ICU
MANAGEMENT & PRACTICE

Renin as marker of tissue-perfusion, predictor of ICU mortality

Researchers in Europe prospectively characterised renin in an ICU population to determine if it performs well as a marker of tissue-perfusion. In a proof-of-concept analysis, they compared renin with lactate as a predictor of ICU mortality. Based on the results, renin served as a useful marker of circulatory function and outperformed lactate in predicting ICU mortality.

The renin-angiotensin-aldosterone system (RAAS) is fundamental to circulatory homeostasis. Renin is the primary driving force in this system and is secreted in response to decreased tissue-perfusion, sympathetic activation, and hypoxic metabolism. Renin is routinely measured in clinical practice to investigate hypertension but has not been well characterised in acute circulatory failure. These are some issues that could encumber its use in critical care practice:

1) Renin has a diurnal variation in healthy subjects.
2) Its molecular weight (~40 kDa) is at the threshold for removal by hemofiltration.
3) Renin production could be affected by commonly used medications including beta-agonists, RAAS blockers, and furosemide.

But in the current study, researchers found that renin measurement was not significantly affected by diurnal variation, continuous renal replacement therapy, or drugs. The researchers explain: "We found no significant diurnal variation of direct plasma renin in this ICU population; the lowest set of measurements was taken in the morning, going against physiologic diurnal variation where morning values are highest. The half-life of fast-component renin elimination is less than 20 minutes, so regular monitoring of renin levels throughout the day could track the tissue level effects of therapeutic interventions."

This study was conducted in a single-centre, mixed medical-surgical ICU in Europe. Patients over 18 years old with a baseline estimated glomerular filtration rate greater than 30 mL/min/1.73 m2 and anticipated ICU stay greater than 24 hours were enrolled. Informed consent was obtained from the patient or next-of-kin. Direct plasma renin was measured in samples drawn 6-hourly from arterial catheters in recumbent patients and from extracorporeal continuous renal replacement therapy circuits. Physiologic variables and use of drugs that act on the renin-angiotensin-aldosterone system were recorded prospectively. Routine lactate measurements were used for comparison.

In all, 112 arterial samples were drawn from 20 patients (65% male; mean ± SD, 60 ± 14 years old) with septic shock (30%), haemorrhagic shock (15%), cardiogenic shock (20%), or no circulatory shock (35%). Renin correlated significantly with urine output (repeated-measures correlation coefficient = –0.29; $p = 0.015$) and mean arterial blood pressure (repeated-measures correlation coefficient = –0.35; $p < 0.001$). There was no diurnal variation of renin or significant interaction of renin-angiotensin-aldosterone system drugs with renin in this population. Continuous renal replacement therapy renin removal was negligible (mass clearance ± SD 4% ± 4.3%).

Data also revealed a significant difference in the rate of change of renin over time between survivors and nonsurvivors (–32 ± 26 µU/timepoint vs. +92 ± 57 µU/timepoint $p = 0.03$; mean ± SEM), but not for lactate (–0.14 ± 0.04 mM/timepoint vs. 0.15 ± 0.21 mM/timepoint; $p = 0.07$). Maximum renin achieved significant prognostic value for ICU mortality (receiver operator curve area under the curve 0.80; $p = 0.04$), whereas maximum lactate did not (receiver operator curve area under the curve, 0.70; $p = 0.17$).

While the study is limited by a small sample size, the research team notes that their cohort was heterogeneous and representative of a broad range of ICU patients. Other limitations are that patients were enrolled at various points during their ICU admission, and patients with stage IV or V CKD were excluded from the study. "We have not demonstrated a direct relationship between renin levels and microcirculation function," according to the researchers, adding that further studies should be performed to investigate the utility of renin in guiding the management of critically ill patients.

Source: Critical Care Medicine
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