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### Authors

Upfill-Brown, Alexander

Wu, Shannon Y

Hart, Christopher

et al.

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## Revision total knee arthroplasty outcomes in solid organ transplant Patients, a matched cohort study of aseptic and infected revisions

Alexander Upfill-Brown<sup>a</sup>, Shannon Y. Wu<sup>a</sup>, Christopher Hart<sup>a</sup>, Peter P. Hsiue<sup>a</sup>, Clark J. Chen<sup>a</sup>, Danielle Ponzio<sup>b</sup>, Christos Photopoulos<sup>c</sup>, Alexandra I. Stavrakis<sup>a,\*</sup>

<sup>a</sup>Department of Orthopaedic Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

<sup>b</sup>Rothman Institute at Thomas Jefferson University, Egg Harbor Township, NJ, USA

<sup>c</sup>Cedars-Sinai Kerlan-Jobe Orthopaedic Institute, Los Angeles, CA, USA

### Abstract

**Background:** Previous studies have demonstrated that solid organ transplant (SOT) patients undergoing primary total knee arthroplasty (TKA) are at an increased risk of postoperative complications. The purpose of this study is to utilize a large, national database to investigate revision TKA (rTKA) outcomes in SOT patients.

**Methods:** This was a retrospective review utilizing the Nationwide Readmissions Database (NRD) and ICD-9 codes to identify patients who underwent rTKA from 2010–2014 with a history of at least one SOT. Propensity-score-matching (PSM) was used to compare rTKA outcomes in SOT patients compared to matched patients without SOT.

**Results:** A total of 303,867 rTKAs, with 464 of those being performed in SOT patients, were included in the study. Of these, 71,903 and 182 were performed for PJI in non-SOT and SOT patients, respectively. rTKA was performed most frequently in kidney transplant patients (53.0%) followed by liver transplant patients (34.3%). For non-PJI patients, SOT patients had a higher 90-day readmission rate than matched non-SOT rTKA patients (23.2% vs 12.6%,  $p = 0.006$ ). However, there were no differences in 90-day readmission rates for specific rTKA complications, subsequent revision rTKA, or mortality. Among patients undergoing rTKA for PJI, there was no difference in overall 90-day readmission rate, readmission for specific rTKA complications, subsequent revision rTKA, or mortality.

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\*Corresponding author at: 1250 16<sup>th</sup> Street, Suite 2100, Santa Monica, CA 90404, USA. [astavrakis@mednet.ucla.edu](mailto:astavrakis@mednet.ucla.edu) (A.I. Stavrakis).

Ethics approval

Ethics approval by the IRB of UCLA was not required as we make use of a publicly available administrative database without personal identifying information.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Conclusions:** While the increased medical comorbidities associated with SOT place patients at increased risk for complications following rTKA, it appears that SOT alone does not do so when patients are matched based on overall medical comorbidity.

### Keywords

Revision total knee arthroplasty; Solid organ transplant; Surgical outcomes; Prosthetic joint infection

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## 1. Introduction

There has been an upward trend in most types of solid organ transplants (SOT) from 2007 to 2018, and advancements made in organ procurement, surgical technique, and medical management have significantly prolonged recipient survivorship [1,2]. More transplant patients are therefore living longer and more likely to develop end-stage knee osteoarthritis (OA) requiring total knee arthroplasty (TKA). In addition, due to lifelong immunosuppression and increased medical comorbidities, organ recipients are also at increased risk of developing avascular necrosis which may also necessitate TKA [3–6]. The percentage of patients undergoing primary TKA with a history of SOT increased by 50% from 1998 to 2011, now are now estimated to account for 0.1% of all TKA performed [7]. As more SOT patients receive TKA, more are also requiring revision TKA (rTKA).

Most prior studies have demonstrated that SOT patients undergoing primary TKA are at an increased risk of postoperative complications compared to non-SOT patients, including surgical site infection and periprosthetic fracture [3,7,8]. The consequences of such complications are serious, as these complications require readmission and surgical management, most commonly revision total knee arthroplasty (rTKA) [8]. Klika et al. found in a comparison of early post-operative outcomes between transplant and non-transplant patients undergoing total knee arthroplasty that transplant patients experienced longer lengths of stay, higher costs, and were at higher risk of overall complications following the procedure [7]. Ledford et al. found that although primary TKA had no impact on SOT patient survivorship, SOT patients had a higher risk of perioperative complication and lower implant survivorship at 5-year follow-up compared to the general TKA population [9]. As a result, transplant patients are more likely to require revision arthroplasty, and the increased complexity of these operations could possibly place SOT patients an increased risk for complications [10]. Ledford *et al* reported poor outcomes in a small series of SOT rTKA patients with 22% of patients required re-revision due to acute periprosthetic joint infection (PJI), and 67% of patients experienced complications such as intraoperative fracture and instability [11]. Labaran *et al* examined rTKA and revision total hip arthroplasty (rTHA) outcomes in renal transplant patients alone and found increased LOS and increased rates of septicemia and 1-year mortality following rTKA [12]. There has been no large study of rTKA in SOT patients generally, and no study has examined outcomes in patients undergoing revision for aseptic and infectious indications separately.

An accurate understanding of complication rates following rTKA in transplant patients may facilitate improved surgical planning and decision making. The purpose of this study is

to utilize a large, nationally representative database to investigate rTKA outcomes in SOT patients compared to those with similar comorbidities. We hypothesized that SOT patients, especially those undergoing revision for infectious reasons, would have higher rates of re-admission and revision operations following rTKA compared to similar, non-transplant patients.

## 2. Methods

The study cohort was identified from the Nationwide Readmissions Database (NRD) over a 5-year study period (2010–2014). The NRD is a nationally representative database developed and validated through a federal–state–industry partnership sponsored by the Agency for Healthcare Research and Quality. It is based on 22 state inpatient databases that track patients across multiple hospitals. Approximately 51.2% of the U.S. population and 49.3% of all U.S. hospitalizations were sampled in a stratified algorithm, designed to allow for estimation of nationally representative statistics. Available variables include demographic data, diagnoses, procedures, cost, length of inpatient stay (LOS), and hospital characteristics. Because the NRD database has been sufficiently deidentified, this study was deemed exempt by the institutional review board at our institution.

Patients older than 18 years of age who were admitted for rTKA were considered for this study. Patients were identified using the International Classification of Diseases, 9th Revision, (ICD-9) procedure codes (81.55, 00.80, 00.81, 00.82, 00.83, 00.84). Patients were separated into groups based on whether or not they had a diagnosis of SOT (Table 1). Indication for rTKA was determined based on associated ICD-9 diagnostic codes, as has been done in previous epidemiological analyses [25]. All subsequent readmissions were considered for these groups. Baseline comorbidity was quantified using the Elixhauser Comorbidity Index (ECI), a composite score of 30 comorbid conditions using all admission diagnoses and the comorbidity package in R [13]. Higher ECI scores corresponded to greater burden of comorbid conditions. ECI score component variables were also extracted.

The primary outcomes of interest included 90-day mortality, all-cause readmission rates, readmission stratified by associated rTKA indication, as well as subsequent revision rTKA. Secondary outcomes included complications during index hospitalization and length of stay. ICD-9 codes were used to identify cardiac arrest, respiratory complications, pneumonia, pulmonary embolism (PE), deep vein thrombosis (DVT), acute renal failure, urinary tract infection, decubitus ulcer, neurologic changes, wound complications, post-operative blood transfusion or any in-hospital complications. Complications and associated ICD-9 codes can be found in supplementary materials (Table S1).

Propensity score matching (PSM) was performed to compare relative risks (RR) of re-admissions and complications transplant and non-transplant patients [14]. A propensity score multivariate logistic regression model was created using patient age, sex, ECI, hospital type, hospital size, insurance status, and zip code income quartile. Specific medical comorbidities were also in the model, including history of CHF, cardiac arrhythmia, pulmonary hypertension, chronic pulmonary disease, essential hypertension, diabetes, obesity, coagulopathy, solid tumor and alcohol abuse. Patients undergoing rTKA for PJI

were analyzed separately from those undergoing rTKA for other reasons (i.e. loosening, instability). Propensity scores were used to match transplant patients to non-transplant patients at a ratio of 1:3 with replacement improve balance using the MatchIt package in R [15]. Relative risk was estimated using weighted logistic regression.

All result sample sizes represented national estimates accounting for the NRD's stratified 2-stage cluster design incorporating individual discharge-level weights. Descriptive analysis was used to describe both baseline characteristics and outcome parameters within each comparison group. Categorical variables were compared using the chi-squared statistic, except when individual cell counts were less than 10, in which case the Fisher exact test was used. Continuous variables were reported using mean, 95% confidence interval (CI), and P values and were compared using the Student t-test after ensuring normal distributions. For skewed distributions, continuous variables were presented as median (interquartile range) and the Wilcoxon rank-sum test. All tests were unpaired with a significance level defined as a 2-tailed P of 0.05. Statistical analyses were performed using R 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria).

### 3. Results

#### 3.1. Baseline characteristics

A total of 303,867 patients underwent rTKA during the study period, 303,366 non-transplant patients and 464 transplant patients (Table 2). Of these, 71,903 (29.8%) and 182 (39.2%) were performed for PJI in non-SOT patients and SOT patients, respectively ( $p < 0.001$ ). Within the SOT rTKA group, renal transplant was the most common (53.0%), followed by liver (34.3%) and heart transplant (11.6%) (Table 3). SOT patients tended to be younger than other rTKA patients (61.6 years vs 65.4 years,  $p < 0.001$ ). SOT patients were also less likely to be female (39.4% vs 58.4%,  $p < 0.001$ ). They also tended to have a higher baseline level of medical comorbidity (ECI mean 3.88 vs 2.44,  $p < 0.001$ ) and a longer LOS (mean 7.1 days vs 4.9 days,  $p < 0.001$ ). SOT patients were more likely to undergo rTKA at an urban teaching hospital (69.7% vs 57.8%,  $p = 0.015$ ).

#### 3.2. PJI versus Non-PJI patients

In univariate analysis of differences in outcomes of PJI rTKA versus non-PJI rTKA, significant differences were identified between SOT and non-SOT patients. SOT patients undergoing rTKA for PJI had a significantly longer LOS (9.4 days vs 5.5 days,  $p = 0.003$ ), higher likelihood of readmission (42.2% vs 24.0%,  $p = 0.0499$ ), and a higher likelihood of subsequent revision (35.1% vs 4.5%,  $p < 0.001$ ) compared to those revised for non-PJI indications. Non-SOT patients undergoing rTKA for PJI had a significantly longer LOS (8.7 vs 3.7 days,  $p < 0.001$ ), higher likelihood of readmission (36.4% vs 10.2%,  $p < 0.001$ ) and a higher likelihood of subsequent revision (28.0% vs 3.6%,  $p < 0.001$ ) compared to those revised for non-PJI indications.

#### 3.3. PSM analysis of Non-PJI patients

A total of 272 non-PJI SOT patients were matched to 803 non-PJI control patients, with good balance across variables (Table S2). Among non-PJI rTKA patients, SOT patients had

a higher all-cause 90-day readmission rate than matched rTKA patients (23.2% vs 12.6%,  $p = 0.006$ , Table 4). There were no differences in 90-day readmission due to specific rTKA complications including loosening, infection, instability or periprosthetic fracture when specific indications were analyzed separately. There was no difference in 90-day revision rTKA or mortality (Table 4).

There was no difference in index hospitalization wound complications (4.0% vs 3.5%,  $p = 0.78$ , Table S3). There were no differences between groups with regard to overall complications or specifically cardiac, pulmonary or renal complications. The rates of PE and DVT were also not significantly different between groups. The higher post-operative blood transfusion rate in SOT patients was not statistically significant (24.4% vs 16.1%,  $p = 0.055$ ). There was no difference in length of stay (4.6 vs 4.4 days,  $p = 0.673$ , Table S3).

### 3.4. PSM analysis of PJI patients

A total of 172 PJI SOT patients were matched to 514 PJI control patients, with good balance across variables (Table S4). There was no difference in all-cause 90-day readmission rate (40.4% vs 39.5%,  $p = 0.89$ ) or readmission secondary to loosening, PJI, instability or fracture, subsequent revision rTKA or mortality (Table 5).

During the index hospitalization, SOT patients had lower rates of concurrent systemic infection than matched rTKA patients (7.2% vs 18.7%,  $p = 0.037$ ) and higher rates of post-operative blood transfusion (43.1% vs 30.4%,  $p = 0.041$ , Table S5). There was no difference during the index hospitalization for wound, cardiac, pulmonary or renal complications. The rates of PE and DVT were not significantly different between groups. The rates of wound and surgical site complications did not differ between groups. There was no difference in LOS (10.1 vs 11.9 days,  $p = 0.268$ , Table S5).

## 4. Discussion

While prior studies have identified higher rates of complications in SOT patients following primary total joint arthroplasty, few studies have examined the post-operative complications of SOT patients following revision arthroplasty. In this analysis, we found a higher rate of all-cause re-admission following rTKA in non-PJI SOT patients compared to matched controls. Otherwise, we found no differences in rates of post-operative re-admission for complications related to rTKA, subsequent re-revision, or mortality in non-PJI SOT patients compared to matched controls. PJI SOT patients were similar to matched PJI patients with regard to 90-day re-admission, revision and mortality after rTKA. The rate of post-operative blood transfusion was significantly higher for SOT patients revised for infection compared to matched controls.

Labaran *et al* investigated outcomes following revision hip and knee arthroplasty in renal transplant patients using a large Medicare database from 2005 to 2015 [12]. In a matched analysis they found that renal transplant patients had a significantly longer LOS, increased 1-year mortality and 1-year septicemia than matched non-transplant patients; they found no difference in 90-day overall re-admissions. They did not analyze re-operations or re-admissions for specific rTKA complications. In comparison, we found higher rates of

overall re-admission in SOT patients and no differences in 90-day mortality or LOS when PJI and non-PJI SOT patients were analyzed separately. While non-PJI SOT patients had a higher all-cause rate of readmission, we found no difference between non-PJI SOT patients and controls with regard to readmission for reasons related to rTKA. These readmissions are likely related to medical issues, which may have been exacerbated by their recent surgery. In our experience with this high-risk population, close monitoring by a multidisciplinary team in the post-operative period is helpful to identify both surgical and medical issues early in their presentation. In a much smaller, single institution case series of 9 rTKA patients, Ledford et al. described outcomes in 9 SOT patients undergoing rTKA, of which 2 underwent re-revision acutely for PJI [10]. This is comparable to the 90-day rate of re-operation following rTKA for PJI in SOT patients in this study. We found the rate of re-operation following rTKA for other reasons to be substantially lower.

While prior studies have suggested a higher post-operative infection rate in SOT patients following primary TJA, results have not been conclusive [4,7,8,16]. PJI is the most feared complication following arthroplasty in SOT patients given the hypothesized higher risk posed by the use of chronic immunosuppressive medications in these patients. However, across surgical specialties, in comparative studies of elective surgical procedures adjusting for underlying medical comorbidity, SOT patients have similar rates of surgical site infections and wound complications [17,18]. The reasons for this may be twofold. First, immunosuppression is not unique to SOT – many different types of patients are on immunosuppressive medications or immunosuppressed as a consequence of chronic disease [24]. Second, SOT patients often have higher levels of medical literacy and access to care than average [19]. Multiple studies have found that advanced kidney disease patients with low health literacy were less likely to be referred for organ transplant in the first place [20,21], and similar findings have been identified in liver transplant populations as well [22]. As a result, the SOT patient population may be uniquely equipped to successfully navigate complex medical issues and less likely to forgo medical care due to barriers imposed by low health literacy [23]. Furthermore, SOT patients are more likely to be treated at specialized academic centers, and consequently, as we find in this study, are more likely to receive their arthroplasty care at these same institutions. These studies suggest that although SOT patients' immunosuppressive regimens may pose additional risk, some of that may be offset by increased access to specialized care and ease of navigating the healthcare system.

The present study is not without its limitations. First, we recognize the inherent weaknesses in a large database study including potential for errors in coding and data entry. It is possible that some re-admission events were missing from the NRD, biasing complication estimates downwards in this study compared to single institution studies. Furthermore, the NRD allows for the analysis of short-term outcomes and therefore likely underestimates the true incidence of complication following rTKA. Important clinical outcomes such as functional status, patient reported outcome measures (PROMs), and pain scores are not recorded in the NRD. Despite controlling for demographic variables and comorbidities in our multivariate PSM analysis, there are some important confounding factors for which we were not able to control. Important surgical factors, including surgical complexity, were not available for analysis. Lastly, information regarding surgical details such as implants used, procedure duration, intraoperative complications, and blood loss were unavailable in the NRD. Despite

the above limitations, our study, to the best of our knowledge, reports on the largest number of rTKA performed in SOT patients and provides a useful contribution to the post-operative risks facing this unique group of patients.

## 5. Conclusion

While the increased medical comorbidities associated with SOT place patients at greater risk for complications following rTKA, it appears that SOT alone does not do so when patients are matched based on overall level of medical comorbidity. In this analysis, we find higher rates of overall re-admission following rTKA for non-PJI reasons in SOT patients compared to matched controls. Otherwise, we find no difference in post-operative re-admission related to rTKA, re-operations or mortality following rTKA for SOT patient compared to matched controls when rTKA was performed for either infectious or noninfectious reasons. While most patients with SOT are taking immunosuppressive agents, they also have relatively high access to medical care and high medical literacy which may offset this expected risk factor when compared to patients with similar levels of medical comorbidity.

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**Table 1.**

Table of diagnostic codes used to identify indications for revision arthroplasty and solid organ transplant patients.

	<b>ICD-9 Diagnostic Codes</b>
<b>Indications for Revision</b>	
<b>Implant and Periprosthetic fracture</b>	996.43,996.44
<b>Aseptic loosening</b>	996.41,996.45,996.46
<b>Instability</b>	996.42
<b>Prosthetic joint infection</b>	996.65,996.66,996.67
<b>Solid Organ Transplant</b>	
<b>Kidney</b>	V42.0
<b>Liver</b>	V42.7
<b>Heart</b>	V42.1
<b>Lung</b>	V42.6
<b>Pancreas</b>	V42.83

**Table 2.**

Baseline characteristics of rTKA transplant and non-transplant patients identified over study period.

	No Transplant	Transplant	P
	n=303,366	n=464	
<b>Sex, Female</b>	177,087 (58.4%)	183 (39.4%)	<0.001
<b>Age</b>			
<b>Mean</b>	65.4	61.6	<0.001
<b>&lt;60</b>	90,485 (29.8%)	190 (40.9%)	0.004
<b>60–75</b>	66,990 (22.1%)	43 (9.3%)	
<b>&gt;75</b>	145,891 (48.1%)	231 (49.8%)	
<b>Indication</b>			
<b>PJI</b>	71,903 (23.7%)	182 (39.2%)	<0.001
<b>Fracture</b>	8683 (2.9%)	6(1.3%)	
<b>Instability</b>	24,642 (8.1%)	27 (5.8%)	
<b>Loosening</b>	73,079(24.1%)	71 (15.3%)	
<b>Other</b>	125,058 (41.2%)	178(38.4%)	
<b>ECI, mean</b>	2.44	3.88	<0.001
<b>LOS, mean</b>	4.89	7.08	<0.001
<b>Payer</b>			
<b>Medicaid</b>	11,750(3.9%)	11 (2.4%)	0.074
<b>Medicare</b>	180,360 (59.6%)	317 (68.2%)	
<b>Private</b>	90,837 (30%)	126(27.1%)	
<b>Other</b>	19,827 (6.5%)	11 (2.4%)	
<b>Income, Quartile</b>			
<b>0–25%</b>	75,173 (25.2%)	99 (22%)	0.600
<b>25–50%</b>	80,537 (27%)	120(26.6%)	
<b>50–75%</b>	77,464 (25.9%)	140(31%)	
<b>75–100%</b>	65,426 (21.9%)	92 (20.4%)	
<b>Hospital Type</b>			
<b>Rural</b>	23,802 (7.8%)	31 (6.7%)	0.015
<b>Urban Non-Teach</b>	104,250 (34.4%)	110(23.7%)	
<b>Urban Teaching</b>	175,314 (57.8%)	324 (69.7%)	
<b>Hospital Size</b>			
<b>Large</b>	170,222 (56.1%)	312 (67.2%)	0.057
<b>Medium</b>	72,705 (24%)	84(18.1%)	
<b>Small</b>	60,439(19.9%)	68(14.7%)	
<b>Emergent</b>	58,258(19.2%)	103 (22.2%)	0.400

**Table 3.**

Number of transplant patients by type of transplant.

	n	%
<b>All Transplants</b>	464	
<b>Kidney</b>	246	53.0%
<b>Liver</b>	159	34.3%
<b>Heart</b>	54	11.6%
<b>Pancreas</b>	26	5.6%
<b>Lung</b>	6	1.3%

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**Table 4.**

Propensity score matched analysis of probability of re-admission and subsequent revision rTKA for non-PJI patients.

	<b>SOT Patients</b>	<b>Matched Controls</b>	<b>Relative Risk</b>	<b>95% CI</b>	<b>P-Value</b>
<b>All-Cause Readmission</b>	23.1%	12.6%	1.84	(1.19, 2.85)	0.006
<i>Loosening</i>	0.0%	0.0%	1.00	(0.81,1.24)	0.999
<i>PJI</i>	2.6%	3.8%	0.69	(0.2,2.43)	0.562
<i>Instability</i>	0.9%	0.3%	3.00	(0.18,49.75)	0.439
<i>Periprosthetic Fracture</i>	0.0%	0.0%	1.00	(0.81,1.24)	0.999
<b>Revision rTKA</b>	4.3%	3.8%	1.15	(0.41,3.21)	0.782
<b>Mortality</b>	0.0%	0.3%	0.00	(0, Inf)	0.996

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**Table 5.**

Propensity score matched analysis of probability of re-admission and subsequent revision rTKA for PJI patients.

	<b>SOT Patients</b>	<b>Matched Controls</b>	<b>Relative Risk</b>	<b>95% CI</b>	<b>P-Value</b>
<b>All-Cause Readmission</b>	40.4%	39.5%	1.02	(0.73,1.43)	0.887
<i>Loosening</i>	1.4%	0.0%	>10000	(0, Inf)	0.994
<i>PJI</i>	18.8%	20.4%	0.93	(0.53, 1.64)	0.796
<i>Instability</i>	0.0%	1.0%	0.00	(0, Inf)	0.995
<i>Periprosthetic Fracture</i>	0.0%	1.0%	0.00	(0, Inf)	0.995
<b>Revision rTKA</b>	24.8%	18.9%	1.31	(0.79,2.17)	0.296
<b>Mortality</b>	0.0%	2.0%	0.00	(0, Inf)	0.992

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