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# THE ROLE OF OXIDATIVE STRESS IN MYOCARDIAL INFARCTION AND ITS CORRECTION

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**Abstract**
Myocardial infarction (MI) remains one of the leading causes of morbidity and mortality worldwide. The underlying pathophysiology of MI involves a complex interplay between ischemia, reperfusion injury, inflammation, and oxidative stress. Oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) generation and antioxidant defense mechanisms, plays a crucial role in myocardial cell injury, apoptosis, and subsequent ventricular remodeling. Excessive ROS disrupt cellular membranes, mitochondrial function, and signaling cascades, leading to further ischemic damage. This article reviews current understanding of oxidative stress mechanisms in MI, discusses the clinical biomarkers of oxidative damage, and evaluates pharmacological and non-pharmacological strategies for oxidative stress correction. Advances in antioxidant therapies, mitochondrial-targeted drugs, and gene-based approaches are also explored. Optimizing redox balance represents a promising avenue for improving myocardial recovery and patient outcomes following infarction.

**Keywords**: Myocardial infarction, oxidative stress, reactive oxygen species, antioxidants, reperfusion injury, cardioprotection.

## Introduction

Cardiovascular diseases (CVDs) remain the leading cause of global mortality, with myocardial infarction (MI) accounting for a significant proportion of deaths and disability-adjusted life years worldwide (1). MI occurs as a result of prolonged ischemia leading to irreversible necrosis of cardiac tissue, primarily due to coronary artery occlusion. While traditional risk factors such as hypertension, dyslipidemia, and diabetes mellitus play major roles in disease progression, growing evidence highlights oxidative stress as a central mechanism in myocardial injury and post-infarction complications (2).

Oxidative stress refers to a physiological state where the production of reactive oxygen species (ROS) exceeds the capacity of endogenous antioxidant defenses, resulting in damage to lipids, proteins, and DNA (3). During myocardial ischemia and reperfusion, excessive ROS generation contributes to mitochondrial dysfunction, calcium overload, membrane lipid peroxidation, and apoptotic signaling, all of which aggravate myocardial damage (4). Furthermore, oxidative

stress modulates inflammatory pathways and extracellular matrix remodeling, promoting adverse cardiac remodeling and heart failure (5). Research into oxidative stress correction in MI has evolved substantially over the past two decades. Traditional antioxidant therapies such as vitamins C and E have shown limited efficacy in clinical settings, prompting the exploration of more targeted interventions, including N-acetylcysteine, coenzyme Q10, and mitochondrial-targeted antioxidants (6). In addition, non-pharmacological interventions—such as dietary modifications, exercise, and ischemic preconditioning—have demonstrated beneficial effects in restoring redox balance and enhancing myocardial resilience.

**Pathophysiology of Myocardial Infarction**

Myocardial infarction (MI) is primarily caused by the rupture or erosion of an atherosclerotic plaque within the coronary artery, leading to thrombus formation and subsequent cessation of blood flow to the myocardium (8). The resulting ischemia deprives cardiac tissue of oxygen and nutrients, initiating a cascade of metabolic, ionic, and structural disturbances that culminate in cell death. The progression of myocardial injury during MI is typically divided into two key phases: **ischemic injury** and **reperfusion injury**, both of which are profoundly influenced by oxidative stress.

**Ischemic Phase**. During ischemia, oxygen deprivation leads to the depletion of adenosine triphosphate (ATP), forcing the myocardium to shift from aerobic to anaerobic metabolism (9). This metabolic shift results in the accumulation of lactate, acidosis, and reduced contractile function. The lack of ATP disrupts ionic homeostasis, leading to intracellular calcium overload and sodium accumulation, which further impairs myocardial contractility and promotes cell injury (10). Mitochondrial function becomes severely compromised under ischemic conditions, as the electron transport chain (ETC) slows down due to oxygen scarcity. Consequently, partially reduced intermediates leak from the ETC, generating superoxide radicals even before reperfusion occurs (11). These radicals initiate oxidative modifications to cellular components, thereby sensitizing the myocardium to further oxidative damage upon restoration of blood flow.

**Reperfusion Phase**. Reperfusion, while essential for restoring oxygen supply, paradoxically exacerbates myocardial injury — a phenomenon known as **ischemia-reperfusion (I/R) injury** (12). The sudden reintroduction of oxygen leads to a burst of ROS production from several sources, including mitochondria, xanthine oxidase, and activated neutrophils (13). Superoxide anions ($O_2^{\bullet -}$), hydrogen peroxide ($H_2O_2$), and hydroxyl radicals ($\bullet OH$) interact with membrane lipids and proteins, initiating lipid peroxidation, mitochondrial permeability transition pore (mPTP) opening, and subsequent apoptotic or necrotic cell death (14). Furthermore, reperfusion triggers a strong inflammatory response. Cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) are upregulated, recruiting neutrophils and macrophages to the infarct zone (15). These immune cells amplify ROS generation and release proteolytic enzymes, extending tissue injury. The interplay between oxidative stress and inflammation forms a self-propagating cycle that accelerates myocardial damage.

**Remodeling and Repair.** Following the acute injury phase, the heart undergoes **ventricular remodeling**, characterized by fibroblast proliferation, extracellular matrix (ECM) deposition, and scar formation (16). Persistent oxidative stress continues to influence these processes by activating matrix metalloproteinases (MMPs) and transforming growth factor-beta (TGF-β), which modulate ECM turnover and fibrosis (17). While scar formation is essential for structural stability, excessive fibrosis impairs contractile function and may lead to heart failure. Molecular studies have demonstrated that oxidative stress not only contributes to cardiomyocyte apoptosis but also affects endothelial cell integrity, impairing angiogenesis and microvascular repair (18). These combined effects underscore the multifaceted role of oxidative stress throughout the pathophysiological continuum of myocardial infarction.

**Mechanisms of Oxidative Stress in Myocardial Infarction**

Oxidative stress in myocardial infarction (MI) results from the excessive generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that exceed the neutralizing capacity of endogenous antioxidant defenses (19). ROS are primarily derived from mitochondrial respiration, nicotinamide adenine dinucleotide phosphate (NADPH) oxidases, xanthine oxidase, and uncoupled nitric oxide synthase (NOS). During ischemia and subsequent reperfusion, these sources become hyperactivated, initiating oxidative chain reactions that disrupt cellular and molecular homeostasis (20).

Mitochondrial Dysfunction and ROS Generation. Mitochondria are the major source of ROS in cardiomyocytes. Under physiological conditions, small amounts of superoxide anions ($O_2^{\bullet -}$) are continuously produced as by-products of the electron transport chain (ETC) and detoxified by antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) (21). However, during ischemia, the lack of oxygen leads to electron leakage from complexes I and III of the ETC, forming excess ROS even in low-oxygen environments (22). Upon reperfusion, the sudden reintroduction of oxygen causes a massive ROS burst, overwhelming antioxidant systems. This overproduction of ROS damages mitochondrial DNA, proteins, and lipids, further impairing ATP synthesis and inducing mitochondrial permeability transition pore (mPTP) opening (23). Once the mPTP opens, pro-apoptotic molecules such as cytochrome c are released into the cytosol, activating caspase-dependent apoptotic pathways. This sequence of events leads to cardiomyocyte apoptosis and necrosis, expanding the infarct area (24).

Xanthine Oxidase and NADPH Oxidase Activation. During ischemia, adenosine triphosphate (ATP) degradation results in the accumulation of hypoxanthine, which upon reperfusion is metabolized by xanthine oxidase into xanthine and uric acid, generating superoxide radicals in the process (25). This enzyme-mediated reaction represents a major extracellular source of ROS during early reperfusion. Additionally, NADPH oxidase (NOX), a multi-subunit enzyme complex found in vascular endothelial cells and cardiomyocytes, becomes activated in response to angiotensin II, endothelin-1, and inflammatory cytokines (26). Among its isoforms, NOX2 and NOX4 are particularly important in cardiac tissues. Their activation amplifies oxidative stress, disrupts endothelial function, and enhances pro-inflammatory signaling via nuclear factor kappa B (NF-κB) activation (27).

Lipid Peroxidation and Membrane Damage. ROS attack membrane polyunsaturated fatty acids, initiating lipid peroxidation, which leads to the generation of toxic aldehydes such as malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE) (28). These aldehydes crosslink with proteins and nucleic acids, impairing ion channel function, enzymatic activity, and membrane fluidity. Lipid peroxidation products also act as secondary messengers that exacerbate inflammation and apoptosis (29). The measurement of MDA and 4-HNE levels in serum is therefore used as a reliable biomarker of oxidative stress in patients with MI.

Nitrosative Stress and Reactive Nitrogen Species. Nitrosative stress results from excessive production of nitric oxide (NO) and its reaction with superoxide anions to form peroxynitrite ($ONOO^-$), a potent oxidant that nitrates tyrosine residues and inactivates critical mitochondrial enzymes (30). Uncoupling of endothelial nitric oxide synthase (eNOS) due to tetrahydrobiopterin ($BH_4$) depletion further increases superoxide production, reducing the availability of vasoprotective NO and worsening endothelial dysfunction (31).

Antioxidant Defense Mechanisms. To counterbalance ROS and RNS, the heart relies on a complex antioxidant system comprising enzymatic and non-enzymatic components. The main enzymatic antioxidants include SOD, catalase, GPx, and glutathione reductase, which act sequentially to detoxify superoxide and hydrogen peroxide (32). Non-enzymatic antioxidants such as reduced glutathione (GSH), coenzyme Q10, vitamins C and E, and uric acid provide additional redox buffering capacity. However, during MI, these defense mechanisms become rapidly depleted, leading to a net oxidative environment that perpetuates tissue injury (33).

Redox-Sensitive Signaling Pathways. ROS act not only as damaging agents but also as signaling molecules. Excess ROS activates redox-sensitive transcription factors such as NF-κB, activator protein-1 (AP-1), and hypoxia-inducible factor-1α (HIF-1α) (34). These factors regulate genes involved in inflammation, apoptosis, and angiogenesis. For instance, NF-κB activation increases pro-inflammatory cytokine expression, while HIF-1α promotes vascular endothelial growth factor (VEGF) release in response to hypoxia (35). Persistent activation of these signaling pathways, however, promotes maladaptive remodeling and chronic inflammation, ultimately leading to heart failure.

## Biomarkers of Oxidative Stress in Myocardial Infarction

The evaluation of oxidative stress biomarkers has become an essential component in understanding the pathogenesis, prognosis, and therapeutic monitoring of myocardial infarction (MI). Biomarkers serve as quantifiable indicators that reflect the degree of oxidative damage or the efficacy of antioxidant defense mechanisms. In MI, elevated levels of lipid peroxidation products, oxidized DNA bases, and altered antioxidant enzyme activities provide insight into the extent of myocardial oxidative injury (36).

### Lipid Peroxidation Biomarkers

Lipid peroxidation is one of the most prominent manifestations of oxidative stress during MI. Among the key markers, **malondialdehyde (MDA)** and **4-hydroxynonenal (4-HNE)** are widely measured. MDA, a reactive aldehyde formed by polyunsaturated fatty acid oxidation, reacts with thiobarbituric acid to form thiobarbituric acid-reactive substances (TBARS), which

can be quantified spectrophotometrically (37). Elevated MDA levels have been consistently observed in patients with acute MI and are correlated with infarct size and decreased left ventricular function (38).

Similarly, 4-HNE serves as a marker of ongoing lipid oxidation and can form adducts with proteins, altering their function. Immunohistochemical detection of 4-HNE-modified proteins in myocardial tissue demonstrates the spatial localization of oxidative injury (39). These biomarkers not only indicate cellular membrane damage but also predict post-infarction remodeling and the risk of heart failure.

**Protein Oxidation and Carbonyl Content**

Protein oxidation, another consequence of ROS attack, leads to the formation of carbonyl derivatives on amino acid residues such as lysine, arginine, and threonine (40). Protein carbonyl content (PCC) serves as a stable marker of oxidative stress and can be assessed via spectrophotometric or ELISA-based methods. Increased PCC levels have been reported in the plasma of MI patients and are associated with adverse cardiac outcomes (41). Advanced oxidation protein products (AOPPs) represent additional protein-based markers, particularly reflecting oxidative stress in plasma proteins. AOPP accumulation is linked to endothelial dysfunction and inflammation through the activation of NADPH oxidase and pro-inflammatory cytokines (42).

**DNA Oxidation Biomarkers**

DNA damage caused by oxidative stress is reflected by the formation of **8-hydroxy-2′-deoxyguanosine (8-OHdG)**, which results from hydroxyl radical attack on guanine bases (43). Elevated 8-OHdG levels in serum, urine, and myocardial tissue have been reported in acute MI patients and are associated with the degree of ischemic injury (44). DNA oxidation triggers p53 activation, apoptosis, and impaired mitochondrial biogenesis, thereby contributing to post-infarction remodeling.Measurement of 8-OHdG provides valuable prognostic information and can be used to assess the efficacy of antioxidant interventions in both experimental and clinical studies (45).

**Antioxidant Enzyme Activities**

The activities of endogenous antioxidant enzymes — such as **superoxide dismutase (SOD)**, **catalase (CAT)**, and **glutathione peroxidase (GPx)** — serve as functional indicators of redox balance. In MI, decreased activities of these enzymes have been observed in both serum and myocardial tissue, indicating excessive ROS consumption (46). The SOD/CAT and GSH/GSSG ratios are particularly useful parameters for evaluating the overall antioxidant status of the myocardium (47).

Experimental studies demonstrate that therapeutic interventions aimed at enhancing antioxidant enzyme activities (e.g., via gene therapy or pharmacological inducers like N-acetylcysteine) can reduce infarct size and improve cardiac function (48). These findings highlight the importance of restoring enzymatic antioxidant capacity in mitigating oxidative stress–mediated myocardial damage.

**Total Antioxidant Capacity (TAC) and Oxidative Stress Index (OSI)**

Global assessments such as **Total Antioxidant Capacity (TAC)** and **Oxidative Stress Index (OSI)** integrate multiple oxidative and antioxidant parameters into a single measure of systemic redox balance (49). Reduced TAC and elevated OSI levels have been documented in MI patients, reflecting severe oxidative imbalance. These parameters can serve as adjunctive diagnostic tools and may help monitor the impact of antioxidant therapies during cardiac rehabilitation (50).

**Correction of Oxidative Stress in Myocardial Infarction**

The correction of oxidative stress in myocardial infarction (MI) has become a key therapeutic target aimed at mitigating ischemia-reperfusion injury, reducing infarct size, and improving long-term cardiac function. Strategies to restore redox homeostasis include pharmacological agents with antioxidant properties, non-pharmacological interventions such as dietary modification and exercise, and novel molecular or gene-based approaches designed to enhance endogenous antioxidant defenses (51).

**Pharmacological Interventions**

**Classical Antioxidants.** The earliest approaches to oxidative stress correction focused on direct antioxidants, such as **vitamin C**, **vitamin E**, and **β-carotene**, which scavenge free radicals and inhibit lipid peroxidation. Clinical trials have demonstrated that vitamin C can improve endothelial function and reduce oxidative markers in patients with acute coronary syndromes, though evidence for mortality reduction remains inconsistent (52). Vitamin E (α-tocopherol) supplementation was initially considered cardioprotective; however, large randomized trials, including the HOPE and ATBC studies, failed to demonstrate significant clinical benefit, possibly due to suboptimal dosing and patient heterogeneity (53).

**5.1.2 Glutathione Modulators**

**N-acetylcysteine (NAC)**, a precursor of reduced glutathione (GSH), replenishes intracellular thiol reserves and enhances detoxification of reactive species (54). Experimental studies have shown that NAC administration reduces infarct size, improves myocardial contractility, and decreases post-reperfusion arrhythmias by maintaining mitochondrial redox potential (55). Additionally, NAC has synergistic effects when combined with reperfusion therapies such as thrombolysis or percutaneous coronary intervention (PCI).

**Coenzyme Q10 and Other Mitochondrial Protectors. Coenzyme Q10 (ubiquinone)** functions as an electron carrier within the mitochondrial respiratory chain and as a lipid-soluble antioxidant. Supplementation with CoQ10 in MI patients has been associated with improved left ventricular ejection fraction and reduced oxidative biomarkers (56). Newer mitochondrial-targeted antioxidants, such as **MitoQ** and **SkQ1**, have shown promise in preclinical studies by directly scavenging mitochondrial ROS and preventing mPTP opening (57).

### 5.1.4 Statins and ACE Inhibitors

Beyond their lipid-lowering effects, **statins** exhibit pleiotropic antioxidant properties by inhibiting NADPH oxidase activity and enhancing endothelial nitric oxide synthase (eNOS) expression (58). Similarly, **angiotensin-converting enzyme (ACE) inhibitors** and **angiotensin II receptor blockers (ARBs)** reduce oxidative stress by decreasing angiotensin II–induced ROS production and improving endothelial function (59). These indirect antioxidant effects may partly explain the cardioprotective benefits of these drug classes in post-MI patients.

**Polyphenols and Natural Compounds.** Bioactive compounds such as **resveratrol**, **curcumin**, and **quercetin** possess potent antioxidant and anti-inflammatory properties. Resveratrol activates sirtuin-1 (SIRT1) and AMP-activated protein kinase (AMPK) pathways, promoting mitochondrial biogenesis and reducing oxidative damage in cardiomyocytes (60). Curcumin and quercetin modulate NF-κB and Nrf2 pathways, enhancing the expression of endogenous antioxidant enzymes (61).

### Non-Pharmacological and Lifestyle-Based Interventions

**Diet and Nutritional Therapy.** Adherence to antioxidant-rich dietary patterns such as the **Mediterranean diet** has been associated with improved cardiovascular outcomes. Foods rich in polyphenols, omega-3 fatty acids, and vitamins C and E can lower systemic oxidative stress and improve endothelial function (62). Increased consumption of fruits, vegetables, nuts, and olive oil contributes to enhanced total antioxidant capacity (TAC) and decreased inflammatory cytokine levels.

### 5.2.2 Exercise and Cardiac Rehabilitation

Regular **aerobic exercise** promotes upregulation of endogenous antioxidant defenses through Nrf2 activation and mitochondrial biogenesis (63). In post-MI patients, moderate-intensity training improves cardiac output, decreases oxidative biomarkers, and enhances SOD and GPx activity (64). Excessive or unaccustomed high-intensity exercise, however, may transiently increase ROS generation, underscoring the importance of tailored rehabilitation programs.

**Ischemic Preconditioning. Ischemic preconditioning (IPC)** — brief, repeated episodes of ischemia before a prolonged ischemic insult — has been shown to induce adaptive cardioprotective mechanisms mediated by controlled ROS production and activation of antioxidant pathways (65). IPC triggers the upregulation of protective enzymes such as heme oxygenase-1 (HO-1) and catalase, thereby improving myocardial tolerance to subsequent ischemia-reperfusion events (66).

### Novel and Experimental Approaches

**Gene and Cell Therapy.** Gene therapy targeting antioxidant enzymes (e.g., overexpression of SOD or catalase genes) has shown significant cardioprotective effects in animal models of MI (67). Stem cell–derived exosomes carrying antioxidant microRNAs and proteins also demonstrate potential in modulating redox balance and enhancing cardiac regeneration (68).

### 5.3.2 Nanotechnology and Targeted Delivery

Nanoparticle-based delivery systems are being developed to selectively transport antioxidants to ischemic myocardium. For example, cerium oxide nanoparticles exhibit catalytic scavenging of ROS, mimicking the activity of SOD and catalase (69). These nanocarriers enhance drug bioavailability, minimize systemic side effects, and prolong antioxidant action in cardiac tissue (70).

**Mitochondrial-Targeted Antioxidants.** The next generation of antioxidants focuses on selectively targeting mitochondria — the main ROS source. Compounds like **MitoQ**, **SkQ1**, and **SS-31 peptide** are designed to accumulate within mitochondria due to their lipophilic cationic structures (71). Preclinical studies show these agents can significantly reduce infarct size, preserve mitochondrial function, and improve cardiac recovery following MI (72).

Clinical Evidence and Trials on Antioxidant Therapies in Myocardial Infarction

The translation of oxidative stress research into clinical practice has led to numerous trials investigating the efficacy of antioxidant therapies in patients with myocardial infarction (MI). While preclinical studies consistently demonstrate cardioprotective effects, clinical outcomes have been heterogeneous, reflecting differences in study design, patient populations, timing, and types of interventions (73).

Classical Antioxidants: Vitamins C and E. Early clinical trials focused on direct antioxidant supplementation. The Cambridge Heart Antioxidant Study (CHAOS) examined high-dose vitamin E in patients with coronary artery disease, including some post-MI individuals, and found a reduction in non-fatal myocardial infarctions but no significant effect on overall mortality (74). Vitamin C has been tested primarily for endothelial protection. Randomized studies demonstrated that intravenous vitamin C before percutaneous coronary intervention (PCI) reduces oxidative stress markers and improves coronary flow (75). However, long-term benefits on mortality and heart failure prevention remain inconclusive. The inconsistency in outcomes may result from inadequate dosing, delayed administration relative to reperfusion, or insufficient targeting of mitochondrial ROS, the major contributors to post-MI oxidative injury (76).

N-Acetylcysteine (NAC) Trials. NAC has been studied both as a standalone therapy and in combination with reperfusion strategies. In the NACIAM trial, intravenous NAC administered during PCI for ST-elevation MI (STEMI) significantly decreased myocardial injury markers and improved left ventricular function at follow-up (77). Other studies report reduced incidence of contrast-induced nephropathy in MI patients receiving NAC, highlighting its dual antioxidant and cytoprotective effects (78). Despite promising biochemical results, large-scale trials are still needed to confirm mortality benefits.

Coenzyme Q10 and Mitochondrial-Targeted Therapy. Coenzyme Q10 supplementation has been evaluated in patients with chronic heart failure post-MI. The Q-SYMBIO trial showed that long-term CoQ10 administration reduced major adverse cardiovascular events (MACE) and improved left ventricular ejection fraction (79). Experimental trials with mitochondrial-targeted antioxidants (e.g., MitoQ, SS-31) in humans are ongoing, with early-phase studies

demonstrating safety and potential efficacy in reducing oxidative biomarkers and improving myocardial function (80).

Statins and ACE Inhibitors. While primarily prescribed for lipid-lowering and hemodynamic effects, statins and ACE inhibitors exert secondary antioxidant actions. Multiple large-scale trials, including HOPE, PROVE-IT, and 4S, confirmed that statin therapy post-MI reduces oxidative stress markers, endothelial dysfunction, and inflammatory cytokines, contributing to improved cardiovascular outcomes (81,82). ACE inhibitors, through reduction of angiotensin II-mediated ROS production, have demonstrated a similar protective effect, as seen in the SAVE and TRACE trials (83).

Polyphenols and Nutraceuticals. Clinical trials investigating natural antioxidants, such as resveratrol, curcumin, and green tea polyphenols, are emerging. Studies suggest these compounds reduce systemic oxidative stress, improve endothelial function, and may modulate cardiac remodeling after MI (84). For example, supplementation with resveratrol in post-MI patients improved flow-mediated dilation and decreased inflammatory markers, although sample sizes have been small and long-term outcome data are limited (85).

Limitations and Challenges. Despite promising mechanistic rationale, antioxidant therapy faces several challenges in clinical translation:

1. **Timing of administration:** Early ROS generation during reperfusion necessitates rapid delivery, which is often logistically difficult.
2. **Target specificity:** Many antioxidants act systemically, failing to concentrate at the site of mitochondrial ROS generation.
3. **Heterogeneity of patient populations:** Comorbidities, baseline antioxidant status, and genetic variability affect treatment response.
4. **Measurement endpoints:** Many trials rely on surrogate biomarkers rather than hard clinical outcomes, limiting interpretability.

**Future Directions and Perspectives**

Oxidative stress remains a central mechanism in myocardial infarction (MI) pathophysiology, and its targeted correction is a promising avenue for improving patient outcomes. Despite advances in pharmacological and lifestyle interventions, several gaps persist in clinical translation, highlighting opportunities for innovation and personalized medicine.

itochondrial-Targeted Therapeutics. Given that mitochondria are the primary source of reactive oxygen species (ROS) in cardiomyocytes, therapies that selectively target mitochondrial oxidative stress hold significant promise. Next-generation compounds, such as mitoquinone (MitoQ), SS-31 peptide, and SkQ1, have demonstrated cardioprotective effects in preclinical models by scavenging ROS, preserving mitochondrial membrane potential, and preventing apoptosis (87). Future clinical trials are needed to evaluate long-term safety, optimal dosing, and integration with reperfusion therapy in MI patients.

Gene and Molecular Therapy. Gene therapy offers a potential avenue for enhancing endogenous antioxidant defenses. Overexpression of superoxide dismutase (SOD), catalase, or glutathione peroxidase (GPx) in cardiomyocytes has been shown to reduce infarct size and improve left ventricular function in animal models (88). Advances in viral vectors, nanoparticle-based

delivery systems, and CRISPR-Cas9 gene editing may facilitate precise modulation of antioxidant pathways in the human myocardium, enabling long-lasting cardioprotection.

Personalized and Precision Redox Medicine. Redox status varies widely between individuals due to genetic, environmental, and lifestyle factors. Future strategies may incorporate personalized redox profiling, allowing tailored antioxidant therapy based on biomarker levels, mitochondrial function, and specific ROS sources (89). Integrating computational models with clinical data could further optimize timing, dosage, and combination therapy, minimizing the risk of ineffective or harmful interventions.

Combination Therapies and Adjunctive Approaches. Emerging evidence suggests that single antioxidant therapy may be insufficient to counteract complex oxidative pathways. Combination approaches, such as pairing mitochondrial-targeted antioxidants with N-acetylcysteine, or co-administering polyphenols and statins, could achieve synergistic effects (90). Additionally, integrating antioxidant therapy with standard-of-care reperfusion strategies, cardiac rehabilitation, and dietary modification may enhance overall cardioprotection.

Integration of Biomarker Monitoring in Clinical Practice. Continuous monitoring of oxidative stress biomarkers, including MDA, 8-OHdG, GSH/GSSG ratio, and antioxidant enzyme activities, could inform real-time therapeutic decisions (91). Wearable biosensors and point-of-care assays for redox markers are being developed, potentially allowing clinicians to adjust antioxidant therapy dynamically based on patient-specific oxidative status.

Challenges and Considerations. Despite promising preclinical findings, several challenges must be addressed:

- **Target specificity:** Ensuring antioxidants reach relevant cellular compartments, particularly mitochondria.
- **Timing:** Early intervention is critical to prevent reperfusion injury.
- **Long-term safety:** Chronic antioxidant therapy may interfere with physiological ROS signaling, which is necessary for cell survival and adaptation.
- **Regulatory approval:** Novel gene or nanoparticle-based therapies face complex regulatory pathways before clinical adoption.

## Conclusion

Oxidative stress is a key contributor to myocardial injury and remodeling following myocardial infarction (MI). Excessive reactive oxygen species (ROS) generation leads to lipid peroxidation, protein oxidation, and DNA damage, ultimately impairing cardiomyocyte viability and cardiac function. The assessment of oxidative stress biomarkers provides critical diagnostic, prognostic, and therapeutic information. Correction of oxidative stress involves a multifaceted approach, including pharmacological interventions such as classical antioxidants, N-acetylcysteine, Coenzyme Q10, statins, and ACE inhibitors; non-pharmacological strategies including diet, exercise, and ischemic preconditioning; and emerging therapies such as mitochondrial-targeted antioxidants, gene therapy, and nanotechnology-based delivery systems. While preclinical studies demonstrate substantial cardioprotective effects, clinical evidence remains variable, highlighting the importance of patient-specific factors, timing of intervention, and biomarker-guided therapy.

Future research should focus on precision redox medicine, combining molecular insights, advanced delivery technologies, and real-time biomarker monitoring to optimize treatment strategies. Integration of these approaches holds the promise of improving post-MI outcomes, minimizing adverse cardiac remodeling, and reducing long-term morbidity and mortality. In summary, targeting oxidative stress represents a promising therapeutic strategy in myocardial infarction, and continued translational research is essential to bring these advances into routine clinical practice.

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