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Acute Kidney Injury and Outcomes in Children Undergoing Noncardiac Surgery: A Propensity-Matched Analysis

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Abstract

BACKGROUND: Acute kidney injury (AKI) has been well documented in adults after noncardiac surgery and demonstrated to be associated with adverse outcomes. We report the prevalence of AKI after pediatric noncardiac surgery, the perioperative factors associated with postoperative AKI, and the association of AKI with postoperative outcomes in children undergoing noncardiac surgery.

METHODS: Patients 18 years of age who underwent noncardiac surgery with serum creatinine during the 12 months preceding surgery and no history of end-stage renal disease were included in this retrospective observational study at a single tertiary academic hospital. Patients were evaluated during the first 7 days after surgery for development of any stage of AKI, according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Patients were classified into stages of KDIGO AKI for the purposes of describing prevalence. For further analyses, patients

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DISCLOSURES

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Contribution: This author helped in manuscript writing, study design, programming, data acquisition, and data validation.

Conflicts of Interest: None.

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Contribution: This author helped as methodology advisor, with statistical analyses, and with manuscript editing.

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Contribution: This author helped as methodology advisor and with manuscript editing.

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were grouped into those who developed any stage of AKI postoperatively and those who did not. Additionally, the time point at which each patient was first diagnosed with stage I AKI or greater was also assessed. Pre-, intra-, and postoperative factors were compared between the 2 groups. A multivariable Cox proportional hazards regression model was created to examine the time to first diagnosis of AKI using all nonredundant covariates. Analysis of the association of AKI with postoperative outcomes, mortality and 30-day readmission, was undertaken utilizing propensity score-matched controls and a multivariable Cox proportional hazards regression model.

RESULTS: A total of 25,203 cases between 2013 and 2018 occurred; 8924 met inclusion criteria. Among this cohort, the observed prevalence of postoperative AKI was 3.2% (288 cases; confidence interval [CI], 2.9–3.6). The multivariable Cox model showed American Society of Anesthesiologists (ASA) status to be associated with the development of postoperative AKI. Several other factors, including intraoperative hypotension, were significantly associated with postoperative AKI in univariable models but found not to be significantly associated after adjustment. The multivariable Cox analyses with propensity-matched controls showed an estimated hazard ratio of 3.28 for mortality (CI, 1.71–6.32, $P < .001$) and 1.55 for 30-day readmission (CI, 1.08–2.23, $P = .018$) in children who developed AKI versus those who did not.

CONCLUSIONS: In children undergoing noncardiac surgery, postoperative AKI occurred in 3.2% of patients. Several factors, including intraoperative hypotension, were significantly associated with postoperative AKI in univariable models. After adjustment, only ASA status was found to be significantly associated with AKI in children after noncardiac surgery. Postoperative AKI was found to be associated with significantly higher rates of mortality and 30-day readmission in multivariable, time-varying models with propensity-matched controls.

An estimated 6 million children undergo anesthesia each year in the United States.¹ While often considered to be more resilient than adults, when complications do occur, children may carry the effects into adulthood. In the adult population, multiple recent studies have highlighted the previously unrecognized complication of acute kidney injury (AKI), estimated to occur in 7.5% of adults after noncardiac surgery and found to be associated with significant short- and long-term morbidity and mortality.^{2–4} Similar to adults, AKI in children has been increasingly recognized as a source of major morbidity in hospitalized and critically ill children.^{5–8}

AKI has been found to occur in 27% of children in intensive care units (ICUs) and 5% of hospitalized noncritically ill pediatric patients.^{7,9} AKI after pediatric cardiac surgery has been extensively studied, with an estimated prevalence of 25%–60%.^{10–12} Perioperative factors repeatedly found to be associated with pediatric postcardiac surgical AKI are young age and cardiopulmonary bypass time.^{12–14} AKI in children has been found to have significant associations with in-hospital mortality and longer length of stay (LOS), as well as far-reaching consequences such as development of chronic kidney disease (CKD), hypertension, and proteinuria.^{5–7,15–22} Chronic renal pathology at a young age is known to have profound multisystemic effects.²³

Additionally, strong associations have been demonstrated between intraoperative hypotension and AKI in the adult noncardiac surgical population, with successively higher probability of AKI with longer and lower mean arterial blood pressure thresholds.^{24–27} The

association of adult perioperative AKI with mortality is also quite strong, with those experiencing AKI postoperatively found to be 8 times more likely to die within 30 days of surgery.²⁸

Despite the known prevalence of AKI in children who are critically ill or undergoing cardiac surgery, there are currently no investigations of the burden of AKI in children undergoing noncardiac surgery. In this article, we hypothesized that AKI is a significant and underrecognized complication in the noncardiac pediatric surgical population. As a primary aim, we examined the prevalence of pediatric AKI after noncardiac surgery. Secondarily, we assessed the association between preoperative and intraoperative factors, including intraoperative hypotension, on the occurrence of AKI in this population. Lastly, we evaluated the association of AKI as an exposure variable with respect to short-term postoperative outcomes, namely in-hospital mortality and readmission.

METHODS

Patients and Data Collection

The University of California Los Angeles (UCLA) Institutional Review Board approved and waived the requirement for informed consent (IRB318–000098) for this single-center retrospective observational study. All patients 18 years of age undergoing noncardiac surgery or procedures under anesthesia between April 2013 and January 2018 at the Ronald Reagan and Santa Monica UCLA Medical Center and affiliated surgery centers were considered eligible for inclusion if they had at least 1 preoperative serum creatinine (Cr) measurement within 1 year before the procedure. As a major referral center and academic institution, our patient population included many children with high degree of complexity and need for high acuity and/or subspecialist care. In patients with >1 surgery during a single admission, only the first case was included in the analysis. Patients with end-stage renal disease (ESRD), preoperative need for renal replacement therapy (RRT), and those undergoing central venous catheter placement specifically for the purpose of RRT were excluded. The presence of ESRD was determined based on clinician-entered data in the preoperative evaluation form or presence of preoperative need for hemodialysis or peritoneal dialysis. Anesthetics for central venous catheter placement specifically for RRT were confirmed by single clinician chart review to ensure appropriate exclusion of these cases.

Preoperative and intraoperative data were obtained from routine clinical documentation entered by anesthesiology residents, attending staff, and certified registered nurse anesthetists. These data and all laboratory, medication, billing, and all clinical documentation are housed in a large perioperative data warehouse (PDW). This PDW was developed at the Department of Anesthesiology and Perioperative Medicine at UCLA and is continually validated and improved and has been described in detail elsewhere.²⁹

Definition of Terms

Perioperative Characteristics.—Preoperative patient characteristics included age, sex, height, weight, American Society of Anesthesiologists (ASA) status, procedure type, inpatient versus outpatient status, and laboratory values. The presence of preoperative CKD

and ESRD was obtained from clinician-entered data in the preoperative evaluation form. History of prematurity was determined from information obtained from UCLA birth records, as well as clinician-entered data in the preoperative evaluation form and the patient problem list. History of congenital heart disease was determined from clinician-entered data in the patient problem list. Intraoperative characteristics included type of anesthetic, duration of anesthesia, estimated blood loss (EBL), red blood cell transfusion, intraoperative antibiotics administered, and intraoperative hemodynamic monitoring data. Presence of arterial blood pressure monitoring was also noted to assess whether this could have introduced any confounding. LOS was measured as days between the surgery and discharge alive. ICU LOS was defined as any ICU time after surgery before discharge alive. Similarly, ventilator time was defined as total duration mechanical ventilation after surgery before discharge alive. Floor-to-ICU transfer were patients who received care on floor wards who required upgrade of care during their postoperative course. Outpatient to ICU transfer were cases that came from home but required immediate ICU admission postoperatively. Because of the inherent bias expected to occur in the analysis of one postoperative event (AKI) with other postoperative outcomes, these variables are included and reported in a purely descriptive manner.

Determination of Intraoperative Hypotension.—Intraoperative blood pressure thresholds were defined according to relationship to age- and sex-adjusted reference values for children undergoing anesthesia during the preparation (also referred to commonly as the preincisional) phase.³⁰ At our institution, blood pressure values are recorded automatically into the electronic medical record every minute for patients with invasive blood pressure monitoring and every 3 to 5 minutes for patients with noninvasive blood pressure monitoring. Blood pressure values examined were those that occurred between the documented anesthesia start and anesthesia stop times. The total intraoperative time in minutes with blood pressure values under the aforementioned reference thresholds were calculated for each patient, with each blood pressure value assumed to be the blood pressure during the minutes preceding the next blood pressure measurement.

Outcomes.—AKI was diagnosed using the definition of the Kidney Disease: Improving Global Outcome (KDIGO) Group definition, which looks at the serum Cr during the first 7 postoperative days.³¹ For the present analyses, we grouped all KDIGO stages of AKI into a single group and compared them to patients with no diagnosis of AKI. The KDIGO definition is more sensitive than the AKI network (AKIN) criteria and adult Risk for renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and ESRD (RIFLE) criteria. Urine output criteria were not utilized due to the inconsistency of charting. While we are aware of this shortcoming, we were cognizant that our reported prevalence of AKI may be less than the true prevalence. Patients were characterized into KDIGO stages of AKI according to whether they had a Cr increase 1.5–1.9 times baseline or a 0.3 mg/dL absolute increase (KDIGO stage 1), 2.0–2.9 times baseline (KDIGO stage 2), or 3 times baseline or greater (KDIGO stage 3). Patients were also considered to have KDIGO stage 3 if Cr reached 4.0 mg/dL, estimated glomerular filtration rate (GFR) dropped <35 mL/min/1.73 m², or new hemodialysis or new continuous RRT was initiated. For the purposes of this study, AKI was defined as KDIGO stage 1, 2, 3, or no AKI. The timestamp

for the time of the first AKI diagnosis was individualized for each patient and taken to be the time at which the patient was diagnosed with stage 1 KDIGO AKI (or higher stage if this occurred first).

Mortality evaluated was in-hospital, thus defined as death occurring within the UCLA hospital system. Thirty-day readmission also only included admission back into the UCLA system. Care was taken to ensure that no AKI diagnoses were made after a readmission. Our third aim involved studying AKI as an exposure rather than an outcome; thus, it was important that we only examine outcomes that occurred after the diagnosis of AKI.

Statistical Analysis

Differences in patient characteristics between the patients who developed postoperative AKI and those who did not were summarized using means (standard deviation) or frequencies (%) and formally assessed using univariable logistic regression models (Table 1).

Univariable and multivariable Cox models for time to AKI were then used to more rigorously evaluate association with AKI (Table 2). For this model, all variables were included except those with potential for biologic redundancy; thus, between transfusion and EBL, only transfusion was included in the model. A Cox proportional hazard regression model was utilized, which looked at the time of first AKI diagnosis as the outcome variable. In this model, patients who did not develop AKI were censored at their time of discharge. Additionally, to address the potential bias introduced by patients who died before they could develop postoperative AKI, patients who died within the first 7 days postoperatively in this model were manually censored at 7 days (the last day AKI diagnoses were observed). Type I error was addressed with Bonferroni correction with an adjusted significance criterion of 0.003 (obtained using 0.05 divided by 15, the number of variables assessed).

To assess the association of AKI with inpatient mortality and readmission (given the inherent differences between groups), we fit a propensity score model for AKI with logistic regression with AKI as outcome using all terms in Table 1 following the basic framework of Rosenbaum and Rubin.³² Patients were matched with nearest neighboring matching without replacement, with a 3:1 ratio of patients who did not develop AKI to patients who did develop AKI. An absolute standardized difference <10% was achieved with all variables, a threshold considered to represent satisfactory balance between the 2 groups.³³ We then ran “doubly robust” Cox multivariable models for both time-to-inpatient death and time-to-readmission using our propensity-matched data with AKI as a time-varying covariate (patients who did not die were censored at time of discharge after surgery). The doubly robust method, which involves including all covariates in the outcome analyses that were originally included in propensity matching, has been shown to protect against misspecification.³⁴ *P* values <0.025 for this model were considered statistically significant, with Bonferroni correction using a significance criterion of 0.05 divided by 2 for the number of variables. Statistical analyses were performed using IBM SPSS V23 (Armonk, NY), R V3.1.2 (Vienna, Austria), and SAS V9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 25,203 noncardiac surgeries or procedures were performed during the 4.8-year study time period. Of these, 23,050 index cases remained after removing subsequent cases within a patient's single admission. Out of these index cases, 13,701 (59.4%) cases were excluded for lack of preoperative Cr and 425 were excluded for ESRD. The data from the remaining 8924 cases were analyzed (Figure).

Patients had a median age of 9.0 years, median weight of 28.7 kg, and 56.6% were male. Preoperative CKD occurred at a rate of 1.6%. Congenital heart disease was present at a rate of 18.5%, and prematurity was present at a rate of 8.2%. Nearly 45% of cases were an ASA I or II, and 50% were an ASA III. Most cases were general anesthetics (70.6%). The highest represented surgical services were pediatric and general surgery, which accounted for 20% of cases, gastroenterology which accounted for 15% of cases, and cardiology which accounted for 11% of cases. Otolaryngology, urology, orthopedics, and neurosurgery accounted for 6.3%, 5.5%, 4.7%, and 4.6% of cases, respectively. Further demographic and clinical characteristics of patients are seen in Table 1 and Supplemental Digital Content, Table 1, <http://links.lww.com/AA/D141>.

Postoperative AKI was observed at an overall prevalence of 3.2% (confidence interval [CI], 2.9–3.6), with prevalence of 1.8%, 1.2%, and 0.2%, respectively, of KDIGO stages 1, 2, and 3. Univariable analysis in Table 1 shows several perioperative characteristics associated with or observed to occur in children who developed AKI. *P* values are included in Table 1 for pre-, intraoperative factors, as well as mortality and readmission to display univariable analysis results. However, no univariable analyses are shown in respect to LOS and other short-term hospitalization characteristics out of concern for bias related to timing of AKI in relationship to these variables. These variables are presented descriptively only.

Perioperative Factors Associated With AKI

All measured, nonredundant variables were inputted into a Cox proportional hazard regression model with time to any stage of AKI as the dependent variable with patients who did not develop AKI being censored at their discharge time. ASA status was found to be significantly associated with the development of postoperative AKI in children undergoing noncardiac surgery ($P < .001$) (Table 2). Estimated hazard ratios (HRs) with 95% CIs for each of these variables are shown in Table 2. Several factors which have physiological basis for hypothesizing an association were examined, including preoperative CKD and age- and sex-adjusted measures of hypotension; however, none of these variables other than ASA status was found to be significantly associated after adjustment.

Association of Intraoperative Hypotension and AKI

The association between different degrees of hypotension and AKI was evaluated to better characterize the relationship of hypotension with AKI. Unadjusted analyses showed significant associations between the development of postoperative AKI and the minutes during a case with mean arterial pressure (MAP) between 1 and 2 standard deviations below, and >2 standard deviations below, the age- and sex-adjusted mean. With inclusion of ASA

status and presence of arterial catheter within the multivariable model, the association between hypotension and AKI was no longer significant.

Association of AKI With Short-term Outcomes

Propensity score–matched analysis to examine the association between AKI and short-term outcomes started with the creation of non-AKI cohort that was matched in terms of patient and case characteristics (Supplemental Digital Content, Table 2, <http://links.lww.com/AA/D141>). A 3-to-1 match was achieved for the 284 patients who developed AKI and 852 matched patients who did not develop AKI. The unadjusted rate of all-cause in-hospital mortality observed was 8.0% vs 0.7% ($P < .001$) in children who developed AKI compared to children who did not (Table 1). All-cause in-hospital mortality in the Cox regression model using the propensity-matched dataset demonstrated an estimated 3.28 times greater HR of mortality for children who developed AKI compared to children who did not (HR = 3.28; CI, 1.71–6.32; $P < .001$). The unadjusted rate of 30-day readmission was 20.8% vs 6.8% ($P < .001$) in children who developed AKI compared to children who did not (Table 1). The estimated HR of 30-day readmission was 1.55 times higher for children who developed AKI compared those who did not, after propensity-matched adjustment (HR = 1.55; CI, 1.08–2.23; $P = .018$). After propensity-matching and time-varying adjustment, we see clearly that postoperative outcomes were significantly worse for children who developed AKI compared those who did not (Table 3).

DISCUSSION

In our cohort, AKI occurred in 3.2% of pediatric patients who underwent noncardiac surgery. Higher ASA status was found to be strongly associated with a higher risk of developing postoperative AKI in children undergoing noncardiac surgery. Time-varying Cox models with propensity-matched controls found an estimated 3.28 times higher HR of in-hospital mortality and an estimated 1.55 times higher HR of 30-day readmission among children who developed AKI after noncardiac surgery. These results point to the conclusion that AKI is a significant, and possibly underappreciated, complication in children undergoing noncardiac surgery.

The rate we observed in this cohort, 3.2% or 1 in about every 31 children, is similar to the 5% prevalence seen in hospitalized children, and much below the 27% reported prevalence in children admitted to ICUs and the 25%–60% reported prevalence after pediatric cardiac surgery.^{7,9–12} Notably, it is 4 times higher than the equivalent prevalence seen in adults, which is estimated at 0.8%.³⁵

Direct comparison between our findings and adult epidemiologic studies of postoperative AKI is fraught due to the markedly different comorbidities and physiology; however, some comparisons can be made. Adults with preexisting renal dysfunction were found to have higher prevalence of postoperative AKI, a finding not replicated in our cohort.³⁵ In some studies, female sex has been found to be associated with AKI; however, this was not found in our study.³⁵ Indeed, several factors which have physiological basis for hypothesizing an association were examined, including preoperative CKD and age- and sex-adjusted measures of hypotension; however, none of these variables other than ASA status was found to be

significantly associated after adjustment. Most importantly, the findings in regard to AKI and outcomes here mirror some of the early studies of AKI in the adult noncardiac surgical population, as they demonstrate a correlation between AKI and outcomes, in this case mortality and readmission.

In looking to examine the association between intraoperative hypotension and AKI, we were faced with the challenge of setting a threshold to identify hypotension in the pediatric population. While blood pressure almost invariably drops under anesthesia, defining hypotension in children under anesthesia is a much debated topic.³⁶ Thus, we utilized a large, multicentered observational study which recently reported age- and sex-adjusted reference nomograms for noninvasive blood pressure in children during anesthesia during the preparation or “preincisional” phase where blood pressures are frequently low.³⁰ While we looked at cumulative intraoperative duration with blood pressure levels falling <1 and 2 standard deviations of age- and sex-adjusted blood pressure levels, there may be better ways to measure hypotension in children. It is also possible that high-risk groups may have a predisposition to developing AKI that healthier children do not.

While our univariable analysis showed a significant association with intraoperative hypotension and development of postoperative AKI, our Cox proportional hazard regression model did not. Unfortunately, retrospective studies are inadequate to determine the presence of a causative relationship between intraoperative hypotension and postoperative AKI. It may simply be that sicker children are more likely to develop AKI and incidentally also more likely to be hypotensive, and indeed there is no causal relationship between pediatric hypotension and AKI. Or it may be that further delineation of covariates or high-risk pediatric populations may elucidate a relationship. Either way, the study of hypotension in pediatrics is an area with immense work still to be done.

Our propensity-matched analysis found a large and significant association between AKI and in-hospital mortality with an estimated 3.28 times higher HR of mortality for patients who developed AKI versus those who did not (Table 3). Similarly, 30-day readmission was also significantly associated with AKI, with an estimated 1.55 times higher HR of mortality for patients who developed AKI versus those who did not. We found that the development of AKI after noncardiac surgery in children is strongly associated with worse outcome. We believe that these results are of tremendous import and implicate that the development of AKI in a child appears unlikely to be a short-lived, well-tolerated phenomenon as may have previously been thought.

Our study did have some limitations. It was a single-center study at an academic tertiary institution, thus interhospital variation and variation between academic and community hospitals are bound to occur and not be captured in our study. We recognize that the patient population in our cohort likely has a higher prevalence of comorbidities than what is likely to be found in the community, and thus, results must be interpreted with appropriate attention to this factor. Also, while we did our best to identify and quantify all major potential covariates, there are several other potential factors, such as other nephrotoxic medications, vasoactive medications, fasting times, intravenous fluids, anemia, urinary tract infections, specific urologic conditions, among others that could have influenced our results.

Our models may be also subject to immortal time bias, such that patients who develop AKI (the exposure of interest) later in the study period are more likely to develop outcomes of interest. Although modeling AKI as a time-varying covariate helps adjust for this, this is still a potential limitation that cannot be completely overcome or precluded based on the data we have. Finally, as noted above, this was an observational cohort study; therefore, it is not possible to make conclusions about causal relationships between AKI, risk factors, and outcomes. Thus, while there is a physiological basis to an association between perioperative factors and AKI and AKI with postoperative outcomes, we cannot differentiate correlation from causation.

Additionally, our study was retrospective in nature and restricted to children who had a known preoperative Cr level. Healthy children frequently may not have chemistry panels ordered on a routine basis. Furthermore, similar to adult populations, for many outpatient and low-risk surgeries, a postoperative chemistry panel may never be ordered.³⁷ If the overall denominator was expanded to include patients without preoperative Cr measurements, the prevalence of AKI would have been 1.2%. However, patients with unknown Cr levels may have also had unrecognized AKI, thus 1.2% is likely an underestimate of the true prevalence. Additionally, our reported prevalence is likely below the true prevalence as we did not include urine output criteria for AKI. Regardless of the exact prevalence of AKI in our population, we believe that the overall associations between AKI and other outcomes are robust and likely clinically and physiologically significant.

From our study, we report 3 major conclusions. First, we found AKI to be a fairly common complication in children after noncardiac surgery occurring at a rate of 3.2%. Second, we found ASA status to be significantly associated with the development of AKI. Third, AKI was found to be significantly associated with worse outcomes, with over 3-fold higher estimated mortality and 1.55-fold higher estimated readmission rate, both independent of patient comorbidities and intraoperative factors. We believe that these results may be a starting point for many future studies to better identify and understand postoperative AKI in children undergoing noncardiac surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

GLOSSARY

AKI	acute kidney injury
AKIN	AKI network
ASA	American Society of Anesthesiologists
CI	confidence interval
CKD	chronic kidney disease
CONSORT	Consolidated Standards of Reporting Trials

Cr	creatinine
EBL	estimated blood loss
ESRD	end-stage renal disease
GFR	glomerular filtration rate
HR	hazard ratio
ICU	intensive care unit
KDIGO	Kidney Disease: Improving Global Outcomes
LOS	length of stay
MAP	mean arterial pressure
n/a	not applicable
PDW	perioperative data warehouse
PS	physical status
RBC	red blood cell
RIFLE	Risk for renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and ESRD
RRT	renal replacement therapy
SD	standard deviation
UCLA	University of California Los Angeles

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KEY POINTS

- **Question:** What are the prevalence, perioperative factors, and outcomes associated with acute kidney injury (AKI) after pediatric noncardiac surgery?
- **Findings:** The observed prevalence of pediatric postoperative AKI was 3.2% after noncardiac surgery, American Society of Anesthesiologists (ASA) status was found to be associated with the development of postoperative AKI, and AKI was found to be significantly associated with mortality and higher rates of 30-day readmission.
- **Meaning:** AKI after pediatric noncardiac surgery is not a rare occurrence, higher rates of AKI are seen in children with higher ASA status, and AKI is associated with adverse short-term outcomes—mortality and 30-day readmission.

Figure.
CONSORT diagram. CONSORT indicates Consolidated Standards of Reporting Trials.

Table 1.**Patient Characteristics**

	No AKI N = 8636	Any Stage AKI N = 288	P Value
Age, y	8.93 (6.02)	7.54 (6.20)	<.001
Age group			<.001
Neonate (0–30 d)	263 (3.0%)	24 (8.3%)	
Infant (31 d to 2 y)	1219 (14.1%)	57 (19.8%)	
Young child (2–6 y)	1654 (19.2%)	53 (18.4%)	
Child (6–12 y)	2013 (23.3%)	59 (20.5%)	
Adolescent (12–18 y)	3487 (40.4%)	95 (33.0%)	
Weight, kg	35.1 (24.6)	27.7 (23.1)	<.001
Sex (% male)	4896 (56.7%)	157 (54.5%)	.463
Chronic kidney disease	134 (1.6%)	11 (3.8%)	.004
Congenital heart disease	1593 (18.4%)	62 (21.5%)	.186
Prematurity	703 (8.1%)	26 (9.0%)	.589
Emergent status	475 (5.5%)	35 (12.2%)	<.001
ASA PS			<.001
I	1179 (13.7%)	6 (2.1%)	
II	2762 (32%)	36 (12.5%)	
III	4283 (49.7%)	182 (63.2%)	
IV	375 (4.3%)	58 (20.1%)	
V	22 (0.3%)	6 (2.1%)	
VI	2 (0%)	0 (0%)	
General anesthetic	6094 (70.6%)	210 (72.9%)	.389
Anesthesia duration, min	169.71 (1538.9)	186.35 (164.1)	.857
Intraoperative arterial line	771 (8.9%)	63 (21.9%)	<.001
Intraoperative nephrotoxic antibiotic	649 (7.5%)	35 (12.2%)	.004
Outpatient procedure	1523 (17.6%)	12 (4.2%)	<.001
Transfusion RBC, mL/kg	0.68 (5.54)	3.63 (12.42)	<.001
Estimated blood loss, mL/kg	0.92 (5.42)	2.15 (10.15)	<.001
Total intraoperative duration MAP <2 SD, min	2.32 (10.9)	5.43 (19.2)	<.001

	No AKI N = 8636	Any Stage AKI N = 288	P Value
Total intraoperative duration MAP 1–2 SD, min	14.00 (27.7)	18.20 (32.5)	.012
Surgical or procedural service			<.001
Cardiology	970 (11.2%)	41 (14.2%)	
Gastroenterology	1304 (15.1%)	42 (14.6%)	
General surgery	890 (10.3%)	27 (9.4%)	
Liver transplant	123 (1.4%)	26 (9%)	
Neurosurgery	411 (4.8%)	8 (2.8%)	
Orthopedics	421 (4.9%)	2 (0.7%)	
Otolaryngology	558 (6.5%)	8 (2.8%)	
Pediatric surgery	874 (10.1%)	40 (13.9%)	
Pediatrics	1403 (16.2%)	47 (16.3%)	
Radiology	509 (5.9%)	22 (7.6%)	
Urology	489 (5.7%)	21 (7.3%)	
Hospitalization characteristics			
Length of stay, d	0 (0–3)	9 (2–19)	n/a
ICU length of stay, h	0 (0–0)	0 (0–174.5)	n/a
Ventilator time, h	0 (0–0)	0 (0–4.09)	n/a
Floor-to-ICU transfer	278 (3.2%)	41 (12.9%)	n/a
Outpatient ICU admission	12 (0.1%)	4 (1.4%)	n/a
Outcomes			
Mortality, in-hospital	57 (0.7%)	23 (8.0%)	<.001
Readmission, 30 d	584 (6.8%)	60 (20.8%)	<.001

Total intraoperative duration MAP <2 SD and MAP 1–2 SD refers to the total duration of time intraoperatively in which patients' MAP was <2 SD or between 1 and 2 SD of age- and sex-adjusted reference values, respectively.³⁰

Data reported as mean (standard deviation) for continuous variables, number (percent) for binary variables, and mean (interquartile range) for time-based variables. Additional surgical or procedural services seen in Supplemental Digital Content, Table 1, <http://links.lww.com/AA/D141>. LOS was measured as days between the surgery and discharge alive. ICU LOS was defined as any ICU time after surgery before discharge alive. Similarly, ventilator time was defined as total duration mechanical ventilation after surgery before discharge alive. Floor-to-ICU transfer were patients received care on floor wards who required upgrade of care during their postoperative course. Outpatient to ICU transfer were cases that came from home but required immediate ICU admission postoperatively. Because of the inherent bias expected to occur in the analysis of one postoperative event (AKI) with other postoperative outcomes, hospitalization characteristics are reported in a purely descriptive manner.

Abbreviations: AKI, acute kidney injury; ASA PS, American Society of Anesthesiologists physical status; ICU, intensive care unit; LOS, length of stay; MAP, mean arterial pressure; n/a, not applicable; RBC, red blood cell; SD, standard deviation.

Table 2.

Multivariable and Univariable Cox Analysis of Factors Associated With AKI

N = 8924	Univariable Cox Analysis		Multivariable Cox Analysis		Units/Reference for Hazard Ratio
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	
Age	0.99 (0.98–1.01)	.488	1.04 (1.00–1.09)	.038	1 y
Weight	1.00 (0.99–1.00)	.048	0.99 (0.98–1.00)	.039	1 kg
ASA PS	1.85 (1.59–2.15)	<.001	1.96 (1.64–2.34)	<.001	1 unit
Sex	0.94 (0.75–1.19)	.626	0.89 (0.70–1.12)	.324	Male
Chronic kidney disease	1.89 (1.00–3.54)	.049	1.56 (0.82–2.95)	.175	
Congenital heart disease	1.13 (0.85–1.50)	.395	0.89 (0.65–1.21)	.324	
Prematurity	0.78 (0.52–1.17)	.229	0.66 (0.42–1.02)	.061	
Emergent status	1.49 (1.05–2.12)	.027	1.28 (0.85–1.92)	.235	
General anesthetic	0.75 (0.58–0.98)	.033	0.74 (0.55–1.01)	.055	
Anesthesia duration	0.98 (0.94–1.03)	.442	0.98 (0.93–1.04)	.516	1 h
Intraoperative arterial catheter	1.18 (0.89–1.57)	.240	0.94 (0.65–1.35)	.727	
Intraoperative nephrotoxic antibiotic	1.01 (0.71–1.44)	.971	1.04 (0.71–1.51)	.843	
Outpatient procedure	1.27 (0.87–1.86)	.222	1.32 (0.90–1.96)	.160	
Transfusion RBC	1.12 (1.04–1.20)	.001	1.07 (0.99–1.16)	.104	10 mL/kg
Total intraoperative duration MAP <2 SD	1.03 (0.97–1.09)	.413	1.00 (0.93–1.07)	.987	10 min

Total intraoperative duration MAP <2 SD refers to the total duration of time intraoperatively in which patients' MAP was <2 SD of age- and sex-adjusted reference values.³⁰ All measured, nonredundant pre- and intraoperative variables were included in the multivariable Cox proportional hazard regression model for time to development of AKI; no variable selection methods were considered. Patients who did not develop AKI were censored at their time of discharge, and patients who died within the first 7 d postoperatively were manually censored at 7 d (the last day AKI diagnoses were recorded). Bonferroni adjusted significance criterion 0.003.

Abbreviations: AKI, acute kidney injury; ASA PS, American society of anesthesiologists physical status; CI, confidence interval; MAP, mean arterial pressure; RBC, red blood cell; SD, standard deviation.

Table 3.**Propensity-Matched Adjusted Outcomes**

Propensity-Matched Cohorts	AKI n = 284	No AKI n = 852	Hazard Ratio (95% CI)	P Value
Mortality, in-hospital	23 (8.1%)	22 (2.6%)	3.28 (1.71–6.32)	<.001
Readmission, 30 d	60 (21.1%)	93 (10.9%)	1.55 (1.08–2.23)	.018

Data reported as number (percentage). These results are based on propensity-matched cohorts created using a propensity score model for AKI with logistic regression with AKI as outcome which included all terms in Table 1; a 3:1 matching ratio and absolute standardized difference <10% was achieved with all variables (Supplemental Digital Content, Table 2, <http://links.lww.com/AA/D141>). Multivariable Cox regression models with AKI as a time-dependent covariate for mortality and 30-day readmission were then applied to these cohorts. Bonferroni adjusted significance criterion 0.025.

Abbreviations: AKI, acute kidney injury; CI, confidence interval.