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Plasma neutrophil gelatinase-associated lipocalin is an early marker of acute kidney injury in adult critically ill patients: A prospective study☆,☆☆

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Abstract

Purpose: The aim of the study was to assess the ability of plasma neutrophil gelatinase-associated lipocalin (pNGAL) to predict acute kidney injury (AKI) in adult intensive care unit (ICU) patients.

Methods: All consecutives patients admitted to 3 ICUs were enrolled in this prospective-observational study. Plasma neutrophil gelatinase-associated lipocalin was analyzed at ICU admission. Risk, injury, failure, loss, and end-stage kidney (RIFLE) criteria were calculated at admission and for each day during the first week. Patients were classified according to whether they met the threshold for RIFLE criteria (RIFLE 0 or 1) at admission and during the first week. Four groups were identified: RIFLE (0-0), (1-1), (1-0), and (0-1).

Results: During this 1-month period, 88 patients were included in the study. Thirty-six patients met the criteria for RIFLE 0-0 with a mean pNGAL of 98 ± 60 nmol/L, 22 for RIFLE 1-1 with a mean pNGAL of 516 ± 221 nmol/L, and 20 patients had no AKI at admission but develop AKI at 48 hours (24-96 hours) (RIFLE 0-1) with a pNGAL of 342 ± 183 nmol/L. Ten patients met the criteria for RIFLE 1-0 and had a mean pNGAL of 169 ± 100 nmol/L. Using a cutoff of 155 nmol/L, sensitivity and specificity to predict AKI were 82% and 97%, respectively (area under the curve [AUC] = 0.92 [0.852-0.972];

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$P = .001$). Looking at the patients without AKI at admission (n = 56) and who developed (n = 20) or did not develop (n = 36) AKI, receiver operating characteristic curve analysis was as follows: AUC = 0.956 (0.864-0.992). Sensitivity was 85% and specificity was 97%. Of the 7 patients who required renal replacement therapy, all of them had pNGAL of more than 303 nmol/L (AUC = 0.788 [0.687-0.868]). **Conclusion:** Plasma neutrophil gelatinase-associated lipocalin at ICU admission is an early biomarker of AKI in adult ICU patients. Plasma neutrophil gelatinase-associated lipocalin increased 48 hours before RIFLE criteria.

1. Introduction

Acute kidney injury (AKI) is a common complication of critical illness and is associated with high mortality and has a separate independent effect on the risk of death [1]. In the overall population of patients who present with AKI during their intensive care unit (ICU) stay (7%-10% of ICU patients), 60% present AKI at ICU admission, and 40% within the first week [2]. An early detection of patients at high risk of AKI may allow for the clinical application of early renoprotective interventions. By the time renal dysfunction is detected by using serum creatinine (SCr) level, a substantial portion of renal function may have already been lost [3] and interventions may not be possible to correct the renal dysfunction.

An early marker of AKI, similar to troponin in acute myocardial disease, may permit the treatment and prevention of renal injury extension (avoid glycopeptides and aminoglycosides, prevent or avoid contrast-induced nephropathy, maintain positive fluid balance…) and help physicians for the timing of renal replacement therapy (RRT) [4]. Neutrophil gelatinase-associated lipocalin (NGAL) is a novel biomarker for which levels are increased within hours after a nephrotoxic, ischemic, or septic insult [5-9]. Recently, Dent et al [5] have shown that rapid and reliable measurements of plasma NGAL (pNGAL) are obtained using the newly developed point-of-care Triage NGAL Test device. In this study, pNGAL is described as an early predictive biomarker of AKI, morbidity, and mortality after pediatric cardiopulmonary bypass. It is unknown whether this association between pNGAL and AKI can be extrapolated to the adult critical care setting, in which the population is heterogeneous, and AKI etiology and timing are often unclear. We studied pNGAL concentrations in a cohort of adult critically ill patients with the following goals: to determine whether there is an association between pNGAL and AKI in this heterogeneous group; to determine the extent to which pNGAL concentrations increase before SCr level in the setting with unknown timing of initial kidney injury; and to evaluate the sensitivity and specificity of pNGAL to predict the clinical course of AKI.

2. Methods

After written informed consent was obtained, all consecutive patients admitted in 3 ICUs of the same institution during a 1-month period were enrolled in this observational study. Patients with end-stage renal disease (patients who need chronic RRT), recent renal transplantation, or medical history of chronic kidney disease (patient with a known decrease in filtration glomerular rate) were excluded. The study protocol and consent forms were approved by the ethic committee of our institution.

2.1. Clinical data collection

The following clinical variables were evaluated: patient age, sex, height, and weight; admission and discharge diagnoses; vasopressor use; RRT; mechanical ventilation; presence of sepsis; and 28-day mortality. Hemodynamic was monitored continuously and urine output every 2 hours. Simplified Acute Physiologic Score 2 and Sequential Organ Failure Assessment score were calculated at ICU admission and on each day for the Sequential Organ Failure Assessment score.

2.2. Laboratory data collection

We measured NGAL concentration in patient plasma samples. Blood samples were collected within the first 2 hours of ICU admission. Serum creatinine level and other standard biologic parameters required by the clinician were analyzed in the biochemistry department where the blood sample for NGAL measurement was centrifuged and quickly frozen at −80°C. All samples were analyzed in duplicate after the inclusion period with the Triage Meter (Boisite, San Diego, CA); intraassay and interassay coefficient of variation was, respectively, 11% and 13.5% (Biosite, Inverness Medical Innovations Inc, San Diego, Calif). The NGAL concentration was blinded to the clinical staff managing the patients, and laboratory personnel was blinded to AKI state of patients. A cutoff value of 150 pg/mL was used to separate normal from higher values [5]. Serum creatinine level values (Modular P, Roche Diagnostics GmbH, Mannheim, Germany) were obtained prospectively as part of routine patient care from the day of admission in ICU up until ICU discharge. Patients were classified by risk, injury, failure, loss, and end-stage kidney (RIFLE) criteria for AKI at ICU admission [10]. Development of AKI was defined as a 50% or greater increase in SCr level from baseline. If baseline creatinine level was not known in the recent medical history of the patient, it was