THE ROLE OF INSULIN RESISTANCE AND ENDOCRINE FACTORS

IN THE DEVELOPMENT OF CARDIOVASCULAR RISK
IN PATIENTS WITH AGE-ASSOCIATED METABOLIC DISORDERS

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Abstract

Insulin resistance represents one of the key pathogenetic mechanisms linking age-associated metabolic alterations with the development of cardiovascular risk. Disturbances of carbohydrate and lipid metabolism, chronic low-grade inflammation, endothelial dysfunction, and age-related hormonal shifts form a multilevel cascade contributing to cardiovascular complications even in the absence of clinically overt diabetes mellitus.

This article presents an integrative analysis of endocrine–cardiovascular mechanisms, conceptualizing insulin resistance as a systemic and potentially modifiable determinant of cardiovascular risk during aging. Pathophysiological pathways, clinical implications,

diagnostic approaches, and preventive and therapeutic strategies aimed at reducing cardiometabolic risk in older populations are discussed.

Keywords: insulin resistance, metabolic syndrome, endocrine aging, cardiovascular risk, chronic inflammation, endothelial dysfunction.

Introduction

The contemporary concept of cardiovascular risk has expanded beyond traditional factors such as arterial hypertension and dyslipidemia. Increasing attention is being directed toward metabolic and endocrine disturbances that create an adverse cardiovascular milieu long before the manifestation of clinically overt disease.

Insulin resistance occupies a central role in the pathogenesis of age-associated metabolic changes. It underlies the development of metabolic syndrome and contributes to endothelial dysfunction, chronic inflammation, and microcirculatory impairment. Importantly, these alterations may remain subclinical for prolonged periods, complicating early diagnosis and prevention of cardiovascular complications.

1. Insulin Resistance as a Systemic Pathogenetic Factor

Insulin resistance is defined as a reduced biological response of target tissues to insulin at normal or elevated circulating concentrations. Skeletal muscle, liver, and adipose tissue represent the principal insulin-sensitive organs; however, the systemic consequences of insulin resistance affect virtually all organs and regulatory systems.

With aging, physiological reductions in insulin sensitivity are observed, associated with sarcopenia, redistribution of adipose tissue toward a visceral phenotype, and decreased physical activity. These changes promote hyperinsulinemia and dysregulation of vascular tone.

Insulin resistance should therefore be regarded not as an isolated metabolic abnormality but as part of a broader endocrine–metabolic continuum influencing vascular structure and myocardial function.

2. Age-Related Endocrine Changes and Cardiovascular Risk

2.1. Adipose Tissue as an Endocrine Organ

Adipose tissue is now recognized as an active endocrine organ secreting adipokines and cytokines that influence metabolic and vascular homeostasis. Aging is associated with qualitative and quantitative changes in adipose tissue, leading to an imbalance between pro-inflammatory and anti-inflammatory mediators.

Increased secretion of leptin, resistin, and pro-inflammatory cytokines occurs in parallel with reduced adiponectin production. This shift promotes chronic low-grade inflammation, a hallmark of both insulin resistance and cardiovascular aging.

2.2. Hormonal Alterations and Vascular Regulation

Declining levels of sex hormones, growth hormone, and insulin-like growth factor-1 contribute to impaired metabolic regulation and diminished endothelium-dependent vasodilation. These endocrine changes exacerbate insulin resistance and accelerate arterial stiffening, thereby increasing cardiovascular risk.

3. Insulin Resistance and Endothelial Dysfunction

Insulin exerts vasoprotective effects by stimulating nitric oxide synthesis and promoting vasodilation. In states of insulin resistance, this signaling pathway is selectively impaired, whereas mitogenic and vasoconstrictive pathways remain active or become upregulated.

Consequently, endothelial dysfunction develops, characterized by reduced nitric oxide bioavailability, increased expression of adhesion molecules, and activation of prothrombotic processes. These alterations compromise microvascular perfusion and facilitate the progression of cardiovascular disease.

4. Chronic Inflammation and Oxidative Stress

Both insulin resistance and aging are accompanied by chronic low-grade inflammation. Activation of inflammatory signaling cascades damages the endothelium, increases oxidative stress, and accelerates vascular remodeling.

Oxidative stress further diminishes nitric oxide availability and disrupts intracellular signaling pathways, reinforcing endothelial dysfunction. Together, these mechanisms establish a persistent pathogenic background that elevates cardiovascular risk.

5. Clinical Implications and Diagnostic Approaches

Insulin resistance frequently remains clinically silent in its early stages, underscoring the importance of proactive screening in older individuals. Assessment of insulin resistance indices, visceral adiposity, inflammatory markers, and endothelial function enhances cardiovascular risk stratification.

Integrating metabolic, hormonal, and vascular parameters may facilitate earlier identification of high-risk individuals and support the implementation of personalized preventive strategies in endocrinology and cardiology.

6. Preventive and Therapeutic Strategies

Targeting insulin resistance is a cornerstone of cardiovascular prevention in patients with age-associated metabolic disorders. Lifestyle interventions—including increased physical activity, weight reduction, and dietary modification—remain the most effective strategies.

Pharmacological therapy should be individualized, addressing not only glycemic control but also inflammation, endothelial dysfunction, and coexisting cardiovascular risk factors.

Conclusion

The integrative synthesis presented in this article supports the concept of an endocrine–cardiovascular continuum as a unified pathogenetic framework in which insulin resistance acts as a central and potentially modifiable determinant of cardiovascular risk during aging.

Chronic inflammation, endothelial dysfunction, and hormonal alterations form an interconnected cascade that promotes cardiometabolic pathology even in the absence of overt diabetes mellitus. This perspective emphasizes the importance of early detection and comprehensive prevention of age-associated cardiovascular disease.

Integration of endocrinological and cardiological approaches enables more accurate risk assessment and the development of personalized preventive interventions aimed at slowing cardiometabolic aging and improving quality of life.

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