A Clinical Approach to the Acute Cardiorenal Syndrome

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KEYWORDS

• Cardiorenal syndrome • Heart failure • Acute kidney injury • Diuretics
• Chronic kidney disease • Ultrafiltration • Acute heart failure syndromes

KEY POINTS

- Acute cardiorenal syndrome represents a unique form of acute kidney injury specific to acute heart failure syndromes that is associated with adverse outcomes.
- Acute cardiorenal syndrome results from renal venous congestion, ineffective forward flow, and impaired renal autoregulation caused by neurohormonal activation.
- Biomarkers reflecting different aspects of acute cardiorenal syndrome pathophysiology may allow patient phenotyping to inform prognosis and treatment.
- Aggressive diuretic therapy to relieve congestion is the cornerstone of treatment in acute cardiorenal syndrome.
- Adjunctive therapies may relieve congestive symptoms and/or improve renal function, but no single therapy has been conclusively shown to reduce mortality in acute cardiorenal syndrome.

INTRODUCTION

The medical community has increasingly recognized the complex relationship between the heart and kidneys over recent years. The term cardiorenal syndromes (CRSs) encompasses a spectrum of disease states involving mutually interacting cardiac and renal dysfunction. CRSs are defined as "disorders of the heart and kidneys

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whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other."[1,2] The term cardiorenal applies when cardiac dysfunction drives renal dysfunction, as opposed to renocardiac, in which renal dysfunction drives cardiac dysfunction.[1,2] Patients may develop more than 1 CRS simultaneously because of the bidirectional nature of cardiorenal interactions and shared risk factors for cardiac and renal disease.[3] Acute CRS represents a unique form of acute kidney injury (AKI) developing in patients with acute cardiac dysfunction. For a broader overview of the CRSs, we refer readers to recent comprehensive reviews.[3–5]

EPIDEMIOLOGY OF ACUTE CARDIORENAL SYNDROME

Acute CRS is the best-recognized of the CRSs, and the subtype most frequently encountered in acutely ill patients. Acute CRS was initially described as diuretic-refractory volume overload with worsening renal function (WRF) during treatment of decompensated heart failure (HF), which is considered forme fruste acute CRS. The definition of acute CRS has broadened to include patients with declining glomerular filtration rate (GFR) and increasing serum creatinine levels caused by acutely worsening cardiac function, most often during hospitalization for an acute HF syndrome (AHFS).[1–9] AHFSs are a common and morbid complication of chronic HF, leading to millions of hospitalizations each year worldwide.[10,11] At least one-fourth of patients hospitalized with AHFS may develop WRF, depending on the definition of WRF; an increase in creatinine level greater than or equal to 0.3 mg/dL or greater than or equal to 25% from baseline has been used most commonly.[4,6,7,9,12–15] Not all increases in creatinine level during AHFS have the same prognostic relevance, and we suggest that acute CRS should only include patients with treatment failure and persistent congestion.[7]

Chronic kidney disease (CKD) is present in approximately half of all patients with AHFS, so many patients with acute CRS have concomitant chronic CRS.[6,9,12,16] The most important risk factor for WRF in AHFS is CKD, reflected by reduced GFR with increased serum creatinine and cystatin C levels (**Box 1**).[13–15,17–20] AKI is an important contributor to the progression of CKD and HF, and both AKI and CKD are associated with adverse outcomes in diverse patient populations.[21] Patients with CKD or WRF complicating AHFS have significantly increased mortalities compared with patients with preserved renal function, and renal dysfunction is the most important prognostic marker in AHFS.[12,22–28] WRF during AHFS portends an adverse prognosis independently of baseline renal function, and mortality increases progressively with incremental increases in serum creatinine.[1,2,6,7,12,26–29] The adverse prognosis conferred by baseline renal dysfunction seems greater than the effect of WRF.[12,23,26–31] Transient WRF reflecting a reversible reduction in GFR seems less harmful than persistent WRF suggesting established AKI, but even decreases in creatinine during hospitalization representing WRF on presentation may be associated with adverse outcomes.[5,32,33]

BIOMARKERS IN ACUTE CARDIORENAL SYNDROME

Cardiorenal biomarkers reflecting different aspects of cardiac and renal dysfunction predict acute CRS outcomes, but there are no definitive diagnostic tests for acute CRS.[36] Four major groups of cardiorenal biomarkers have been studied in acute CRS, including clearance biomarkers reflecting GFR, natriuretic peptides reflecting congestion, tubular injury biomarkers, and miscellaneous biomarkers reflecting neurohormonal and/or inflammatory activation (**Box 2**). Levels of cardiac injury biomarkers