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Diagnostic Significance of Immuno-Inflammatory Biomarkers of Cardiorenal Syndrome

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Abstract Cardiorenal syndrome (CRS) is a pathological interdependent condition involving the heart and kidneys, developing as a result of acute or chronic dysfunction of one of the organs, followed by acute or chronic dysfunction of another organ. The author conducted a review of scientific studies devoted to the study of the pathogenesis and diagnosis of cardiorenal syndrome, analyzed the latest meta-analysis data on the immunological aspects of the cardiorenal continuum, identified the most informative biomarkers of the disease that can serve for early diagnosis and prevention.

Keywords Cardiorenal syndrome, Immunity, Cytokines, Coronary heart disease, Kidneys, Heart, Diagnosis

1. Introduction

CRS includes various acute and chronic disorders in which both the heart and the kidney may be the primary affected organ. The kidneys, being an organ involved in important metabolic processes, regulate humoral The systems involved in microcirculation processes are susceptible to acute and chronic effects in various cardiovascular diseases (CVD) and affect the formation and progression of cardiovascular pathology [9].

Renal dysfunction is associated with a higher incidence of recurrence of myocardial ischemia, myocardial infarction (MI), stroke, serious hemorrhagic complications, acute heart failure, atrial and ventricular fibrillation. Even a slight decrease in kidney function significantly worsens the course of the underlying cardiac pathology, at the same time angiotensin converting enzyme, angiotensin II receptor antagonists, nitrates, methods of renal replacement therapy) increasing the incidence of complications and the risk of death, and, conversely, a decrease in myocardial contractile function affects the kidneys in the most negative way. The need for early detection of kidney damage in cardiovascular pathology in order to assess risk, develop strategies and tactics for patient management contributed to the emergence of such concepts as "cardiorenal anemia syndrome" and "cardiorenal continuum" [1,4].

The purpose of the study: To review and analyze foreign and domestic studies on the diagnostic value of immunological markers in cardiorenal syndrome.

The incidence of combined kidney and heart damage is very high. Renal dysfunction determines high cardiac morbidity and mortality even with an initial decrease in kidney function. Cardiac pathology is 64% higher in patients with impaired renal function than in healthy patients [2]. It is the heart pathology that determines the significant risk in chronic kidney disease (CKD). Cardiac complications develop more often than terminal chronic renal failure (CRF) [14]. According to the results of the NHANES II Study, In patients with CKD, the prevalence of CVD increases as the glomerular filtration rate (GFR) decreases. As CKD worsens, hypertrophy of the left ventricle of the heart develops, systolic and/or diastolic dysfunction, atherosclerosis, vascular calcification. In terminal CKD, signs of heart failure are detected in 40% of cases, and changes in the left ventricle of the heart are detected in 85% of cases [5].

Ischemic heart disease (CHD) and arterial hypertension (AH) are common in this category of patients. According to the ARIC study, in patients with stage 2 CKD, new cardiac complications account for 4.8%, and at stages 3-4 CKD, their frequency almost doubles. A large number of studies have proven an association between a decrease in GFR <60 ml/min/1.73 m2 and an increased risk of death from cardiovascular events. More than half of the deaths in patients with terminal CRF are cardiac. Cardiac mortality in CKD is 20-50 times higher than the general population. Also in patients receiving hemodialysis treatment, cardiovascular complications are the leading cause of death [3].

There are two important aspects in the development of any type of CRS: the first is the sequence of organ involvement and the second is the bi–directionality of action leading to a vicious circle. These disorders are time-limited (chronic or acute) [10]. The development of cattle is associated with the action of pathological factors that negatively affect the function of the myocardium and kidneys. Genetic, metabolic, hemodynamic, neurohumoral factors, disorders of mineral and lipid metabolism are involved in the development of this syndrome. Predispose to CRS: hypertension, metabolic

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syndrome, dyslipidemia, anemia, DM, coronary heart disease, renovascular and parenchymal kidney diseases [16].

CRS is a complex of pathophysiological changes occurring in kidney tissues in response to heart damage, or in heart tissue in response to kidney damage. Primary dysfunction of one organ entails secondary damage or dysfunction of another, worsening the prognosis and course of both HF and PN [8,22]. In the conditions MI develops AKI against the background of sudden deterioration of cardiac activity due to hemodynamic stress and ischemia. In turn, it is worth noting that in the conditions of IM CRS is also a trigger for the progression and development of the renocardial syndrome, thereby forming a “vicious circle". With MI, the kidneys continue to control the processes of sodium excretion and reabsorption, maintaining volumetric homeostasis of extracellular fluid, while the heart is responsible for controlling systemic hemodynamics [12]. A decrease in the left ventricular ejection fraction by a quarter leads to a decrease in renal perfusion by 2 times, which, along with a decrease in cardiac output against the background of an increase in central venous pressure, contributes to the development of stagnation in the kidneys [15].

The kidney-heart axes play one of the key roles in the development of cattle and remodeling of the kidneys and heart in MI mf. Their participation in these processes is due to the realization of such basic functions as the secretion of pro- and anti-inflammatory factors, phagocytosis of dead cells, participation in the formation of connective tissue and apoptosis processes, isolation of angiogenesis and fibrogenesis factors. Monocytes/mf both in healthy tissues and in various pathologies have been the subject of scientific interest for the last ten years [20].

Two main mf phenotypes have been conditionally identified: M1 mf participating in the processes of inflammation or classically activated, as well as alternatively activated mf type 2 — M2, having anti-inflammatory, adaptive, regenerative functions [18]. MF is also divided into tissue (resident), involved in maintaining homeostasis and originating from the yolk sac and hematopoietic precursors, and newcomers — penetrating with blood flow from the bone marrow into damaged tissues, and transforming either into tissue mf or dendritic cells [24]. There are tissue mf in the kidneys they have been present since the formation of the organ and demonstrate an M2-like phenotype, realizing the functions of homeostasis and immune control, and represent a part of the reticuloendothelial system [19]. In the mouse model, 5 populations of kidney tissue mf were identified with expression on their surface of CD (differentiation cluster) 11b and CD11c, as well as surface expression of F4/80, CD103, CD14, CD16 and CD64. However, the definition of phenotypic The characteristics of tissue and “alien” mf in vivo in humans, both in the presence of pathology and in healthy kidneys, require further study [21].

In ischemic kidney damage, in addition to local proliferation of mf from embryonic precursors, recruitment of foreign mf with a proinflammatory phenotype into the kidney through chemokine receptors (CC) R2 and CX3CR1 is noted [16]. They make a huge contribution to the population of mf M2 type, since the supply of tissue mf M2 type in the kidney is gradually depleted [13].

The physiological relationship between the activity of the kidneys, heart and blood vessels leads to the fact that the dysfunction of each of these systems exacerbates disorders throughout the cardiorenal continuum. During the search for new predictive markers of cardiovascular diseases, it was found that pKIM-1 reflects the severity of the condition of patients with heart failure. In elderly men with diabetes mellitus, an increase in uKIM-1 regardless of other indicators, it is associated with the risk of death from cardiovascular complications. P. Egli et al. in the framework of a clinical examination of 2060 conditionally healthy individuals aged 25 to 41 years, they found that in this population pKIM-1 does not correlate with indicators of impaired renal function (creatinine and cystatin C), but is statistically significantly associated with risk factors for cardiovascular disease. vascular diseases: high blood pressure, low and high density lipoproteins in the blood, as well as M.T. Wybraniec et al. [17] observed 95 patients with heart failure during 12 months after coronary angiography and found that an increase in uKIM-1 after performing this diagnostic procedure is an independent predictor of heart attack or stroke in patients in the long term. Some researchers believe that an increase in uKIM-1 can serve as an early diagnostic indicator of AKI in patients who have undergone cardiological surgery [13], and correlates with the duration of the acute period of renal impairment [20]. According to other data, uKIM-1 is not informative enough to assess the development of renal complications in patients after heart surgery, but its increase is associated with a fatal outcome. At the same time, a more accurate prognostic assessment can be obtained when uKIM-1 is combined with other markers of kidney damage — NGAL in blood plasma and interleukin-18 in urine or cysteine C in serum and NGAL in urine. It has been shown that in patients with heart failure or atherosclerosis, uKIM-1 in combination with cysteine C can serve as an early marker of AKI and a risk factor for the progression of renal failure to the terminal stage of the disease [4], and the prognostic significance of uKIM-1 in this assessment surpasses other urinological markers of kidney damage (NAG, NGAL and L-FABP) [12].

2. Conclusions

At the moment, the assessment of the effect of innate immunity on the development of post-infarction remodeling of the kidneys and heart has a fundamental focus. However, a holistic approach to analyzing the mutual effect of macrophage infiltration of the kidneys and heart on both changes in composition, microenvironment, metabolism, efferocytosis and epigenetics, as well as on the remodeling processes of these organs, will increase the likelihood of success in translating experimental data to the clinic. This fundamental knowledge is necessary for us to further understanding and the possibility of intervention in the development of adverse

postinfarction remodeling of both kidneys and heart.

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