ZAMONAVIY TIBBIYOT VA TABIIY FANLARDA ILMIY-INNAVATSION TADQIQOTLAR

XXI-RESPUBLIKA ILMIY-AMALIY KONFERENSIYA

YAKUNLARI BO'YICHA ILMIY ISHLAR TO'PLAMI

Issue - 10(2025) Available at www.uznauka.uz

PATHOPHYSIOLOGICAL MECHANISMS OF HEART FAILURE DEVELOPMENT IN PATIENTS WITH DIABETES MELLITUS

Azizova Noilaxon Saidolimxon qizi
Assistent of Central Asian Medical University

Abstract: *this thesis examines the multifactorial pathophysiological mechanisms underlying heart failure development in diabetic patients, integrating metabolic, structural, and molecular perspectives. The investigation elucidates how chronic hyperglycemia, insulin resistance, and metabolic derangements converge to precipitate myocardial dysfunction through oxidative stress, mitochondrial dysfunction, advanced glycation end-product accumulation, and neurohormonal dysregulation. These findings illuminate critical therapeutic targets and underscore the imperative for integrated cardiovascular-metabolic risk management strategies.*

Keywords: *myocardial insulin resistance, advanced glycation end-products, mitochondrial dysfunction, oxidative stress, cardiac remodeling, diastolic dysfunction, lipotoxicity, renin-angiotensin-aldosterone system, endothelial dysfunction*

In contemporary medical practice, the intersection of diabetes mellitus and cardiovascular disease represents a paramount clinical challenge, with heart failure emerging as a leading cause of morbidity and mortality among diabetic populations. Epidemiological evidence demonstrates that diabetic patients exhibit a two to fivefold increased risk of developing heart failure independent of conventional risk factors such as hypertension and coronary artery disease. This phenomenon has catalyzed intensive investigation into the concept of diabetic cardiomyopathy, a distinct clinical entity characterized by structural and functional

myocardial abnormalities occurring in the absence of coronary atherosclerosis, valvular disease, or hypertension.

The pathogenesis of heart failure in diabetes mellitus encompasses a complex interplay of metabolic, cellular, and molecular mechanisms that collectively compromise myocardial structure and function. Chronic hyperglycemia initiates a cascade of deleterious processes, beginning with the nonenzymatic glycation of proteins to form advanced glycation end-products, which accumulate within the myocardial interstitium and promote collagen cross-linking, resulting in increased myocardial stiffness and impaired diastolic relaxation. Concurrently, hyperglycemia-induced oxidative stress overwhelms endogenous antioxidant defense systems, generating excessive reactive oxygen species that damage mitochondrial DNA, impair oxidative phosphorylation, and compromise cellular energy production. Insulin resistance, the hallmark metabolic derangement in type 2 diabetes, profoundly affects cardiac metabolism by shifting myocardial substrate utilization away from glucose oxidation toward increased fatty acid metabolism. This metabolic inflexibility leads to intramyocardial lipid accumulation, a process termed lipotoxicity, which induces cellular dysfunction through ceramide formation, endoplasmic reticulum stress, and apoptotic pathway activation. Furthermore, impaired insulin signaling disrupts calcium homeostasis within cardiomyocytes, compromising both systolic contractility and diastolic relaxation. The diabetic milieu activates neurohormonal systems, particularly the renin-angiotensin-aldosterone system and sympathetic nervous system, which promote adverse cardiac remodeling through fibroblast proliferation, extracellular matrix deposition, and cardiomyocyte hypertrophy. Endothelial dysfunction,

mediated by reduced nitric oxide bioavailability and increased endothelin-1 expression, further compromises coronary microvascular function, leading to myocardial ischemia even in the absence of epicardial coronary stenosis. Inflammatory pathways are simultaneously upregulated, with elevated circulating cytokines such as tumor necrosis factor-alpha and interleukin-6 contributing to myocardial inflammation and fibrosis. These interconnected mechanisms culminate in progressive left ventricular hypertrophy, interstitial fibrosis, and ultimately clinical heart failure with either preserved or reduced ejection fraction.

The development of heart failure in diabetic patients reflects a multifaceted pathophysiological process integrating metabolic dysregulation, oxidative injury, mitochondrial dysfunction, and neurohormonal activation. Understanding these mechanisms is essential for developing targeted therapeutic interventions that address both glycemic control and cardioprotection. Future research directions should prioritize elucidating molecular signaling pathways amenable to pharmacological modulation and identifying biomarkers for early detection of diabetic cardiomyopathy before irreversible structural damage occurs.

REFERENCES:

1. Jia, G., Hill, M. A., & Sowers, J. R. (2018). Diabetic cardiomyopathy: An update of mechanisms contributing to this clinical entity. Circulation Research, 624-638 pages

2. Matsushita, K., Harada, K., Kohno, T., Nakano, H., Kitano, D., Matsuda, J., Takei, M., Yoshino, H., Yamamoto, T., Nagao, K., & Takayama, M.

(2024). Prevalence and clinical characteristics of diabetic cardiomyopathy in patients with acute heart failure. Nutrition, Metabolism and Cardiovascular Diseases, 34 page

3. Sarabhai, T., & Kahl, S. (2024). Pathophysiology and advances in the therapy of cardiomyopathy in patients with diabetes mellitus. Life, 14 page