INVESTIGATION OF OXIDATIVE STRESS MARKERS IN THE PATHOGENESIS OF MYOCARDIAL INFARCTION

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Introduction

The investigation of oxidative stress markers in the pathogenesis of myocardial infarction (MI) has received increasing scientific attention because of the pivotal role oxidative stress plays in cardiovascular diseases. Oxidative stress refers to a biochemical imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms. When the generation of ROS exceeds the capacity of the antioxidant system, it leads to cellular and molecular damage that contributes to endothelial dysfunction, ischemia, and ultimately, myocardial injury.

Understanding how oxidative stress contributes to MI is essential, not only for clarifying disease mechanisms but also for developing novel therapeutic interventions. Elevated oxidative stress markers have been consistently associated with adverse outcomes in patients with MI, making them valuable prognostic indicators. Key biomarkers such as lipid peroxidation products—particularly F2-isoprostanes and malondialdehyde—are closely linked to infarct severity and myocardial tissue damage. The quantification of these markers provides clinicians with critical insights into the extent of ischemic injury and the effectiveness of therapeutic interventions.

Despite significant progress in elucidating the role of oxidative stress in cardiovascular pathology, challenges remain regarding the most effective therapeutic strategies. Although antioxidant supplementation has been proposed to reduce oxidative damage, clinical results have been inconsistent, with some trials showing only partial improvement in patient outcomes. Factors such as differences in antioxidant types, dosages, and bioavailability likely contribute to these discrepancies. Furthermore, comorbid conditions—such as diabetes mellitus and metabolic syndrome—can exacerbate oxidative stress, further complicating the management of MI. These complexities emphasize the need for personalized therapeutic approaches that consider both systemic oxidative burden and metabolic background.

Oxidative Stress

Oxidative stress (OS) is defined as a physiological state resulting from an imbalance between the production of reactive oxygen species (ROS) and the body's capacity to detoxify these reactive intermediates or repair the resulting damage. It is a key factor in the progression of multiple pathological conditions, including aging, chronic inflammation, atherosclerosis, and cardiovascular disorders such as myocardial infarction.

Mechanisms of Oxidative Stress

Sources of Reactive Oxygen Species

Endogenous sources of ROS include mitochondrial oxidative phosphorylation, inflammatory responses, and immune cell activation—especially macrophages and neutrophils, which release ROS as part of pathogen defense mechanisms. Exogenous sources, such as air pollution, radiation exposure, psychological stress, and excessive physical exertion, also contribute to increased ROS production. Moreover, reactive nitrogen species (RNS),

including nitric oxide (•NO), play dual roles: they act as physiological signaling molecules while also participating in oxidative stress under pathological conditions, amplifying damage to lipids, proteins, and nucleic acids.

Effects of Oxidative Stress

Excessive oxidative stress disrupts endothelial homeostasis, leading to endothelial dysfunction characterized by impaired vasodilation, increased vascular stiffness, and heightened inflammatory responses. These changes contribute directly to myocardial ischemia, reperfusion injury, and pulmonary arterial hypertension. In addition, oxidative modification of low-density lipoproteins (LDL) promotes atherogenesis by stimulating macrophage infiltration and plaque formation within arterial walls. Over time, these processes accelerate coronary artery disease and increase susceptibility to myocardial infarction.

Biomarkers of Oxidative Stress

The evaluation of oxidative stress involves the measurement of specific biomarkers that reflect oxidative damage at the cellular level. Among these, lipid peroxidation products such as malondialdehyde (MDA), 4-hydroxynonenal (4-HNE), and F2-isoprostanes are widely recognized indicators of oxidative damage to cell membranes. Protein oxidation products and oxidized DNA bases (e.g., 8-hydroxy-2'-deoxyguanosine) provide additional evidence of oxidative stress–induced injury.

Monitoring these biomarkers, together with antioxidant enzyme activities such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), allows for a comprehensive assessment of oxidative balance in patients. Such measurements are particularly valuable in clinical cardiology, as they can help predict disease severity, therapeutic response, and recovery potential after myocardial infarction.

Myocardial Infarction

Myocardial infarction (MI), commonly referred to as a heart attack, occurs when blood flow to a portion of the heart muscle is severely reduced or completely obstructed, resulting in ischemic injury and necrosis of cardiac tissue. The underlying pathophysiology of MI involves complex interactions between vascular, metabolic, and inflammatory mechanisms, among which oxidative stress plays a central role. Oxidative stress is defined as an imbalance between the excessive generation of reactive oxygen species (ROS) and the body's antioxidant defense capacity, leading to cellular and molecular damage. This imbalance contributes significantly to myocardial ischemia, reperfusion injury, and subsequent cardiac remodeling and dysfunction.

Mechanisms of Oxidative Stress in Myocardial Infarction

During myocardial infarction, oxidative stress acts as a critical mediator of myocardial injury. Elevated ROS levels disrupt calcium homeostasis in cardiomyocytes, impairing excitation–contraction coupling and contributing to contractile dysfunction. This disruption exacerbates ischemic damage and increases the risk of arrhythmogenesis.

In addition, oxidative stress activates inflammatory signaling pathways such as NF-κB and MAPK, which stimulate the production of pro-inflammatory cytokines and adhesion molecules. These cascades amplify tissue injury and promote apoptosis. During reperfusion—the restoration of blood flow after ischemia—there is a sudden oxygen influx that paradoxically intensifies ROS production, leading to myocardial reperfusion injury. This secondary wave of oxidative stress worsens mitochondrial dysfunction, damages membrane lipids and proteins, and further reduces myocardial viability.

Clinical Implications of Oxidative Stress Markers

Oxidative stress biomarkers have emerged as valuable diagnostic and prognostic indicators in patients with myocardial infarction. Elevated levels of oxidative markers correlate strongly with disease severity, left ventricular dysfunction, and increased post-infarction mortality risk. Monitoring these markers provides clinicians with crucial insights into the extent of myocardial injury, therapeutic response, and prognosis.

Biochemical indicators such as lipid peroxidation products (e.g., malondialdehyde, F2-isoprostanes), protein oxidation markers (e.g., protein carbonyls), and DNA oxidation products (e.g., 8-hydroxy-2'-deoxyguanosine) reflect the systemic oxidative burden. Longitudinal studies assessing these parameters in MI patients have demonstrated that persistent oxidative stress following infarction is associated with delayed recovery and higher incidence of heart failure, reinforcing the importance of oxidative marker assessment in clinical practice.

Relationship with Comorbid Conditions

The presence of comorbidities, particularly diabetes mellitus, further intensifies oxidative stress in patients with myocardial infarction. Diabetic individuals exhibit higher baseline ROS levels due to chronic hyperglycemia, increased advanced glycation end products (AGEs), and mitochondrial dysfunction. This heightened oxidative environment impairs endothelial function, disrupts nitric oxide signaling, and exacerbates ischemic myocardial damage. Consequently, patients with diabetes are at greater risk of post-infarction complications such as heart failure, arrhythmias, and reduced ejection fraction, even when traditional cardiovascular risk factors are controlled.

This interrelationship highlights the necessity of integrating antioxidant and metabolic management strategies in the treatment of MI—especially in diabetic and metabolic syndrome populations—where mitigating oxidative injury may substantially improve prognosis.

Oxidative Stress Markers

Oxidative stress is one of the most significant biochemical mechanisms involved in the onset and progression of myocardial infarction. It arises from an imbalance between ROS generation and antioxidant defense systems, resulting in oxidative damage to lipids, proteins, and nucleic acids. Quantifying oxidative stress biomarkers allows for the assessment of the extent of tissue injury and the prediction of disease progression or recovery potential.

Biomarkers of Oxidative Stress

A variety of biomarkers have been developed to assess oxidative stress in clinical and experimental cardiology. Among the most reliable are F2-isoprostanes (F2-IsoPs)—stable products formed by the non-enzymatic peroxidation of polyunsaturated fatty acids. These compounds serve as robust indicators of in vivo oxidative damage and have shown strong correlations with cardiovascular risk and myocardial infarction severity. Elevated plasma and urinary levels of F2-IsoPs have been associated with extensive coronary atherosclerosis and larger infarct sizes, making them valuable for both diagnostic and prognostic purposes.

Other important markers include malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE), which reflect lipid peroxidation intensity; oxidized low-density lipoproteins (ox-LDL), which indicate atherogenic oxidative modification; and protein carbonyl content, a measure of protein oxidation. Together, these biomarkers provide a comprehensive profile of oxidative damage at different molecular levels.

Implications for Myocardial Infarction

The accumulation of oxidative stress markers has far-reaching implications for understanding and managing myocardial infarction. Elevated oxidative stress contributes to endothelial dysfunction, chronic inflammation, and thrombotic activity—all of which are central to the development of atherosclerosis and acute coronary events. Moreover, persistent oxidative imbalance accelerates biological aging by promoting the senescence-associated secretory phenotype (SASP), a process that increases inflammation and tissue vulnerability.

Addressing oxidative stress through lifestyle modification, dietary antioxidants, pharmacological agents, and mitochondrial-targeted therapies could reduce ischemic injury and improve clinical outcomes in patients with MI. Continued research in this field remains essential for identifying novel therapeutic targets and refining antioxidant strategies to achieve optimal cardioprotection.

References:

1. Madamanchi, N. R., Vendrov, A., & Runge, M. S. (2005). Oxidative stress and vascular disease. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 25(1), 29–38.

2. Tsutsui, H., Kinugawa, S., & Matsushima, S. (2011). Oxidative stress and heart failure. *American Journal of Physiology-Heart and Circulatory Physiology*, 301(6), H2181–H2190.

3. Packer, M. (2020). Derangements in redox signaling as a major determinant of oxidative stress in heart failure. *Circulation*, 141(12), 907–929.

4. Rodrigo, R., Libuy, M., Feliú, F., & Hasson, D. (2013). Oxidative stress-related biomarkers in essential hypertension and ischemia–reperfusion myocardial damage. *Disease Markers*, 35(6), 773–790.

5. Dalle-Donne, I., Rossi, R., Colombo, R., Giustarini, D., & Milzani, A. (2006). Biomarkers of oxidative damage in human disease. *Clinical Chemistry*, 52(4), 601–623.

6. Patel, R. S., Al Mheid, I., Morris, A. A., Ahmed, Y., Kavtaradze, N., Ali, S., & Alexander, R. W. (2016). Oxidative stress is associated with impaired arterial elasticity in patients with coronary artery disease. *Free Radical Biology and Medicine*, 97, 319–325.

7. Griendling, K. K., Touyz, R. M., Zweier, J. L., Dikalov, S., Chilian, W., Chen, Y. R., Harrison, D. G., & Bhatnagar, A. (2016). Measurement of reactive oxygen species, reactive nitrogen species, and redox-dependent signaling in the cardiovascular system. *Circulation Research*, 119(5), e39–e75.

8. Münzel, T., Camici, G. G., Maack, C., Bonetti, N. R., Fuster, V., & Kovacic, J. C. (2017). Impact of oxidative stress on the heart and vasculature: Part 2—Clinical aspects, drug therapy, and prevention. *European Heart Journal*, 38(13), 949–959.

9. Anderson, E. J., Kypson, A. P., Rodriguez, E., Anderson, C. A., Lehr, E. J., & Neufer, P. D. (2009). Substrate-specific derangements in mitochondrial metabolism and redox balance in the atrium of the type 2 diabetic human heart. *Journal of the American College of Cardiology*, 54(20), 1891–1898