Development and Validation of a Web-Based Prediction Model for AKI after Surgery

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Abstract

Background AKI after surgery is associated with high mortality and morbidity. The purpose of this study is to develop and validate a risk prediction tool for the occurrence of postoperative AKI requiring RRT (AKI-dialysis).

Methods This retrospective cohort study had 2,299,502 surgical patients over 2015–2017 from the American College of Surgeons National Surgical Quality Improvement Program Database (ACS NSQIP). Eleven predictors were selected for the predictive model: age, history of congestive heart failure, diabetes, ascites, emergency surgery, hypertension requiring medication, preoperative serum creatinine, hematocrit, sodium, preoperative sepsis, and surgery type. The predictive model was trained using 2015–2016 data (n=1,487,724) and further tested using 2017 data (n=811,778). A risk model was developed using multivariable logistic regression.

Results AKI-dialysis occurred in 0.3% (n=6853) of patients. The unadjusted 30-day postoperative mortality rate associated with AKI-dialysis was 37.5%. The AKI risk prediction model had high area under the receiver operating characteristic curve (AUC; training cohort: 0.89, test cohort: 0.90) for postoperative AKI-dialysis.

Conclusions This model provides a clinically useful bedside predictive tool for postoperative AKI requiring dialysis.

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Introduction

Postoperative dialysis-requiring AKI is a serious medical complication of surgery, with a rising incidence and significant morbidity and mortality. Postoperative AKI increases 5-year mortality regardless of level of injury and extent of kidney recovery (1). For patients who develop AKI requiring RRT (AKI-dialysis) after elective surgery, 90-day mortality rate was reported to be 42%; among patients undergoing cardiac surgery, dialysis conferred a 30-day mortality rate of 63.7% as compared with 4.3% without AKI (2,3). Of patients who survived the episode of AKI-dialysis, 27.2% required chronic dialysis, with its attendant morbidity and cost (3,4). It is important to identify patients at high risk of postoperative AKI as preventative measures may lower the risk. Implementation of the Kidney Disease Improving Global Outcomes (KDIGO) care bundles consisting of optimization of volume status and hemodynamics, avoidance of nephrotoxic drugs, and preventing hyperglycemia showed reduction of postoperative AKI (5).

Preoperative assessment of surgical risk is valuable for determining appropriateness of surgery, facilitating multidisciplinary surgical planning, and engaging patients in shared decision making (6). Tools for cardiac and pulmonary risk stratification have been widely adopted. Even though AKI prediction tools have been reported in the literature, these tools have not been incorporated into daily clinical practice (7–10). Existing postoperative AKI models are on the basis of small datasets or are specific to patients undergoing cardiac surgery (11–15). The universal American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) Surgical Risk Calculator includes postoperative renal failure as one of its eight outcomes (16). The NSQIP surgical risk calculator does not use preoperative serum creatinine as a predictor, which makes it difficult to differentiate postoperative AKI risk between patients with normal kidney function and patients with advanced CKD.

Establishing an AKI risk prediction model for surgical patients, including the risk for RRT, is an unmet clinical need. The objective of this study is to develop and validate an AKI risk calculator using data from the NSQIP database.

Materials and Methods

Study Participants

Data were obtained from the ACS NSQIP database, which collects clinical data from >500 United States hospitals, including patient demographics, medical conditions, laboratory data, and 30-day postoperative outcomes, collected by trained surgical clinical

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reviewers (17,18). Patients undergoing surgery at participating hospitals from 2015 to 2017 were included (19). The dataset from 2015 to 2016 was used to develop the model, whereas the dataset from 2017 was held for validation. Patients who already had an NSQIP-assessed procedure within the previous 30 days were excluded (20). The study was approved by the Thomas Jefferson University Institutional Review Board, and informed consent was waived.

Outcome

The primary outcome of interest was AKI-dialysis within 30 days of surgery, a time frame chosen on the basis of the ACS NSQIP definition. ACS NSQIP defines AKI-dialysis as "worsening of renal dysfunction postoperatively requiring hemodialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, or ultrafiltration in a patient who did not require dialysis preoperatively" (20). Instructions from the organization state that if a patient refuses a recommendation for dialysis, they should still be coded as developing AKI-dialysis as dialysis was deemed necessary (20).

The secondary outcome was postoperative major adverse kidney event (Postop-MAKE), a composite of AKI-dialysis or 30-day postoperative AKI (a rise in serum creatinine of >2 mg/dl from preoperative value but with no requirement for postoperative dialysis).

Data Analyses

We analyzed previously described risk factors for AKI, including demographic factors, medical history, current medical condition (*e.g.*, presence of sepsis and American Society of Anesthesiologists class), and preoperative functional status. Multiple preoperative laboratory tests were analyzed, including serum sodium, creatinine, platelets, and hematocrit. Participant risk factors were compared using the chi-squared test for categorical variables and the Wilcoxon test for continuous variables. Multivariable logistic regression was performed with predictor candidates to determine the significance of their associations with the outcome.

Separate categories were made for missing values of laboratory concentrations of serum hematocrit. Backward elimination with P-value cutoff of 0.01 was used to select predictor variables with lowest P values. The model was trained on 2015–2016 cohort data and tested on 2017 cohort.

GridSearchCV was used to perform five-fold crossvalidation to select the best model parameters. The dataset from year 2017 (n=811,778) was used to further test and validate the predictive model. Area under the receiver operating characteristic curve (AUC) was used for model evaluation. Sensitivity analysis was performed after removing emergency cases from the cohort. TRIPOD statement was followed for this study.

Statistical analysis was performed with Python (version 3.65), Statsmodels (version 0.8.0), and R programming (RStudio version 1.1.463). Scikit-learn was used for the web-based model.

Results

Study Population

The study included 2,299,502 patients from 2015 to 2017; 56.4% were women. Patients from 2015 to 2016 (n=1,487,724) were included in the cohort to develop the model; 811,778 patients from 2017 were included in the validation cohort. Table 1 shows the characteristics of study patients for the years from 2015 to 2017. In total, 0.3% (n=6853) of patients developed AKI-dialysis, and 0.59% (n=13,482) of patients developed Postop-MAKE.

Patients who required dialysis were older (66.2 versus 58.5 years, P<0.001); had higher preoperative serum creatinine level (1.97 versus 0.92 mg/dl, P<0.001); and were

Table 1. Patient characteristics (2015–2017)

Characteristics	No AKI with Dialysis, n=2,292,649	AKI with Dialysis, n=6853
Age, mean (±SD)	58.5 (±16.4)	66.2 (±13.6)
Men, %	43.52	61.67
American Society of Anesthesiologists class, %		
1	5.80	0.28
2	42.41	6.89
3	45.35	45.56
4	6.27	40.62
5	0.17	6.65
Diabetes, %	17.22	34.26
Disseminated cancer, %	2.72	5.92
Smoker within 1 yr, %	17.77	24.19
Chronic obstructive pulmonary disease, %	4.94	14.59
Ascites, %	0.34	3.71
Congestive heart failure, %	0.90	8.84
Hypertension requiring medication, %	49.32	74.20
Steroid, %	4.03	9.54
Weight loss, %	1.38	4.71
Bleeding disorder, %	4.53	17.82
Emergency surgery, %	10.08	37.84
Serum sodium, mEq/L	139.2	138.1
Serum creatinine, mg/dl	0.92	1.97
White blood cell, $\times 10^9$/L	8.2	11.4
Hematocrit, %	39.8	35.3
Platelet, $\times 10^9$/L	249.5	233.0

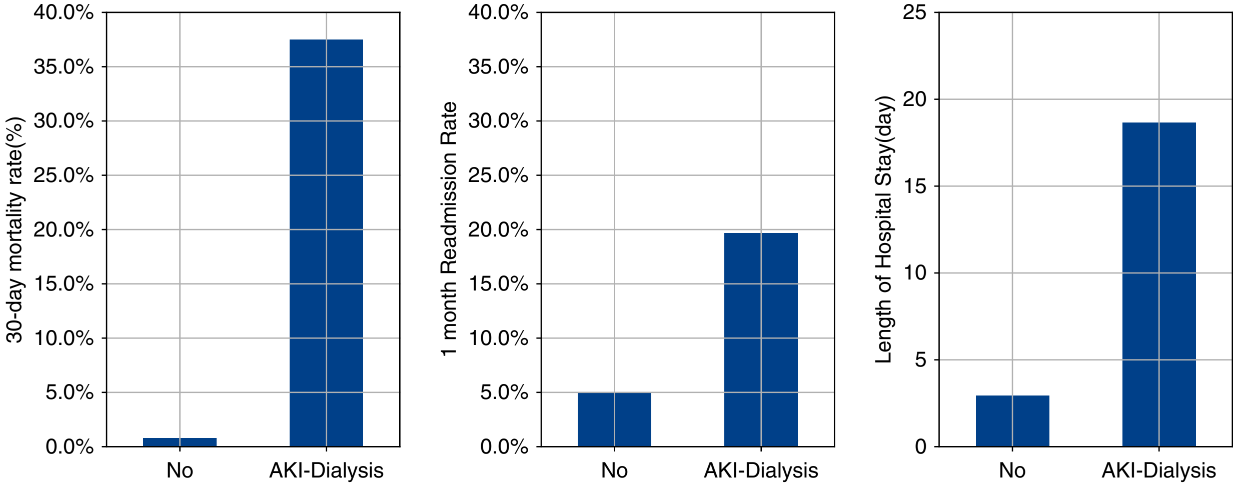

Figure 1. | **Significant differences in thirty-day unadjusted mortality, hospital readmission rate and length of stay in patients who developed AKI requiring dialysis.** AKI-dialysis, AKI requiring RRT.

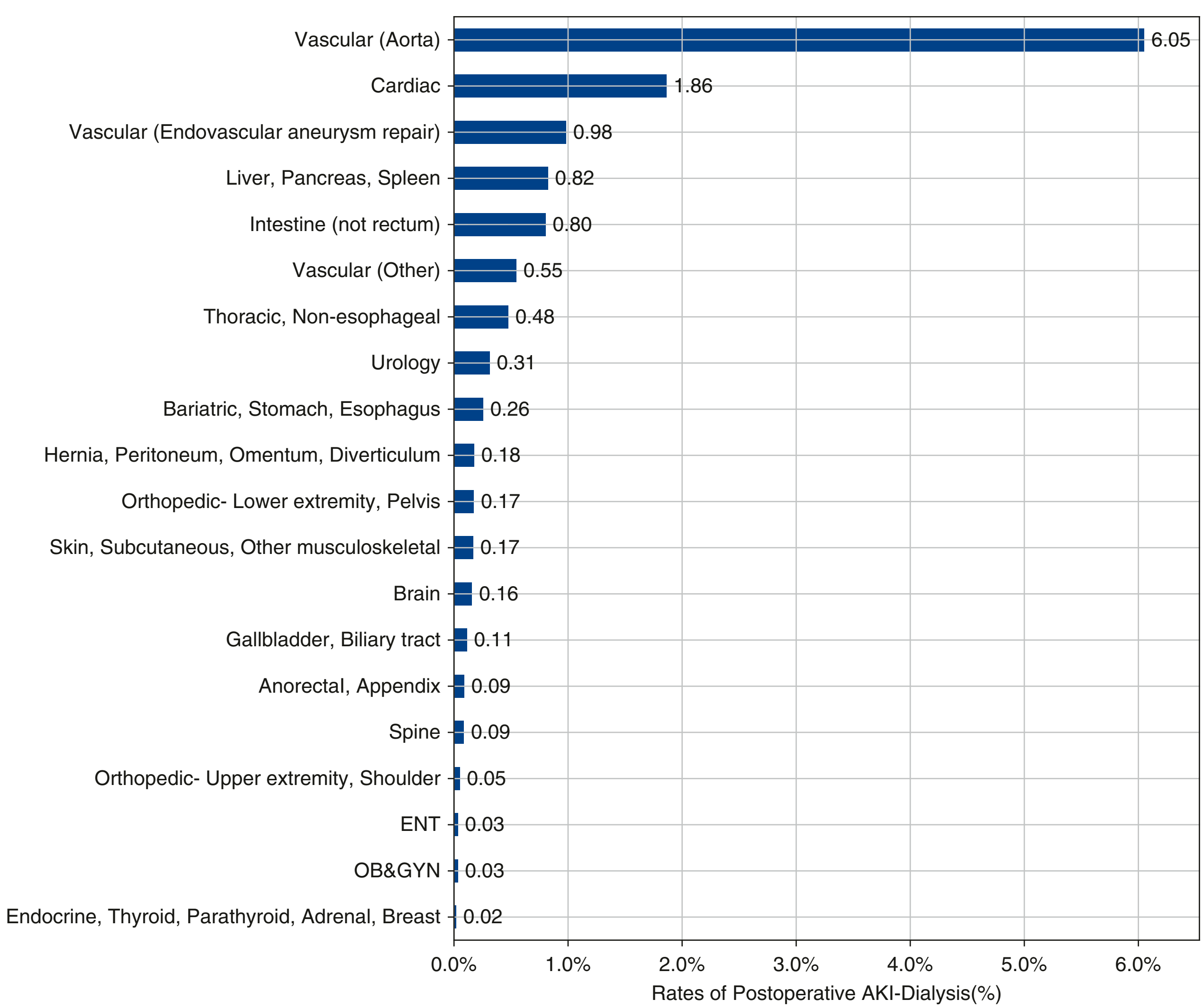

Figure 2. | **Differences in unadjusted rates of postoperative AKI requiring dialysis according to surgery type.** AKI-dialysis, AKI requiring RRT; ENT, Ear, Nose, Throat: OB&GYN, Obstetrics and Gynecology.

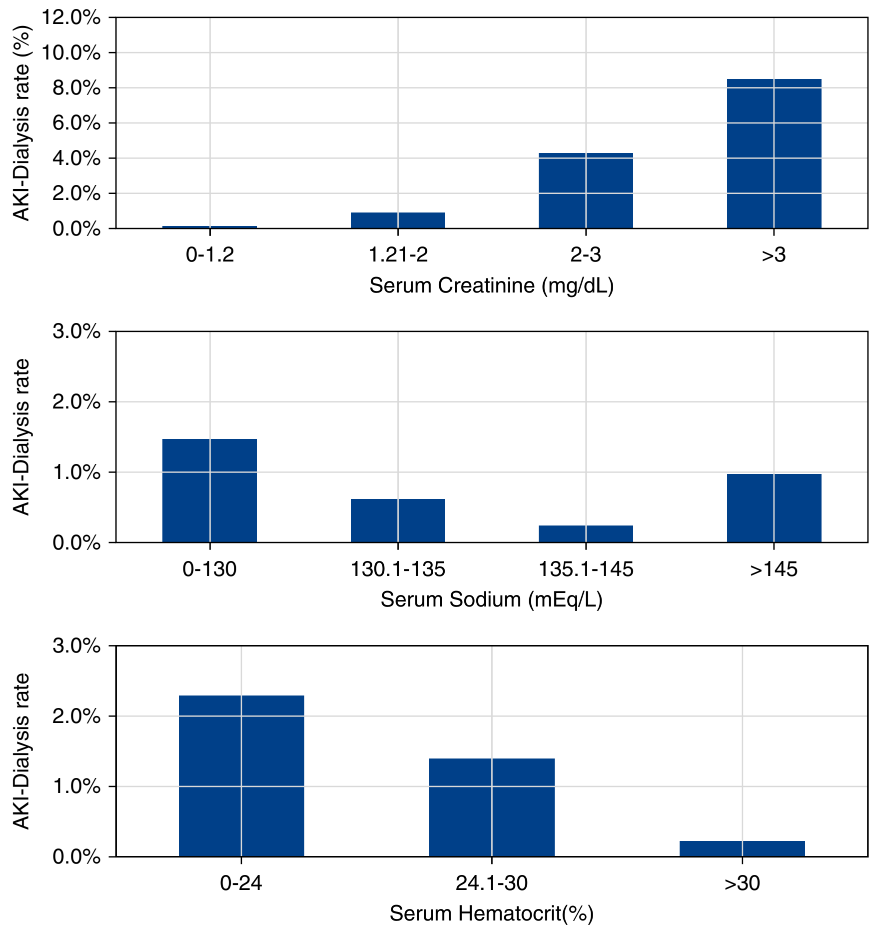

Figure 3. | Significant differences in unadjusted risk of postoperative AKI requiring dialysis according to preoperative serum creatinine, sodium, and hematocrit. AKI-dialysis, AKI requiring RRT.

more likely to have congestive heart failure (8.84% versus 0.90%, $P<0.001$), diabetes (34.26% versus 17.22%, $P<0.001$), or other comorbidities. They were more likely to have undergone emergency surgery (37.84% versus 10.08%, $P<0.001$). Ascites was defined by the presence of fluid accumulation in the peritoneal cavity noted on physical examination, abdominal ultrasound, or abdominal computed tomography/magnetic resonance imaging within 30 days prior to primary procedure (20).

Supplemental Figure 1 shows a flowchart of study participants. Supplemental Tables 1 and 2 show training and validation cohort patient characteristics.

Mortality, Readmission, and Length of Stay Associated with AKI

Figure 1 shows a high unadjusted 30-day postoperative mortality rate (37.5%) from 2015 to 2017 for patients who developed AKI-dialysis compared with those who did not. The rate of 30-day hospital readmission was also higher in these patients (19.7% versus 5.0%). The patients who developed AKI-dialysis also had increased length of hospital stay (18.7 versus 2.9 days).

Supplemental Figure 2 illustrates unadjusted 30-day mortality rates after operation among patients who developed AKI requiring dialysis according to surgery types from 2015 to 2017. These varied widely, ranging from 16.2% to 53.3%. Although patients undergoing ENT surgery had a high mortality rate, the incidence of AKI-dialysis was low at 0.03%; 1.86% of patients who underwent cardiac surgery developed AKI-dialysis, with a mortality rate of 37.9%. Another study showed that the unadjusted all-cause mortality among patients requiring RRT after cardiac surgery was 64% at 1 year (21). Figure 2 shows unadjusted rates of postoperative AKI-dialysis according to surgery types. Aorta surgery has the highest risk of AKI-dialysis at 6.05%, with a mortality rate of 41.4%. Endovascular aneurysm repair has a lower AKI-dialysis rate at 0.98% compared with aorta surgery. Other surgery types that have higher AKI risk include liver, pancreas, spleen surgery (0.82%), intestinal surgery (0.8%), vascular surgery (0.59%), and thoracic surgery (0.48%). Surgery types in lower-risk categories include orthopedic upper extremity surgery (0.05%) and spine surgery (0.09%).

Effect of Preoperative Renal Function, Serum Sodium, and Hematocrit

As shown in Figure 3, preoperative renal dysfunction was associated with increased unadjusted risk of AKI-dialysis.

Table 2. **Predictors of postoperative AKI requiring dialysis**

Characteristics	Coefficient	SEM	*P* Value	Adjusted Odds Ratio (95% Confidence Interval)
Intercept	−9.228	0.122	<0.001	
Age, per yr	0.012	0.001	<0.001	1.01 (1.01 to 1.02)
Ascites	0.971	0.089	<0.001	2.64 (2.22 to 3.14)
Congestive heart failure	0.832	0.059	<0.001	2.30 (2.05 to 2.58)
Emergency surgery	0.773	0.042	<0.001	2.17 (2.00 to 2.35)
Hypertension requiring medication	0.440	0.038	<0.001	1.55 (1.44 to 1.67)
Diabetes, reference: no diabetes				
Insulin dependent	0.667	0.043	<0.001	1.95 (1.79 to 2.12)
Noninsulin dependent	0.219	0.046	<0.001	1.25 (1.14 to 1.36)
Serum sodium, reference: 135.1–145, mEq/L				
0–130	0.328	0.071	<0.001	1.39 (1.21 to 1.60)
130.1–135	0.193	0.041	<0.001	1.21 (1.12 to 1.31)
>145	0.390	0.090	<0.001	1.48 (1.24 to 1.76)
Missing	−0.165	0.181	0.36	0.85 (0.59 to 1.21)
Serum hematocrit, reference: >30, %				
0–24	0.802	0.073	<0.001	2.23 (1.93 to 2.57)
24.1–30	0.688	0.041	<0.001	1.99 (1.83 to 2.16)
Missing	−0.582	0.167	<0.001	0.56 (0.40 to 0.78)
Preoperative sepsis, reference: no				
SIRS	0.959	0.056	<0.001	2.61 (2.34 to 2.91)
Sepsis	1.238	0.056	<0.001	3.5 (3.09 to 3.85)
Septic shock	2.116	0.062	<0.001	8.30 (7.35 to 9.38)
Surgery type, reference: anorectal, appendix				
ENT	0.255	0.372	0.49	1.29 (0.62 to 2.68)
Bariatric, stomach, esophagus	1.425	0.127	<0.001	4.16 (3.24 to 5.33)
Brain	0.872	0.210	<0.001	2.39 (1.58 to 3.61)
Cardiac	2.864	0.141	<0.001	17.53 (13.30 to 23.09)
Endocrine, thyroid, parathyroid, adrenal, breast	−0.427	0.203	0.04	0.65 (0.44 to 0.97)
Gallbladder, biliary tract	0.555	0.140	<0.001	1.74 (1.33 to 2.29)
Hernia, peritoneum, omentum, diverticulum	0.920	0.121	<0.001	2.51 (1.98 to 3.18)
Intestine (not rectum)	1.690	0.111	<0.001	5.42 (4.36 to 6.73)
Liver, pancreas, spleen	2.565	0.126	<0.001	13.00 (10.16 to 16.64)
OBGYN	0.203	0.173	0.24	1.23 (0.87 to 1.72)
Orthopedic lower extremity, pelvis	0.732	0.118	<0.001	2.08 (1.7 to 2.62)
Orthopedic upper extremity, shoulder	0.020	0.260	0.94	1.02 (0.61 to 1.70)
Skin, subcutaneous, other musculoskeletal	0.909	0.129	<0.001	2.48 (1.93 to 3.20)
Spine	0.593	0.148	<0.001	1.81 (1.35 to 2.42)
Thoracic (nonesophageal)	1.913	0.149	<0.001	6.77 (5.06 to 9.07)
Urology	1.590	0.124	<0.001	4.90 (3.85 to 6.25)
Vascular (endovascular aneurysm repair)	2.310	0.151	<0.001	10.07 (7.50 to 13.53)
Vascular (open aorta surgery)	3.993	0.128	<0.001	54.20 (42.19 to 69.64)
Vascular (other)	1.709	0.119	<0.001	5.53 (4.37 to 6.98)
Preoperative serum creatinine per 1 mg/dl, mg/dl	0.449	0.008	<0.001	1.57 (1.54 to 1.59)

SIRS, systemic inflammatory response syndrome; ENT, Ear, Nose, Throat: OBGYN, Obstetrics and Gynecology.

The risk of AKI was higher with higher preoperative serum creatinine levels. Patients with hyponatremia and hypernatremia had higher incidence of AKI-dialysis (≤130 mEq/L: 1.5%; 130.1–135 mEq/L: 0.6%; 135.1–145 mEq/L: 0.2%; >145 mEq/L: 1.0%; P <0.001). Anemia also increased the risk of AKI-dialysis, with higher unadjusted rates among patients with hematocrit <30% (hematocrit ≤24%: 2.3%; 24.1%–30%: 1.4%; >30%: 0.2%; P<0.001).

Prediction of AKI-Dialysis

Table 2 lists clinical factors that were strongly associated with the occurrence of postoperative 30-day AKI-dialysis, and these variables were incorporated into the prediction model. History of congestive heart failure was a significant predictor, with increased adjusted odds ratio (OR) of the outcome of 2.3 (95% confidence interval [95% CI], 2.05 to 2.58; P<0.001). Diabetes was also associated with an increased risk (OR, 1.95; 95% CI, 1.79 to 2.12; P<0.001 if insulin dependent and OR, 1.25; 95% CI, 1.14 to 1.36; P<0.001 if noninsulin dependent), a finding consistent with a previous study (22). Preoperative conditions, such as systemic inflammatory response syndrome (OR, 2.61; 95% CI, 2.34 to 2.91; P<0.001), sepsis (OR, 3.5; 95% CI, 3.09 to 3.85; P<0.001), and septic shock (OR, 8.3; 95% CI, 7.35 to 9.38; P<0.001), were strongly associated with postoperative AKI-dialysis. Laboratory findings associated with increased risk included preoperative serum sodium and hematocrit. Serum sodium abnormalities in either direction had an increased adjusted risk of the outcome: for serum sodium ≤130 mEq/L, OR of AKI-dialysis was 1.39 (95% CI, 1.21 to 1.6; P<0.001); for serum sodium of 130.1–135 mEq/L, OR was 1.21 (95% CI, 1.12 to 1.31; P<0.001); and for serum sodium >145 mEq/L, OR was 1.48 (95% CI, 1.24 to 1.76; P<0.001). Surgery type was also a predictive factor, with the highest rates of AKI-dialysis in patients undergoing aortic surgery, followed by cardiac surgery and surgery of the liver, pancreas, or spleen. Intestinal and other vascular procedures were also strongly associated.

These predictors were used to develop a model for AKI-dialysis as described in Materials and Methods. Brier score for the training cohort was 0.003. The model has a training AUC of 0.89. Sensitivity analysis after removing emergency cases from the cohort showed training AUC of 0.87 and validation AUC of 0.87. The model has sensitivity of 0.89 and specificity of 0.717 with cutoff of 0.002 and sensitivity of 0.667 and specificity of 0.908 with cutoff of 0.005.

Supplemental Figure 3A shows the calibration plot of the prediction model, which is well matched with a 45° line.

Prediction of Postop-MAKE

Supplemental Table 3 shows predictors of Postop-MAKE. Anemia had an increased risk of Postop-MAKE: for serum hematocrit ≤24%, adjusted OR was 2.04 (95% CI, 1.82 to 2.29), and for hematocrit 24.1%–30%, OR was 1.90 (95% CI, 1.79 to 2.02). Systemic inflammatory response syndrome (OR, 2.38; 95% CI, 2.2 to 2.58), sepsis (OR, 3.07; 95% CI, 2.83 to 3.33), and septic shock (OR, 5.85; 95% CI, 5.29 to 6.47) also had an increased risk. The model had a training AUC of 0.85. Brier score for the training cohort was 0.006. Supplemental Figure 3B shows the excellent calibration plot of the prediction model.

Validation of the AKI Risk Model

The trained model was tested by applying the model to a validation cohort of 811,778 from 2017. The prediction model has excellent predictive power, with an AUC of 0.90 for the AKI-dialysis model and an AUC of 0.85 for the Postop-MAKE model. Five-fold crossvalidation from the training cohort also showed high average AUC (0.89) for AKI-dialysis model and AUC (0.85) for the Postop-MAKE model. Figure 4 shows the AUC of model validation for AKI-dialysis.

Examples of AKI Risk Calculator

A calculator for AKI-dialysis risk was programmed from coefficients and intercepts from multivariable logistic regression and the Scikit-learn machine learning library (23). The examples in Supplemental Figure 4 demonstrate the bedside applicability of this model as well as the effect of various clinical factors on the risk of the outcome. The mobile web model is available at https://www.prediction-model.org/. The mobile web model and hypothetical cases are shown in Supplemental Figure 4.

Discussion

Preoperative evaluation has often focused on cardiac risk assessment, but AKI risk assessment has not been routinely incorporated in clinical practice, even though patients with CKD have high morbidity and mortality after surgery (24–26).

Accurate risk assessment of postoperative AKI will help clinicians to identify patients at high risk and implement individualized preventative measures. For high-risk patients, KDIGO bundle and biomarker-guided intervention may lower AKI risk after major surgery (5,27–30).

In addition, accurate risk assessment can allow appropriate anticipatory guidance to be given to patients in advance of emergent surgeries, allowing patients at high risk of postoperative AKI-dialysis to prepare themselves for that possibility (31).

In this study, a risk model was developed for postoperative AKI-dialysis in patients undergoing broad types of surgery. This model uses simple, easily available clinical data to deliver excellent predictive ability for the outcome, with a validation AUC of 0.90.

This study has strengths compared with prior models to predict postoperative AKI. A prior machine learning algorithm to predict postoperative AKI requires a complex set of electronic health record (EHR)–extracted data (32). There are also previously described machine learning prediction models for AKI in hospitalized patients, which are not specific to the postoperative population and often rely on complex data extracted from the EHR (33–36).

Other strengths of this study include the very large (2,299,502 patients) and recent (2015–2017) cohort used to build our model. The study population includes various surgery types, including cardiac surgery, and the risk model was validated across surgery types.

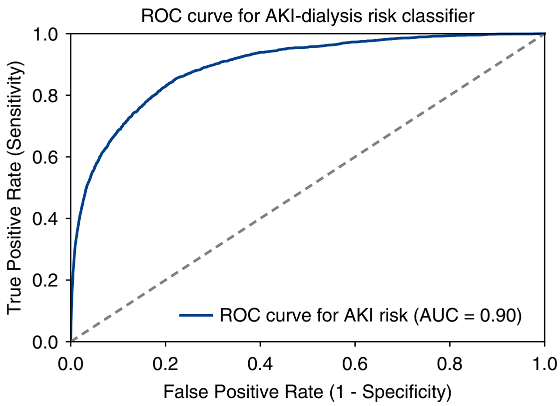

Figure 4. | Showing excellent predictive model performance with validation cohort for postoperative AKI requiring dialysis. AKI-dialysis, AKI requiring RRT; AUC, area under the receiver operating characteristic curve; ROC, receiver operating characteristic.

A limitation of our model is an inability to account for multiple factors as is possible in an EHR-integrated model: for example, zip code as a predictor of socioeconomic factors. The simplicity of our model was an intentional choice, making it useful in a variety of settings without requiring institutional investment in EHR integration. Additionally, the large dataset used to develop and validate the model portends a high degree of external validity. This could be further tested by using this model at institutions that do not participate in NSQIP and evaluating its performance in that population, which will assure the generalizability of the model.

Another limitation pertains to the clinical use of this model. Although certain factors investigated are modifiable (for example, preoperative hematocrit and sodium), this analysis cannot determine causality or the effect of modifying these factors on ultimate risk of AKI-dialysis. An individual with sodium <130 mEq/L can be counseled on an elevated postoperative risk of AKI-dialysis, but it is not known if correcting the sodium prior to surgery will be protective.

This analysis shows that preoperative renal function, older age, congestive heart failure, diabetes, and anemia are all significantly associated with the development of postoperative AKI-dialysis. A clinical model incorporating 11 readily available patient factors can be easily used by the clinician at bedside and has high predictive ability for this outcome, making it a useful and individualized tool for shared surgical decision making. Further study will be needed to see if optimizing modifiable predictors can improve renal outcomes.

Disclosures

All authors have nothing to disclose.

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The ACS NSQIP and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Author Contributions

S.H. Woo conceptualized the study; S.H. Woo was responsible for data curation, formal analysis, project administration, software, validation, and visualization; L. Ackermann, S.W. Cowan, O.H. Maarouf, S.H. Woo, J. Zavodnick, and J. Zhang were responsible for investigation; S.H. Woo and J. Zavodnick were responsible for methodology; S.H. Woo provided supervision; L. Ackermann, S.H. Woo, and J. Zavodnick wrote the original draft; and L. Ackermann, S.W. Cowan, O.H. Maarouf, S.H. Woo, J. Zavodnick, and J. Zhang reviewed and edited the manuscript.

Supplemental Material

This article contains supplemental material online at http://kidney360.asnjournals.org/lookup/suppl/doi:10.34067/KID.0004732020/-/DCSupplemental.

Supplemental Figure 1. Study participant flow chart.

Supplemental Figure 2. 30-day postoperative unadjusted mortality rates of patients who developed AKI requiring dialysis according to surgery types.

Supplemental Figure 3. (A) Calibration plot for postoperative acute kidney injury requiring dialysis. Observed vs predicted AKI-Dialysis risk. (B) Calibration plot for Postoperative major adverse kidney event (Postop-MAKE). Observed vs predicted AKI-MAKE risk.

Supplemental Figure 4. Mobile web application of AKI risk model.

Supplemental Table 1. Training cohort patient characteristics (2015–2016).

Supplemental Table 2. Validation cohort patient characteristics (2017).

Supplemental Table 3. Predictors of postoperative major adverse kidney event (Postop-MAKE).

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