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Monitoring of patients with Cardiorenal syndromes

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Abstract.
Cardiac and renal diseases often coexist and patients with cardiac and renal failure have high morbidity and mortality. Cardiorenal syndromes (CRSs) are disorders of the heart and kidneys whereby dysfunction in one organ may induce dysfunction in the other organ. Five subtypes of CRSs have been defined by the Acute Dialysis Quality Initiative Consensus Group. There is a need for early detection and monitoring of patients with CRSs. Biomarkers play a key role in the diagnosis and monitoring of acute myocardial infarction, chronic heart failure, and chronic kidney disease. In recent years, new biomarkers have been identified that may play a role in the early diagnosis of acute kidney injury. Herein, we review the use of serum and urine biomarkers in the diagnosis and management of CRSs. The established cardiac and renal biomarkers such as the cardiac troponins, natriuretic peptides, urine albumin, and creatinine, as well as the new renal biomarkers cystatin C and neutrophil gelatinase–associated lipocalin are reviewed in detail. The recent advances in assay methods, clinical studies, and recommendations in clinical guidelines are discussed. With advances in biomarker research, in future, perhaps a multimarker approach will become feasible to stratify the diagnosis of CRS for individualized treatment and prognosis.
Keywords: heart failure, osteoporosis, bone mineral density, bone metabolism.

Introduction

The cardiorenal syndromes (CRSs) are a heterogeneous group of conditions comprising both cardiac and renal dysfunction, whereby dysfunction in one organ may induce dysfunction in the other organ[1] (Table I). Type 1 CRS (acute CRS) is characterized by an acute cardiac event resulting in acute renal deterioration. The acute cardiac event commonly includes acute coronary syndrome (ACS), acute decompensated heart failure (HF), cardiogenic shock, and cardiac surgery.[2] The acute cardiac insult results in reduced cardiac output, which leads to reduced renal perfusion pressure, increased renal vascular resistance, and reduced glomerular filtration rate (GFR).[2] Type 2 CRS (chronic CRS) is characterized by chronic heart disease resulting in renal disease. Approximately 50% of patients with chronic HF have chronic kidney disease (CKD), and CKD is associated with high mortality in patients with HF.[3] Type 3 CRS (acute renocardiac syndrome) is characterized by an acute worsening of renal function, which causes acute cardiac dysfunction such as arrhythmia, HF, or ischemia. The development of acute kidney injury (AKI) is the primary event.[3] Type 4 CRS (chronic renocardiac syndrome) is characterized by CKD leading to decreased cardiac function, ventricular hypertrophy, diastolic dysfunction, and increased risk of adverse cardiovascular events. Patients with CKD have an increased risk of cardiovascular mortality, with cardiovascular causes representing up to 50% of all deaths in patients with CKD.[4] Type 5 CRS or secondary CRS is characterized by systemic conditions leading to simultaneous injury and dysfunction of the heart and kidney. Chronic inflammatory conditions such as systemic lupus erythematosus, vasculitis, amyloidosis, and diabetes mellitus can affect both the kidney and the heart.[5] In the acute setting, sepsis is the most common condition causing type 5 CRS.[5] In the chronic setting, diabetes mellitus is the most common condition causing simultaneous cardiac and renal dysfunction.[5] The 5 subtypes reflect the primary and secondary pathophysiology, time frame, and simultaneous cardiac and renal dysfunction. The classification is based on clinical presentation alone and often it is not easy to distinguish between acute and chronic disease. The Acute Dialysis Quality Initiative working group recognized that many patients may populate or move between different subtypes during the course of the disease.[1] The different subtypes create new definitions of disease to identify diagnostic biomarkers, identify patients at risk, and develop strategies to prevent and manage CRS. Although it is recognized that biomarkers play an important role in diagnosis of acute and chronic HF, as well as acute and chronic renal disease, biomarkers have not yet been integrated into the diagnosis of the various CRS.[1] Further studies are needed to identify whether the biomarkers can be used to classify CRS, to risk stratify patients, and as treatment targets to monitor the efficacy of treatment. Although multiple clinical guidelines exist to manage acute and chronic

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heart disease, as well as acute and CKD, there are no guidelines for the management of the various CRS. Currently, early risk recognition with careful monitoring using biomarkers appears essential to developing treatment and prevention strategies. For example, the measurement of procalcitonin may play a role in acute type 5 CRS by early identification of acute sepsis. In chronic type 5 CRS, the measurement of urine albumin plays a role in the early identification of renal disease.

Cardiac and renal diseases often coexist and patients with cardiac and renal failure have high morbidity and mortality;[1] hence, there is a need for early detection and monitoring of patients with cardiac and renal diseases. The pathophysiology of CRS involves complex multiple interactions between the heart and the kidney[2] (Fig 1). Biomarkers play a key role in the diagnosis and monitoring of acute myocardial infarction (MI), chronic HF, and CKD. In recent years, new biomarkers have been identified that may play a role in the early diagnosis of AKI. Herein, we review the role of cardiac and renal biomarkers in the diagnosis and management of CRS.

Section snippets

Cardiac troponin

An acute cardiac ischemic event is often the primary event in type 1 CRS. ACS also features in types 3 and 5 CRSs, where an MI may be triggered by AKI in type 3 CRS and by sepsis in type 5 CRS. The cardiac troponins (cTns) have a central role in the diagnosis of ACS: in the Third Universal Definition of MI, the criteria for diagnosis of MI is a rise or fall in cTn value with at least one value greater than the 99th percentile upper reference limit (URL) plus at least one evidence of myocardial

Albuminuria

Proteinuria has long been known to be a marker of renal damage, and quantification of proteinuria or albuminuria is widely used for identifying and monitoring patients with CKD. Albumin is the predominant protein in urine in renal damage, and measurement of the albumin-to-creatinine ratio (ACR) in first morning or random spot urine is generally recommended for annual screening of patients with type 2 diabetes mellitus for CKD.[50] The Kidney Disease: Improving Global Outcomes (KDIGO) 2012

Conclusions

Although there has been significant progress in the recent decade in biomarker discovery for the diagnosis and prognosis of CRS, further work needs to be done before translation of the newer biomarkers into clinical utility. A clinically useful biomarker is one that is easily measured at low cost with a low turnaround time, and can provide information in addition to clinical assessment to influence medical decision. The cTns, BNP, NT-proBNP, and creatinine have proven to be essential in the

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