Difference of Admission Neutrophil Gelatinase-Associated Lipocalin Concentration Between Patients Developing and Not Developing Acute Kidney Injury or Need for Acute Dialysis: An Ancillary Individual-Study Data Meta-Analysis (INDICATE–AKI)

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Abstract

Rationale & ObjectivePatients admitted to the emergency department, the intensive care unit (ICU), and after cardiac surgery are at increased risk of developing adverse kidney events. Assessment of neutrophil gelatinase-associated lipocalin (NGAL) may facilitate renal risk prediction. However, the difference in NGAL-concentrations at admission in patients developing and not developing adverse events is unclear.Study DesignAn ancillary meta-analysis to a previous systematic review and meta-analysis using reanalyzed individual study-data from prospective clinical studies to compare NGAL concentrations measured using clinical laboratory platforms at patient admission. The study followed the Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data guideline.Setting & Study PopulationsStudies of adults investigating acute kidney injury (AKI) of all stages, severe AKI (stage injury or failure), and acute initiation of renal replacement therapy (RRT) in the setting of cardiac surgery, emergency department, or intensive care unit using either urinary or plasma NGAL concentrations measured on clinical laboratory platforms.Selection Criteria for StudiesData inclusion was limited to the individual study-level data from the predecessor study.Data ExtractionThis study used individual study-level data acquired using the protocol of a previous study, which was accomplished by individual authors' reassessment of their study data.Analytical ApproachClassification of AKI was harmonized among studies. Prespecified data comparison was performed for urine and plasma specimens for the outcome measures AKI, severe AKI, and acute RRT-initiation. Random effects meta-analyses were performed using the inverse variance method and the DerSimonian and Laird heterogeneity estimator.ResultsIn total, 30 data sets from 26 studies were included. The estimated mean difference of urine NGAL concentrations was 125 (95% CI, 57.33-193.54) ng/mL for AKI, 317 (95% CI, 134.95-499.82) ng/mL for severe AKI, and 331 (95% CI, 71.36-592.06) ng/mL for RRT. For plasma NGAL concentrations, the estimated mean differences were 86.04 (95% CI, 51.74-120.34) ng/mL for AKI, 150.52 (95% CI, 80.27-220.76) ng/mL for severe AKI, and 129.83 (95% CI, 79.03-180.63) ng/mL for RRT. There were subgroup differences for the clinical setting, but not for the use of the urine output criterion. Multiple studies showed elevated NGAL concentrations in patients without serum creatinine concentration-based AKI, likely identifying patients with suspected AKI stage 1S (subclinical AKI).LimitationsImperfect harmonization of data across studies because of their original protocols.ConclusionsNGAL concentration differences may facilitate identification of patients at risk of AKI or with suspected AKI stage 1S at admission. Heterogeneity and variability across studies, specimen types, and settings emphasize the importance of interpreting NGAL values within the specific clinical context and patient population.Study RegistrationThe International Database of Prospectively Registered Systematic Reviews reg. no.: CRD42016042735. Version of Record 1.2.Plain-language SummaryPatients admitted to the intensive care unit, the emergency department, or following cardiac surgery are at increased risk of acute kidney injury (AKI). Neutrophil gelatinase-associated lipocalin (NGAL) is a biomarker that may help stratify AKI risk. This meta-analysis pooled and reanalyzed data from prospective studies measuring NGAL levels at patient admission and systematically compared them in those patients who developed AKI or required renal replacement therapy with those who did not. Higher NGAL levels were found to be associated with unfavorable outcomes. However, variability across studies and settings was observed. Interestingly, some patients showed elevated NGAL levels despite not being affected by serum creatinine-based AKI, suggesting

NGAL levels may reflect subclinical AKI (stage 1S). These findings highlighted the need to interpret NGAL concentrations contextually within clinical settings.

Author keywords

Acute kidney injury; clinical decision making; meta-analysis; neutrophil gelatinase-associated lipocalin; NGAL; renal replacement therapy; renal risk assessment; subclinical AKI

Indexed keywords

EMTREE drug terms

neutrophil gelatinase associated lipocalin

EMTREE medical terms

acute kidney failure; adverse event; Article; blood level; clinical chemistry; comparative study; dialysis; emergency ward; heart surgery; hospital admission; human; injury severity; medical intensive care unit; meta analysis; outcome assessment; patient identification; patient risk; post hoc analysis; Preferred Reporting Items for Systematic Reviews and Meta-Analyses; renal replacement therapy; risk assessment; time factor; urine level

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