Acta Scientific Cardiovascular System

Volume 1 Issue 5 October 2022

Review Article

Cardiorenal Relationships

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Received: September 15, 2022

Published: September 29, 2022

Abstract

The combination of cardiac and renal pathologies is one of the frequent manifestations of comorbidity. Comorbidity can complicate the diagnosis and pharmacotherapy of diseases. Renal dysfunction is believed to be associated with high overall and cardiovascular mortality. The review highlights the relationship and prognostic role of renal and cardiac pathology.

Keywords: Diseases of the Cardiovascular System; Renal Dysfunction; Renal Dysfunction; Comorbidity; Chronic Kidney Disease; Risk Factors

An important feature of modern clinical medicine is a significant increase in comorbidity, which complicates the diagnosis of diseases and the choice of rational pharmacotherapy.

The term «comorbidity», introduced into clinical practice in 1970 by the American physician A.R. Feinstein, is defined as the presence simultaneously of several diseases (conditions, syndromes, complications) that have more than two common pathogenetic mechanisms of development that coincide in time in one patient. Comorbidity is not just a combination of several diseases, but a certain relationship of conditions that leads to the formation of a pathomorphologically distinct new new «nadnozology» with other qualitative and quantitative manifestations [1]. Comorbidity is actually observed in the vast majority of patients. According to various authors, its prevalence can vary from 21% to 98%, with the frequency most often increasing with age [2].

Another negative point: a patient with a combination of several diseases receives a larger number of drugs, which increases the likelihood of violating the rules of rational pharmacotherapy, increasing the number of complications associated with forced polypharmacy. The presence of comorbidity also increases the likelihood of adverse outcomes and repeated hospitalizations, determines the prognosis of the disease and life, causes diagnostic errors, non-core hospitalization of patients [3].

One of the frequent manifestations of comorbidity is a combination of cardiac and renal pathologies. Cardiac and renal pathology often have a close relationship on issues related to common risk factors for kidney and cardiovascular diseases, pathogenetic mechanisms, a mutually aggravating prognosis, as well as the therapeutic strategy of nephro- and cardioprotection. In recent decades, there has been a steady trend towards an increase in the number of patients with comorbid cardiac and renal diseases.

Undoubtedly, the important question is the influence of the state of kidney function on the course of cardiovascular diseases, as well as on the extent to which these disorders determine the prognosis of the disease. On the one hand, patients with cardiac pathology develop renal dysfunction as a consequence of cardiac pathology, leading to the development of chronic kidney disease (CKD). On the other hand, in persons with renal dysfunction that has arisen against the background of any disease of the urinary system, damage to the cardiovascular system develops, which, in turn, aggravates the course of the underlying disease.

The development of renal dysfunction is one of the most common comorbid conditions with cardiac pathology, in particular, with chronic heart failure (CHF). However, to date, there is no doubt that any kidney damage, both acute and chronic, is also associated with high overall and cardiovascular mortality. For example, an increase in cardiovascular mortality in patients who have had myocardial infarction (MI) is observed even with a moderate decrease in the glomerular filtration rate (GFR) [4,5]. As well as a slight decrease in kidney function, it significantly aggravates the course of the underlying cardiac pathology, while increasing the frequency of complications and the risk of death. The HOPE (Heart Outcomes Prevention Evaluation) study, which included persons over the age of 55 who have risk factors for coronary heart disease (CHD), showed a 2-fold higher incidence of cardiovascular mortality in individuals with microalbuminuria (UIA) compared with patients without kidney pathology. Moreover, even a slight impairment of kidney function, regardless of other risk factors and treatment, is associated with a 40% increase in cardiovascular events [6]. Other researchers have shown that a decrease in myocardial contractility also leads to a deterioration in kidney function [7,8].

In a Russian study with lower GFR was observed in 30-40% of patients with acute coronary syndrome (ACS) and in 70% of patients with acute heart failure (OSN). In coronary artery disease, a moderate decrease in renal function after coronary artery bypass surgery worsens the prognosis, leads to an increase in the duration of hospitalization and increases the likelihood of hemodialysis. Progressive decrease in GFR is a predictor of an unfavorable outcome of MI, OSN, ischemic stroke, bleeding. It is believed that that a decrease in GFR of less than 60 ml/min/1.73 m^2 contributes to a 50% increase in cardiovascular mortality [9].

As early as 1999, the Hoorn Study showed that albuminuria is an independent cardiac risk factor, especially in patients with hypertension (AH) [10]. According to the results of the INSIGHT study (2004), a decrease in renal function in patients with hypertension significantly increased the risk of fatal outcomes [11]. Similar conclusions were drawn from the results of the Framingham Study [12]. In a 2001 study, the authors found an association between albuminuria and the risk of fatal and nonfatal cardiovascular events [13]. J. Redon (2002) determined that albuminuria is a predictor of adverse cardiovascular events as well as renal dysfunction [14]. The LIFE study (2003) linked albuminuria and cardiac risk to left ventricular hypertrophy (LVH) [15].

It is estimated that a third of all patients with CHF simultaneously have chronic renal failure, and about half of them have a deterioration in renal function when hospitalized due to decompensation of CHF. Renal dysfunction is an independent predictor of a poor prognosis of CHF, although the pathogenesis of impaired renal function during decompensation of CHF remains unclear. The functional state of the kidneys in patients with the initial stages of CHF without concomitant extracardiac pathology has not been sufficiently studied, since most of the previously performed studies were devoted to patients with severe CHF and/or concomitant diseases (in particular, with diabetes mellitus).

Kidney dysfunction significantly worsens the prognosis in patients with CHF and low left ventricular ejection fraction (LVF). Two randomized trials (SOLVD and SAVE) found an association between decreased renal function and mortality in patients with left ventricular systolic dysfunction [16]. With GFR <60 ml/min/1.73 m^2, the risk of mortality increased by 2.1, with reduced systolic function of the left ventricle - by 3.8, with preserved systolic function - by 2.9 times [16]. Obviously, kidney dysfunction may be one of the important independent causes of the unfavorable outcome of any cardiac pathology. This is facilitated by the aging of the world's population and the improvement of diagnostic methods.

The wide prevalence of renal dysfunction in various diseases, the unfavorable prognostic significance of reduced GFR and albuminuria in relation to cardiovascular and renal outcomes, determined the need to develop unified approaches to the management of patients with impaired renal function. In 2002, the suprasological concept of «chronic kidney disease» was introduced, the first recommendations on CKD were presented. To clarify the relationship between cardiorenal relationships, the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA)) put forward an initiative aimed at promoting cooperation between nephrologists and doctors of other specialties. At the ERA-EDTA Congress (Stockholm, 2008), a special working room was created. group on cardiorenal medicine EURECA-m (European Renal and Cardiovascular Medicine),

which promotes cooperation between European research centers and specialists of various profiles, as well as the development of educational programs for doctors and patients [17].

In various studies, a high prevalence of CKD has been demonstrated, competing even with the incidence of coronary artery disease and diabetes mellitus [18]. According to large epidemiological studies, the prevalence of CKD is at least 10%, reaching 20% or more in certain categories of persons [19-21]. With progressive CKD, there is a high incidence of death. In particular, among patients with end stage of chronic renal disease (ESRD), the value of cardiovascular mortality is almost 500 times higher than in the general population with preserved renal function [18]. CKD reflects the presence of kidney damage and/or the characteristic of GFR, since the renal and cardiovascular prognosis is significantly dependent on the magnitude of GFR [22].

Various epidemiological studies indicate a high incidence of damage to the cardiovascular system in patients with CKD. Thus, the prevalence of hypertension, as the most important risk factor for coronary artery disease and LVH, in CKD is 87-90% [23].

In turn, in patients with coronary artery disease, concomitant CKD is a predictor of an unfavorable prognosis of the disease. It is believed that cardiovascular diseases are the most common cause of death in CKD, and the latter is an independent risk factor for the development of cardiovascular pathology and death [17]. There is evidence that 35% of patients with renal pathology at the time of contacting a nephrologist have various manifestations of coronary artery disease in the anamnesis. The prevalence of LVH increases with a decrease in renal function, reaching 75% by the time of dialysis [23]. It is believed that the presence of coronary artery disease at the start of renal replacement therapy increases the risk of death on hemodialysis by 45%, and heart failure by 93% [24].

Nevertheless, the effect of CKD on the functional state of the cardiovascular system is not fully understood, although the main mechanisms contributing to the development of left ventricular myocardial dysfunction in patients with CKD have been identified: pressure overload against the background of prolonged hypertension and increased vascular stiffness; volume overload and a number of non-hemodynamic factors associated with CKD that alter the structure and function of the myocardium, resulting in the progression of LVH and diastolic dysfunction [25,26]. It is believed that UIA reflects the presence of generalized endothelial dysfunction in the body, which, in turn, is the cause of accelerated atherogenesis and progression of renal fibrosis [27]. An increase in mineralocorticoid activity and a violation of mineral metabolism are important in the development of cardiovascular complications in CKD [28].

However, the heat of exposure to the main traditional risk factors does not allow to explain the high prevalence of cardiovascular pathology in terminal renal failure. Patients suffering from CKD of any stage are at risk for the development of diseases of the cardiovascular system and acute cerebral circulation disorders. Patients with CKD are more likely to die from cardiovascular disease than from the progression of CKD and even the development of terminal renal failure with the need for hemodialysis or kidney transplantation. A significant number of patients with CKD die due to cardiovascular complications even before they reach terminal renal failure, and kidney dysfunction in patients with primary cardiac pathology poses a significantly higher risk of morbidity and mortality from cardiovascular disease [26,28,29]. Ultimately, the state of the cardiovascular system determines both the duration and quality of life of patients with CKD.

The interdependence of cardiac and renal pathology defines cardiorenal relationships as a continuous chain of events that make up a vicious circle - the cardiorenal continuum [27]. This concept confirms the fact that the kidney is not just a «target organ» in cardiac pathology, as was previously believed, but an organ that is actively involved in the chain of pathogenetic events due to biochemical changes in the body.

Thus, damage to the kidneys as a target organ is often found in patients with cardiovascular diseases, which activates a cascade of pathological mechanisms in the kidneys and aggravates the prognosis of cardiovascular diseases. Obviously, in order to improve the life prognosis of patients with a combination of cardiac and renal pathologies, a unified approach to diagnosis and treatment is needed, especially in terms of early warning of cardiac and renal complications. Optimal pharmacotherapy, based on objective criteria for assessing the structure and function of the kidneys, can reduce the risk of developing cardiovascular and renal complications, and even slow down the progression of comorbid pathology.

Conflict of Interest

There is no conflict of interest.

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