

ADIPONECTIN, METABOLIC SYNDROME, AND CARDIOVASCULAR RISK: A NARRATIVE REVIEW ON THE LINK BETWEEN METABOLIC DYSFUNCTION AND VASCULAR COMPLICATIONS

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RESUMO

ADIPONECTIN, METABOLIC SYNDROME, AND CARDIOVASCULAR RISK: A NARRATIVE REVIEW ON THE LINK BETWEEN METABOLIC DYSFUNCTION AND VASCULAR COMPLICATIONS Rafael Gago Paulino^{1 2}, Ana Luiza Fracone Milani¹, Sandra Maria Barbalho^{1 3} ¹Universidade de Marília (UNIMAR), Marília, SP; ² Graduated in Medicine from the University Center of Votuporanga-SP - Medical Course (UNIFEV), Brazil; ³Post- graduate Program in Structural and Functional Interactions in Rehabilitation, University of Marília (UNIMAR), Marília, São Paulo, Brazil

Abstract: Introduction: Adiponectin is an adipokine with anti-inflammatory, insulin-sensitizing, and vasculoprotective effects. In metabolic syndrome, its circulating levels are reduced, contributing to insulin resistance and endothelial dysfunction. Adiponectin activates AMPK and PPAR- α , promoting fatty acid oxidation and improving glucose metabolism. Its deficiency favors chronic inflammation, with increased pro-inflammatory cytokines. Furthermore, it reduces nitric oxide bioavailability, impairing vascular function. Hypoadiponectinemia is associated with oxidative stress and atherogenesis. These effects contribute to greater arterial stiffness and progression of atherosclerosis. Adiponectin also modulates vascular endothelial and smooth muscle cells. Low levels of this adipokine correlate with a higher risk of cardiovascular events. Thus, it represents an important link between metabolic dysfunction and increased vascular risk. Objective: Considering the role of this adipokine, the aim of this study was to conduct a narrative review on the role of this marker in metabolic syndrome and cardiovascular complications. Methods: This narrative review was based on a structured search in PubMed/MEDLINE and Scopus, covering the period from 2021 to 2026. The keywords included “adiponectin,” “metabolic syndrome,” and “cardiovascular risk.” Relevant original studies and reviews were selected, and the data were qualitatively synthesized, focusing on metabolic and vascular mechanisms. Discussion: Adiponectin is a hormonal protein secreted mainly by adipocytes in white adipose tissue, acting through AdipoR1 and AdipoR2 receptors. AdipoR1 predominates in skeletal muscle, endothelial cells, and cardiomyocytes, whereas AdipoR2 is mainly expressed in the liver. Hypoadiponectinemia impairs signaling through AdipoR1/AdipoR2, decreasing insulin sensitivity by reducing AMPK and PPAR- α activation. It also reduces glucose uptake via GLUT-4 and increases hepatic glucose production by stimulating gluconeogenic enzymes, such as G6Pase and PEPCK. In lipid metabolism, reduced adiponectin signaling decreases free fatty acid oxidation through mechanisms involving acetyl-CoA carboxylase. It may also reduce HDL-C levels by decreasing hepatic apolipoprotein A-I expression. In the endothelium, hypoadiponectinemia favors the adhesion of atherogenic molecules, such as ICAM-1, VCAM-1, and E-selectin. It may also decrease nitric oxide production through PI3K and AMPK pathways and impair M2 macrophage polarization, which is involved in atherosclerotic plaque stability. Adiponectin plays a relevant role in the anti-inflammatory response by inhibiting reactive oxygen species, promoting the release of anti-inflammatory cytokines, such as IL-10 and IL-1RA, suppressing pro-inflammatory cytokines, such as TNF- α , IL-6, and IL-8, increasing nitric oxide bioavailability, and inhibiting the activation of nuclear factor kappa B, or NF- κ B. Metabolic syndrome comprises metabolic risk factors, including abdominal obesity, arterial hypertension, insulin resistance, and dyslipidemia. Thus, hypoadiponectinemia is related to metabolic syndrome through the modulation of multiple pathophysiological pathways. This metabolic stress contributes to diseases associated with high cardiovascular risk, such as obesity, type 2 diabetes,

hypertension, atherosclerosis, and coronary syndromes. Conclusion: Adiponectin regulates glucose and lipid metabolism, as well as angiogenesis, inflammatory stress, and oxidative stress. These mechanisms participate in the pathogenesis of metabolic syndrome, linking hypoadiponectinemia to vascular complications. Therefore, adiponectin represents a marker and possible mediator of cardiometabolic risk, reinforcing the endocrine role of adipose tissue.

Keywords: Adiponectin; Metabolic syndrome; Insulin resistance; Endothelial dysfunction; Cardiovascular risk. Palavras-chave: Adiponectina; Metabolic Syndrome; Insulin Resistance; Endothelial Dysfunction; Cardiovascular Risk.