

Comparison of Total Knee Arthroplasty Outcomes Between Renal Transplant and End Stage Renal Disease Patients

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ABSTRACT

Introduction: Patients with end-stage renal disease (ESRD) have increased risk for periprosthetic joint infection (PJI) due to their predisposition for bacteremia and subsequent implant inoculation secondary to dialysis. PJI risk is also elevated in transplant patients secondary to chronic immunosuppressive therapy. The purpose of this study was to compare medical and surgical complications after primary total knee arthroplasty (TKA) in patients with ESRD or renal transplant (RT).

Methods: This was a retrospective review from the PearlDiver database. International Classification of Diseases and Current Procedural Terminology codes were used to identify patients with ESRD or RT who underwent primary TKA for osteoarthritis from 2015 to 2019. Univariate and multivariable logistic regression analyses were done for medical complications up to 90 days and surgical complications up to 2 years.

Results: Within 90 days of TKA, patients with RT were less likely to develop pneumonia (odds ratio [OR] 0.46, 95% confidence interval [CI] 0.23 to 0.84, $P = 0.018$) and wound dehiscence (OR 0.46, 95% CI 0.21 to 0.90, $P = 0.015$). Patients with RT had a lower risk for PJI at 1 year (OR 0.61, 95% CI 0.36 to 0.99, $P = 0.017$) and at 2 years (OR 0.56, 95% CI 0.34 to 0.88, $P = 0.017$) after primary TKA.

Discussion: Consideration should be given to delaying TKA in patients with ESRD who are RT candidates.

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Periprosthetic joint infection (PJI) remains one of the most devastating complications of arthroplasty, oftentimes necessitating multiple surgeries, an extended course of antibiotics, and inferior clinical outcomes. It is also the most common indication for revision total knee arthroplasty (TKA), accounting for more than 25% of these procedures.^{1,2} Revision TKAs not only place a notable financial burden on the United States

healthcare system³ but also lead to clinically notable reductions in quality of life when compared with primary TKA.⁴ Moreover, when comparing outcomes of revision TKA for PJI versus non-PJI etiologies, PJI revision TKA is associated with worse knee range of motion and patient-reported outcomes scores and even increased mortality.^{1,5} Zmistowski et al¹ found that revision TKA for PJI had a 10.6% and 25.9% mortality rate at 1 and 5 years, respectively. This was lower than 5-year relative survival rates of the most common malignancies, including prostate cancer, breast cancer, and melanoma.

Several risk factors have been associated with an increased risk of PJI, including obesity, liver disease, diabetes, and renal disease.^{6,7} The relationship between renal disease and PJI is not fully understood, but it has been hypothesized that electrolyte imbalances⁸ and the blunting of the immune system caused by uremia and systemic inflammation are possible mechanisms.⁹⁻¹¹ Moreover, as the condition progresses to renal failure, the two treatment options available, dialysis and renal transplant (RT), both further increase PJI risk. Dialysis access sites in patients with end-stage renal disease (ESRD) are a potential source of bacteremia and therefore total joint arthroplasty (TJA) implant seeding. RT requires chronic immunosuppressive therapy to prevent transplant rejection, thereby increasing PJI risk. This is particularly problematic because both treatments have been associated with amyloid deposition, osteonecrosis, renal osteodystrophy, and osteoarthritis, all of which increase the need for TJA.^{6,12-15} Thus, a deeper understanding of the interplay between ESRD, RT, and TJA outcomes is necessary to better care for patients who simultaneously have a greater need for TJA and a greater risk for adverse complications after TJA.

Previous studies evaluating PJI risk in patients undergoing these two treatments for renal failure have consisted of small cohorts, lacked longitudinal follow-up, and included total hip arthroplasty and TKA patients together.¹⁵⁻¹⁷ The purpose of this study was to compare the medical and surgical complications after primary TKA in patients with ESRD or RT.

Methods

This study was a retrospective review of the MKnee data set of the PearlDiver Patient Record Database (Pearl-

Diver [www.pearliver.inc]). The MKnee subset is a commercial registry of 1.5 million insured patients who have undergone knee procedures from October 2015 through December 2019. Clinical diagnoses from patient records can be queried using International Classification of Diseases (ICD) and Current Procedural Terminology codes. All data are deidentified and are considered exempt from Institutional Review Board requirements.

ICD-10 and Current Procedural Terminology codes were used to identify patients who had undergone primary TKA. From this group, we only analyzed patients who had undergone surgery for osteoarthritis as identified by the use of ICD-9 and ICD-10 diagnosis codes (Appendix, <http://links.lww.com/JG9/A185>). Patients without a minimum 2-year follow-up were excluded from the study.

Demographic data for each record included the patient's age (reported as 5-year bins), sex, year of procedure, and comorbidities. Comorbidities were defined when at least one instance of comorbidity was diagnosed under any encounter in the patient record within 1 year before index TKA. The two cohorts, dialysis-dependent patients, herein after referred to as patients with ESRD, and patients with RT, were then queried to identify those who had postoperative complications. Medical complications were collected as prerecorded categories using the PearlDiver analysis package and analyzed up to 90 days after TKA. ICD-10 codes, including those for periprosthetic fracture (PPF), PJI, aseptic loosening, and stiffness, were used to identify surgical complications within 90 days, 1 year, and 2 years from the index procedure (Appendix, <http://links.lww.com/JG9/A185>).

Data analysis was done using the PearlDiver R analysis package (PearlDiver [www.pearliver.inc]). Raw/unadjusted univariate analysis of demographic, comorbidity, and complications data was done using χ^2 testing and Welch's *t*-test where appropriate. Multivariable logistic regression was done for medical and surgical outcomes of interest while controlling for age, sex, Charlson Comorbidity Index, and all other factors found to be markedly different in the univariate analysis.

Results

Patient Demographics

There were 3533 patients with ESRD and 646 patients with RT included in the study. Women made up a larger

proportion of the ESRD group (59.81%) versus the RT group (50.31%) ($P < 0.001$). Patients with RT undergoing TKA tended to be younger than patients with ESRD undergoing TKA. A larger percentage of patients in the ESRD group had a Charlson Comorbidity Index ≤ 3 (50.64% ESRD versus 41.33% RT, $P < 0.001$) (Table 1).

Baseline Patient Comorbidities

Patients with RT were less likely to have a history of hypertension (79.41% RT versus 86.78% ESRD, $P < 0.001$), coronary artery disease (20.12% RT versus 29.30% ESRD, $P < 0.001$), anemia (9.91% RT versus 15.85% ESRD, $P < 0.001$), acute myocardial infarction (4.02% RT versus 6.99% ESRD, $P = 0.007$), peripheral vascular disease (10.83% RT versus 16.76% ESRD, $P < 0.001$), and cardiac arrhythmias (15.94% RT versus 24.79% ESRD, $P < 0.001$) (Table 2).

Patients with RT were less likely to have a history of asthma (6.35% RT versus 8.83% ESRD, $P = 0.044$) and chronic pulmonary disease (14.55% RT versus 23.94% ESRD, $P < 0.001$). Patients with RT were less likely to have diabetes (43.34% RT versus 53.10% ESRD, $P < 0.001$), obesity (22.14% RT versus 29.18% ESRD, $P < 0.001$), hypothyroidism (13.93% RT versus 20.89%

ESRD, $P < 0.001$), and cancer (7.43% RT versus 10.16% ESRD, $P = 0.037$) (Table 2).

Liver disease was more common in patients with RT (10.06%) compared with patients with ESRD (7.13%), $P = 0.01$. No other notable differences in baseline comorbidities were observed between patients with RT and ESRD (Table 2).

Medical Complications

Patients with a history of RT were less likely to develop pneumonia (PNA) within 90 days of TKA (odds ratio [OR] 0.46, 95% confidence interval [CI] 0.23 to 0.84, $P = 0.018$). Patients with RT were also less likely to develop wound dehiscence within 90 days of index TKA (OR 0.46, 95% CI 0.21 to 0.90, $P = 0.015$). No difference was observed between the ESRD and RT groups for risk of deep vein thrombosis (DVT), hematoma, transfusion, urinary tract infection, or sepsis (Table 3).

Surgical Complications

Within 90 days of TKA, the RT group was more likely to develop knee stiffness (OR 1.36, 95% CI 1.02 to 1.80, $P = 0.034$). No statistically significant difference was observed in risk of PJI, PPF, or aseptic loosening at 90 days (Table 4). At 1 year, the RT group was less likely to develop a PJI than the ESRD group (OR 0.61,

Table 1. Baseline Patient Demographics and Charlson Comorbidity Index

Patient Demographics	ESRD (N = 3533)		Renal Transplant (N = 646)		P
	N	%	N	%	
Age					
<40	10	0.28	<11	N/A	N/A
40-49	61	1.73	30	4.64	<0.001
50-59	414	11.72	151	23.27	<0.001
60-69	1038	29.38	261	40.40	<0.001
70-79	1856	52.53	190	29.41	<0.001
≥ 80	154	4.36	<11	N/A	N/A
Sex					
Male	1420	40.19	321	49.69	<0.001
Female	2113	59.81	325	50.31	<0.001
CCI					
≤ 3	1789	50.64	267	41.33	<0.001
4	365	10.33	112	17.34	<0.001
5	381	10.78	90	13.93	0.023
6	271	7.67	59	9.13	0.235
≥ 7	727	20.58	118	18.27	0.197

CCI = Charlson Comorbidity Index, ESRD = end-stage renal disease, N/A = not available

Table 2. Baseline Patient Comorbidities

Patient Comorbidities	ESRD (N = 3533)		Renal Transplant (N = 646)		P
	N	%	N	%	
Cardiovascular					
Hypertension	3066	86.78	513	79.41	<0.001
Coronary artery disease	1035	29.30	130	20.12	<0.001
Anemia	560	15.85	64	9.91	<0.001
Congestive heart failure	234	6.62	51	7.89	0.274
Acute myocardial infarction	247	6.99	26	4.02	0.007
Peripheral vascular disease	592	16.76	70	10.83	<0.001
Cardiac arrhythmias	876	24.79	103	15.94	<0.001
Coagulopathy	235	6.65	43	6.66	1
Pulmonary					
Asthma	312	8.83	41	6.35	0.044
Chronic pulmonary disease	846	23.94	94	14.55	<0.001
Metabolic					
Diabetes	1876	53.10	280	43.34	<0.001
Obesity	1031	29.18	143	22.14	<0.001
Liver disease	252	7.13	65	10.06	0.01
Hypothyroidism	738	20.89	90	13.93	<0.001
Cancer	359	10.16	48	7.43	0.037
Other					
Tobacco use	179	5.07	21	3.25	0.059
Alcohol use	81	2.29	12	1.86	0.586
Drug abuse	140	3.96	17	2.63	0.128
Depression	582	16.47	87	13.47	0.06

ESRD = end-stage renal disease

95% CI 0.36 to 0.99, $P = 0.017$). The RT group was more likely to develop stiffness at 1 year (OR 1.32, 95% CI 1.11 to 1.71, $P = 0.046$). No statistically significant

difference was observed for risk of PPF and aseptic loosening between the two groups at 1 year (Table 5). The RT group also had a lower risk of PJI at 2 years (OR

Table 3. Frequency and Adjusted Odds Ratio of Medical Complications at 90 Days

Patient Comorbidities	ESRD (N = 3533)		Renal Transplant (N = 646)		Transplant Odds Ratio (95% Confidence Interval)	P
	N	%	N	%		
DVT	40	1.13	11	1.70	0.73 (0.28-1.89)	0.518
Pulmonary embolism	<11	N/A	0	0	N/A	N/A
Pneumonia	129	3.65	11	1.70	0.46 (0.23-0.84)	0.018
Hematoma	21	0.59	<11	N/A	0.84 (0.30-2.32)	0.733
Transfusion	109	3.09	17	2.63	0.89 (0.52-1.52)	0.673
Urinary tract infection	276	7.81	49	7.59	1.08 (0.77-1.50)	0.652
Sepsis	65	1.84	16	25.00	1.40 (0.76-2.44)	0.252
Wound dehiscence	78	2.21	12	1.86	0.46 (0.21-0.90)	0.015

ESRD = end-stage renal disease

Table 4. Frequency and Adjusted Odds Ratio of Surgical Complications at 90 days

Patient Comorbidities	ESRD (N = 3533)		Renal Transplant (N = 646)		Transplant Odds Ratio (95% Confidence Interval)	P
	N	%	N	%		
Periprosthetic joint infection	94	2.66	11	1.70	0.54 (0.27-0.98)	0.057
Periprosthetic fracture	22	0.62	<11	N/A	0.28 (0.02-1.40)	0.223
Stiffness	277	7.84	73	11.3	1.36 (1.02-1.80)	0.034
Aseptic loosening	<11	N/A	0	0	N/A	N/A

ESRD = end-stage renal disease, N/A = not available

0.56, 95% CI 0.34 to 0.88, $P = 0.017$). No notable difference was observed in risk of PPF, stiffness, or aseptic loosening at 2 years (Table 6).

Discussion

Because outcomes after RT continue to improve, more patients with ESRD are undergoing this procedure. However, there remains some concern in doing TJA in this patient population because both dialysis and RT have been associated with increased complications and worse outcomes, including increased DVT, PJI, implant loosening, and mortality.^{15,16,18,19} Current literature comparing TJA complications and outcomes between patients receiving dialysis and RT is lacking, and most are limited by small sample sizes.¹⁵⁻¹⁷ Furthermore, the current available studies that do include larger patient cohorts are limited by short-term outcomes.¹² In our retrospective cohort study, we included a much larger patient cohort with the 2-year follow-up.

Compared with patients with ESRD, patients with RT had a nearly onefold decrease in risk of PJI at both 1 and 2 years after TKA. A similar difference was observed at 90 days after TKA, although statistical significance was not reached ($P = 0.057$). In 2015, Cavanaugh et al¹² demonstrated decreased rates of surgical site infection after TJA in patients with RT compared against dialysis

patients. In a more recent single center study, Inoue et al²⁰ also reported a decreased risk of surgical site infection or PJI after TJA in patients with RT compared with dialysis patients. Although these two studies grouped both hip and knee arthroplasty patients together, the results of our study, which evaluated TKA patients only, are consistent with their findings. It is also important to note that these previous studies only reported postoperative infection rates during the index hospitalization or within 90 days after surgery. Thus, our current study builds on these observations by focusing on TKA and by demonstrating that the differences in risk persist up to 2 years after index arthroplasty. Our findings support the suggestions made by previous studies to consider RT before TJA in patients with severe kidney disease.^{12,16,17,20}

Interestingly, patients with RT were found to have increased knee stiffness at 90 days and 1 year after TKA. This is a cause for concern because patients with arthrofibrosis have poor functional outcomes and increased knee pain,^{21,22} both of which are major determinants of patient satisfaction with TKA.²³ Arthrofibrosis is characterized by excessive proliferation of scar tissue.²⁴ Although the precise mechanism of pathogenesis is unclear, it has been posited that derangements in type-I collagen deposition during scar formation or fibrinolysis during scar remodeling play a

Table 5. Frequency and Adjusted Odds Ratio of Surgical Complications at 1 Year

Patient Comorbidities	ESRD (N = 3533)		Renal Transplant (N = 646)		Transplant Odds Ratio (95% Confidence Interval)	P
	N	%	N	%		
Periprosthetic joint infection	133	3.76	19	2.94	0.61 (0.36-0.99)	0.017
Periprosthetic fracture	26	0.74	<11	N/A	0.46 (0.07-1.58)	0.30
Stiffness	322	9.11	82	12.69	1.32 (1.11-1.71)	0.046
Aseptic loosening	16	0.45	<11	N/A	N/A	N/A

ESRD = end-stage renal disease, N/A = not available

Table 6. Frequency and Adjusted Odds Ratio of Surgical Complications at 2 years

Patient Comorbidities	ESRD (N = 3533)		Renal Transplant (N = 646)		Transplant Odds Ratio (95% Confidence Interval)	P
	N	%	N	%		
Periprosthetic joint infection	183	5.18	21	3.25	0.56 (0.34-0.88)	0.017
Periprosthetic fracture	32	0.91	<11	N/A	0.39 (0.06-1.31)	0.199
Stiffness	333	9.43	83	12.85	1.28 (0.98-1.67)	0.067
Aseptic loosening	27	0.76	<11	N/A	0.15 (0.01-0.71)	0.062

ESRD = End-stage renal disease, N/A = not available

role in joint contracture.^{25,26} Following this line of thought, one possible explanation for increased knee stiffness observed in patients with RT in our study is that the use of glucocorticoids—one of the most common agents in combination immunosuppressive therapy after solid organ transplant—has been shown to diminish fibrinolysis.²⁷ The resultant inadequate tissue remodeling could contribute to stiffness in patients with RT. Although arthrofibrosis is associated with worse post-operative outcomes, the morbidity associated with PJI is graver.^{1,2} The previously mentioned decrease in risk of PJI arguably outweighs the higher rates of stiffness in patients with RT. As such, consideration should be given to delaying TKA in patients with ESRD who are RT candidates.

Although our study found that rates of medical complications were similar between patients with ESRD and RT, the latter cohort did demonstrate markedly lower rates of PNA within 90 days of TKA. This is important because studies have shown that chronic kidney disease is a risk factor for community-acquired and nosocomial PNA,²⁸ and patients with kidney disease experience more severe bouts with this lower respiratory tract infection.²⁹ Moreover, PNA is one of the most common nonsurgical complications after surgery,³⁰ including after TJA surgery.³¹ Postoperative PNA prolongs length of stay after surgery, increases medical costs, and is associated with increased morbidity and mortality.^{30,32,33} This is yet another reason why clinicians may consider RT before TKA in transplant candidates to avoid placing patients, who already have an increased predisposition for acquiring PNA, at even greater risks.

There are some limitations to our current study that should be considered. First, as a retrospective database study, there is an inherent possibility for inaccuracies in data entry and coding. Second, we were unable to identify the microorganism responsible for PJI, which may be an important factor to consider. Finally, information regarding implant design and fixation technique was unavailable.

Despite these limitations, it is our understanding that this study is the first to investigate longitudinal differences in rates of medical and surgical complications between these two patient cohorts, specifically in patients with TKA. Our study demonstrates that compared with patients with ESRD, patients with RT are at a decreased risk for PJI after TKA. This finding is consistent with results from smaller previous studies with short-term outcomes.^{12,16,17,20} In addition, our results also agree with the recommendations made by the second International Consensus Meeting on orthopaedic infections to conduct TJA after solid organ transplant to reduce rates of PJI.³⁴ Although not all patients with ESRD are candidates for RT, those who are should be made aware of the differences in complication and infection risks to avoid adverse outcomes and further improve patient outcomes with TKA.

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