Elevated renin and acute respiratory distress syndrome in patients with vasodilatory shock treated with angiotensin ii

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Introduction:
Elevated renin is associated with an increased risk of death in patients with vasodilatory shock (VS). Recent data show that patients with VS and elevated renin levels have improved survival when treated with angiotensin II (Ang II) + standard care (SC) vs placebo + SC. Patients with acute respiratory distress syndrome (ARDS) can develop angiotensin-converting enzyme (ACE) defects that can lead to elevated renin levels and insufficient endogenous Ang II production. We hypothesized that patients with severe ARDS and elevated renin shock would have improved survival when treated with Ang II + SC vs placebo + SC.

Methods:
In the randomized, placebo-controlled, double-blind ATHOS-3 study, 321 patients with severe VS receiving >0.2 µg/kg/min of norepinephrine or the equivalent were randomized to intravenous Ang II (n=163) or placebo (n=158). In a post hoc analysis, we assessed the subset of patients with elevated renin (defined as a renin level greater than the median value of the overall ATHOS-3 population) and ARDS (defined by a PaO2/FiO2 ratio <300) at the time of randomization. Survival to 28 days was compared between the Ang II group (n=41) and the placebo group (n=61).

Results:
In patients with elevated renin and ARDS, baseline age, Acute Physiology and Chronic Health Evaluation II score, and blood pressure were similar in the Ang II and placebo groups. The median serum renin level was 459.5 pg/ml (IQR: 285.8-1036.0) compared to the normal range for serum renin: 5-58 pg/ml. A significantly higher proportion of patients receiving Ang II survived to day 28 compared to those in the placebo group (51% vs 31%; p=0.01).

Conclusion:
Elevated renin identified patients with VS and ARDS who were most likely to gain a survival benefit from Ang II. Elevated renin is likely caused by an ACE defect and may describe an important subset of patients with a biotype that responds well to Ang II therapy.