

# Development and Validation of an Acute Kidney Injury Risk Index for Patients Undergoing General Surgery

## Results from a National Data Set

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**Background:** The authors sought to identify the incidence, risk factors, and mortality impact of acute kidney injury (AKI) after general surgery using a large and representative national clinical data set.

**Methods:** The 2005–2006 American College of Surgeons–National Surgical Quality Improvement Program participant use data file is a compilation of outcome data from general surgery procedures performed in 121 US medical centers. The primary outcome was AKI within 30 days, defined as an increase in serum creatinine of at least 2 mg/dl or acute renal failure necessitating dialysis. A variety of patient comorbidities and operative characteristics were evaluated as possible predictors of AKI. A logistic regression full model fit was used to create an AKI model and risk index. Thirty-day mortality among patients with and without AKI was compared.

**Results:** Of 152,244 operations reviewed, 75,952 met the inclusion criteria, and 762 (1.0%) were complicated by AKI. The authors identified 11 independent preoperative predictors: age 56 yr or older, male sex, emergency surgery, intraperitoneal surgery, diabetes mellitus necessitating oral therapy, diabetes mellitus necessitating insulin therapy, active congestive heart failure, ascites, hypertension, mild preoperative renal insufficiency, and moderate preoperative renal insufficiency. The c statistic for a simplified risk index was 0.80 in the derivation and validation cohorts. Class V patients (six or more risk factors) had a 9% incidence of AKI. Overall, patients experiencing AKI had an eightfold increase in 30-day mortality.

**Conclusions:** Approximately 1% of general surgery cases are complicated by AKI. The authors have developed a robust risk index based on easily identified preoperative comorbidities and patient characteristics.

ACUTE kidney injury (AKI) after cardiac and vascular surgery has been well studied but remains a prevalent, devastating, and costly complication.<sup>1-5</sup> Depending on

the definition of AKI, it affects from 2% to 25% of cardiovascular surgery patients and increases the mortality and costs associated with these procedures by two to five times.<sup>1,3,6</sup> Although more than 6 million general surgery procedures are performed each year in the United States,<sup>7</sup> AKI in this group of patients has been largely unstudied.<sup>4</sup> In a study of 15,000 patients without significant preexisting kidney dysfunction, Kheterpal *et al.*<sup>8</sup> recently demonstrated that approximately 1% of major noncardiac surgery procedures were complicated by AKI, defined as a significant reduction in calculated creatinine clearance to less than 50 ml/min.

The American College of Surgeons–National Surgical Quality Improvement Program (ACS–NSQIP) data set offers a unique opportunity to study perioperative morbidity and mortality in a broadly representative, national sample of patients. At the time of publication, more than 200 community hospitals, moderate-sized private hospitals, and tertiary care academic centers participated in ACS–NSQIP data collection and process improvement.<sup>9-13</sup> The ACS–NSQIP publishes an annual participant use data file with national deidentified data for research and quality improvement purposes. The 2005–2006 participant use data file includes data from 121 centers and more than 150,000 cases. We used these data to identify the incidence of and preoperative risk factors for AKI after general surgery. We also sought to create a risk index using these risk factors and to establish the mortality associated with the development of AKI after general surgery. We hypothesized that general surgery procedures would demonstrate an AKI risk factor model distinct from cardiac and vascular surgery procedures. Second, we hypothesized that the development of AKI after general surgery would be associated with an increased mortality independent of underlying comorbidities.

## Materials and Methods

### Patients and Data Collection

Institutional review board approval (University of Michigan Medical School, Ann Arbor, Michigan) was obtained for the data analysis of these prospectively collected data. Because no care interventions were mandated and no protected health information was collected or analyzed, signed patient consent was waived.

The ACS–NSQIP methodology has been described in detail elsewhere and is summarized here.<sup>10,12</sup> Operations ne-

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cessitating general, epidural, or spinal anesthesia are prospectively divided into 8-day cycles. The first 40 general surgery and vascular surgery operations within each 8-day cycle are included. The 2005–2006 ACS-NSQIP participant use data file is a compilation of operations from 121 participating US medical centers submitted over a 1-yr period spanning 2005 and 2006. To maintain institutional, provider, and patient anonymity, no site- or region-specific data elements are included in the participant use data file. The following case types were excluded from the data analysis: procedures performed by the vascular, cardiac, urology, ophthalmology, podiatry, or obstetric services. If any concurrent cardiac, obstetric, or urologic procedures were performed, the case was excluded. Because of their low-acuity nature, outpatient procedures were excluded. Patients with preexisting acute renal failure (defined as rapid steadily increasing azotemia and serum creatinine  $\geq 3.0$  mg/dl within 24 h of surgery) or preexisting dialysis dependence were excluded.

For each operation, a trained risk assessment nurse prospectively collected preoperative patient demographics, preoperative comorbidities, operative information, selected intraoperative elements, and postoperative adverse occurrences up to 30 days after the operation. Detailed, standardized definitions of ACS-NSQIP preoperative patient demographics and comorbidities are available in appendix 1. High-risk procedures were defined as intraperitoneal procedures excluding hernia repairs.<sup>8</sup> Preoperative serum creatinine values were defined as the most recent serum creatinine (mg/dl) measured within 90 days of the surgery. Mild preoperative renal insufficiency was defined as a serum creatinine between 1.2 and 1.9 mg/dl, whereas moderate preoperative renal insufficiency was defined as a serum creatinine of 2.0 mg/dl or greater. Diabetes mellitus was evaluated as two separate clinical elements: (1) diabetes mellitus necessitating oral hypoglycemic therapy without insulin therapy and (2) diabetes mellitus necessitating insulin therapy with or without oral hypoglycemic therapy.<sup>3,14</sup>

Surgical nurse data collectors completed standardized and detailed training regarding the definitions of study variables. Regular conference calls, annual meetings, and site visits were used to maintain data reliability. Sites with interrater reliability audit scores demonstrating 5% or greater disagreement were excluded from the ACS-NSQIP participant use data file.

### Outcomes

On the 30th postoperative day, the nurse obtained outcome information through chart review, reports from morbidity and mortality conferences, and communication with each patient by letter or by telephone. The primary outcome was AKI defined as either ACS-NSQIP renal morbidity outcome: progressive renal insufficiency or acute renal failure necessitating dialysis. Progressive renal insufficiency was defined as “the reduced capacity of the kidney to perform its function as evidenced by an

increase in creatinine of  $> 2$  mg/dl from preoperative value, but with no requirement for dialysis.” Acute renal failure necessitating dialysis is defined as “in a patient who did not require dialysis preoperatively, worsening of renal dysfunction postoperatively requiring hemodialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, or ultrafiltration.” Two secondary outcomes were recorded: (1) 30-day all-cause mortality and (2) a composite non-AKI morbidity endpoint of pneumonia, pulmonary embolus, stroke, cardiac arrest, myocardial infarction, sepsis, or septic shock. Detailed definitions for these outcomes are listed in appendix 2.

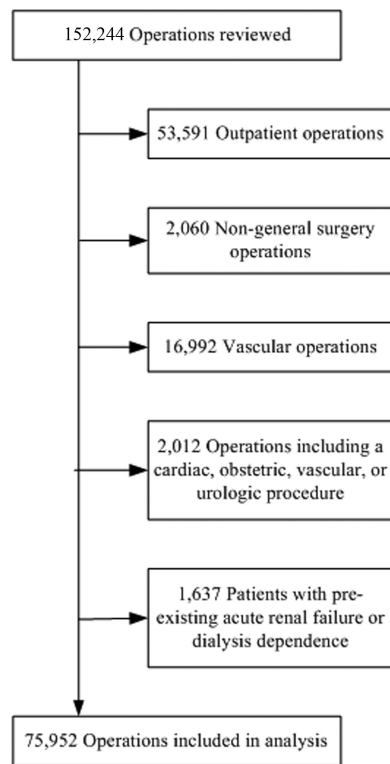
### Statistical Analysis

Statistical analysis was performed using SPSS<sup>®</sup> versions 15 and 16 (SPSS Inc., Chicago, IL). Patients meeting inclusion criteria were randomly assigned to a derivation (75%) or validation (25%) cohort data set. The derivation cohort was used to build the AKI preoperative risk stratification model and score. The validation cohort was used to assess for internal validity as described by Harrell and as used by others.<sup>9,14,15</sup> First, descriptive statistics were performed on each preoperative variable to compare patients with and without postoperative AKI. All patient and operative characteristics were compared using the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables.

Because of the large number of patients with a missing preoperative serum creatinine, we used the Missing Value Analysis module of SPSS version 16 to assess the impact of imputation on the model.<sup>16,17</sup> Collinearity diagnostics and Pearson correlations were evaluated for all preoperative predictors in this derivation cohort. To improve clinically usability, continuous variables were transformed into dichotomous variables by identifying the maximal sum of sensitivity and specificity. All remaining variables were entered into a logistic regression full model fit to identify significant independent predictors of AKI. All variables deemed to be significant in the full model fit ( $P < 0.05$ ) were established as independent predictors. The resulting model's predictive value was evaluated using a receiver operating characteristic area under the curve, or c statistic.<sup>18</sup> Each variable was assessed for effect size using adjusted hazard ratios.<sup>19,20</sup>

An unweighted risk score assigning one point to each risk factor was created using the independent risk factors. In addition, a weighted risk score based on the  $\beta$  coefficient of the independent predictors was derived from the logistic regression model.<sup>21</sup> In the weighted score, the points assigned to each risk factor were derived by dividing each  $\beta$  coefficient by the smallest  $\beta$  coefficient of the independent predictors, multiplying by 2, and rounding to the nearest integer.<sup>21</sup> The unweighted and weighted scores were compared using the c statistic.<sup>18</sup>

The model was tested against the validation cohort *via* several mechanisms. First, both the unweighted and the



**Fig. 1. Patient inclusions and exclusions. The number of patients excluded because of each exclusion criterion is demonstrated.**

weighted prediction scores were applied to the validation cohort, and a c statistic was calculated. In addition, the incidence of AKI among patients with similar preoperative risk scores was compared between the derivation and validation cohorts.

Finally, to compare the all-cause 30-day mortality and composite morbidity endpoints, we developed an AKI propensity score based on the logistic regression full model fit to control for coexisting comorbidities. The

propensity score for each patient was the predicted probability (0 to 1) of developing AKI as defined by the output of the logistic regression model performed on the raw (nonimputed) derivation patient data set. AKI patients were matched using a five-digit manual matching algorithm to patients who did not experience AKI. If a five-digit match was not available, the patient was not used in the matched analysis. Mortality was compared using a Cox proportional hazards model that incorporated all AKI risk factors and the development of AKI itself as independent variables. The composite non-AKI morbidity endpoint was compared using a chi-square test.

## Results

A total of 152,244 distinct operations were detailed in the ACS-NSQIP participant use data file spanning a 1-yr period from 2005 to 2006. Thirty-day follow-up was achieved for all patients included in the data set. Of 75,952 operations that met the inclusion criteria for the study, 57,080 were randomly allocated to the derivation cohort and 18,872 were randomly allocated to the validation cohort. The majority of exclusions were for one of two reasons: excluded surgical specialties or outpatient surgery (fig. 1). A wide variety of general surgery procedures were represented in the final data set (table 1).

Of the 75,952 patients included in the final analysis, 762 patients (1.0%) experienced the primary outcome of AKI. Of the 762 patients, 358 met the progressive renal insufficiency criteria and 460 met the acute renal failure criteria. Fifty-six patients were coded as meeting both criteria. In general, patients experiencing AKI were older, more likely to be male, and more likely to have a variety of comorbidities than were patients without AKI (table 2).

Data completion rates were excellent for all historic and demographic elements, with greater than 99.9%

**Table 1. Categorization of Derivation Cohort by Primary Procedure Type**

CPT Range of Primary Procedure	Type of Operation by Organ System or Area of Body	Total Patients, N = 56,519 n (% of Total Population)	Patients with Acute Kidney Injury, N = 561 n (% Incidence within CPT Group)
10000–29999	Integumentary and musculoskeletal	4,232 (7.4)	22 (0.5)
30000–39999	Respiratory system, hemic and lymphatic system, mediastinum, and diaphragm	1,294 (2.3)	18 (1.4)
40000–42999	Head and neck	37 (0.1)	0 (0)
43000–43499	Esophageal procedures	1,341 (2.3)	5 (0.4)
43500–43999	Foregut (stomach, including gastric bypass procedures)	7,007 (12.3)	56 (0.8)
44000–46999	Hindgut (small bowel, large bowel, rectum, and anus)	21,019 (36.8)	269 (1.3)
47000–47419	Liver	1,007 (1.8)	23 (2.3)
47420–47999	Biliary system (gallbladder, ducts)	9,152 (16.0)	51 (0.6)
48000–48999	Pancreatic procedures	1,727 (3.0)	23 (1.3)
49000–49499	Miscellaneous peritoneal procedures	2,022 (3.5)	58 (2.9)
49500–49999	Herniorrhaphy	4,714 (8.3)	33 (0.7)
50000–59999	Pelvic organs	128 (0.2)	0 (0)
60000–60999	Endocrine	3,380 (5.9)	3 (0.1)
61000–64999	Nervous system structures	20 (0.0)	0 (0)

CPT = common procedural terminology.

**Table 2. Preoperative Patient Characteristics of the Derivation Cohort**

Risk Factor*	No Acute Renal Failure, N = 56,519	Yes Acute Renal Failure, N = 561	P Value†
Age, yr‡	53.5 ± 17.3	64.8 ± 14.8	< 0.001
Body mass index, kg/m <sup>2</sup> ‡	30.1 ± 8.5	30.0 ± 8.3	0.73
Male sex	21,959 (39%)	319 (57%)	< 0.001
Diabetes mellitus—oral therapy	4,894 (8.7%)	83 (15%)	< 0.001
Diabetes mellitus—insulin therapy	2,808 (5.0%)	82 (15%)	< 0.001
Chronic obstructive pulmonary disease	2,274 (4.0%)	61 (11%)	< 0.001
Active congestive heart failure	517 (0.9%)	46 (8.2%)	< 0.001
Recent myocardial infarction	314 (0.6%)	19 (3.4%)	< 0.001
Ascites	1,257 (2.2%)	75 (13%)	< 0.001
Hypertension	23,374 (41%)	387 (69%)	< 0.001
Previous cardiac intervention§	4,257 (7.5%)	99 (18%)	< 0.001
Peripheral vascular occlusive disease	798 (1.4%)	30 (5.3%)	< 0.001
Cerebrovascular disease	2,613 (4.6%)	66 (12%)	< 0.001
Long-term steroid therapy	2,392 (4.2%)	51 (9.1%)	< 0.001
Renal insufficiency—mild	4,215 (8.5%)	139 (27%)	< 0.001
Renal insufficiency—moderate#	916 (1.9%)	123 (24%)	< 0.001
Emergency surgery	11,260 (20%)	232 (41%)	< 0.001
Intraperitoneal surgery	40,975 (73%)	512 (91%)	< 0.001
General anesthesia	56,147 (99%)	555 (99%)	0.23

\* Detailed definitions of all American College of Surgeons—National Surgical Quality Improvement Program data elements are available in appendix 1. † All patient and operative characteristics were compared using Mann–Whitney U test for continuous variables and chi-square for categorical variables. ‡ Mean ± SD. § Defined as previous percutaneous coronary interventions or previous cardiac surgery. || Preoperative serum creatinine value between 1.2 and 1.9 mg/dl. # Preoperative serum creatinine value ≥ 2.0 mg/dl.

valid data. Preoperative serum creatinine was not available for 7,167 patients (9.4%). Patients missing a preoperative serum creatinine were more likely to be younger and healthier (data not shown) and less likely to experience AKI (0.6% vs. 1.0%;  $P < 0.001$ ). Of the 762 patients who experienced AKI, 40 (5.2%) had a missing preoperative serum creatinine value, whereas 7,127 (9.5%) of the 75,190 patients without AKI had a missing preoperative serum creatinine value ( $P < 0.001$ ).

Missing value analysis demonstrated that the preoperative creatinine data were missing at random. The expectation-maximization algorithm with a tolerance of 0.001 and convergence of 0.0001 was used to impute missing preoperative creatinine values only.<sup>17</sup> The logistic regression full model fit was performed on both the raw and imputed derivation cohort data set (table 3).

Collinearity diagnostics demonstrated a condition index above 30, so the construction of a bivariate correlation matrix was necessary. No correlation issues were identified; therefore, no variables were removed. Age was transformed into a dichotomous variable; the maximal sum of sensitivity and specificity was 56 yr. Body mass index was not entered into the logistic regression model because it demonstrated a poor c statistic of 0.51 and the mean body mass index of the AKI and control groups were both 30 kg/m<sup>2</sup> ( $P = 0.73$ ). All remaining variables listed in table 2 were entered into a logistic regression full model fit with AKI as the dependent dichotomous variable.

The imputed data set logistic regression model included 57,075 patients (> 99.9%) and demonstrated that the independent predictors of AKI ( $P \leq 0.05$ ) were age 56 yr or older, male sex, emergency surgery, intraperitoneal surgery, diabetes mellitus necessitating oral hypoglycemic therapy, diabetes mellitus necessitating insulin therapy, active congestive heart failure, ascites, hypertension, mild preoperative renal insufficiency, and moderate preoperative renal insufficiency (table 3). The omnibus test of model coefficients demonstrated a chi-square value of 1,024.5 with 18 degrees of freedom and a  $P$  value less than 0.001. The c statistic of the model was  $0.83 \pm 0.01$ . The raw (nonimputed) data set logistic regression model included 49,929 patients (88%) and demonstrated excellent agreement with the imputed data set, with a c statistic of  $0.83 \pm 0.01$ . Adjusted hazard ratios are reported for each predictor (fig. 2 and table 3). In the raw (nonimputed) data set logistic regression model, diabetes mellitus necessitating oral hypoglycemic therapy demonstrated borderline statistical significance at 0.058. However, because the adjusted hazard ratio was significant (1.3; 95% confidence interval, 1.0–1.7) and it was significant in the imputed model, it was retained in the weighted and unweighted prediction scores. All subsequent analyses and descriptive statistics were performed on the raw (nonimputed) data set (tables 4–6).

The unweighted and weighted prediction scores were based on the 11 independent predictors. Comparison of receiver operating characteristic curves demonstrated an area under the curve of  $0.82 \pm 0.01$  for the weighted score and  $0.81 \pm 0.01$  for the unweighted score. Unweighted scores ranged from 0 to 9 because the two severity classes for diabetes mellitus and preoperative renal insufficiency were each mutually exclusive. To improve clinical usability, we created five General Surgery AKI Risk Index classes: class I (zero, one, or two points), class II (three points), class III (four points), class IV (five points), and class V (six or more points). The classes were created by identifying groups of scores that resulted in “highly significant” ( $P < 0.001$ ) differences in the incidence of AKI between consecutive classes (*i.e.*, class I vs. class II, class II vs. class III, *etc.*). The incidence of AKI and hazard ratios increased with risk class and demonstrated consistency across the derivation and validation cohort (table 5). The c

**Table 3. Independent Predictors of Acute Kidney Injury Derived from Logistic Regression Full Model Fit Performed on the Derivation Cohort of 57,080 Patients**

Risk Factor	Imputed Data Set*		Raw (Nonimputed) Data Set*			
	$\beta$ Coefficient	P Value	$\beta$ Coefficient	P Value	Adjusted Hazard Ratio (95% Confidence Interval)	Points in Weighted Scoring Model†
Intraperitoneal surgery	1.149	< 0.001	1.207	< 0.001	3.3 (2.4–4.7)	9
Renal insufficiency–moderate	1.126	< 0.001	1.172	< 0.001	3.2 (2.8–3.7)	9
Renal insufficiency–mild	1.058	< 0.001	1.139	< 0.001	3.1 (2.5–3.9)	9
Ascites	1.046	< 0.001	1.096	< 0.001	3.0 (2.2–4.0)	9
Active CHF	0.724	< 0.001	0.705	< 0.001	2.0 (1.4–3.0)	6
Emergency surgery	0.725	< 0.001	0.619	< 0.001	1.9 (1.5–2.3)	5
Age $\geq$ 56 yr	0.617	< 0.001	0.555	< 0.001	1.7 (1.4–2.2)	4
DM–insulin therapy	0.550	< 0.001	0.545	< 0.001	1.7 (1.3–2.3)	4
Hypertension	0.388	< 0.001	0.402	< 0.001	1.5 (1.2–1.9)	3
Male sex	0.377	< 0.001	0.333	< 0.001	1.4 (1.2–1.7)	3
DM–oral therapy	0.308	0.017	0.256	0.058	1.3 (1.0–1.7)	2

\* The imputed data set logistic regression model included 57,075 patients (> 99.9%). Preoperative serum creatinine values only were imputed using the expectation-maximization algorithm. The raw (nonimputed) data set logistic regression model included 49,929 patients with complete data (88%). † In the weighted score, the points assigned to each risk factor were derived by dividing each  $\beta$  coefficient by the smallest  $\beta$  coefficient of the independent predictors, multiplying by 2, and rounding to the nearest integer.

CHF = congestive heart failure; DM = diabetes mellitus.

statistic for the General Surgery AKI Risk Index was  $0.80 \pm 0.01$  (fig. 3) in the derivation cohort and  $0.80 \pm 0.02$  in validation cohort ( $n = 18,872$ ).

Propensity score matching based on the preoperative likelihood of developing AKI allowed the creation of two patient groups from the derivation cohort that were similar in terms of patient and operative characteristics (table 6). Each patient's propensity score was the predicted probability of AKI as derived in the logistic regression full model fit performed on the raw (nonimputed) data set. The predicted probability is based on the  $\beta$  coefficient for each risk factor in the full model.<sup>22</sup> A one-to-one five-digit match was achieved for 499 patients. All-cause 30-day mortality for the patients who developed AKI was 42%, whereas it was only 8.6% for their matched cohorts that did not develop AKI, correlating with a hazard ratio of 7.5 (95% confidence interval, 5.2–10.8). Cox proportional hazard analysis demonstrated that the development of AKI was a significant independent predictor of 30-day mortality ( $P < 0.001$ ). The omnibus test of model coefficients demonstrated a chi-square value of 241.187, 12 degrees of freedom, and

$P < 0.001$ . The incidence of the composite morbidity endpoint for the patients who developed AKI was 66%, whereas it was only 19% for their matched cohorts who did not develop AKI, correlating with a hazard ratio of 8.3 (95% confidence interval, 6.2–11.2;  $P < 0.001$ ; table 6).

## Discussion

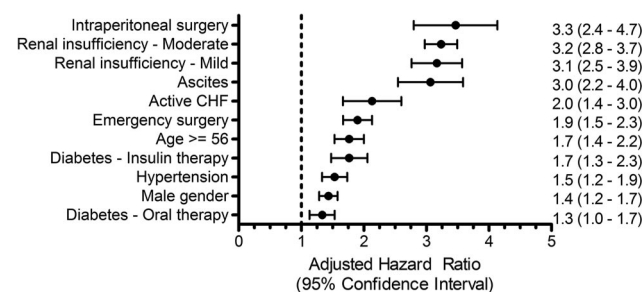
We have reviewed the incidence, predictors, and mortality impact of AKI in a general surgery population using a large national clinical research data set. Our data demonstrate that AKI occurs in approximately 1% of patients undergoing general surgery procedures and that the development of AKI was associated with an eightfold increase in all-cause 30-day mortality. Furthermore, we have developed an effective preoperative risk prediction model that can be used for patient education, postoperative observation, and patient selection for prospective studies.

**Table 4. General Surgery Acute Kidney Injury Risk Index**

Risk factor
Age $\geq$ 56 yr
Male sex
Active congestive heart failure
Ascites
Hypertension
Emergency surgery
Intraperitoneal surgery
Renal insufficiency–mild or moderate*
Diabetes mellitus–oral or insulin therapy

Five General Surgery Acute Kidney Injury Risk Index classes are based on the number of risk factors the patient possesses: class I (zero, one, or two risk factors), class II (three risk factors), class III (four risk factors), class IV (five risk factors), and class V (six or more risk factors).

\* Preoperative serum creatinine value > 1.2 mg/dl.



**Fig. 2. General surgery acute kidney injury independent predictor adjusted hazard ratios. The hazard ratios are based on the adjusted odds ratios identified in the logistic regression full model fit. CHF = congestive heart failure.**

**Table 5. General Surgery Acute Kidney Injury Risk Index Classification System**

Preoperative Risk Class	Derivation Cohort, N = 57,080			Validation Cohort, N = 18,872		
	Total Patients, n	Acute Kidney Injury Incidence, % (n)	Hazard Ratio (95% Confidence Interval)	Total Patients, n	Acute Kidney Injury Incidence, % (n)	Hazard Ratio (95% Confidence Interval)
Class I (0–2 risk factors)	31,500	0.2 (66)		10,301	0.2 (25)	
Class II (3 risk factors)	12,576	0.8 (104)	4.0 (2.9–5.4)	4,218	0.8 (32)	3.1 (1.9–5.3)
Class III (4 risk factors)	7,933	1.8 (144)	8.8 (6.6–11.8)	2,625	2.0 (53)	8.5 (5.3–13.7)
Class IV (5 risk factors)	3,615	3.3 (118)	16.1 (11.9–21.8)	1,244	3.6 (45)	15.4 (9.4–25.2)
Class V (6+ risk factors)	1,456	8.9 (129)	46.3 (34.2–62.6)	484	9.5 (46)	46.2 (26.3–70.9)

Patients are assigned to a risk class based on the number of preoperative risk factors they possess: age  $\geq$  56 yr, male sex, active congestive heart failure, ascites, hypertension, emergency surgery, intraperitoneal surgery, renal insufficiency (serum creatinine  $>$  1.2 mg/dl), and diabetes mellitus (oral or insulin therapy).

Our findings shed light on a clinical problem with limited existing literature. Approximately 1–5% of hospitalized patients experience AKI.<sup>23–25</sup> Previous studies on AKI among hospitalized patients have been limited by the inclusion of very heterogeneous patient populations, poorly defined reasons for admission, variant surgical types, and administrative data sources for concomitant disease information. There are no current data on the incidence, predictors, or impact of AKI after general surgery. Using single-center data, we have previously demonstrated that 0.8% of patients with previously normal renal function undergoing noncardiac surgery would experience AKI defined as a postoperative esti-

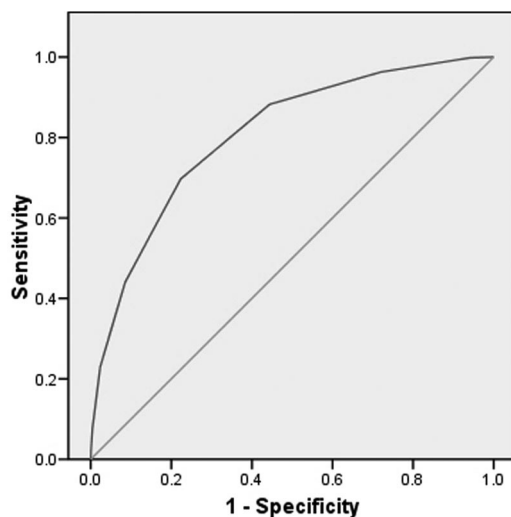
mated creatinine clearance less than 50 ml/min.<sup>8</sup> These data, however, included patients undergoing high-risk vascular surgery procedures and focused on patients without preexisting renal insufficiency.

The cardiac surgery literature has extensively evalu-

**Table 6. Acute Kidney Injury Propensity Score Matched 30-Day Mortality Comparison**

Risk Factor*	No Acute Kidney Injury, N = 499	Yes Acute Kidney Injury, N = 499	P Value†
Age, yr‡	64.1 $\pm$ 15.0	65.0 $\pm$ 14.9	0.31
Body mass index, kg/m <sup>2</sup> ‡	29.4 $\pm$ 8.0	30.0 $\pm$ 8.2	0.29
Male sex	282 (57%)	282 (57%)	1.00
Diabetes mellitus—oral therapy	70 (14%)	70 (14%)	1.00
Diabetes mellitus—insulin therapy	73 (15%)	73 (15%)	1.00
Chronic obstructive pulmonary disease	52 (10%)	57 (11%)	0.61
Active congestive heart failure	30 (6.0%)	30 (6.0%)	1.00
Recent myocardial infarction	9 (1.8%)	16 (3.2%)	0.16
Ascites	61 (12%)	61 (12%)	1.00
Hypertension	352 (71%)	352 (71%)	1.00
Peripheral vascular occlusive disease	19 (3.8%)	27 (5.4%)	0.23
Cerebrovascular disease	51 (10%)	61 (12%)	0.32
Long-term steroid therapy	49 (9.8%)	44 (8.8%)	0.59
Renal insufficiency—mild§	133 (27%)	133 (27%)	1.00
Renal insufficiency—moderate	109 (22%)	109 (22%)	1.00
Emergency surgery	198 (40%)	198 (40%)	1.00
Intraperitoneal surgery	462 (93%)	462 (93%)	1.00
General anesthesia	495 (99%)	495 (99%)	1.00
Mortality—30 day	43 (8.6%)	207 (42%)	$<$ 0.001#
Composite morbidity**	94 (19%)	329 (66%)	$<$ 0.001†

\* Detailed definitions of all American College of Surgeons—National Surgical Quality Improvement Program data elements are available in appendix 1. † All patient and operative characteristics were compared using Mann–Whitney U test for continuous variables and chi-square for categorical variables. ‡ Mean  $\pm$  SD. § Preoperative serum creatinine value between 1.2 and 1.9 mg/dl. || Preoperative serum creatinine value  $\geq$  2.0 mg/dl. # Derived using the Cox regression survival analysis. \*\* Pneumonia, pulmonary embolus, stroke, cardiac arrest, myocardial infarction, sepsis, or septic shock. Does not include acute kidney injury.



**Fig. 3. General Surgery Acute Kidney Injury Risk Index receiver operating characteristic curve.** A receiver operating characteristic curve evaluating the sensitivity and specificity of the General Surgery Acute Kidney Injury Risk Index is demonstrated. Eleven independent preoperative predictors were identified in the derivation cohort ( $P <$  0.05): age 56 yr or older, male sex, emergency surgery, intraperitoneal surgery, diabetes mellitus necessitating oral therapy, diabetes mellitus necessitating insulin therapy, active congestive heart failure, ascites, hypertension, mild preoperative renal insufficiency, and moderate preoperative renal insufficiency. To improve clinical usability, we created five General Surgery Acute Kidney Injury Risk Index classes: class I (zero, one, or two risk factors), class II (three risk factors), class III (four risk factors), class IV (five risk factors), and class V (six or more risk factors). The c statistic for this simplified risk class model was  $0.80 \pm 0.01$ .

ated AKI, demonstrating that between 1% and 15% of patients exposed to cardiopulmonary bypass will experience a marked increase in serum creatinine, with 2% requiring renal replacement therapy.<sup>1-4,6,26-28</sup> However, these data also have questionable applicability to general surgery patients given the unique pathophysiology associated with cardiopulmonary bypass.<sup>4,29</sup> Similarly, the vascular surgery literature demonstrates rates of renal dysfunction of approximately 5% with less than 1% of patients requiring renal replacement therapy.<sup>30</sup> Because of the marked alterations in renal blood flow induced by suprarenal or infrarenal aortic cross-clamping, it is unlikely that general surgery patients experiencing AKI are subjected to similar physiologic derangements.

Our data demonstrate a 1% incidence of AKI in a broad general surgery population across the United States. Facilities contributing data to the ACS-NSQIP participant use data file include tertiary care academic centers, moderate-sized private hospitals, and community hospitals. In addition, because we are not using an administrative data set, the patients are not limited to Medicare beneficiaries and the concomitant skewing of age distribution.<sup>25</sup> The resulting broad array of patients and medical centers involved in the ACS-NSQIP offers a truly representative sample. The inclusion of nearly 76,000 patients makes this analysis the most comprehensive to date as well. For these reasons, the data serve as the first definitive literature establishing the incidence of AKI after general surgery in the United States. They serve as a foundation for a more informed patient consenting process. In addition, they establish postoperative AKI as a complication not limited to high-risk cardiovascular procedures. The 1% incidence rivals that of other feared perioperative complications, such as cardiac adverse events<sup>9</sup> or venous thromboembolism,<sup>31</sup> but AKI after general surgery has not been the focus of risk reduction strategies.<sup>32</sup>

The General Surgery AKI Risk Index demonstrates an excellent predictive capability, with a c statistic of 0.80. The Risk Index is easy to calculate and can be readily incorporated into clinical practice because it is based on commonly acquired history, physical, and laboratory data elements. It has a predictive value superior to other landmark cardiovascular outcome prediction models such as the Lee Revised Cardiac Risk Index for perioperative cardiac events (c statistic = 0.76) and the Preoperative Renal Risk Stratification for cardiac surgery (c statistic = 0.76) of Chertow *et al.*<sup>6,14</sup> In addition, the General Surgery AKI Risk Index demonstrated excellent consistency in the validation cohort (c statistic = 0.80), providing internal validity to the analysis (table 5).

Several of the AKI predictors in this study have also been identified for patients undergoing cardiovascular surgery: advanced age, diabetes mellitus, active congestive heart failure, hypertension necessitating medication, pre-existing renal dysfunction, and emergent surgery.<sup>1-4,6,27,28,33</sup> We have also confirmed intraperitoneal surgery as an

independent predictor of AKI, consistent with previously published general surgery data.<sup>8</sup> We have identified, for the first time, that the presence of ascites is an independent risk factor for AKI after general surgery. Existing literature indicates that preoperative liver dysfunction and jaundice predispose a patient to AKI.<sup>8,34-37</sup> It is not immediately clear from the available data why ascites itself may predispose to AKI after general surgery. It is possible that other mechanisms related to fluid shifts or common therapies for ascites (*e.g.*, diuretics) may be involved in predisposing these patients to postoperative AKI. These hypotheses will necessitate further investigation and a more detailed data set.

Previous cardiac surgery literature has suggested that sex either plays no role in AKI or that female sex confers independent risk.<sup>3,6,28</sup> However, our data suggest that male sex doubles the risk of AKI after general surgery. Unfortunately, few of the risk factors we have identified can be easily corrected before an operation. However, clinicians may be able to optimize ascites and congestive heart failure. The use of general anesthesia was not associated with AKI, but we are reticent to draw conclusions from these data given that few patients in the derivation cohort underwent regional or neuraxial techniques (378 patients, 0.6%). Many of the risk factors associated ( $P < 0.05$ ) with AKI in the univariate analysis (table 2) were not found to be independent predictors in the multivariate logistic regression full model fit: chronic obstructive pulmonary disease, recent myocardial infarction, previous cardiac intervention, peripheral vascular occlusive disease, cerebrovascular disease, and long-term steroid use.

Our data and the resulting AKI risk index are an important first step toward identifying strategies to reduce the incidence of AKI after general surgery. Historically, most trials of therapeutics (diuretics, intravenous hydration, *n*-acetylcysteine, *etc.*) purported to prevent AKI have focused on high-risk vascular procedures because these prospective trials require high events rates to be sufficiently powered.<sup>4,38</sup> Our data offer the ability to identify high-risk patients and develop prospective, randomized risk reduction trials focused on the patients most likely to experience AKI.

Our data also demonstrate that the development of AKI is independently associated with 30-day all-cause mortality. This is consistent with previous single-center data for general surgery patients<sup>8</sup> and larger data sets for cardiac surgery patients.<sup>5,28</sup> Our observed mortality association is independent of underlying comorbidities that may be associated with mortality. However, because of the observational nature of the study, we cannot comment on causality.

There are several limitations to our study. First, the observational nature of the study did not enable specific detailed data collection on patients exhibiting the outcome. Therefore, our ability to provide additional descriptive information regarding this important group of patients is limited. In addition, because the data were

collected as part of a large prospective observational study, some data elements pertinent to AKI pathophysiology were not collected and cannot be retrospectively acquired. These include preoperative and intraoperative hydration, use of nephrotoxic agents, use of specific volatile agents associated with perioperative renal dysfunction, and postoperative medical management. Next, the ACS-NSQIP participant use data file lacks any regional or facility specific information. As a result, we are not able to comment on specific practice patterns or regional factors and their impact on the risk of AKI. In addition, although we chose to define preexisting renal dysfunction on the basis of serum creatinine, some may argue that estimated creatinine clearance may be a better predictor of outcome.<sup>1</sup> In addition, we lacked preoperative serum creatinine data for approximately 9% of patients in the data set. Finally, although this data set uses rigorous and validated definitions, these definitions could not be adjusted for the purposes of this specific study.

In summary, these data are of interest to patients, surgeons, anesthesiologists, nephrologists, and intensivists alike as they attempt to decrease the risk of AKI after general surgery. We have established an incidence of 1% and an eightfold increase in mortality independent of underlying comorbidities. We have derived a General Surgery AKI Risk Index that demonstrates excellent discriminating capability. These data can be used to target populations for prospective trials attempting to reduce the risk of this devastating complication.

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**Appendix 1. American College of Surgeons–National Surgery Quality Improvement Program Data Element Definitions**

Data Element	Definition
Orally controlled diabetes mellitus	Report the treatment regimen of the patient's chronic, long-term management. Do not include a patient if diabetes is controlled by diet alone. A diagnosis of diabetes necessitating therapy with an oral hypoglycemic agent
Insulin controlled diabetes mellitus	Insulin: a diagnosis of diabetes necessitating daily insulin therapy Report the treatment regimen of the patient's chronic, long-term management. Do not include a patient if diabetes is controlled by diet alone. A diagnosis of diabetes necessitating daily insulin therapy
Alcohol use	The patient admits to drinking > 2 oz hard liquor or > two 12-oz cans of beer or > two 6-oz glasses of wine per day in the 2 weeks before admission. If the patient is a binge drinker, divide out the numbers of drinks during the binge by 7 days and then apply the definition.
History of chronic obstructive pulmonary disease	Chronic obstructive pulmonary disease (such as emphysema and/or chronic bronchitis) resulting in any of the following: <ul style="list-style-type: none"> <li>● Functional disability from chronic obstructive pulmonary disease (e.g., dyspnea, inability to perform activities of daily living)</li> <li>● Hospitalization in the past for treatment of chronic obstructive pulmonary disease</li> <li>● Necessitates long-term bronchodilator therapy with oral or inhaled agents</li> <li>● A forced expiratory volume in 1 s of &lt; 75% of predicted on pulmonary function testing</li> </ul> Do not include patients whose only pulmonary disease is asthma, an acute and chronic inflammatory disease of the airways resulting in bronchospasm. Do not include patients with diffuse interstitial fibrosis or sarcoidosis.
Ascites	The presence of fluid accumulation in the peritoneal cavity noted on physical examination, abdominal ultrasound, or abdominal computed tomography or magnetic resonance imaging within 30 days before the operation
Active congestive heart failure	Congestive heart failure is the inability of the heart to pump a sufficient quantity of blood to meet the metabolic needs of the body or can do so only at increased ventricular filling pressure. Only newly diagnosed congestive heart failure within the previous 30 days or a diagnosis of chronic congestive heart failure with new signs or symptoms in the 30 days before surgery fulfills this definition. Common manifestations are: <ul style="list-style-type: none"> <li>● Abnormal limitation in exercise tolerance due to dyspnea or fatigue</li> <li>● Orthopnea (dyspnea on lying supine)</li> <li>● Paroxysmal nocturnal dyspnea (awakening from sleep with dyspnea)</li> <li>● Increased jugular venous pressure</li> <li>● Pulmonary rales on physical examination</li> <li>● Cardiomegaly</li> <li>● Pulmonary vascular engorgement</li> </ul> Should be noted in the medical record as congestive heart failure, congestive heart failure, or pulmonary edema
Acute renal failure	The clinical condition associated with rapid, steadily increasing azotemia (increase in blood urea nitrogen) and an increasing creatinine > 3 mg/dl. Acute renal failure should be noted within 24 h before surgery.
Preoperative dialysis dependence	Acute or chronic renal failure necessitating treatment with peritoneal dialysis, hemodialysis, hemofiltration, hemodiafiltration, or ultrafiltration within 2 weeks before surgery
Cerebrovascular disease	History of transient ischemic attacks: Transient ischemic attacks are focal neurologic deficits (e.g., numbness of an arm or amaurosis fugax) of sudden onset and brief duration (usually < 30 min) that usually reflect dysfunction in a cerebral vascular distribution. These attacks may be recurrent and, at times, may precede a stroke or Cerebrovascular accident/stroke with or without neurologic deficit: history of a cerebrovascular accident (embolic, thrombotic, or hemorrhagic) lasting at least 30 min with or without persistent residual motor, sensory, or cognitive dysfunction
History of myocardial infarction within past 6 months	History of a non-Q-wave or a Q-wave infarct in the 6 months before surgery as diagnosed in the patient's medical record
Previous cardiac intervention	The patient has undergone percutaneous coronary intervention at any time (including any attempted intervention). This includes either balloon dilatation or stent placement. This does not include valvuloplasty procedures or Any major cardiac surgical procedure (performed either as an "off-pump" repair or using cardiopulmonary bypass). This includes coronary artery bypass graft surgery, valve replacement or repair, repair of atrial or ventricular septal defects, great thoracic vessel repair, cardiac transplant, left ventricular aneurysmectomy, insertion of left ventricular assist devices, etc. Do not include pacemaker insertions or automatic implantable cardioverter defibrillator insertions

(continued)

Appendix 1. *Continued*

Data Element	Definition
History of angina within 1 month before surgery	Pain or discomfort between the diaphragm and the mandible resulting from myocardial ischemia. Typically angina is a dull, diffuse (fist-sized or larger) substernal chest discomfort precipitated by exertion or emotion and relieved by rest or nitroglycerine. Radiation to the arms and shoulders often occurs, and occasionally to the neck, jaw (mandible, not maxilla), or interscapular region. Documentation in the chart by the physician should state "angina" or "anginal equivalent." For patients taking antianginal medications, enter "yes" <i>only</i> if the patient has had angina at any time within 1 month before surgery
Hypertension necessitating medication	The patient has a persistent elevation of systolic blood pressure > 140 mmHg or a diastolic blood pressure > 90 mmHg or requires an antihypertensive treatment (e.g., diuretics, $\beta$ -blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers) at the time the patient is being considered as a candidate for surgery (which should be no longer than 30 days before surgery). Hypertension must be documented in the patient's chart
History of peripheral vascular occlusive disease	Any type of angioplasty (including stent placement) or revascularization procedure for atherosclerotic peripheral vascular disease (e.g., aorta-femoral, femoral-femoral, femoral-popliteal) or a patient who has had any type of amputation procedure for peripheral vascular disease (e.g., toe amputations, transmetatarsal amputations, below-the-knee or above-the-knee amputations). Patients who have had amputation for trauma or a resection of abdominal aortic aneurysms should not be included
Serum creatinine $\geq 2$	The most recent serum creatinine drawn before the patient's arrival in the operating room
Emergency surgery	An emergency case is usually performed as soon as possible and no later than 12 h after the patient has been admitted to the hospital or after the onset of related preoperative symptomatology. Answer "yes" if the surgeon and anesthesiologist report the case as emergent

## Appendix 2. American College of Surgeons–National Surgery Quality Improvement Program Data Outcome Definitions

Postoperative Outcome	Definition
Pneumonia	Inflammation of the lungs caused primarily by bacteria, viruses, and/or chemical irritants, usually manifested by chills, fever, pain in the chest, cough, and purulent, bloody sputum. Enter “yes” if the patient has pneumonia meeting the definition of pneumonia below and pneumonia not present preoperatively. Pneumonia must meet one of the following two criteria: Criterion 1: Rales or dullness to percussion on physical examination of chest <i>and</i> any of the following: a. New onset of purulent sputum or change in character of sputum b. Organism isolated from blood culture c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy <i>or</i> Criterion 2: Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion <i>and</i> any of the following: a. New onset of purulent sputum or change in character of sputum b. Organism isolated from blood culture c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy d. Isolation of virus or detection of viral antigen in respiratory secretions e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen f. Histopathologic evidence of pneumonia
Pulmonary embolus	Lodging of a blood clot in a pulmonary artery with subsequent obstruction of blood supply to the lung parenchyma. The blood clots usually originate from the deep leg veins or the pelvic venous system. Enter “yes” if the patient has a ventilation/perfusion scan interpreted as high probability of pulmonary embolism or a positive computed tomography spiral examination, pulmonary arteriogram, or computed tomography angiogram. Treatment usually consists of: <ul style="list-style-type: none"> <li>● Initiation of anticoagulation therapy</li> <li>● Placement of mechanical interruption (e.g., Greenfield filter), for patients in whom anticoagulation is contraindicated or already instituted</li> </ul>
Stroke/cerebral vascular accident	Patient develops an embolic, thrombotic, or hemorrhagic vascular accident or stroke with motor, sensory, or cognitive dysfunction (e.g., hemiplegia, hemiparesis, aphasia, sensory deficit, impaired memory) that persists for 24 or more hours.
Cardiac arrest necessitating cardiopulmonary resuscitation	The absence of cardiac rhythm or presence of chaotic cardiac rhythm that results in loss of consciousness necessitating the initiation of any component of basic and/or advanced cardiac life support. Patients who have an automatic implantable cardioverter defibrillator that fires but who have no loss of consciousness should be excluded.
Myocardial infarction	A new transmural acute myocardial infarction occurring during surgery or within 30 days after surgery as manifested by new Q waves on electrocardiogram
Sepsis	Sepsis is the systemic response to infection. Report this variable if the patient has two of the following clinical signs and symptoms of systemic inflammatory response syndrome: 1. Temperature > 38°C or < 36°C 2. Heart rate > 90 beats/min 3. Respiratory rate > 20 breaths/min or PaCO <sub>2</sub> < 32 mmHg 4. White blood cell count > 12,000 cell/mm <sup>3</sup> , < 4,000 cells/mm <sup>3</sup> , or > 10% immature (band) forms 5. Anion gap acidosis <i>and</i> one of the following: positive blood culture, clinical documentation of purulence, or positive culture from any site thought to be causative
Severe sepsis	Sepsis is considered severe when it is associated with organ and/or circulatory dysfunction. Report this variable if the patient has the clinical signs and symptoms of system inflammatory response syndrome or sepsis and documented organ and/or circulatory dysfunction. Examples of organ dysfunction include oliguria, acute alteration in mental status, and acute respiratory distress. Examples of circulatory dysfunction include hypotension and requirement for inotropic or vasopressor agents

Ig = immunoglobulin; PaCO<sub>2</sub> = arterial carbon dioxide tension.