

THE INFLUENCE OF MITOCHONDRIAL DYSFUNCTION, OXIDATIVE STRESS, AND METABOLIC SYNDROME ON CARDIOVASCULAR DISEASES: A LITERATURE REVIEW

Ana Flávia Pontes Sodré

Lucca Gonsales Rodrigues - Student of the Medicine course at the University of Marília (UNIMAR); Marília; São Paulo; Kauanne Martins - Student of the Medicine course at the University of Marília (UNIMAR); Marília; São Paulo; Sandra Maria Barbalho - Post-graduate Program in Structural and Functional Interactions in Rehabilitation; University of Marília (UNIMAR); Marília; São Paulo; Brazil

RESUMO

INTRODUCTION: Metabolic Syndrome (MetS) is a growing global health concern associated with sedentary lifestyles and frequent consumption of ultra-processed, high-fat, and high-sugar foods, negatively impacting health and quality of life. MetS is characterized by obesity, insulin resistance, glucose metabolism dysfunction, increased abdominal circumference. These alterations affect white adipose tissue, promoting adipocyte hypertrophy and changes in adipokine secretion, which contribute to a chronic pro-inflammatory state and systemic metabolic imbalance. Mitochondrial dysfunction and oxidative stress play key roles in MetS progression by increasing reactive oxygen species (ROS) production and reducing ATP synthesis, leading to inflammation, cellular damage, and increased cardiovascular risk. **OBJECTIVE:** This review aims to elucidate the relationship between inflammation, metabolic syndrome (MetS), oxidative stress, and mitochondrial dysfunction in the development and progression of cardiovascular diseases (CVD). **METHODOLOGY:** This literature review was based on a PubMed search using descriptors related to metabolic syndrome, mitochondrial dysfunction, oxidative stress, and cardiovascular risk. Original articles, systematic reviews, and narrative reviews that investigated the association between mitochondrial dysfunction, metabolic syndrome, oxidative stress, and the development of cardiovascular disease were included. **RESULTS:** In MetS, excessive caloric intake and chronic inflammation in white adipose tissue (WAT) alter lipid metabolism and promote mitochondrial dysfunction. During oxidative phosphorylation, an overload of nutrients increases electron transfer in the respiratory chain, generating excessive ROS and an imbalance between oxidant and antioxidant defenses. These oxidative molecules can damage DNA, proteins, and cellular signaling pathways, leading to apoptosis and tissue dysfunction. Mitochondria generate ATP through oxidative phosphorylation by transferring electrons from NADH and FADH₂ through the electron transport chain. In MetS, excess nutrients and low energy expenditure increase NADH accumulation and electron leakage, resulting in ROS overproduction. ROS activate NF-κB signaling and stimulate the release of pro-inflammatory cytokines such as TNF-α, IL-6, IL-1β, and MCP-1, creating a chronic inflammatory environment that enhances insulin resistance, lipolysis, and systemic metabolic dysfunction. Oxidative stress also causes vascular endothelial dysfunction through lipid peroxidation, protein oxidation, and LDL oxidation. Oxidized LDL (ox-LDL) is phagocytosed by macrophages, generating foam cells that accumulate in the vascular intima and initiate atherosclerotic plaque formation. Increased vascular permeability, platelet aggregation, and matrix metalloproteinase activation contribute to plaque rupture and thrombus formation, increasing the risk of myocardial infarction and cardiovascular disease. Mitochondrial dysfunction in MetS is also associated with reduced ATP production, impaired beta-oxidation, decreased AMPK activity, mtDNA damage, and deregulated mitophagy. These alterations increase ROS production, inflammatory signaling, apoptosis, and insulin resistance, affecting multiple tissues, including liver, skeletal muscle, kidneys, and cardiovascular tissue. Consequently, MetS promotes systemic metabolic dysfunction and increases the risk of cardiovascular and chronic degenerative diseases. **CONCLUSION:** In summary, mitochondrial dysfunction and oxidative stress play central roles in the progression of MetS and

cardiovascular diseases by promoting chronic inflammation, endothelial dysfunction, insulin resistance, and cellular damage. Future studies should focus on therapeutic strategies targeting mitochondrial function and oxidative balance, as well as on identifying biomarkers associated with early cardiovascular and metabolic alterations

Palavras-chave: Metabolic Syndrome/MetS Oxidative Stress Mitochondrial Dysfunction Cardiovascular Diseases Inflammation.