HHS Public Access
Author manuscript
BJOG. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:
BJOG. 2015 September ; 122(10): 1340–1348. doi:10.1111/1471-0528.13026.

ACUTE KIDNEY INJURY IN MAJOR GYNECOLOGICAL SURGERY: AN OBSERVATIONAL STUDY

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Abstract

Objective—To assess the prevalence, outcomes and cost associated with acute kidney injury (AKI) defined by consensus Risk, Injury, Failure, Loss, and End-stage kidney (RIFLE) criteria after gynecologic surgery.

Design—Retrospective single-center cohort study.

Setting—Academic medical center.

Sample—2341 adult patients undergoing major inpatient gynecologic surgery between January 2000 and November 2010.

Methods—AKI was defined by RIFLE criteria as an increase in serum creatinine greater than or equal to 50% from the reference creatinine. We used multivariable regression analyses to determine the association between perioperative factors, AKI, mortality and cost.

Main Outcome Measure(s)—AKI, combined major adverse events (hospital mortality, sepsis or mechanical ventilation), 90-days mortality and hospital cost.

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Disclosure of Interests

The authors have no conflicts of interest to declare.

Contribution to Authorship

The authors were involved as follows: AB – conception, design, data acquisition and supervision, data analysis and interpretation, and drafting and revising the article; AJV– conception, data interpretation, drafting and revising the article; TOB – data acquisition, data analysis and interpretation, and drafting and revising the article; AJ –data analysis and interpretation, and drafting the article; LM – revising the article; CEH – data interpretation, and drafting and revising the article. All authors approved the final version of the article to be published.

Details of Ethics Approval

The study was approved by the UF Privacy Office and the UF Institutional Review Board (#5–2009) on 05/15/2009.

Results—Overall prevalence of AKI was 13%. The prevalence of AKI was associated with the primary diagnosis: 5% (43/801) of patients with benign tumor surgeries experienced AKI compared to 18% (211/1159) among patients with malignant disease (p<0.001). Only 1.3% of the whole cohort had evidence of urologic mechanical injury. In a multivariable logistic regression analysis AKI patients had nine times the odds of a major adverse event compared to patients without AKI (adjusted odds ratio 8.95, 95% confidence interval 5.27–15.22). We have identified several readily available perioperative factors that can be used to identify patients at high risk for AKI after in-hospital gynecologic surgery.

Conclusion—AKI is a common complication after major inpatient gynecologic surgery associated with an increase in resource utilization and hospital cost, morbidity and mortality.

Keywords

acute kidney injury; gynecologic procedure; outcomes

Introduction

Acute kidney injury (AKI) is a serious complication among hospitalized patients associated with increased morbidity and mortality. With the introduction of the consensus RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney) criteria, the adverse effects of less severe AKI characterized by changes in serum creatinine (sCr) level reflecting acute decline in glomerular filtration rate were increasingly recognized.[1, 2] While the RIFLE definition was based on at least a 50% change in sCr relative to the reference sCr [3] the recent KDIGO (Kidney Disease: Improving Global Outcomes) clinical practice guideline have further expanded RIFLE to include sCr changes as small as 0.3 mg/dl.[4] Furthermore, recommendations in this guideline provide a series of stage-based management clinical steps to be considered on all patients with AKI or at high risk of developing it.

Among surgical patients an association between small sCr changes and short and long-term mortality has emerged in the literature.[5–10] While the prevalence and risk factors for AKI have been increasingly studied in general surgical patients,[7, 10] studies describing the prevalence and outcomes of AKI defined by RIFLE criteria among gynecologic surgical patients are lacking. Although an increasing number of gynecologic procedures are being performed on an outpatient basis, in-hospital gynecologic procedures comprise almost 12% of all surgical procedures[11, 12] In the absence of data based on consensus AKI definitions in such a large surgical population, the health-care burden of AKI after gynecological surgeries is difficult to determine and insight into the clinical risk stratification is unavailable for practicing surgeons.

In a large single-center cohort of patients undergoing major inpatient gynecologic surgery we assessed the prevalence, outcomes, risk factors and cost for AKI defined using consensus RIFLE criteria.

Methods

Data source and patient population

Using the University of Florida (UF) Integrated Data Repository we assembled a single center retrospective cohort by integrating multiple clinical databases. We included patients 18 years and older admitted to the hospital for longer than 24 hours following in-hospital gynecologic procedure between January 1, 2000 and November 2010. We excluded patients with chronic kidney disease prior to admission[13] and those with any obstetric procedure (n=214). We used the combination of operating physician's specialty and first two diagnostic and procedure International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to identify gynecologic procedures and to group them based on the primary diagnosis and anatomic location. The study was approved by the University of Florida Institutional Review Board and the Privacy Office.

Definition of AKI

We applied two AKI definitions using sCr changes only: RIFLE (AKI) and the American College of Surgeons National Surgical Quality Improvement Program (NSQIP-AKI). RIFLE defines AKI using at least a 50% sCr change from a reference sCr (corresponding to at least 25% decline in glomerular filtration rate) [3] and NSQIP defines AKI as a rise in sCr greater than 2 mg/dl from the preoperative value or as the acute requirement for renal replacement therapy.[14] We defined reference sCr either as the minimum sCr within six months of the admission (used for the main results), or as the mean and minimum sCr within seven days of the admission (used for sensitivity analyses).[15] Patients with AKI were stratified according to the worst RIFLE stage reached during the hospitalization. RIFLE Risk corresponds to a 50% increase in sCr or 25%–50% decline in glomerular filtration rate, RIFLE Injury to a doubling in sCr or 51–75% decline in glomerular filtration rate and RIFLE Failure to a tripling in sCr or > 75% decline in glomerular filtration rate compared to preoperative renal function. Complete renal recovery existed if the discharge sCr returned to a level less than 50% above reference sCr, whereas partial renal recovery existed if there was a persistent increase in sCr more than 50% above reference sCr but no need for renal replacement therapy. We encountered less than 5% missing sCr values in overall cohort.

Outcomes and Covariates

The main outcomes included AKI, combined major adverse events (hospital mortality, severe sepsis or mechanical ventilation, 90-days mortality and hospital cost. Patient survival status was determined using hospital discharges and the Social Security Death Index. We defined severe sepsis by adding ICD-9-CM codes for acute organ dysfunction to the sepsis diagnosis.[16, 17] The exact dates were used to calculate the duration of mechanical ventilation, intensive care unit (ICU) and hospital stay. Cost of hospitalization was estimated using the ratio of cost-to-charge for urban hospitals in the South Atlantic division.[18] We converted all costs to 2012 dollars using the Consumer Price Index to adjust for inflation over the years. Postoperative complications were defined as previously described.[19, 20] We identified urologic injuries related to gynecologic procedure using validated ICD-9-CM codes for bladder and ureteral injuries and manual review of medical records.[21]

The presence of underlying comorbidities and gynecologic tumors was identified by ICD-9-CM codes using previously validated criteria[22, 23] and by calculating the Charlson-Deyo comorbidity index.[24] Emergent surgery was defined as either non-elective surgery or emergent admission using clinical data. Using residency zip code we linked to US Census data[25] to calculate residing neighborhood characteristics and distance from hospital.[26]

Statistical analysis

The analytical plan followed the STROBE recommendations.[27] The Pearson χ^2 test or Fisher's exact test were used to test independence between categorical variables while Student's T-test, analysis of variance and Kruskal-Wallis test where used for comparison of continuous variables as appropriate. All significance tests were two-sided with $\alpha<0.05$ considered statistically significant unless Bonferroni correction was used to adjust for multiple comparisons. In those cases $\alpha<0.0083$ was considered statistically significant. Statistical analyses were performed with SAS (v.9.3, Cary, N.C.).

For all multivariable analyses we selected explanatory variables based on their significance in a prior univariate analysis and reported association in the literature. We used separate logistic models to determine the association between a) perioperative factors (age, gender, ethnicity, primary diagnosis, emergent surgery status, weekend admission, socio-economic status and comorbid conditions on admission), and occurrence of any stage of AKI and b) AKI and combined major adverse eventswhile adjusting for other postoperative complications in addition to perioperative factors listed above. Adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were reported for logistic regression models. We used the area under the receiver operating characteristics curve values (AUC) and Hosmer-Lemeshow goodness of fit test to assess model fit and discrimination. We performed sensitivity analyses by restricting analyses only to patients within each primary diagnosis group and by comparing the effect of different definitions for reference sCr on the model fit.

We constructed risk-adjusted generalized log-linear models[28] for hospital cost with logarithmic transformation due to the skewness of the distribution. Each model was adjusted for perioperative risk factors and other postoperative complications. to. Adjusted incremental cost with 95% CI was calculated using non-parametric transformation of the regression coefficients to US dollars. Standard errors were calculated using the smearing estimate to adjust for bias due to the transformation of costs back to the original scale.[29]

Results

Prevalence of acute kidney injury

Among 2341 adult patients undergoing major gynecologic surgery the most common admission diagnoses were malignant (n=1159) and benign neoplastic disease (n=801) accounting for 84% of the cohort. The most common primary procedures were abdominal hysterectomies among uterine/fallopian surgeries (n=1349), salpingo-oophorectomies among ovarian surgeries (n=345), vulvectomy (n=41) and repair of colorectovaginal fistulas and rectoceles(n=39) among vulva/perineum/vaginal surgeries.

The overall prevalence of AKI was 13% (295/2341). The prevalence of AKI was strongly associated with the primary diagnosis: only 5% (43/801) of patients with benign tumor surgeries experienced AKI compared to 18% (211/1159) among patients with malignant disease (p<0.001) (Table S1). Mild to moderate AKI (stages Risk and Injury) comprised the majority of all AKI with only 15% (45/295) of AKI patients developing RIFLE Failure stage and 3% (8/295) requiring renal replacement therapy. AKI was significantly more prevalent when defined using RIFLE criteria compared to the NSQIP criteria, which captured only 7% of the patients with RIFLE AKI. Only 14% of all AKI patients had a diagnosis of AKI listed in their discharge summaries (Table 1).

Most AKI episodes developed within 72 hours of admission, while only 9% of AKI patients had onset of AKI after seventh day of admission. AKI was more likely to occur among patients undergoing emergent surgery and those admitted on the weekend. The majority of emergent surgeries were related to benign and malignant uterine and ovarian neoplasms, abscess of the vulva, menorrhagia, torsion of the ovary, and infections. Only 1.3% of the whole cohort had evidence of urologic mechanical injury. Although patients with AKI have a higher prevalence of urologic mechanical injury compared to the no AKI patients (5.4%, 16/295 versus 0.7%, 14/2046), this subgroup of patients represented only a small proportion of AKI.

Perioperative Factors Associated with Acute Kidney Injury

We constructed a multivariable logistic regression model to determine perioperative factors independently associated with the occurrence of any stage AKI (Table 2). The model demonstrated good discrimination and model fit. Increasing age, emergent surgery and weekend admission as well as the presence of congestive heart failure and chronic pulmonary disease on admission were associated with AKI. Patients with benign gynecologic tumors had lower odds for AKI while those with any type of cancer and especially those with metastatic cancer had significantly higher odds for AKI. Diabetes mellitus was risk factor for AKI only among patients with surgeries for benign tumors and non-neoplastic disease (OR 2.36, 95% CI 1.32–4.21) but not among patients with surgery for malignant tumors.

Adverse hospital outcomes and acute kidney injury

Although the overall hospital mortality and 90-day mortality were only 0.9% and 1.7%, patients with AKI had increases in hospital mortality to 7% and 90-day mortality to 10%. Among the 22 patients who died in hospital 91% had AKI during their hospitalization. The primary causes of hospital death were neoplastic disease (19/22), chronic liver disease (1/22), immune disorders (1/22) and sepsis (1/22). (Table 3)

Increasing severity of AKI was associated with increasing rates of most of the postoperative complications, including surgical infections, pulmonary and cardiovascular complications. Close to half of the patients with AKI (120/295, 42%) had at least one other postoperative complication, while the majority of patients without AKI had no other postoperative complication (1757/2046, 86%). Renal recovery from AKI was promising with full recovery noted 89% of the time and only 11% of all AKI patients having partial or no renal recovery.

We constructed two multivariable logistic regression models using a composite of major adverse events (occurrence of hospital death, sepsis or mechanical ventilation) as an outcome and using AKI stages separately or together while adjusting for perioperative factors and other complications. Both models had good discrimination, showing that AKI had a significant association with major adverse events proportional to the severity of AKI (AUC 0.88, 95% CI 0.84–0.92) (Table 4). Patients with AKI had nine times higher adjusted odds of major adverse event compared to patients without AKI. The adjusted odds increased with the severity of AKI, with RIFLE-F having an odds ratio of 23.56 (10.46–53.06). The number of other postoperative complications and emergent surgery also showed an increase in odds of major adverse events.

The strong association between AKI and major adverse events remained in sensitivity analyses where we limited analyses to patients with malignant tumor surgeries only (OR 5.60, 95% CI 3.11–11.54), benign tumor surgeries (OR 33.03, 95% CI 7.85–139.02) and non-neoplastic disease surgeries (OR 12.42, 95%CI 3.67–42.07). The sensitivity analyses examining the effect of different methods of assigning the RsCr demonstrated no significant change in model fit for each outcome (data not shown).

Utilization of Hospital Resources

Patients with AKI stayed almost a week longer in the hospital compared to patients without AKI, and were less likely to be discharged home (Table 3). When compared to patients with no AKI, patients with AKI were ten times more likely to have ICU admission and also had a significantly prolonged ICU stay. Among patients admitted to ICU, those with AKI had a significant increase in resource utilization, including prolonged mechanical ventilation (17/109,16% of AKI patients versus 0/72, 0% of no AKI patients, $p<0.05$) and increased use of invasive monitoring-arterial line placement (29/109, 27% of AKI patients versus 6/72, 8% of no AKI patients, $p<0.05$), central venous line placement (74/109, 68% of AKI patients versus 13/72, 18% of no AKI patients, $p<0.05$), and tracheostomy (13/109, 12% of AKI patients versus 0/72, 0% of no AKI patients). A majority of ICU patients with AKI (95/109, 87%) were ordered at least one unit of packed red blood cells compared to 47% (34/72) of those without AKI.

In a multivariable regression analysis of hospital cost, when gynecologic surgical patients had no other adverse events besides AKI, risk-adjusted average hospital cost doubled ($18,900 with AKI versus $8700 without AKI). However, the adjusted incremental cost for major adverse event was four-times higher if patients had concomitant AKI ($54,700 with AKI versus $13,200 without AKI). We found a similar relationship for almost all postoperative complications, as the presence of AKI significantly increased the incremental cost of each complication (Table 5).

Discussion

Main Findings

In a large single-center cohort of patients undergoing major in-hospital gynecologic surgery we have demonstrated that acute kidney injury defined by the RIFLE criteria is a common complication associated with significant increases in mortality, hospital cost and resource utilization, even after adjustment for other postoperative complications. The gynecologic surgeries for malignant cancer were associated with the highest prevalence of AKI. Patients with AKI had nine times higher odds of a major adverse event regardless of whether the primary diagnosis was a malignant or benign tumor or non-neoplastic disease. Consistent with other reports, AKI occurred early, within 72 hours of admission for most patients, emphasizing the importance of early detection and intervention in the management of this disease process.[30] The use of hospital resources increased among AKI patients even after excluding those not requiring ICU admission: AKI patients had a two-fold increase in ICU length of stay, and prolonged MV and invasive monitoring were more utilized among ICU patients with AKI compared to those without. Not surprisingly, the incremental cost of any other postoperative complication was quadrupled in the presence of AKI. While the average cost for laparoscopic and vaginal hysterectomy ranges from $7000-$8521 [31] the risk-adjusted cost in our cohort doubled from $8700 to $18,900 for those patients who developed AKI only and quadrupled to $54,700 when AKI was further complicated with additional postoperative complication. The three-fold increase in median hospital length of stay of 11 days among patients with the least severe AKI (RIFLE-R) compared to the reported average length of stay between 2.6 and 3.9 days for patients undergoing abdominal and laparoscopic hysterectomies[32] is reflective of the strong association between higher cost and resource utilization once a complication develops, and reinforces the importance of early risk assessment and diagnosis. Any effort to intervene in the course of AKI prior to a severe and often irreversible stage will require preventive techniques that can be deployed after early risk stratification by frontline clinical providers. The KDIGO clinical practice guideline for AKI was intended specifically for such practitioners and offers a variety of kidney sparing strategies including hemodynamic and renal monitoring, adequate volume status and avoidance of radiographic and nephrotoxic medications among patients at-risk for AKI. [4] Our study demonstrates that several readily available perioperative factors can be used to identify such patients at high risk for AKI after gynecologic surgery allowing primary surgical providers to apply preventive strategize in a timely manner.

Strengths and limitations and Interpretation

Similar to other surgical populations, the American College of Surgeons National Surgical Quality Improvement Program criteria for AKI underestimated the prevalence of AKI at only 1% in our cohort thus failing to identify 90% of the AKI patients, mostly those with mild to moderate stages.[5] The lack of reports of AKI in the gynecologic population may reflect this misconception of AKI as a rare surgical complication. In contrast to reports of AKI prevalence of < 2% when utilizing the American College of Surgeons National Surgical Quality Improvement Program criteria,[33] the prevalence of AKI defined by RIFLE in the surgical population is much higher ranging from 25% to 50%, depending on the type of procedure. [5–8, 10, 34] Not only is AKI one of the most prevalent postoperative complication but it is associated with other adverse events, an increase in resource utilization, and both short and long term mortality.[6–8, 35] This is true not only for the most severe AKI that requires renal replacement therapy but also for the whole spectrum of AKI severity including only small changes in sCr.[5] With a prevalence of 13% after major gynecologic surgery, AKI was more common than previously reported postoperative ileus (3%),[36] infections and pelvic abscesses (3–10%),[37] vaginal dehiscence (0.29–4.9%),[38] ureteral injury (0.3–4.8%),[39, 40] and bowel injury (0.3%).[41]

Perioperative AKI is a complex syndrome associated with preoperative patient susceptibilities and intraoperative exposures to nephrotoxins, hypotension, bleeding and surgical stress. In our cohort AKI patients were more likely to require invasive hemodynamic monitoring and use of vasopressors and blood products all of which may reflect unstable perioperative hemodynamic status.[42] Urinary output is a common end-point during resuscitation and its decrease often precedes use of invasive monitoring for assessment of volume status.[8, 34] The increased risk of blood loss and hypotension during the large debulking procedures for gynecologic cancer and exposure to nephrotoxic agents may contribute to the high odds for AKI among patients with cancer.[43] The increased risk for AKI in congestive heart failure and chronic pulmonary disease may be associated with decreased renal perfusion due to low cardiac output or neurohormonal response to hypercapnea.[44] Mechanical urologic injuries did not appear to be a significant mechanism of AKI as only 1.28% of the patients had any evidence of the injury, consistent with previous reports. [39, 40] Although we have used a validated approach for identifying urologic injuries with ICD-9-CM codes we acknowledge that underestimation could occur. However the cumulative urologic injury rate reported with the use of universal intraoperative cystoscopy of 4.3% still cannot account for the reported prevalence of AKI in our study.[40]

Our study is a retrospective cohort analysis and we cannot exclude bias from unmeasured factors although we attempted to control for selection bias with multivariable statistical methods. Although we included only major inpatient surgeries for patients with considerable comorbidity burden that may not reflect the patient profile seen in outpatient setting, in-hospital gynecologic procedures still comprise almost 12% of all surgical procedures.[11] The major strength of our study was the ability to use longitudinal changes in sCr to define AKI using consensus RIFLE criteria rather than relying on ICD-9-CM diagnostic codes. While we assessed comorbidities and complications using previously validated criteria, this approach relies on accurate coding thus the potential for underassessment of risk exists.

Conclusion

In conclusion, AKI is a common complication after major inpatient gynecologic surgery associated with a marked increase in major adverse events. The presence of AKI significantly increases hospital costs associated with other postoperative complications. We have identified several risk factors for AKI that can allow early risk stratification in the preoperative setting in order to improve the delivery of recommended kidney sparing interventions.[4]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Azra Bihorac is supported by Award Number K23GM087709 from the National Institutes of Health - National Institute of General Medical Sciences. The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health. Funding agency had no involvement in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. AB has received grant funding from Astute Medical, Inc. Mr. Adnan Javed was supported by the University of Florida Medical Student Summer Research Fellowship. The preliminary report from this research was presented as oral presentation and awarded at the 38th annual Gulf Atlantic Anesthesia Residents' Research Conference hosted by the University of Puerto Rico Department of Anesthesiology from April 27 through April 29, 2012, in Puerto Rico.

Funding

Azra Bihorac is supported by Award Number K23GM087709 from the National Institutes of Health - National Institute of General Medical Sciences. AB has received grant funding from Astute Medical, Inc. Mr. Adnan Javed was supported by the University of Florida Medical Student Summer Research Fellowship.

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Table 1

Clinical characteristics of the patients stratified by severity of acute kidney injury.

Variables	No AKI (n=2046)	All AKI (n=295)	AKI Stage RIFLE Risk (n=185)	AKI Stage RIFLE Injury (n=65)	AKI Stage RIFLE Failure (n=45)
Age (years), Mean (SD)	53 (15)	60 (15)[a]	60 (15)[a]	59 (14)[a]	61 (14)[a]
Ethnicity, n (%)					
Caucasian	1475 (72)	226 (77)	141 (76)	54 (83)	31 (69)
African-American	380 (18)	44 (15)	26 (14)	7 (11)	11 (24)
Hispanic	55 (3)	9 (3)	8 (4)	0 (0)	1 (2)
Other or missing	136 (7)	16 (5)	10 (6)	4 (6)	2 (4)
Rural area residency, n (%)	800 (39)	97 (33)[a]	61 (33)	20 (31)	16 (36)
Distance from residing neighborhood to hospital (km), Median (25^{th},75^{th})	33 (15, 71)	36 (21, 79)	36 (19, 77)	38 (27, 102)	29 (9, 67)
Population living in poverty in residing neighborhood, % (SD)	16 (8)	16 (8)	15 (8)	14 (7)	18 (9)
Insurance, n (%)					
Medicare	621 (30)	143 (48)[a]	87 (47)[a]	29 (45)	27 (60)[a]
Medicaid	394 (19)	50 (17)	30 (16)	14 (22)	6 (13)
Private	878 (43)	84 (28)[a]	57 (31)[a]	16 (25)	11 (24)
Uninsured	153 (7)	18 (6)	11 (6)	6 (9)	1 (2)
Emergent surgery, n (%)	244 (12)	108 (37)[a]	60 (32)[a]	25 (38)[a]	23 (51)[a]
Weekend admission, n (%)	60 (3)	29 (10)[a]	15 (8)[a]	7 (11)[a]	7 (16)[a]
Weekend discharge, n (%)	695 (34)	54 (18)[a]	37 (20)[a]	13 (20)[a]	4 (9)[a]
Charlson's Comorbidity Index, Median (25^{th}, 75^{th})	1 (0, 3)	5 (2, 8)[a]	5 (2, 8)[a]	8 (2, 8)[a]	3 (2, 8)[a]
Comorbid conditions on admission, n (%)					
Diabetes Mellitus	306 (15)	61 (21)[a]	38 (21)	14 (22)	9 (20)
Chronic obstructive pulmonary disease	246 (12)	54 (18)[a]	37 (20)[a]	9 (20)	8 (18)
Cardiovascular disease	104 (5)	38 (13)[a]	24 (13)[a]	5 (8)	9 (20)[a]
Cerebrovascular disease	24 (1)	10 (3)[a]	7 (4)	2 (1)	1 (2)
Metastatic tumor	307 (15)	144 (49)[a]	91 (49)[a]	37 (57)[a]	16 (36)[a]
Admission serum creatinine (mg/dl), Median (25^{th}, 75^{th})	0.7 (0.6, 0.8)	0.8 (0.6, 1.1)	0.7 (0.6, 1.0)[a]	0.85 (0.6, 1.1)[a]	1.3 (0.75, 2.1)[a,b,c]

Variables	No AKI (n=2046)	All AKI (n=295)	AKI Stage RIFLE Risk (n=185)	AKI Stage RIFLE Injury (n=65)	AKI Stage RIFLE Failure (n=45)
AKI onset in the first 72 hours, n (%)		265 (68)	85 (46)	49 (75)[b]	35 (78)[b]
AKI by NSQIP definition, n (%)		22 (7)	0 (0)	0 (0)	22 (49)[b,c]
ICD-9-CM AKI diagnostic code in discharge summary, n (%)		40 (14)	11 (6)	12 (18)[b]	17 (38)[b]

Abbreviations. AKI, Acute kidney injury; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; NSQIP, National Surgical Quality Improvement Program; SD, Standard Deviation. RIFLE, Risk, Injury, Failure, Loss, and End-stage kidney.

P<0.0083 when comparing to

[a] no AKI group

[b] RIFLE Risk group and

[c] RIFLE Injury group (using Bonferroni correction for Pearson $\chi 2$ test or Fisher's exact test for categorical variables and Kruskal-Wallis test for continuous variables).

Table 2

Perioperative factors associated with acute kidney injury.

Variables	Adjusted Odds Ratio (95% confidence interval)
Age, per one-year increase	1.015 (1.005, 1.03)[a]
African-American ethnicity (vs. others)	1.15 (0.78, 1.69)
Primary diagnosis (vs. Benign tumor)	
Malignant tumor	1.80 (1.17, 2.76)[a]
Non-neoplastic disease of female organs	1.57 (0.94, 2.63)
Emergent Surgery (vs. Elective)	4.10 (2.84, 5.67)[a]
Weekend Admission (vs. Weekday Admission)	1.84 (1.08, 3.13)[a]
Metastatic Cancer (Yes vs. No)	4.01 (2.84, 5.67)[a]
Congestive Heart Failure (Yes vs. No)	2.25 (1.23, 4.11)[a]
Chronic Pulmonary Disease (Yes vs. No)	1.80 (1.24, 2.61)[a]
Diabetes mellitus (Yes vs. No)	1.40 (0.98, 1.99)

Adjusted odds ratios were derived using the multivariable logistic regression that included all listed variables in the model simultaneously. The modeled outcome was any stage of acute kidney injury. The cross-validation estimate of the area under receiver operator curve (95% confidence interval) was 0.79 (0.77, 0.82) by bootstrap resampling, and the Hosmer–Lemeshow test indicated good fit (P = 0.64).

[a]p-value<0.05.

Table 3

Postoperative Complications and Hospital Outcomes stratified by severity of acute kidney injury.

Variables	No AKI (n=2046)	All AKI (n=295)	AKI stage RIFLE Risk (n=185)	AKI stage RIFLE Injury (n=65)	AKI stage RIFLE Failure (n=45)
Hospital Outcomes					
Major adverse event (mortality, sepsis, or mechanical ventilation), n (%)	29 (1.4)	72 (24.4)[a]	27 (15)[a]	21 (32)[ab]	24 (53)[ab]
Hospital mortality, n (%)	2 (0.1)	20 (7)[a]	1 (0.5)[a]	9 (14)[ab]	10 (22)[ab]
90-days mortality, n (%)	10 (0.5)	29 (10)[a]	7 (4)[a]	11 (17)[ab]	11 (24)[ab]
Days in hospital, Median (25th, 75th)	4 (3, 5)	10 (7, 17)[a]	10 (7, 13)[a]	10 (7, 26)[ab]	19 (10, 43)[ab,c]
Discharge to home, n (%)	1997 (98)	232 (79)[a]	162 (88)[a]	48 (74)[ab]	22 (49)[ab]
Resource Utilization					
Intensive care unit admission, n (%)	73 (3.6)	110 (37)[a]	50 (27)[a]	32 (49)[ab]	28 (62)[ab]
Days in intensive care unit, Median (25th, 75th)	2 (1, 4)	4 (2, 9)[a]	2 (1, 4)	5 (2, 9)[ab]	13 (5, 28)[ab]
Mechanical ventilation, n (%)	25 (1)	61 (21)[a]	24 (13)[a]	16 (25)[a]	21 (47)[ab]
Days on mechanical ventilation, Median (25th, 75th)	1 (1, 2)	5 (2, 16)[a]	2 (2, 4)[a]	7 (2, 19)[ab]	15 (5, 27)[ab]
Postoperative Complications					
Mechanical wound complications, n(%)	30 (1)	23 (8)[a]	9 (5)[a]	4 (6)[a]	10 (22)[ab]
Surgical infections, n (%)	56 (3)	18 (6)[a]	7 (4)	8 (12)[a]	6 (13)[ab]
Pulmonary complications, n (%)	50 (2)	44 (15)[a]	20 (11)[a]	10 (15)[a]	14 (31)[a]
Cardiovascular complications, n (%)	30 (1)	17 (6)[a]	6 (3)[a]	7 (10)[a]	4 (9)[a]
Venous thromboembolism, n (%)	15 (0.7)	14 (5)[a]	8 (4)[a]	2 (3)[a]	4 (9)[a]
Gastrointestinal complications, n (%)	62 (3)	36 (12)[a]	23 (12)[a]	6 (9)[a]	7 (16)[a]
Number of postoperative complications, n (%)					
None	1757 (86)	172 (58)[a]	120 (65)[a]	34 (52)[a]	18 (40)[a]
1	257 (13)	77 (26)[a]	46 (25)[a]	21 (32)[a]	10 (22)[ab]
≥2	32 (1)	46 (16)[a]	19 (10)[a]	10 (15)[a]	17 (38)[ac]

Abbreviations. AKI, acute kidney injury. CI, confidence interval. RIFLE, Risk, Injury, Failure, Loss, and End-stage kidney. Hospital cost is inflation adjusted using values for 2012.

P<0.0083 when comparing to

[a] no AKI group

[b] RIFLE Risk group

[c] RIFLE Injury group (using Bonferroni correction for Pearson $\chi 2$ test or Fisher's exact test for categorical variables and Kruskal-Wallis test for continuous variables).

Table 4

The risk-adjusted association between acute kidney injury and major adverse events

Variables	Adjusted Odds Ratio (95% Confidence Interval)
Acute kidney injury (vs. no acute kidney injury)	
Acute kidney injury, all stages[a]	8.95 (5.27, 15.22)[b]
Acute kidney injury, stage RIFLE-Risk	5.39 (2.96, 9.80)[b]
Acute kidney injury, stage RIFLE-Injury	13.26 (6.42, 27.41)[b]
Acute kidney injury, stage RIFLE-Failure	23.56 (10.46, 53.06)[b]
Age, per 1-year increase	1.01 (0.99, 1.04)
African-American Ethnicity (vs. others)	1.67 (0.91, 3.08)
Charlson Comorbidity Index Score, per unit increase	1.05 (0.96, 1.12)
Emergent surgery (vs. Elective)	2.90 (1.74, 4.82)[b]
Weekend Admission (vs. Weekday Admission)	1.16 (0.50, 2.71)
Primary diagnosis (vs. Benign tumor)	
Malignant tumor	1.23 (0.56, 2.75)
Non-neoplastic diseases of female organs	1.64 (0.74, 3.63)
Insurance type (vs. Private)	
Medicare	1.00 (0.49, 2.04)
Medicaid	1.04 (0.51, 2.10)
Uninsured	1.37 (0.54, 3.50)
Number of postoperative complications[c] (vs No complications)	
One	3.53 (2.07, 6.00)[b]
≥ Two	10.20 (5.23, 19.89)[b]

Abbreviations: RIFLE, Risk, Injury, Failure, Loss, and End-stage kidney. Major adverse events were defined as any occurrence of death, sepsis or mechanical ventilation during hospitalization.

[a] Adjusted odds ratios were derived using the multivariable logistic regression that included all listed variables in the model simultaneously. We used two separate multivariable logistic regression models to calculate odds ratios for all stages of acute kidney injury together and separately. The cross-validation estimate of the area under receiver operator curve (95% confidence interval) was 0.88 (0.84, 0.92) by bootstrap resampling, and the Hosmer–Lemeshow test indicated good fit (P = 0.49).

[b] p-value<0.05.

[c] Number of complications sums all postoperative complications from Table 3.

Table 5

Risk-adjusted incremental cost of postoperative complications stratified by acute kidney injury occurrence.

Additional Complications	No acute kidney injury (n= 2,046)	Acute kidney injury (n=295)
Patient with no other postoperative complication, n (%)	1738 (85.0%)	156 (52.9%)
Adjusted average cost ($1000) (95% CI)	8.7 (8.6, 8.9)	18.9 (17.3, 20.4)[a]
Major adverse event, n (%)	29 (1.4%)	72 (24.4%)
Adjusted average cost ($1000) (95% CI)	13.2 (11.5, 14.9)	54.7 (47.2, 62.2)[a]
Postoperative pulmonary complications, n (%)	50 (2.4%)	44(14.9%)
Adjusted average cost ($1000) (95% CI)	10.9 (9.8, 12.0)	45.9 (38.3, 53.5)[a]
Postoperative procedural complications, n (%)	91 (4.5%)	42 (14.2%)
Adjusted average cost ($1000) (95% CI)	10.8 (10.1, 11.6)	37.9 (31.4, 44.4)[a]
Postoperative gastrointestinal complications, n (%)	62 (3.0%)	36 (12.2%)
Adjusted average cost ($1000) (95% CI)	12.1 (11.0, 13.1)	33.2 (27.1, 39.3)[a]
Postoperative surgical infections or wound complications, n (%)	79 (3.9%)	35 (11.9%)
Adjusted average cost ($1000) (95% CI)	11.6 (10.7, 12.5)	46.2 (37.7, 54.8)[a]
Postoperative cardiovascular complications, n (%)	30 (1.5%)	17 (5.8%)
Adjusted average cost ($1000) (95% CI)	11.1 (9.7, 12.5)	49.0 (35.9, 62.1)[a]
Postoperative venous thromboembolism, n (%)	10 (0.5%)	11 (3.7%)
Adjusted average cost ($1000) (95% CI)	13.0 (10.0, 15.9)	37.4 (25.0, 49.8)[a]

Abbreviations: CI, confidence interval.

Adjusted average cost was calculated using non-parametric transformation of the regression coefficients generated using generalized log-linear models adjusted for age, ethnicity, Charlson Comorbidity Index, emergent surgery status, admission day, procedure type, primary insurance, and each postoperative complication.

[a] $P<0.001$ calculated using two independent samples t-test to compare to no AKI group.