ОГЛЯД ЛІТЕРАТУРИ

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THE MODERN VIEW ON CARDIORENAL SYNDROM

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Summary: In recent years, due to increased prevalence of cardiovascular diseases, increased life expectancy of cardiac patients and the use of interventional research methods and treatment also increases the incidence of acute renal failure [5]. However, with the development of medical science, it was found that renal dysfunction often accompanies heart failure and cardiac dysfunction – renal failure. This interdependent relationship became known as " cardiorenal syndrome " [1-2]. This statement was announced in Virginia in 2004 [5], but in spite of the large number of publications and discussions in thematic conferences cardiorenal syndrome has not yet become world deadlines, and many key questions remain unanswered [3-4].

Key words: cardiorenal syndrome, heart failure, renal failure, aldosterone antagonists, edema.

Among patients with congestive heart failure renal dysfunction is very common, which negatively reflected in the statistics. Data obtained Acute Decompensated Heart Failure National Registry (ADHERE), who studied nearly 100,000 patients show that a third of them had renal failure [1]. Another study found that among outpatients with congestive heart failure, 39 % of patients with NYHA class for 4 and 31 % of patients with grade 3 had hard deterioration of renal function (creatinine clearance less than 30 ml/min) [6]. Prognostically important adverse markers on ejection fraction and NYHA functional class are basic kidney function [7].

Similarly, renal insufficiency is associated with increased adverse cardiovascular risk. Among patients with end-stage renal disease 44% had died according to cardiovascular disease, and meta-analysis in

2006 found that patients with end-stage renal disease likely to die from cardiac causes than from kidney failure [8]. Death from cardiovascular vascular lesions in 10 – 20 times more frequent in patients with chronic renal failure than in the corresponding part of the general population. Increased myocardial mass (left ventricular hypertrophy), which in turn increases the oxygen demand of the myocardium, causes an increasing of stage of renal disease from mild to moderate or even severe [9]. Treatment of renal failure can improve cardiac function. The study of more than 100 dialysis patients diagnosed with heart failure who had a kidney transplant, shows an increase in ejection fraction from 32% to 52 % and more than 2/3 of the patients had complete recovery of cardiac function [10].

Cardiorenal syndrome (CRS) – a pathophysiologic disorder of the heart and kidneys, in which acute or chronic dysfunction of one of these organs leads to acute or chronic dysfunction of the other. Thus, CRS includes acute and chronic disorders in which the primary affected organ can be both heart and kidney. A special feature is a declaration of fundamental heterogeneity of cardiorenal syndrome and highlight its five main types depending on the presence of acute / chronic heart failure (HF), and primacy / secondary occurrence of heart disease or kidney disease in relation to each other [12].

At the conciliation conference ADQI in Venice in 2008, C. Ronco and colleagues presented a classification, which was allocated five types of cardiorenal syndrome [13].

Acute kardiorenal syndrome (CRS type 1) : acute decompensation of cardiac function leads to acute renal failure. This syndrome is characterized by the deterioration of kidney function that often complicates acute decompensated heart failure (ADHF) and acute coronary syndrome (ACS) [14]. In 7 studies reported the frequency and type of cattle in relation ADHF and 5 – ACS. Depending on the population 27% – 40% of patients hospitalized with ADHF, had developed acute kidney injury (AKI), which was diagnosed by an increase of serum creatinine $\geq$ 0,3 mg / dl [15].

Table 1

Classification system represented by C. Ronco and colleagues for separating CRS into 5 types depending on the etiology of dysfunction

CRS type	***Name***	***Description***	***Example***	***Markers***
1	Acute cardiorenal	Acute cardiac dysfunction leading to acute kidney injury	Acute coronary syndrome causing acute heart failure and then renal dysfunction	Endothelin-1, troponin,CPK-MB
2	Chronic cardiorenal	Chronic heart failure leading to renal dysfunction	Congestive cardiac failure	Endothelin-1, BNP
3	Acute renocardiac	Acute kidney injury leading to acute cardiac dysfunction	Uraemic cardiomyopathy secondary to acute renal failure	TNF-alfa, IL-1, IL-6, IL-8
4	Chronic renocardiac	Chronic renal failure leading to cardiac dysfunction	Left ventricular hypertrophy and diastolic heart failure secondary to renal failure	Parathyroid hormone, Calcium-phosphate product, cys-tatin C
5	Secondary	Systemic condition causing cardiac and renal dysfunction	Septic shock, vasculitis	–

Predictors of the risk of complications include reduced basic kidney function, diabetes and previous heart failure. These patients require more complex treatments, longer inpatient stay and have a high mortality rate. The study ADHF (who had complications in cardiogenic shock, hypotension, cardiac arrest, sepsis or ACS) and an increase in serum creatinine six month mortality was higher [16]. Conversely, in patients with an increase in serum creatinine ≥ 0,3 mg / dL, but no other complications, there was a higher mortality in the hospital for 30 or 180 days. Thus, most patients with 1 type CRS died because of complications during and ACS. It is important to note that 1 type CRS in patients with ADHF rarely diagnosed in the prehospital phase, usually after admission, because then we can use some of hospital performance, such as diuresis, which speeds diagnosis of CRS [17]. Data from the study Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) demonstrated that the use of high doses of loop diuretics, causing thickening of the blood, leading to more rapid progression of renal dysfunction (5 times faster) [18]. However, in this prospective study on hemodynamic monitoring and active diuresis mortality at 180 days decreased by 69%. Some studies in the present associated increase in central venous pressure and renal venous stagnation in the development 1 type CRS , thus , the relative balance of venous and arterial tone and overload the kidneys are important factors in reducing renal filtration that occurs during treatment in hospital ADHF [19].

Another major clinical scenario in which developing 1 type CRS is an urgent or elective coronary revascularization for patients with acute or chronic ischemic heart disease. A sharp contrast – induced and associated with AKI shunting occurring in 15 % and 30 % of patients, respectively. Importantly, iodine contrast, which causes renal vasoconstriction and has direct cellular toxicity in renal tubular cells, is an important factor that plays an important role in a couple of days before heart surgery. This interference causes renal hypothermia, lack of pulse for reduced perfusion at 30-90 min, and thus represents

an additional ischemic damage in terms of proinflammatory state [20]. It is possible that using artificial blood circulation in coronary artery bypass grafting activates systemic factors that continue to cause AKI, but attempts to limit this exposure did not lead to a significant reduction in the rate of AKI [21]. Thus, these two scenarios are closely related, since almost every cardiac patient operated on urgently spend coronary angiography before surgery. As with ADHF and 1 type CRS with acute and chronic ischemic heart disease has a direct relationship with outcomes. Patients with complications of 1 type CRS marked increase in mortality from 3 to 4 times, despite the presence of dialysis in hospital [20]. In all forms of 1 type CRS are at risk of progression to chronic kidney failure (CKF) highest stage, which ultimately leads to the need for renal transplantation [19]. Increasing and cumulative risk of renal outcomes, according to the above described clinical situations for a single patient currently stay unknown.

Chronic cardiorenal syndrome (CRS type 2): chronic dysfunction of the myocardium leading to deterioration of chronic renal failure. This subtype suggests that chronic cardiovascular disease (CVD) may contribute to the development of CKF. 6 studies reported that CVD causes excess risk of CKF [15]. Established that risk factors for atherosclerosis (diabetes, hypertension, and smoking) are independently associated with the development of CKF [14]. In addition, chronic violations of systolic and diastolic function of the myocardium can lead to changes in neurohormonal activation, renal hemodynamics, and various adverse cellular processes leading to their apoptosis and fibrosis of the kidneys [15]. Approximately 30 % of persons with chronic CVD with CKF and numerous studies have demonstrated the independent contribution of CVD on the degradation of CKF [16]. An important component of the epidemiology of 2 type CRS is the acceleration of atherosclerosis, which leads to premature cardiovascular disease, including myocardial infarction and stroke [5, 18]. Importantly, CKF with metabolic disorders it causes the progression of a calcined atherosclerosis through mineral and bone

disorders in CKF, which is characterized by a delay phosphates [19-21]. Phosphate retention is critical pathophysiological component that stimulates the conversion of vascular smooth muscle cells in osteoblast-like cells that, because of Pit-1 receptor, stimulate the production of extracellular calcium hydroxyapatite crystals in the vascular smooth muscle layer of the arteries [20].

The study showed that 45.0 % – 63.6 % of patients with chronic heart failure have proven CKF defined by calculating the glomerular filtration rate (GFR) < 60 ml / min per 1.73 m ² [21]. Patients with chronic renal failure and end-stage CKF have higher defibrillation thresholds don't have preferences for implanting defibrillators for the purpose of protecting the heart compared with patients with normal renal function. Increased levels of left ventricular hypertrophy and cardiac fibrosis is the biological basis of these electrophysiological results [5, 18-20].

Acute renocardial syndrome (CRS type 3): a sharp deterioration in renal function, resulting in cardiac disorders. The most common scenario for the development of 3 type CRS is AKI, leading to an overload of volume, sodium retention, neurohormonal activation and clinical development of heart failure with pulmonary edema and peripheral edema. This volume overload causes heart failure and 3 type CRS is most clearly reflected in pediatric patients [12]. However, in adults with acute exacerbation of chronic disease, it is difficult to clearly identify cases where AKI leads to cardial decompensation. Thus, the epidemiology of subtype 3 CRS not determined for individual CVD, such as acute coronary syndrome, stroke, arrhythmia, deficiency discharge the functions of the heart and cardiac death [15].

Chronic renocardial syndrome (CRS type 4): chronic kidney disease leading to progression of CVD. Over the past few decades there has been an independent association between the severity and incidence of CKF and CVD incidence [13]. In a meta-analysis of 39 studies (1,371,990 participants) there is a clear correlation between the degree of renal dysfunction and the risk of death from cardiovascular

causes [14]. In 14 of the 39 studies described the risk of mortality from reduced kidney function after adjustment for other established risk factors. Although among the adjusted relative risks ratios were on average 17 % lower than in the unadjusted, they remained significantly higher than the one at 71% of the cohort. The overall mortality significantly influenced significant cardiovascular mortality, which accounted for over 50 % of cases. Specially conducted 13 studies on 4 type CRS, most of them in the population with end-stage renal disease [15]. It should also be noted that CKF causes CVD in patients with 4 type CRS, thus complicating the pharmacological and surgical treatment [16]. For example, azotemia and hyperkalemia restrict the use of drugs that provide antagonistic effects on the renin-angiotensin-aldosterone system, so fewer patients with CKF have a preference for the use of angiotensin-converting enzyme, angiotensin II receptor antagonists and aldosterone receptor blockers. Established that CKF is also worsens manifestations, severity and response to treatment cardiorenal effects of acute and chronic hypertension [15].

Secondary cardiorenal syndrome (CRS type 5): systemic diseases leading to simultaneous heart and kidney failure. It is known that systemic damage, especially in young patients without previous heart disease and kidney failure can result in simultaneous organ dysfunction. It almost always appears critical condition, such as sepsis, multiple trauma, burns. There are limited data on the incidence and factors that determine 5 type CRS, particularly such as hypotension, respiratory failure, liver failure and other organ damage without the involvement of cardiac and renal systems. Sepsis as accelerator 5 type CRS, contributes to morbidity and mortality in this case is estimated at 20 % – 60 %. Approximately 11% – 64 % of septic patients develop AKI, which is associated with higher morbidity and mortality [16]. Abnormalities of cardiac function are common in sepsis, including violations of wall motion and decrease left ventricular ejection fraction. These observations have found about 30 % – 80 % of people with sepsis who had diagnostically significant levels of troponin I or T

levels. These elevated cardiac biomarkers were associated with decreased left ventricular function and increased mortality even in patients with established coronary heart disease [17]. It is important to note that the volume overload as a result of aggressive fluid therapy significantly determines 5type CRS . Among the 3147 patients enrolled in the Sepsis Occurrence in Acutely III Patients (SOAP), was 36 % of the AKI and volume overload, which was the strongest predictor of mortality. Overload capacity increased tension of the walls of the left ventricle and probably contributes to the development of heart failure in patients who are prone to systolic and diastolic heart failure [18].

Thus, by the present time cardiorenal syndrome remains a significant problem for both physicians and patients. Many aspects remain unknown, requiring further research to develop more effective means of diagnosis, treatment and prevention of life-threatening conditions.

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РЕЗЮМЕ

СУЧАСНИЙ ПОГЛЯД НА КАРДІОРЕНАЛЬНИЙ СИНДРОМ

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За останні роки у зв'язку зі зростанням поширеності серцево-судинної патології, збільшенням тривалості життя кардіологічних пацієнтів та використанням інтервенційних методів дослідження та лікування зростає також частота розвитку гострої ниркової не-

достатності. Однак, з розвитком медичної науки, було з'ясовано, що дисфункція нирок часто супроводжує серцеву недостатність, а дисфункції серця – ниркову недостатність. Цей взаємозалежний зв'язок став відомим як "кардіоренальний синдром". Це твердження було оголошено у Вірджинії в 2004 році, але, незважаючи на велику кількість публікацій та обговорень у тематичних конференціях, кардіоренальний синдром ще не став всесвітньо встановленим терміном, а багато ключових питань залишаються без відповіді.

Ключові слова: кардіоренальний синдром, серцева недостатність, ниркова недостатність, набряк.

РЕЗЮМЕ

СОВРЕМЕННЫЙ ВЗГЛЯД НА КАРДИОРЕНАЛЬНЫЙ СИНДРОМ

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За последние годы в связи с ростом распространенности сердечно-сосудистой патологии, увеличением продолжительности жизни кардиологических пациентов и использованием интервенционных методов исследования и лечения возрастает также частота развития острой почечной недостаточности. Однако, с развитием медицинской науки, было выяснено, что дисфункция почек часто сопровождает сердечную недостаточность, а дисфункции сердца – почечную недостаточность. Эта взаимосвязанная патология стала известна как "кардиоренальний синдром". Это утверждение было объявлено в Вирджинии в 2004 году, но, несмотря на большое количество публикаций и обсуждений в тематических конференциях, кардиоренальний синдром еще не стал всемирно установленным термином, а многие ключевые вопросы оставались без ответа.

Ключевые слова: кардиоренальний синдром, сердечная недостаточность, почечная недостаточность, отек.