

## CARDIOVASCULAR DISEASES AS A COMPLICATION LEADING TO CHRONIC KIDNEY DISEASE: CLINICAL SIGNS, EARLY DIAGNOSIS, AND PREVENTION

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**Abstract.** Cardiovascular diseases, particularly chronic heart failure, play a significant role in the development of chronic kidney disease (CKD) and constitute type 2 cardiorenal syndrome. According to Global Burden of Disease study data, chronic kidney disease ranks as the 9th leading cause of death worldwide, associated with 1.48 million deaths annually, and occupies the 12th position in terms of years lived with disability. In patients with CKD, the rate of cardiovascular complications and mortality can reach 40–50%. This article provides an in-depth analysis of the clinical manifestations of chronic kidney disease developing as a complication of cardiovascular diseases, the pathophysiological mechanisms of cardiorenal syndrome, its association with diabetes mellitus, methods of early diagnosis, and modern preventive measures.

**Keywords:** type 2 cardiorenal syndrome, glomerular filtration rate, urinary albumin-to-creatinine ratio, sodium-glucose cotransporter 2 inhibitors, Dapagliflozin in Patients with Chronic Kidney Disease study, Empagliflozin in Patients with Chronic Kidney Disease study, finerenone, biomarkers, early screening, prevention.

**Introduction.** The complex interrelationship between the heart and kidneys in the human body is one of the most pressing issues in modern medicine. This relationship is expressed by the concept of cardiorenal syndrome, in which dysfunction of one organ leads to functional and structural disorders in the other. According to the classification proposed by Ronco and co-authors, cardiorenal syndrome is divided into 5 types, of

which type 2 is characterized by the progressive development of chronic kidney disease as a result of chronic heart failure. According to Global Burden of Disease studies, in 2023 chronic kidney disease was the 9th leading global cause of death, accounting for 1.48 million deaths, and ranked 12th in years of disability. Cardiovascular diseases together with this condition represent not only a biological but also a major social and economic problem — the risk of hospitalization and death is several times higher in patients with chronic kidney disease. The purpose of this article is to professionally highlight the clinical signs, pathophysiological mechanisms, association with diabetes mellitus, methods of early diagnosis, and effective preventive measures of chronic kidney disease developing as a complication of cardiovascular diseases. From a human perspective, these diseases change not only the organs but also the patient's entire lifestyle, family relationships, and social activity. Through early intervention, we can not only reduce mortality but also preserve the quality of life for patients. The article emphasizes the need for a multidisciplinary approach.

## **Main Part.** Pathophysiological Mechanisms of Cardiorenal Syndrome

Type 2 cardiorenal syndrome consists of a complex interaction of hemodynamic and non-hemodynamic factors. According to the traditional view, a decrease in the heart's pumping function reduces renal perfusion. This situation activates the renin-angiotensin-aldosterone system (RAAS), the sympathetic nervous system, and arginine-vasopressin secretion, resulting in increased water and salt retention, elevated preload, and further worsening of heart failure. Modern research shows that low-flow states do not fully explain cardiorenal syndrome. Venous congestion and increased central venous pressure lead to renal venous hypertension, increased intrarenal resistance, and a decrease in glomerular filtration rate (GFR). This mechanism is particularly important in chronic conditions.

The main pathophysiological mechanisms are as follows:

1. Hemodynamic disorders, i.e., renal hypoperfusion and venous congestion;
2. Neurohormonal activation, i.e., hyperactivation of the renin-angiotensin-aldosterone system, activation of the sympathetic nervous system, and arginine-vasopressin secretion;
3. Inflammation and oxidative stress — venous congestion shifts endothelial cells to a pro-inflammatory phenotype, stimulates cytokine production, and chronic inflammation leads to glomerulosclerosis, tubulointerstitial fibrosis, and endothelial dysfunction;

4. Additional factors, including anemia, disorders of mineral-bone metabolism, and vascular remodeling.

These mechanisms form a self-reinforcing cycle and limit the patient's daily life through fatigue, edema, and shortness of breath, increasing the burden on the family and society. Association Between Diabetes Mellitus and Chronic Kidney Disease Diabetes mellitus is one of the leading causes of chronic kidney disease and is referred to as diabetic kidney disease. In patients with diabetes, chronic kidney disease develops in 20–40% of cases. In type 2 diabetes, this rate is higher and is often already present at diagnosis, while in type 1 diabetes it usually manifests 5–15 years later. The pathophysiological mechanisms are complex and include hemodynamic, metabolic, inflammatory, and fibrotic processes. Persistent hyperglycemia leads to glomerular hyperfiltration, which increases intraglomerular pressure and damages podocytes, endothelium, and mesangial cells. Hyperactivation of SGLT2 transporters increases glucose and sodium reabsorption in the proximal tubules, reducing sodium delivery to the macula densa and disrupting tubuloglomerular feedback. Advanced glycation end-products, oxidative stress, and activation of the polyol pathway cause cellular damage. Hyperactivation of mineralocorticoid receptors increases inflammatory cytokines and promotes glomerulosclerosis and tubulointerstitial fibrosis. Diabetes and cardiovascular diseases together form a cardiorenal-metabolic syndrome, accelerating the progression of chronic kidney disease. According to Global Burden of Disease data, the prevalence of chronic kidney disease associated with type 2 diabetes is high, with the greatest burden observed in countries with middle socio-economic development indices.

## Clinical Signs

In the early stages of chronic kidney disease, clinical signs are often asymptomatic and manifest only in laboratory parameters. In later stages, fatigue, weakness, swelling of the legs and face, worsening of arterial hypertension, anemia, and electrolyte disorders are observed. When occurring together with cardiovascular diseases, fluid retention intensifies, leading to worsened shortness of breath, pulmonary edema, and peripheral edema. Studies show that the prevalence of heart failure in patients with chronic kidney disease reaches 25–56%. Decreased renal perfusion and venous congestion activate the renin-angiotensin-aldosterone and sympathetic nervous systems, resulting in increased arterial pressure, cardiac rhythm disturbances, and intensified remodeling. From a human perspective, these signs limit the patient's work capacity, family relationships, and social activity.

## Methods of Diagnosing Cardiorenal Syndrome

Diagnosis of cardiorenal syndrome includes clinical suspicion, laboratory parameters, biomarkers, imaging methods, and hemodynamic assessment. According to the 2024 guidelines of the Kidney Disease: Improving Global Outcomes (KDIGO) organization, chronic kidney disease is identified by a glomerular filtration rate below 60 ml/min/1.73 m<sup>2</sup> or an increase in the urinary albumin-to-creatinine ratio. Regular screening is recommended in high-risk groups. In clinical assessment, symptoms such as fatigue, shortness of breath, edema, and oliguria, as well as physical signs such as jugular venous distension and peripheral edema, are taken into account. Among laboratory parameters, calculation of glomerular filtration rate, urinary albumin-to-creatinine ratio, creatinine, blood urea nitrogen, and electrolytes are important. Among cardiac biomarkers, natriuretic peptide levels confirm heart failure. Kidney injury biomarkers, such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1), detect early signs of tubular damage. Imaging methods include echocardiography and renal ultrasound. In differential diagnosis, causes such as nephrotoxic drugs and glomerulonephritis are excluded. A multidisciplinary approach is necessary.

## Early Diagnosis

For early detection of chronic kidney disease in patients with cardiovascular diseases, calculation of glomerular filtration rate and determination of the urinary albumin-to-creatinine ratio are fundamental. The use of cystatin C increases accuracy. Regular laboratory monitoring is mandatory in high-risk groups. Additionally, biomarkers and renal ultrasound can help identify the disease at an early stage. According to Global Burden of Disease data, early stages of chronic kidney disease often remain undiagnosed (61–95%), which accelerates progression. Early diagnosis and intervention at the initial stage prolong patient life and reduce the economic burden.

## Prevention and Treatment Measures

The main directions in prevention are maintaining arterial blood pressure below 130/80 mmHg, strict control of diabetes mellitus, smoking cessation, and increasing adherence to diet and physical activity. In drug therapy, renin-angiotensin-aldosterone system blockers occupy the primary place. Sodium-glucose cotransporter 2 (SGLT2) inhibitors reduce intraglomerular pressure and attenuate inflammation. The DAPA-CKD study (2020) showed that dapagliflozin slowed CKD progression by 39% and reduced cardiovascular complications by 29% in patients with chronic kidney disease. The EMPA-KIDNEY study (2023) demonstrated that empagliflozin reduced CKD progression by 28%. In studies with finerenone (2020–2021), non-steroidal mineralocorticoid receptor antagonists significantly reduced albuminuria and provided

cardiorenal protection. Statins correct dyslipidemia. In the presence of diabetes, glucose-lowering drugs provide additional benefit. New potassium binders are used to manage hyperkalemia risk. A multidisciplinary approach and patient education form the basis of prevention. From a human perspective, these measures preserve not only numbers but also the patient's ability to spend time with family and work.

**Research Results.** Modern clinical studies clearly confirm the link between chronic kidney disease and cardiovascular diseases. In the DAPA-CKD trial (2020), dapagliflozin slowed disease progression by 39% and reduced cardiovascular complications by 29%. In the EMPA-KIDNEY trial (2023), empagliflozin reduced CKD progression by 28%. In finerenone studies (2020–2021), non-steroidal mineralocorticoid receptor antagonists significantly reduced albuminuria and provided cardiorenal protection. The 2024 KDIGO guidelines mandate monitoring of glomerular filtration rate and urinary albumin-to-creatinine ratio every 3–6 months in high-risk groups. Biomarkers (NGAL and KIM-1) allow detection of tubular damage earlier than traditional indicators. These observations prove the effectiveness of a multidisciplinary approach (collaboration among cardiologist, nephrologist, and endocrinologist).

**Conclusion.** Early diagnosis and prevention of chronic kidney disease developing as a complication of cardiovascular diseases improve patients' quality of life, prevent severe complications, and significantly reduce global mortality rates. The 2024 KDIGO guidelines and modern studies confirm the cardiorenal protective effects of sodium-glucose cotransporter 2 inhibitors and finerenone. Early screening for cardiorenal syndrome, use of biomarkers, and a multidisciplinary approach should be the main focus in medical practice. A deeper understanding of the relationship between diabetes mellitus and chronic kidney disease helps manage this process more effectively. As humans, we must view these diseases not merely as statistics but as the life stories of each patient. Through early intervention, we can restore hope and health. Deepening research and practice on this topic can make a significant contribution to preserving the health of the population. Early diagnosis and prevention of chronic kidney disease as a complication of cardiovascular diseases improve patients' quality of life, prevent severe complications, and significantly reduce global mortality rates. The 2024 KDIGO guidelines and modern studies confirm the cardiorenal protective effects of sodium-glucose cotransporter 2 inhibitors and finerenone. Early screening for cardiorenal syndrome, use of biomarkers, and a multidisciplinary approach should be the main focus in medical practice. A deeper understanding of the relationship between diabetes and chronic kidney disease helps manage this process more effectively. As humans, we must view these diseases not merely as statistics but as the

life stories of each patient. Through early intervention, we can restore hope and health. Deepening research and practice on this topic can make a significant contribution to preserving the health of the population.

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