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In-Hospital Acute Kidney Injury After TKA Revision With Placement of an Antibiotic Cement Spacer

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ABSTRACT

Background: There is mounting evidence that treatment of periprosthetic joint infection of the knee with an antibiotic cement spacer (ACS) may increase risk for acute kidney injury (AKI). We sought to determine the incidence, as well as potential risk factors, of in-hospital AKI in this cohort.
Methods: We retrospectively identified 75 patients that received either a static or articulating ACS at a single institution. In-hospital AKI was defined by a more than 50% rise in serum creatinine from preoperative baseline to at least 1.4 mg/dL. Our secondary outcome was percent change in creatinine from preoperative to peak postoperative value. Variables were analyzed for the outcome of AKI with univariate logistic regression. A final multivariate model for percent change in creatinine was formed while controlling for age, gender, body mass index, and baseline creatinine.
Results: The incidence of AKI was 14.6%, occurring at a mean of 6.3 days (2-8 days). A lower preoperative hemoglobin (odds ratio = 1.82, $P = .015$) significantly increased risk for AKI on univariate analysis. Diagnosis of either hypertension or diabetes also showed a strong statistical trend ($P = .056$). On multivariate regression, lower preoperative hemoglobin significantly correlated with a greater percent rise in creatinine postoperatively ($\beta = 0.30$, $P = .015$).
Conclusion: The incidence of AKI in patients who receive ACS is relatively high, raising clinical concern in the care of periprosthetic joint infection patients. Our results suggest that a lower baseline hemoglobin may be involved in the etiology of AKI in this population. Therefore, it may be clinically appropriate to monitor anemic patients for AKI when implanting an ACS.

Periprosthetic joint infection (PJI) is the most common reason for revision total knee arthroplasty (TKA), accounting for approximately 25% of all revision TKA cases [1]. Gold standard treatment consists of 2-stage revision arthroplasty with use of an antibiotic-loaded cement spacer [2]. This technique has shown successful long-term prevention of reinfection [2,3]. However, there is relatively little data evaluating antibiotic cement spacers (ACSs) for possible systemic complications.

Acute kidney injury (AKI) is of clinical significance, as the antibiotics most commonly used in cement spacers, vancomycin and aminoglycosides, can be nephrotoxic. Recent case reports have illustrated instances of AKI after implantation of an ACS [4–7] and larger cohort studies have reported an incidence of 17% [8]-26% [9]. The incidence of AKI in primary TKA is much lower. Jafari et al [10] found AKI incidence after primary TKA to be 0.55%, and that the use of antibiotic cement in these primary cases increased risk for AKI ($P = .006$). Other studies have also found AKI incidence for primary TJA to be less than 1% [11,12], and have pointed to male gender [13], and higher American Society of Anesthesiologists (ASA) class, body mass index (BMI), and duration of operation as risk factors [12].

In light of recent reports that have identified relatively high rates of AKI in patients receiving ACS for PJI treatment, we conducted a retrospective review of patients undergoing 2-stage revision TKA for infection at our institution. The goal was to

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identify the incidence and potential predisposing risk factors for AKI in these patients. We hypothesized that increased dose of antibiotics in the ACS would increase risk for AKI.

Materials and Methods

After IRB's approval, we retrospectively identified patients who received a static or articulating ACS for an infected TKA at a single institution from 2007-2017.

All surgeons implanted either PALACOS (Zimmer Biomet, Warsaw, IN) or Simplex (Stryker, Kalamazoo, MI) cement, which are premixed with gentamycin and tobramycin antibiotic powder, respectively. Additional antibiotic powder was routinely added into the cement mixture (either gentamycin, tobramycin, vancomycin, daptomycin, or a mixture of any four). Intravenous (IV) antibiotic therapy was tailored to cultures taken at the time of surgery, with consultation from the institution's infectious disease service. Amount of antibiotic powder implanted, as well as type of IV antibiotic used, was collected from operative notes, implant logs, and medical records.

Variables recorded from the electronic health record included age, gender, BMI, ASA score, comorbidities, and the laboratory values of blood urea nitrogen, creatinine, and hemoglobin. The primary outcome of AKI was defined by a greater than 50% rise in creatinine from baseline (within 30 days preoperatively) to a value of at least 1.4 mg/dL [8] during the hospital stay. A sensitivity analysis was performed for the secondary outcome of percent change in creatinine (from preoperative value to peak postoperative value) to analyze variables that may have caused kidney injury, but did not meet the definition of AKI.

Descriptive statistics on demographics, as well as time to AKI and length of stay were calculated. All variables were analyzed for the outcome of AKI via univariate logistic regression. Only comorbidities that were present in 2 or more patients in the outcome group were analyzed to prevent either partial or complete separation on regression analysis. Univariate odds ratios (ORs) and confidence intervals (CIs) are reported. Secondary to a statistically low number of cases in the outcome group, multivariate regression for the outcome of AKI was not performed. Instead, a final multivariate model for the higher-powered linear outcome of log-transformed percent change in creatinine was constructed to observe the effect of variables that achieved significance on univariate regression while controlling for the demographics of age, gender, BMI, and baseline creatinine. Standardized beta (β) and 95% CIs are reported. All statistics were performed on SPSS, version 22 (IBM, Armonk, NY).

The hospital records of patients in the AKI group were reviewed at second stage reimplantation. Diagnosis of chronic kidney disease, creatinine values, antibiotic powder dose, and IV antibiotic type were collected. Surgeons aimed to use lower-dosed antibiotic cement on reimplantation TKA to avoid weakening the cement [9,14–16]. Patients were evaluated for repeat kidney injury using the same criteria as for first-stage spacer insertion [8]. Descriptive statistics are reported.

Results

A total of 75 knees in 74 patients (39 male and 36 female) were identified. Average age was 67 years (range 35-88 years) and average BMI was 31.3 kg/m^2 (range 18.6-53.3 kg/m^2) (Table 1). Incidence of in-hospital AKI was 14.6% (n = 11), at a mean postoperative time of 6.3 days (range 2-18 days) during a median length of stay of 11 days (range 9-113 days) (Table 2). Average blood urea nitrogen/Cr ratio in patients with AKI was 11.2 (range 5.88-15.75; Table 2), which in the setting of acute renal failure, indicates an intrinsic renal process [17].

Table 1
Demographics (Total Population).

	Mean	SD	Range
Age, y	67	10.58	35-88.7
BMI, kg/cm^2	31.3	7.3	18.6-53.3
Female	36	48.0	
Male	39	52.0	
Acute kidney injury	11	14.7%	
Time to acute kidney injury, d	6.27	1.36	2-18
Length of stay, d	8[a]	7.5[b]	3-113
ASA score	2.61	0.69	1-4
Baseline creatinine, mg/dL	0.95	0.53	0.39-4.15
Peak postoperative creatinine	1.29	0.92	0.50-6.24
BUN, mg/dL	18.86	9.98	1-60
Percent change in creatinine	18.75%[a]	50.36%[b]	−29.87% to 746.15%
Baseline hemoglobin, g/dL	11.41	1.66	7.3-15.4
Percent change in hemoglobin	−19.95%	12.68%	−50% to 25%

ASA, American Society of Anesthesiologists; BMI, body mass index; BUN, blood urea nitrogen; SD, standard deviation.
[a] Median.
[b] Interquartile range.

Increased dose of either vancomycin (P = .681), tobramycin (P = .445), or gentamycin (P = .625) cement was not found to be a statistically significant risk factor for AKI (Table 3). The presence of IV vancomycin also did not increase risk for AKI (P = .627; Table 4). Lower baseline hemoglobin (OR = 1.82, 95% CI = 1.12-2.96, P = .015) increased risk for in-hospital AKI on univariate analysis, whereas hypertension and diabetes both showed a strong trend (P = .056) (Table 5). ASA score did not significantly correlate (P = .344; Table 5). Univariate ORs are summarized in Table 6.

When controlling for age (P = .854), gender (female, P = .404), BMI (P = .426), and baseline creatinine (P = .340) on multivariate regression, lower preoperative hemoglobin significantly correlated with a greater percent change in creatinine (β = 0.30, 95% CI = 0.01-0.13, P = .015) (Table 7).

None of the patients in the AKI group presented with a new diagnosis of chronic kidney disease at second-stage spacer removal and reimplantation (with 1 patient lost to follow-up). One patient in this group did develop repeat-AKI. Antibiotic powder dose varied (vancomycin, range = 0-6 g; tobramycin, range = 0-10.2 g; gentamycin, range = 0-5 g), and was on average less than was given in the ACS (vancomycin, mean = 2.0 vs 8.5 g; tobramycin, mean = 3.6 vs 7.3 g; gentamycin, mean = 1.0 vs 1.3 g, respectively). Seven of the 10 patients received the same IV antibiotics that were administered for the interval between the staged procedures. The remaining 3 patients received IV cefazolin, which is standard prophylactic protocol for TKA at our institution.

Discussion

The incidence of AKI in total joint arthroplasty revision with an ACS varies from 2%-26% based on the definition of AKI used

Table 2
Descriptive Statistics in AKI Group.

	Mean	SD	Range
Length of stay, d	11[a]	18[b]	9-113
Days to AKI	6.27	4.52	2-18
BUN, mg/dL	29	16.18	10-60
Peak creatinine	2.75	1.64	1.43-6.24
BUN/Creatinine	11.18	3.54	5.88-15.75

AKI, acute kidney injury; BUN, blood urea nitrogen; SD, standard deviation.
[a] Median.
[b] Interquartile range.