

IMPROVEMENT IN RENAL FUNCTION WHEN TREATING ACUTE DECOMPENSATED HEART FAILURE: PROGNOSTIC IMPORTANCE AND RELATIONSHIP WITH MARKERS OF RENAL TUBULAR INJURY

Peter S Natov, MD¹, Juan B Ivey-Miranda, MD², and Jeffrey M Testani, MD, MTR²

¹ Department of Internal Medicine, Yale School of Medicine, New Haven, CT; ² Department of Internal Medicine, Section of Cardiovascular Medicine, Yale School of Medicine, New Haven, CT

Original Research

Background: During the treatment of acute decompensated heart failure (ADHF), improvement in renal function (IRF) has been shown to be independently associated with adverse outcomes. The mechanisms driving this paradoxical finding are, however, undefined. When managing ADHF, creatinine fluctuations may reflect functional changes glomerular filtration without corresponding histologic renal injury. Well-validated markers are available to quantitatively assess renal tubular injury. This study investigates the characteristics of ADHF patients with IRF and the ability of renal tubular injury markers to predict clinical outcomes in these patients.

Methods: This study is a post hoc analysis of the Renal Optimization Strategies Evaluation–Acute Heart Failure (ROSE-AHF) trial. From the trial cohort, 277 patients met criteria for inclusion in our analysis, and subjects were grouped by renal function status. IRF was defined as a $\geq 20\%$ rise in the estimated glomerular filtration rate (eGFR) at any timepoint during the intervention period of 72 h. Worsening renal failure (WRF) was defined as $\geq 20\%$ fall in the eGFR. Subjects not meeting definitions for IRF or WRF were categorized as stable renal function (SRF). Urinary levels of neutrophil gelatinase-associated lipocalin (NGAL), N-acetyl- β -d-glucosaminidase (NAG), and kidney injury molecule 1 (KIM-1) were used to evaluate renal tubular injury.

Results: Upon admission, ADHF patients with IRF had lower systolic blood pressures and eGFR compared to patients with WRF and SRF ($p=0.01$ across three groups for trend in systolic pressure; $p=0.03$ for trend in eGFR). With intravenous diuresis, the IRF group exhibited greater urine output ($p=0.02$ for trend) and weight loss ($p<0.001$) compared to the WRF and SRF groups, but no statistically significant differences were found in N-terminal pro-B-type natriuretic peptide levels or in symptoms and examination findings of congestion. There were no differences in the change in NGAL, NAG, or KIM-1 when analyzed individually or collectively across the three groups. ADHF patients with IRF exhibited the worst survival (hazard ratio 1.98, 95% confidence interval 1.10–3.58, $p=0.02$) compared to the SRF group, which had the best survival. While there were no differences in survival based on the pattern of change in renal tubular injury markers, patients with IRF and improved markers had the worst survival while those with SRF and stable markers had the best survival ($p=0.02$ for linear trend).

Conclusions: IRF observed during decongestive therapy for ADHF was associated with increased mortality compared to steady or deteriorating renal function. The link between IRF and poor outcomes may be explained by IRF serving as a marker of greater disease severity and the incomplete decongestion in the IRF group. No pattern of change in the renal tubular injury markers was found to be independently associated with survival, but these markers may be used for further risk stratification in conjunction with glomerular filtration measures.