RENAL TUBULAR CELL INJURY IN ACUTE DECOMPENSATED HEART FAILURE: A POTENTIAL PATHOPHYSIOLOGIC MECHANISM, A NOVEL DIAGNOSTIC MARKER AND A THERAPEUTIC TARGET FOR DIURETIC RESISTANCE

Poster Contributions
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Authors: Parta Hatamizadeh, Todd Koelling, Mahboob Chowdhury, Judith Grossi, Su Q. Wang, Roger C. Wiggins, University of Michigan, Ann Arbor, MI, USA

Background: Diuretic resistance is a major challenge in the management of volume overload in patients with acute decompensated heart failure (ADHF) and its pathophysiologic mechanism is unclear. Aquaporin2-containing renal tubular cells are the major contributors of renal water clearance. We hypothesized that injury to aquaporin2-containing renal tubular cells during ADHF may contribute to diuretic resistance associated with ADHF.

Methods: We examined urine pellet aquaporin2 mRNA in 39 patients with ADHF during hospitalization and post-discharge using reverse transcription-polymerase chain reaction technique. Urine aquaporin to creatinine ratio (UaqCr) was used as a marker of severity of damage to the renal tubular cells that detach from the tubules and subsequently appear in the urine.

Results: ADHF patients with diabetes or hypertension had almost 6 times higher UaqCr (475±951 x10−6) compared to ADHF patients without diabetes or hypertension (82±85 x10−6) (P<0.05). Post-discharge UaqCr was not significantly different from ADHF phase when it was measured within one month of hospital discharge (640±1,209 x10−6 vs. 553±1,269 x10−6 P=0.11); however, it was 17-fold lower when it was measured after 3 months of hospital discharge (39±33 x10−6 vs. 671±1,225 x10−6 vs. ; P=0.03).

Conclusion: UaqCr is higher during ADHF compared to stable heart failure, which suggests aquaporin2-containing renal tubular cell injury during ADHF. The UaqCr remains elevated for a month after clinical recovery of ADHF, suggesting persistence of renal tubular cell injury several weeks following clinical stabilization of ADHF. However, it decreases substantially after 3 months. Impairment of aquaporin2-containing renal tubular cells may contribute to diuretic resistance associated with ADHF. Higher levels of UaqCr in diabetic and hypertensive patients found in this study may explain the prior observations of association of diuretic resistance with comorbidities such as diabetes in ADHF. UaqCr can be a potential future diagnostic marker and therapeutic target for diuretic resistance in heart failure.