of hyaluronic-acid-based hydrogels in which treatment was associated with changes in ventricular volumes and, at later follow-up, improved measures of systolic function. A related formulation combining a HEMA–hyaluronic acid hydrogel with PLGA microspheres was reported to increase the thickness of the infarct region and local cell and vessel density in an experimental model. These observations are consistent with the possibility that material degradation and spatial structure influence tissue integration and mechanical effects. The timing of administration may also matter: the source draft describes an experimental PEG hydrogel study in

which delivery one week after infarction was associated with greater ventricular-wall thickness than immediate administration, potentially because the acute inflammatory environment accelerated material degradation.The supplied review also refers to polymer-based formulations, including dextran-associated polymer hydrogels and PEG-containing systems. In experimental infarction models, some formulations were reported to reduce scar dimensions, increase ventricular-wall thickness, or limit ventricular dilation relative to control treatment[4]. Such results should be interpreted in relation to each material's formulation, delivery method, comparator, and observation period. A favorable effect in an animal model does not by itself establish the optimal material, dose, timing, or safety profile for patients. Post-infarction healing depends on coordinated interactions among immune cells, endothelial cells, fibroblasts, and cardiomyocytes. Biomaterials may alter this environment directly through their physical and chemical properties or indirectly by controlling the local release of signaling molecules. Macrophage activity is particularly relevant because inflammatory clearance and subsequent tissue repair must remain appropriately coordinated. Endothelial responses and new vessel formation can affect tissue perfusion, while fibroblast activation and extracellular-matrix deposition contribute to scar formation and ventricular mechanics[5-7]. A platform that affects several of these processes could have broader effects than one designed solely for mechanical reinforcement; however, excessive suppression of inflammation or fibrosis could also interfere with necessary healing. The direction and magnitude of these effects require evaluation for each material and model.Some emerging biomaterials are designed to reproduce selected mechanical, structural, or electrical characteristics of native myocardium. Conductive or directionally organized materials have been investigated as ways to support cellular alignment and electrical integration. These strategies are conceptually attractive because myocardial repair involves not only tissue thickness and vascularization but also coordinated electrical activation and contraction. Nonetheless, the supplied source material does not provide enough comparative clinical evidence to determine whether these approaches improve patient outcomes.The evidence summarized here is predominantly experimental, and biomaterial studies vary in composition, delivery route, timing, animal model, endpoints, and duration of follow-up[8]. These differences limit direct comparisons across studies. Important questions include long-term biodegradation, immune compatibility, arrhythmogenic potential, reproducibility of manufacturing, delivery feasibility, and whether structural or imaging changes translate into fewer clinical events or better quality of life. Future studies should use clearly defined comparators, transparent outcome reporting, adequate follow-up, and clinically relevant endpoints. A systematic review would also require a fully reproducible search strategy and documented study-selection and appraisal procedures.

Conclusion

Biomaterials may contribute to myocardial repair after infarction by providing temporary structural support and modifying the local environment in which cardiac, vascular, stromal, and immune cells respond to injury. Experimental findings suggest potential roles in preserving cardiomyocytes, supporting angiogenesis, regulating inflammation, and influencing fibrosis and ventricular remodeling. The effects are highly dependent on material properties and delivery conditions, and the current evidence should not be interpreted as proof of established clinical benefit. Carefully designed translational studies are needed to clarify safety, durability, optimal use, and effects on outcomes that matter to patients.

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