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Original Investigation

Acute Kidney Injury Incidence in Noncritically Ill Hospitalized Children, Adolescents, and Young Adults: A Retrospective Observational Study

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Background: Acute kidney injury (AKI) has been characterized in high-risk pediatric hospital inpatients, in whom AKI is frequent and associated with increased mortality, morbidity, and length of stay. The incidence of AKI among patients not requiring intensive care is unknown.

Study Design: Retrospective cohort study.

Setting & Participants: 13,914 noncritical admissions during 2011 and 2012 at our tertiary referral pediatric hospital were evaluated. Patients younger than 28 days or older than 21 years of age or with chronic kidney disease (CKD) were excluded. Admissions with 2 or more serum creatinine measurements were evaluated.

Factors: Demographic features, laboratory measurements, medication exposures, and length of stay.

Outcome: AKI defined as increased serum creatinine level in accordance with KDIGO (Kidney Disease: Improving Global Outcomes) criteria. Based on time of admission, time interval requirements were met in 97% of cases, but KDIGO time window criteria were not strictly enforced to allow implementation using clinically obtained data.

Results: 2 or more creatinine measurements (one baseline before or during admission and a second during admission) in 2,374 of 13,914 (17%) patients allowed for AKI evaluation. A serum creatinine difference $\geq$0.3 mg/dL or $\geq$1.5 times baseline was seen in 722 of 2,374 (30%) patients. A minimum of 5% of all noncritical inpatients without CKD in pediatric wards have an episode of AKI during routine hospital admission.

Limitations: Urine output, glomerular filtration rate, and time interval criteria for AKI were not applied secondary to study design and available data. The evaluated cohort was restricted to patients with 2 or more clinically obtained serum creatinine measurements, and baseline creatinine level may have been measured after the AKI episode.

Conclusions: AKI occurs in at least 5% of all noncritically ill hospitalized children, adolescents, and young adults without known CKD. Physicians should increase their awareness of AKI and improve surveillance strategies with serum creatinine measurements in this population so that exacerbating factors such as nephrotoxic medication exposures may be modified as indicated.

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INDEX WORDS: Acute kidney injury (AKI); acute renal failure (ARF); serum creatinine; incidence; nephrotoxicity; medication exposure; inpatient pediatrics; children, adolescents, young adults, electronic medical records (EMRs); KDIGO AKI criteria.

Clinical manifestations of acute kidney injury (AKI) encompass a spectrum from subtle changes in glomerular filtration rate (GFR) to symptomatic end-organ failure. In hospitalized children, adolescents, and adults, AKI is associated with increased mortality, increased length of stay, permanent loss of kidney function, and risk for future chronic kidney disease (CKD).[1-5] Previous studies reporting the incidence and sequelae of AKI in younger patients have focused on high-risk patient populations. Cohorts have been limited to those with nephrotoxic medications,[3,6-8] cardiac surgery/bypass,[9,10] sepsis,[11,12] or admission to an intensive care unit.[3,4,13-15] Due to patient selection, these may not accurately convey overall AKI incidence.

Case definitions for AKI have been based on diagnostic codes, laboratory data, and/or estimated GFR. International expert consensus definitions assess the degree of change from baseline in serum creatinine or estimated creatinine clearance values, and some consider urinary output.[4,16,17] The KDIGO (Kidney Disease: Improving Global Outcomes) definition requires a serum creatinine concentration increase $\geq$0.3 mg/dL or $\geq$1.5-fold increase from baseline. This increase in creatinine level serves as a proxy for significant change in true kidney function from baseline. The KDIGO definition also includes specific threshold and time window requirements for the change in creatinine level (increase by 0.3 mg/dL

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in 48 hours or increase by 1.5-fold in 7 days), urine output cutoffs, and estimated GFRs for establishing the diagnosis of AKI. The incidence of AKI by the KDIGO criteria in noncritically ill young patients has not been established.

Using a large retrospective analysis of electronic medical records (EMRs) of admissions to a tertiary-care children's hospital over a 2-year period, we sought to determine the incidence of AKI in noncritically ill children, adolescents, and young adults using KDIGO serum creatinine criteria with modifications to allow ascertainment from clinically obtained EMR data. We also characterized features that have been associated with AKI in other settings, such as nephrotoxic drug exposure, length of stay, and contrast exposure.

METHODS

This study was approved by the Vanderbilt University Institutional Review Board; individual parental consent was waived.

Population

The most recent admission of patients aged 28 days through 21 years admitted to the Monroe Carell Jr Children's Hospital at Vanderbilt from January 1, 2011, through December 31, 2012, were considered for this study. Exclusion criteria were intensive care during the admission or pre-existing CKD defined as 2 or more related *International Classification of Diseases, Ninth Revision* (*ICD-9*) or *Current Procedural Terminology* codes preceding admission (Table S1, available as online supplementary material). Although those with CKD are also at risk for superimposed AKI, we sought to assess patients without pre-existing kidney disease. Patients were included irrespective of their indication for admission or admitting service.

Clinical Data

Demographic data included age, sex, race, and ethnicity, as recorded in the patient's EMR. Clinical parameters included length of hospital admission, weight, inpatient medications (except those administered during operations), and clinical laboratory values. Weight is represented as a z score, or as standard deviations from the mean for age and sex.[18] Nephrotoxic medications were categorized using a modified Delphi method as follows: group 1 (high risk): nephrotoxin as single agent; or group 2 (moderate risk): nephrotoxin in at-risk clinical situation or in conjunction with additional agent by their relative contribution to the development of AKI (Table S2). The discharge diagnosis, based on *ICD-9* code, for each admission was obtained from the hospital administrative database. Data outliers underwent manual verification, and filters were implemented to ensure data validity. Specifically, all weight measurements with negative values were excluded. Weight z scores above 5 and below -5 were excluded. Laboratory results with non-numeric values were manually reviewed to ensure that no valid results were contained in the entry. Laboratory values that were below or above the limits of the assay were assigned the numeric minimum or maximum, as indicated (Table S3). Extreme values for reported laboratory results were manually verified in the EMR. Comparisons between groups were conducted with Wilcoxon test for continuous data or Pearson χ^2 test for categorical data. Comparisons between stages of AKI were conducted with a proportional odds test. When proportional odds assumptions were violated, the Cochran-Armitage trend test for proportions or Pearson χ^2 test was used.

AKI Definition and Severity

For a patient to qualify for AKI evaluation, at least 2 creatinine measurements were required: one during the baseline time window and a second on a different day during the admission (Fig 1). Baseline was defined as the lowest creatinine value measured 90 days before admission through the first week of admission. This baseline measurement may have occurred before or after the increased creatinine measurement leading to the AKI classification. This allowed evaluation of AKI status for patients for whom no serum creatinine was measured until after the onset of AKI. Inpatient creatinine measurements were defined as those obtained in the 24 hours prior to admission through discharge. In our data set, admission time reflected the entry of the admission order into the EMR. By including the 24 hours prior to the admission order, laboratory evaluations performed in the emergency department or outpatient clinic portion of the patient's hospitalization were also captured. Patients with one creatinine measurement during the admission and no additional creatinine measurements in the 90 days prior to admission were not evaluated for AKI status. Each patient with a baseline (measured up to 90 days prior to admission through the first 7 days of admission) and an inpatient creatinine value measured on a different date was evaluated and further classified as no AKI or assigned an AKI stage. Per KDIGO serum creatinine criteria,[16] a patient was classified as having AKI if any inpatient creatinine measurement was $\geq$0.3 mg/dL greater than the baseline value or $\geq$1.5-fold higher than the baseline value. The KDIGO criteria also specify time windows for the increase in creatinine values, which were not imposed due to the paucity of clinically obtained creatinine measurements in our data set.

AKI severity was defined using KDIGO stages 1 to 3 (Table S4), based on the baseline and maximum inpatient creatinine measurement. Because urine output data were not consistently available in this noncritical population, AKI was defined solely using changes in measured serum creatinine levels. Additionally, we did not estimate GFR for patients because this calculation requires an accurate height measurement during the admission.

RESULTS

During the 2-year study period, admissions for 13,914 unique patients met inclusion and exclusion criteria (Fig 2). Of these, 2,374 (17%) had both a baseline and inpatient creatinine value to allow for AKI evaluation (Table 1). The 11,540 patients not

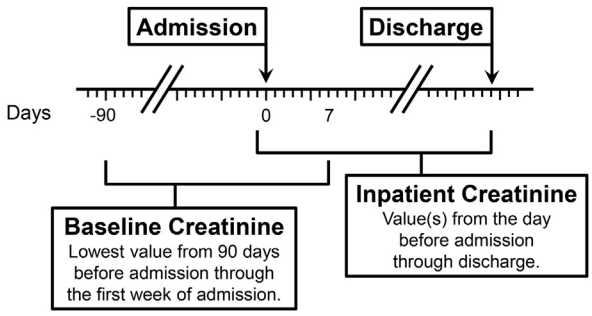

Figure 1. Schematic representation of methodology used to determine acute kidney injury status based on modified KDIGO (Kidney Disease: Improving Global Outcomes) consensus criteria. The lowest value 90 days before through 7 days after admission defined the baseline serum creatinine. The highest value 1 day before admission through discharge defined the peak serum creatinine.

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