ABSTRACT

Cardio-Renal Syndrome is defined as pathophysiological dysfunction of the heart and kidneys in which an acute or chronic abnormality of one organ favours either the acute or chronic disorder of the other one. Due to complex interactions between the heart and kidneys, Cardio-Renal Syndrome is divided into five types: Cardio-Renal Syndrome type 1 (Acute Cardio-Renal Syndrome) is defined as acute kidney dysfunction as a result of acute heart failure. Cardio-Renal Syndrome type 2 (Chronic Cardio-Renal Syndrome) is a progressive chronic kidney disorder as a result of chronic heart failure. Cardio-Renal Syndrome type 3 (Acute Renocardial Syndrome) is defined as an acute heart abnormality due to acute kidney dysfunction. Cardio-Renal Syndrome type 4 (Chronic Renocardial Syndrome) is defined as a chronic heart function disorder as a result of a chronic kidney disorder. Cardio-Renal Syndrome type 5 (Secondary Cardio-Renal Syndrome) is defined as either a permanent or temporary abnormality of both organs due to systemic disease. Early detection of kidney and heart disease and timely and adequate therapy can prevent the development of Cardio-Renal syndrome and reduce the overall expense of therapy.

Keywords: cardiorenal syndrome, acute heart failure, acute kidney injury, chronic kidney disease, chronic heart failure

SAŽETAK


Ključne reči: kardiorenalni sindrom, akutna srčana slabost, akutno oštećenje bubrega, hronična bolest bubrega, hronična slabost srca
INTRODUCTION

Cardio-Renal Syndrome (CRS) is defined as a pathophysiological disorder of the heart and kidneys in which an acute or chronic disorder of one organ favours the acute or chronic disorder of the other [1-6]. Direct and indirect actions due to the insufficiency of one organ may trigger damage to the other via a complex combination of neurohumoral feedback mechanisms [1-6].

METHODS

The MEDLINE database was used for this study. The following keywords were used for searching: cardio-renal syndromes, acute heart failure, acute kidney injury, worsening renal function, chronic kidney disease, chronic heart failure. About 10000 references were found dealing with these types of problems. Systematic review articles and well controlled clinical studies were extracted. Editor’s letters and uncontrolled clinical studies were not used. Systematic review articles were used and analysed by the Acute Dialysis Quality Initiative (ADQI) consensus group, which checked the validity and quality of the selected references.

RESULTS

Types of cardiorenal syndrome

Due to the complex interactions of the heart and kidney, cardiorenal syndrome is divided into five categories [1-6].

Cardiorenal syndrome type 1

Cardiorenal syndrome type 1 (acute cardiorenal syndrome) is defined as acute renal failure caused by sudden worsening of heart function, such as hypertensive pulmonary oedema with preserved systolic function, acute decompensation of chronic congestive heart failure, acute cardiogenic shock and predominant right ventricle failure [1-7].

In acute heart failure (including acutisation of chronic decompensatory heart failure, heart arrhythmia or ischaemia) compromised cardiac output is reflected by an impairment in the strength of glomerular filtration and acute renal failure [acute renal hypoperfusion, lowered oxygen income, apoptosis and necrosis of renal cells, lowered strength of glomerular filtration and inadequate response to natriuretic peptides (ANP - atrial natriuretic peptide, BNP - brain natriuretic peptide)]. A sudden drop in intravascular volume in the renin-angiotensin-aldosterone system (RAAS) and excessive angiotensin 2 stimulates the creation and deliberation of endothelin-1 (ET-1) in the kidney. Endothelin-1 is a potent proinflammatory and profibrotic vasoconstrictive peptide that plays an important role in most pathological mechanisms of acute renal failure by activating an ischaemic cascade during secondary acute renal damage [1-7]. Patients with CRS type 1 have higher concentrations of lipocaline (lipocaline linked with neutrophil gelatinisation) in their urine, indicating the incipient development of renal impairment [1, 8].

The basic goal of treatment for CRS type 1 is the stabilization of impaired heart function, which is the main cause of hemodynamic instability, and generation of better renal perfusion [7]. Acute renal impairment with or without hyperkalaemia has an impact on the choice of drugs used for treatment; angiotensin-1 convertase blockers, angiotensin-1 receptor blockers and aldosterone blockers can all raise the survival of patients with heart failure and myocardial infarction. Monitoring of renal function and serum potassium concentration is necessary in patients with CRS type 1. Acute administration of β-blockers in CRS is not advised. Blockage of inotropic compensation, which is dependent on compensatory tachycardia and on the sympathetic nervous system, can worsen cardiogenic shock [1-7].

In the case of hypovolaemia, eliminating excessive body water can lead to changes in the diuretics used and, in certain situations, require the adjustment of dialysis treatment modality (SCUF - slow continuous ultrafiltration) [5-7]. Adding diuretics that block distal tubules (chlorothiazide 500-1000 mg i.v. or metolazone 2.5-10 mg per os) can significantly improve diuresis in patients who receive diuretics of Henle’s loop [7, 9].

Nitrate doses should be titrated with the goal of lowering blood pressure by 10 mmHg while at the same time maintaining systolic blood pressure above 100 mmHg. The dosage of nitrates should be lowered if systolic blood pressure is between 90 and 100 mmHg and if blood pressure falls below 90 mmHg, nitrate use should be discontinued [7, 9].

Inotropic therapy is used in patients with acute heart failure and systolic blood pressure below 90 mmHg [7, 9]. For the vast majority of patients, dobutamine at a dose of 1.0-2.0 μg/kg/min has an inotropic effect and improves renal function, while high doses (5.0-10.0 μg/kg/min) have simultaneous inotropic and vasoconstrictive effects [7, 9].

Cardiorenal syndrome type 2

Cardiorenal syndrome type 2 (chronic cardiorenal syndrome) is defined as a progressive chronic renal impairment due to the chronic impairment of heart function (chronic congestive heart failure) [1-5]. In chronic heart failure, impaired cardiac output and hypoxia cause excessive sympathetic activity, renin-angiotensin-aldosterone system (RAAS) activity, vasopressin system activity, increased oxidative stress in the kidneys, and a disturbance of the L-arginine/NO system in the endothelium of the kidneys. Activation of RAAS increases the levels of angiotensin-2, aldosterone and endothelin-1 in the kidney, which all cause fibrotic processes in the glomeruli and tubulointerstitium and development of end stage chronic renal failure [1-6]. Chronic heart failure also causes anaemia and microinflammation [increased deliberation of cytokine: TNFα (tumour necrosis factor α), interleukin-1, interleukin-6], which additionally contributes to fibrosis of the renal parenchyma and more rapid impairment of renal function [1-6].
The basic goal of cardiorenal syndrome type 2 treatment is improvement of deteriorated heart function, which is main cause of hemodynamic instability, and better renal perfusion (Figure 1) [9, 10]. However, treatment of chronic heart failure may actually worsen renal function. Increased diuresis, blockage of renin-angiotensin-aldosterone system and hypotension exaggerated by medical treatment may all contribute to the worsening of renal function [1-6]. Treatment of patients with chronic heart failure, chronic renal diseases and anaemia with recombinant human erythropoietin improves heart function, leads to regression of left ventricle enlargement and slowing the progression of chronic renal failure [1-6].

Cardiorenal syndrome type 3

Cardiorenal syndrome type 3 (acute reno-cardial syndrome) is defined as an acute damage of heart function (heart failure, arrhythmia, pulmonary oedema) as the result of acute renal damage (acute renal ischaemia or acute glomerulonephritis) [1-6]. Cardiorenal syndrome type 3 is much less frequent than CRS type 1. Due to a sudden impairment in the strength of glomerular filtration and the development of oligoanuria (retention of sodium with...

Figure 1. Mechanism by which negative sodium and water balance may improve myocardial and renal function in CHF

Figure 2. Risk factors for development of cardiovascular complications in patients with chronic renal failure

Modified according to reference [13].
CHF - Congestive Heart Failure

Modified according to reference [13].
SHPT - secondary hyperparathyroidism, iPTH - intact parathormone, GFR - glomerular filtration rate
acute renal failure [1, 8, 27]. The strategy for preventing acute renal damage in septic patients includes adequate hydration (central venous pressure - CVP 8-12 mmHg, urine output ≥ 0.5 ml/kg/h), maintenance of mean arterial blood pressure (mean arterial blood pressure - MAP ≥ 65 mmHg) and the avoidance of nephrotoxic drugs [28, 29]. Therapy with vasopressors is indicated in patients with hypotension (SAP < 65 mmHg), complete fluid restitution, normal or enlarged cardiac index - SI and absent peripheral vasoconstriction during physical examination [28, 29]. Vasopressors should not be used in patients with a low cardiac index (without inotropics and monitoring), in patients with vasoconstrictive status or those with volume depletion. The most frequently used vasopressin is norepinephrine, also known as noradrenaline. The initial dose used is 0.1 - 0.2 μg/kg/min, while the upper treatment value is 1.0 μg/kg/min [28, 29]. Inotropic therapy (dobutamine) is used in patients with low cardiac index or in patients with lowered cardiac index after the use of, and those with previous fulfillment of intravascular volume (those who reached target restitution). Dobutamine titration begins with a dose of 2.5 μg/kg/min and should be increased by 2.5 μg/kg/min every 15-20 minutes until normal heart function is maintained (cardiac index - SI = 2.5 - 4.5 l/min/m2) [28, 29].

CONCLUSION

The link between the heart and kidneys is more complex than of a simple pump and filter, and knowing more about the complex interactions between these two organs enables the development of adequate therapeutic strategies for preserving heart and renal function [30-34].

REFERENCES