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Chronic Kidney Disease Linearly Predicts Outcomes After Elective Total Joint Arthroplasty

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ABSTRACT

Background: Kidney disease is associated with increased complications in total joint arthroplasty (TJA). The purpose of this study was to determine the association of kidney disease severity as measured by the chronic kidney disease (CKD) staging system with complications after TJA.
Methods: A retrospective review of 12,308 primary TJAs (6361 hips and 5947 knees) from 2008 to 2013 was performed. The following preoperative variables were obtained from medical records: chemistry 7 panel, Elixhauser comorbidities, and demographic factors. CKD stages were defined based on estimated glomerular filtration rate (eGFR) in mL/min/1.73m^2: (1) 90+, (2) 60-89, (3A) 45-59, (3B) 30-44, (4) 15-29, and (5) <15. Multivariate analysis was performed to assess the independent influence of CKD stage on the aforementioned end points.
Results: Patients with CKD stage greater than 2 demonstrated an increased odds of receiving transfusions ($P = .001$), length of stay >3 days ($P = .010$), acute kidney injury ($P < .001$), septic revisions ($P = .002$), and in-hospital complications ($P < .001$) compared with all patients with eGFR ≥60 when controlling for potential confounders. Only CKD stage 3A was significantly associated with septic revisions (90 days, $P = .004$; 2 years $P = .002$). In addition, the relationship between eGFR and the previously mentioned complications increased linearly rather than demonstrating a clear threshold at which the risk increased substantially.
Conclusion: Severe CKD is associated with increased transfusion, length of stay, and in-hospital complications; and complications increased linearly with disease severity. Surgeons should be cognizant of this increase when evaluating TJA patients with renal disease.

The prevalence of chronic kidney disease (CKD) in the United States has recently been described as an "epidemic," [1] increasing from approximately 10% in 1994 to 13% in 2004 [2]. CKD is common in elderly patients undergoing total joint arthroplasty (TJA), and the incidence of patients who require TJA is higher in CKD patients compared with the general population [3,4]. Thus, it is important for surgeons to understand the complications associated with CKD in patients who undergo TJA.

Patients with CKD frequently have significant cardiovascular comorbidities and reduced long-term survival in proportion to the severity of renal disease [5]. In addition, CKD is associated with comorbidities such as obesity, diabetes mellitus, and hypertension, each of which is an independent risk factor for development of complications after TJA [6-8]. Multiple previous studies have illustrated the large impact renal disease can have on outcomes after TJA: a greater likelihood of postoperative mortality, higher rates of infection, and increased risk of developing other complications [9-17]. Because of the elective nature of TJA, medical optimization of patients with high-risk comorbidities such as CKD remains one of the most important strategies for reducing complications. In addition, patients with renal disease frequently require dialysis or kidney transplantation and are immunosuppressed, which further increases the potential risks of complications.

With a growing population of CKD patients [2,18,19] who require TJA [3,4,20], we should anticipate an increase in the number of perioperative complications, which may have significant

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implications for patients, surgeons, and hospitals. Given that renal disease may potentially be reversible and patients may benefit from medical optimization, it is critical to study the influence of creatinine (Cr) clearance on the outcomes of TJA. Furthermore, no studies have been able to establish threshold values for which TJA can be safely performed in this patient population. The aim of this study was to (1) investigate if CKD severity, as measured by the CKD staging system and Cr clearance, impacted the frequency of in-hospital complications and outcomes after TJA and (2) determine if there is an optimal renal function threshold for performing elective arthroplasty.

Methods

Study Design and Sample

After institutional review board approval, a retrospective review of a prospectively collected institutional database of 12,308 primary TJAs (6361 hips and 5947 knees) was conducted between 2008 and 2013. An electronic query of the medical record was performed to obtain the following parameters: chemistry 7 panel (serum Cr and blood urea nitrogen), Elixhauser comorbidities, [21] and demographic factors (age, gender, body mass index, and race). The total number of patients screened was 12,333; however, 25 patients without available preoperative renal function parameters were excluded. Renal function values from the 2 months before surgery were used or the postoperative day zero values if there were no other prior laboratory values. An estimated glomerular filtration rate (eGFR) was then calculated using Cr clearance and adjusted for patient demographics [22,23].

Exposure of Interest

The main exposure of interest in this study was CKD, which was classified by stage according to the CKD staging system. Primary TJA was not performed in patients with acute kidney disease, so all renal function values could thus be categorized into CKD stages. The CKD stages were defined based on eGFR in mL/min/1.73 m^2 (eGFR): (1) 90+, (2) 60-89, (3A) 45-59, (3B) 30-44, (4) 15-29, and (5) <15.

Outcomes of Interest

The following outcomes were evaluated at 90 days and 2 years: acute kidney injury (AKI), in-hospital complications, in-hospital transfusion, periprosthetic joint infection (PJI), aseptic revisions, venous thromboembolism (VTE), and myocardial infarction. In-hospital complication was determined using *International Classification of Diseases, Ninth Revision* codes for the following: mechanical complications, wound complications, PJI, deep vein thrombosis, pulmonary embolism, genitourinary, cardiovascular, and other (Appendix 1). AKI was defined as an increase in serum Cr of 0.3 mg/dL within 48 hours or serum Cr greater than 1.5 times the preoperative levels, which was identified through an electronic query of Cr laboratories for all patients [24]. AKI thus reflects postoperative renal changes from baseline levels, whereas CKD was based on preoperative labels because patients with AKI are unlikely to undergo primary arthroplasty given its elective nature. In-hospital transfusion was determined by an electronic query for transfusion orders from our institution's blood bank. PJI was determined using a cross-match of our prospectively collected infection database that was constructed with *International Classification of Diseases, Ninth Revision* codes followed by a manual review to confirm PJI that fulfilled the Musculoskeletal Infection Society's criteria [25] and to identify the infecting organism. We also examined the length of hospital stay as another independent variable. Because of the number of patients and retrospective nature of this study, patients were not called, and the follow-up for complications and readmissions were based on the hospital and office visits and admissions of the institution at which the primary surgery was performed.

Covariates

Patient characteristics (age, gender, body mass index, and race), patient comorbidities based on the Elixhauser comorbidity index (acquired immune deficiency syndrome, congestive heart failure, chronic pulmonary disease, cardiovascular disease, diabetes mellitus, malignancy, myocardial infarction, liver disease, peptic ulcer, peripheral vascular disease, rheumatoid arthritis, and kidney or liver transplant), and preoperative angiotensin-converting enzyme inhibitor or nonsteroidal anti-inflammatory drug consumption were recorded and controlled for during the multivariate analysis.

Statistics

Multiple logistic regression analyses were used to evaluate the effect of different renal metrics and comorbidities on each of the different end points and complications. Differences in the organism profile of PJIs were evaluated with Fisher's exact test. All statistical analyses were performed with the use of R 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) using the RMS (regression modeling strategies) package for the logistic regression. The model was pruned using the Akaike information criterion. An alpha level of 0.05 was used to determine statistical significance.

Results

When adjusted for potential confounders, the multivariate analysis demonstrated that patients with CKD stage greater than 2 demonstrated an increased odds of receiving transfusions, having length of stay greater than 3 days, developing AKI, and sustaining in-hospital complications compared to all patients with eGFR ≥60 (Table 1). Overall, the relationship between eGFR and transfusion, length of stay, AKI, and in-hospital complications was found to consistently increase linearly rather than exponentially up to a certain threshold, as a lower eGFR was associated with a higher risk of complications (Fig. 1A-D).

Table 1
Chronic Kidney Disease (CKD) Stage and Complications.

CKD Stage[a]	Transfusion	LOS >3 d	AKI	In-Hospital Complications
3A	OR, 1.67; 95% CI, 1.43-1.96; $P < .001$	OR, 1.34; 95% CI, 1.16-1.56; $P < .001$	OR, 11.21; 95% CI, 7.60-16.53; $P < .001$	OR, 1.21; 95% CI, 1.02-1.45; $P = .033$
3B	OR, 2.80; 95% CI, 2.20-3.57; $P < .001$	OR, 1.39; 95% CI, 1.08-1.78; $P = .010$	OR, 38.30; 95% CI, 25.03-58.60; $P < .001$	OR, 1.80; 95% CI, 1.36-2.37; $P < .001$
≥4	OR, 2.24; 95% CI, 1.38-3.62; $P = .001$	OR, 3.57; 95% CI, 2.30-5.53; $P < .001$	OR, 88.18; 95% CI, 50.41-154.26; $P < .001$	OR, 3.36; 95% CI, 2.09-5.41; $P < .001$

AKI, acute kidney injury; LOS, length of stay; OR, odds ratio.
[a] *P* values compared to CKD stages 1 and 2.