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EARLY DIAGNOSIS OF CARDIAC TISSUE INJURY AND REGENERATIVE CARDIOLOGY: STEM CELL-BASED RESTORATION STRATEGIES

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ABSTRACT.

Cardiovascular diseases continue to represent the leading cause of mortality worldwide. Myocardial infarction results in irreversible loss of cardiomyocytes that conventional therapeutic approaches are unable to fully restore, given that the adult human heart lacks meaningful self-renewal capacity. This article reviews the diagnostic value of contemporary biomarkers used in the early detection of cardiac tissue injury — including high-sensitivity cardiac troponin I (cTnI), B-type natriuretic peptide (BNP), and the emerging next-generation biomarker cardiac myosin-binding protein C (cMyC) — alongside a scientific analysis of regenerative cardiology strategies based on mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and embryonic stem cells (ESCs). Conclusions were drawn from clinical trials, systematic reviews, and meta-analyses published between 2015 and 2024, sourced from PubMed, Web of Science, and Google Scholar. Findings indicate that cTnI and cMyC enable detection of cardiac injury at very early stages — even before clinical symptoms become apparent. Clinical trials confirmed that stem cell-based therapy holds significant potential for improving left ventricular ejection fraction (LVEF) and reducing infarct size. Nevertheless, barriers to clinical translation — including the absence of standardized protocols, ethical constraints, and limited follow-up durations — remain unresolved challenges.

Keywords: regenerative cardiology, stem cell therapy, myocardial infarction, early diagnosis, cardiac troponin, mesenchymal stem cells, induced pluripotent stem cells, heart failure

INTRODUCTION. Cardiovascular diseases remain the most formidable threat to human health in the contemporary world. According to the World Health Organization, more than 17 million people die each year from these conditions globally, with myocardial infarction — the acute occlusion of coronary arteries supplying the heart muscle — accounting for a disproportionately large share of these deaths. When myocardial infarction occurs, millions of cardiomyocytes — the contractile cells responsible for cardiac function — are destroyed within minutes.

The fundamental challenge lies in the fact that the adult human heart possesses virtually no capacity for regeneration, meaning it cannot replace lost cells through its own mechanisms. As a result, the necrotic tissue left behind following myocardial infarction is gradually replaced not by healthy functional muscle, but by non-contractile fibrous scar tissue. Over time, this process leads to chronic heart failure, a dramatic decline in quality of life, and ultimately death.

Conventional medicine has achieved partial success in addressing this problem. Thrombolytic therapy, coronary stenting, and bypass surgery have significantly reduced mortality in the acute phase of myocardial infarction. However, all of these approaches share a fundamental limitation — they cannot restore cardiomyocytes that have already been lost; they can only preserve remaining tissue or re-establish blood supply. It is precisely at this juncture

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that regenerative cardiology — a discipline aimed at restoring the function of damaged cardiac tissue through the creation of new cells and structures — has emerged as a compelling scientific frontier.

Regenerative cardiology rests on two essential pillars: first, the earliest possible and most accurate diagnosis of cardiac injury; and second, the biological restoration of damaged tissue. Early diagnosis has always been of decisive importance in medicine, since timely intervention during the first 90 minutes following coronary occlusion — the so-called "golden window" — minimizes cardiomyocyte loss. In this regard, modern laboratory diagnostics, particularly high-sensitivity biomarkers, have opened extraordinary possibilities.

Stem cell-based therapy, in turn, represents a relatively new yet rapidly advancing field. Over the past decade, a substantial body of research has been conducted on the regenerative potential of various cell types — including mesenchymal stem cells, embryonic stem cells, and induced pluripotent stem cells — planting seeds of genuine hope for patients and clinicians alike.

OBJECTIVE. The aim of this article is to analyze the diagnostic significance of contemporary biomarkers employed in the early detection of cardiac tissue injury, and to provide a scientifically grounded review — based on current literature — of the present state, clinical trial outcomes, and future prospects of stem cell-based regenerative therapy strategies in cardiology.

MATERIALS AND METHODS. This article was prepared on the basis of a systematic literature review methodology. Scientific sources were identified through searches of the PubMed, Web of Science, Google Scholar, and Cochrane Library databases. Key search terms included: cardiac regeneration, stem cell therapy, myocardial infarction, cardiac troponin, early diagnosis, mesenchymal stem cells, iPSC cardiomyocytes, and regenerative cardiology. The review was restricted primarily to peer-reviewed articles published between 2015 and 2024. A total of more than 120 scientific articles were screened, of which 18 were directly relevant to the scope of this review and served as primary sources. Inclusion criteria comprised clinical trials, systematic reviews, meta-analyses, and original research published in high-impact journals.

RESULTS. 4.1The Role of Biomarkers in Early Diagnosis

Early and accurate diagnosis of myocardial infarction constitutes one of the most actively investigated areas in contemporary cardiology. Electrocardiography (ECG) and cardiac biomarker measurement currently form the cornerstone of clinical diagnosis. However, ECG alone is frequently insufficient, as ST-segment changes may also be observed in conditions such as pericarditis, left ventricular hypertrophy, or Brugada syndrome.

Cardiac Troponin I (cTnI). Cardiac troponins are structural proteins essential to myocardial contraction, and they are recognized as the most sensitive and specific biological indicators of cardiac injury. According to Duque-Ossa and colleagues (2023), measurement of cTnI concentration in blood plasma or saliva using biosensor technologies has become one of the most widely adopted strategies for diagnosing acute myocardial infarction. Chaulin (2022) demonstrated that the introduction of high-sensitivity troponin assays has fundamentally transformed our understanding of cardiac marker metabolism and has raised the diagnostic bar considerably.

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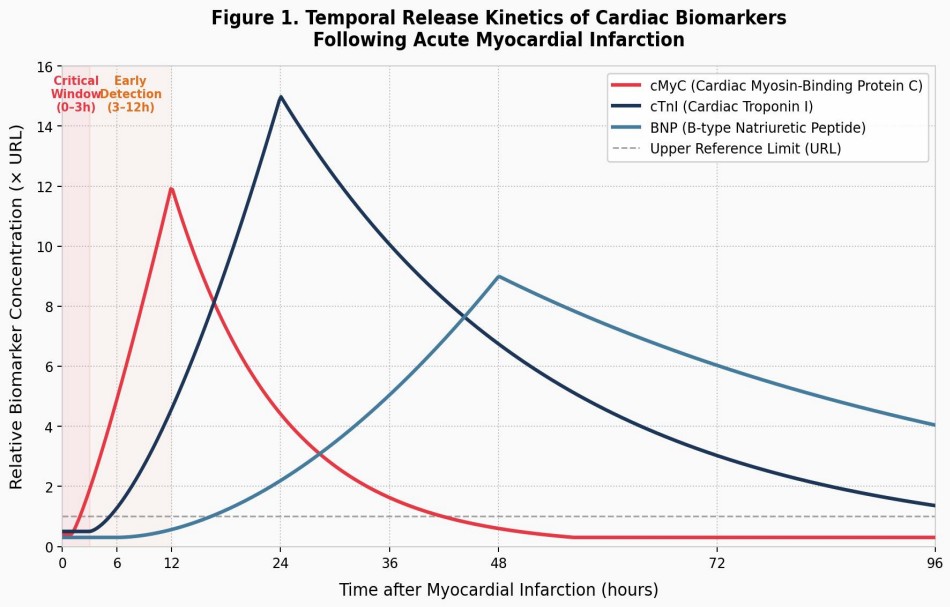

B-Type Natriuretic Peptide (BNP). BNP is a hormone secreted by the cardiac chambers in response to wall stress and volume overload. Multiple studies have confirmed that BNP is more effective than troponin in predicting long-term morbidity and outcomes in heart failure patients, while troponin excels in forecasting short-term events.

Cardiac Myosin-Binding Protein C (cMyC). The most recently characterized biomarker drawing significant scientific attention is cMyC. In a systematic review conducted by Akyuz (2025), cMyC was found to rise and fall more rapidly than high-sensitivity troponins, making it especially valuable for identifying myocardial infarction at the earliest possible time point in emergency settings. The study concluded that cMyC may emerge as a complementary biomarker to troponins for rapid decision-making and short-term monitoring following cardiac events.

Biosensor Technologies. Ullah and colleagues (2025) reported the development of biosensor devices capable of simultaneously and rapidly detecting multiple biomarkers — including cTnI, BNP, and C-reactive protein (CRP) — ushering in a new era of point-of-care diagnostics that can be performed at the bedside rather than in centralized laboratories.

4.2 Stem Cell Types and Their Regenerative Potential.Mesenchymal Stem Cells (MSCs). MSCs are multipotent cells derived from bone marrow, adipose tissue, umbilical cord blood, and several other sources. As documented by Kabat and colleagues (2020), MSCs remain the most frequently used cell type in clinical trials, owing to the relative ease of their isolation and their minimal tendency to form teratomas. MSCs exert their therapeutic effects primarily through paracrine mechanisms — secreting growth factors such as VEGF, HGF, and TGF-beta that promote angiogenesis and tissue repair rather than directly differentiating into cardiomyocytes.

Embryonic Stem Cells (ESCs). Since their first derivation in 1998, ESCs have generated considerable excitement within regenerative medicine due to their unlimited differentiation capacity, which allows large-scale in vitro production of cardiomyocytes. However, clinical application of ESCs remains contested, owing to ethical concerns surrounding the use of embryonic material and the variable regulatory frameworks across different jurisdictions.

Induced Pluripotent Stem Cells (iPSCs). The reprogramming technology pioneered by Yamanaka (2020) represented a genuine revolution in medicine. iPSCs are generated by reverting a patient's own somatic cells — such as skin or blood cells — to a pluripotent state through the introduction of specific transcription factors. This approach fundamentally resolves the problem of immunological rejection and circumvents the ethical constraints associated with ESCs. Sugiura, Shahannaz, and Ferrell (2024) reviewed the current state of iPSC-based cardiac

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therapy and concluded that the technological foundation for its clinical translation has been firmly established.

Cardiac Spheroid Strategy. In 2024, a Japanese research team from Shinshu University and Keio University School of Medicine published landmark findings in the journal Circulation, reporting that injection of cardiac spheroids derived from human iPSCs into monkeys with experimentally induced myocardial infarction produced significant recovery of cardiac function. This result was recognized as one of the most promising outcomes achieved in primate models to date.

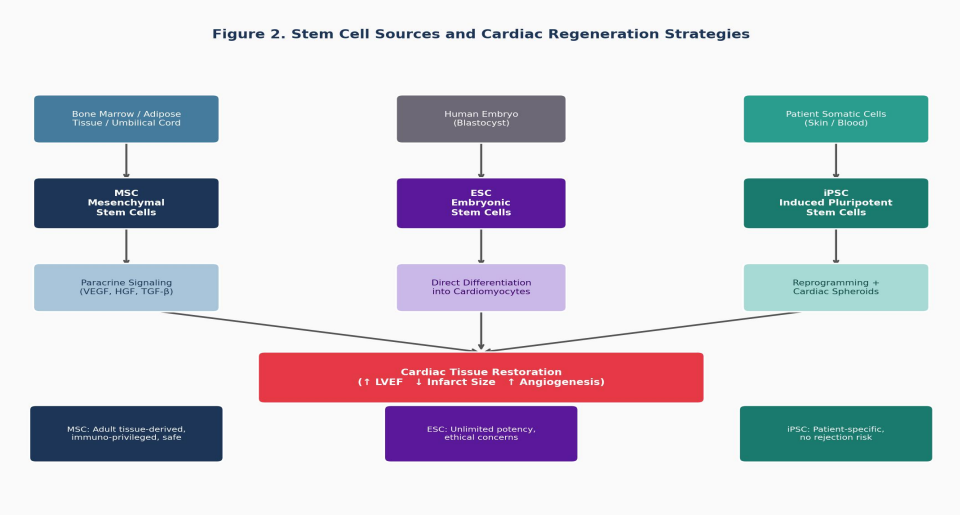

Figure 2. Stem cell sources and cardiac regeneration strategies. MSCs, ESCs, and iPSCs each follow distinct pathways — paracrine signaling, direct differentiation, and cardiac spheroid delivery respectively — all converging on restoration of cardiac tissue function.

4.3 Clinical Trial Outcomes. Several large-scale clinical trials have been conducted to evaluate the efficacy of stem cell-based therapies. The BAMI (Bone Marrow-Derived Mononuclear Cell Therapy in Acute Myocardial Infarction) and C-CURE (Cardiopoietic Stem Cell Therapy in Heart Failure) trials demonstrated that stem cell therapy demonstrated modest but promising improvements in left ventricular ejection fraction and reductions in infarct size. However, the heterogeneity of trial designs, relatively small sample sizes, and short follow-up durations limit the generalizability of these findings.

Cacciapuoti and colleagues (2020) investigated the synergistic role of neuregulin and stem cells in the post-infarction period, arriving at intriguing conclusions regarding their combined regenerative effects. Work by Seow and Ling further suggests that MSCs are poised to occupy a central role in future cardiovascular therapeutics.

CONCLUSION. Early diagnosis of cardiac tissue injury and regenerative cardiology together constitute the most promising and rapidly evolving frontier of contemporary cardiology. High-sensitivity cardiac troponin, BNP, and cMyC enable detection of myocardial infarction from the very first minutes, significantly improving treatment outcomes. The advancement of biosensor technologies further extends these capabilities, enabling rapid and accurate diagnosis not only in hospital settings but directly at the point of patient care.

Stem cell-based therapy, in turn, strives to answer the question that conventional cardiology has been unable to resolve — the restoration of lost cardiomyocytes. The paracrine effects of MSCs, the versatility of iPSCs, and the remarkable results demonstrated by cardiac spheroid technology in primate models all indicate that this field is drawing steadily closer to routine clinical application. Nevertheless, the development of standardized protocols, the accumulation of long-term follow-up data, and the resolution of ethical and regulatory questions remain tasks that lie ahead.

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Future research priorities should include the broad clinical introduction of cMyC, the conduct of large multicenter trials confirming the safety of iPSC-based therapy in human subjects, and the development of integrated medical protocols that employ stem cells and biomarkers jointly for both diagnosis and treatment.

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