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Short Communication

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# Cardiorenal Syndrome Complicating Treatment of Acute Decompensated Heart Failure: Relation to Mitral and Tricuspid Regurgitation

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## Abstract

*Worsening renal function as defined by an increase in creatinine of 0.3 mg/dl during treatment of patients with acute decompensated heart failure (ADHF) is a dire complication and portends a poor prognosis. We studied 80 patients with heart failure and reduced ejection fraction (HFrEF) who presented with ADHF requiring decongestive therapy with diuretics. We divided patients into 2 groups according to their renal function during diuretic therapy: group 1 those with worsening renal function or cardiorenal syndrome (CRS) and group 2 those with stable renal function. Comparison between groups showed that baseline renal function and the magnitude of mitral and tricuspid regurgitation (MR and TR) as studied by color Doppler echocardiography were the most sensitive parameters in predicting worsening renal function during diuretic therapy in patients with ADHF.*

**Keywords:** *Cardiorenal syndrome; Acute decompensated heart failure; Mitral and tricuspid regurgitation*

## Description

There is a complex interaction between the kidney and the heart. This interaction plays a major role both in normal physiology and in pathophysiology of heart and kidney failure. Renal dysfunction is one of the most important complications in patients with heart failure with reduced ejection fraction (HFrEF) and portends a poor prognosis.

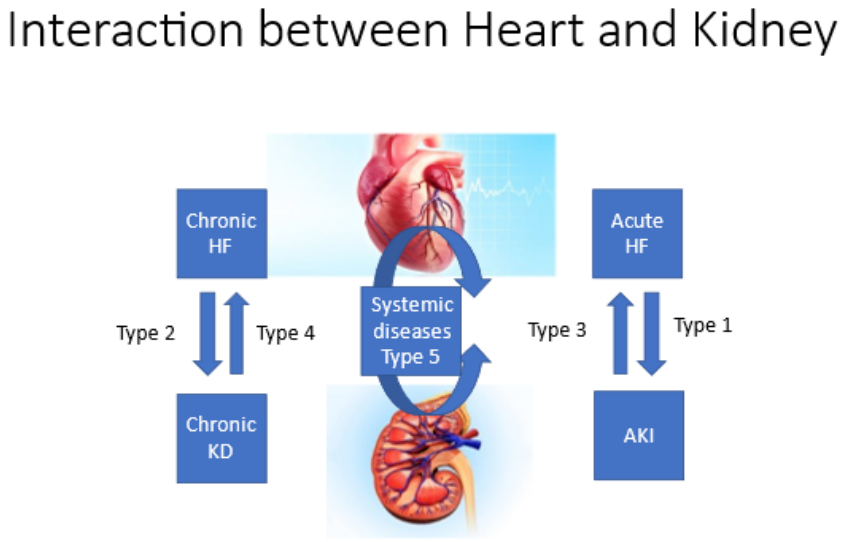


**Figure 1:** Classification and relationship between the heart and the kidney. In type 1 CRS acute HF like in cardiogenic shock leads to decrease cardiac output which leads to decrease renal blood perfusion. In type 2 CRS chronic reduction in blood flow to kidney associated with elevated filling pressure and congestion of splanchnic blood pool will lead to kidney failure through compression of renal veins. In type 3 CRS acute kidney injury will lead to fluid and salt retention which leads to volume overload and elevated filling pressures. In type 4 CRS chronically elevated volume overload leads to congestive heart failure. And type 5 CRS is when systemic diseases such as some forms of vasculitis and diabetes mellitus will affect both the heart and the kidney. (CRS: Cardiorenal Syndrome, HF: Heart Failure)

Cardiorenal syndromes are a group of linked disorders of the heart and kidneys. They are classified according to whether the problem is acute or chronic and whether the primary problem is in the heart (cardiorenal syndrome), the kidneys (renocardiac syndrome), or another organ (secondary cardiorenal syndrome). This classification is still evolving [1-2]. In Acute Decompensated Heart Failure National Registry (ADHERE) of 105000 patients admitted with acute decompensated heart failure (ADHF), 30% of patients had a previous history of renal insufficiency, 20% had creatinine > 2.0 mg/dl and 9% had creatinine >3.0 mg/dl [3].

Renal dysfunction is an independent risk factor for poor outcome and all-cause mortality in patients hospitalized with ADHF. Although worsening renal function was traditionally believed to result from decreasing cardiac output or diuretic-induced intravascular volume depletion, recent insights suggest that venous congestion has an important contributing role especially in the setting of an increasing serum creatinine during decongestive therapy [4].

It is also important to point out that the occurrence of rising serum creatinine has been more closely linked to inadequate fluid loss than drop in right atrial pressure.

However, if congestion persists and the ability for the kidney to mobilize fluid remains intact (e.g., diuretic-responsive), aggressive decongestive strategies may even overcome such counter-regulatory mechanisms [5]. Baseline GFR is a strong predictor of mortality, even more than left ventricular ejection fraction (LVEF) and NYHA functional class. Both elevated creatinine on admission and worsening creatinine during hospitalization predict prolonged hospitalization, re-hospitalization and death [6]. In all types of CRS, multiple pathophysiological processes are implicated in the initiation and progression of organ injury [7].

In our retrospective study we hypothesized that the presence of more than moderate mitral and/or tricuspid regurgitations (MR and/or TR) in patients with severe chronic heart failure with reduced ejection fraction (HFrEF) is associated with higher risk of developing cardiorenal syndrome (CRS). The reason for this hypothesis was that patients with moderate to severe or severe MR and TR are a subset of HFrEF who have both reduced cardiac output and elevated filling pressures. We recruited 80 consecutive patients who were hospitalized with acute decompensated heart failure due to HFrEF either from ischemic or non-ischemic cardiomyopathy.

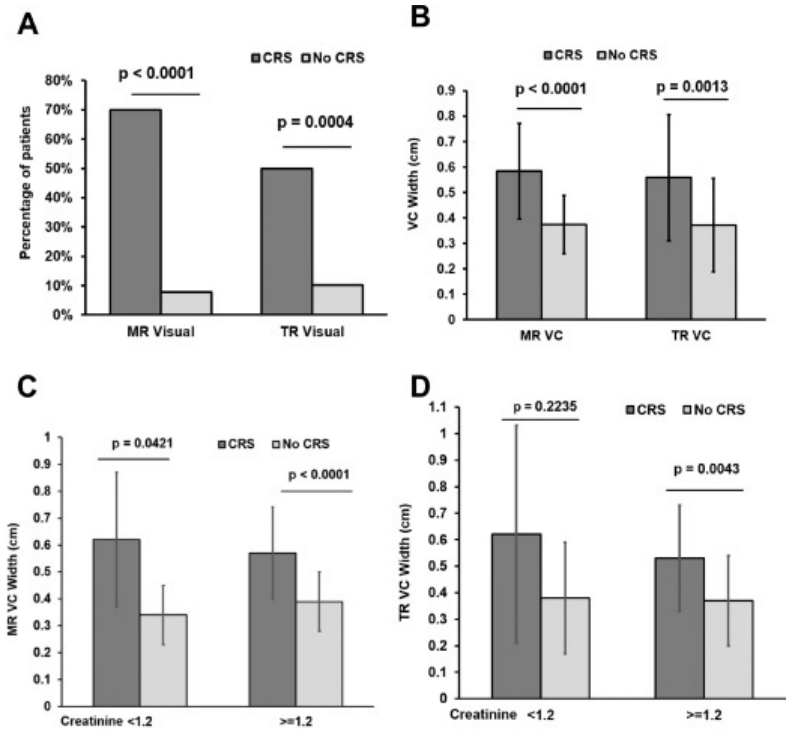


**Figure 2:** Severity of MR and TR is worse in patient with CRS. (A) Prevalence of moderate to severe or severe (3+ and 4+) MR and TR by visual assessment and by CRS status. (B) Mean MR and TR VC by CRS Status. (C) Mean MR VC by CRS Status stratified by baseline creatinine levels. (D) Mean TR VC by CRS Status stratified by baseline creatinine levels (CRS = dark gray bars, no CRS = light gray bars).

All patients underwent comprehensive echocardiography within 24 H of admission. All measurements of cardiac chambers and Doppler evaluation were performed as recommended by the guidelines of the American Society of Echocardiography. The degree of mitral and tricuspid regurgitation (MR and TR) was evaluated semi quantitatively by visual assessment using the conventional views and quantitatively by measuring Vena Contracta (VC). Renal function as measured by BUN and Creatinine was measured on admission and on a daily basis during index hospitalization. An increase in Creatinine of > 0.3 mg/dl from baseline while receiving diuretic therapy was defined worsening renal function or cardio renal syndrome (CRS).

Our study shows that patients who develop CRS are those with baseline renal dysfunction and significant (moderately severe and severe) functional MR and/or TR. Comparison between the 2 groups shows that patients who develop CRS are those who have significant (at least moderate) MR and/or TR. Indeed, we found a statistically significant difference between the 2 groups in both the degree of visually estimated MR and TR (which is a semi-quantitative assessment of severity of regurgitation) and their vena contracta (vc) which is a quantitative measure of regurgitation.

In addition to hemodynamic parameters, a constellation of biologic and molecular factors including endothelial injury, immunological imbalance, cell death, inflammatory cascades, oxidative stress, neutrophil migration, leukocyte trafficking, caspase-mediated apoptosis, extracellular vesicles, small noncoding RNAs, and epigenetics play pivotal roles in the development of CRS [7].

Our study shows the complex interaction between the heart and the kidney: patients with ADHF who develop CRS are those in whom the intrinsic renal function is more often initially abnormal compared to patients in whom renal function is intact. Moreover, our study shows that both decreased cardiac output and elevated filling pressures and elevated pressures in abdominal and splanchnic bed play an important role in the development of CRS.

## Conclusion

Cardiorenal Syndrome has a complex pathophysiology. Chronic kidney disease and significant mitral and/or tricuspid regurgitation and probably RV systolic dysfunction are potential mechanisms of CRS. These factors should be considered when giving diuretic therapy in patients with ADHF and CRS.

## Conflict of Interest Statement

Authors declare to have no conflict of interest relevant to this article.

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