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Complications of total joint arthroplasty in solid organ transplant patients versus a large control group

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ABSTRACT

Background: Solid organ transplant patients are theoretically at increased risk for complications after total joint replacement due to immunosuppressive medication regimens and multiple medical co-morbidities. There are a number of studies that report on outcomes of total joint arthroplasty (TJA) following solid organ transplant, however, the results are heterogeneous. This study evaluated the outcomes of TJA in solid organ transplant patients as compared to non-organ transplant controls at one academic medical center.

Methods: This study was a single institution retrospective review of a consecutive series of patients who underwent joint replacement following solid organ transplant as compared to a control cohort over a 10-year period. Univariable and multivariable generalized linear mixed effects models were used to compare the odds of readmission, infection, mortality, and being discharged home between transplanted (cases) and non-transplanted (control) patients.

Results: Transplant and non-transplant cohorts had similar BMI, although transplant patients were younger (61 versus 65 years) and had a higher incidence of Diabetes (55% vs. 16%). On multivariable analysis, there was no difference in the odds of re-admission or rate of infection, but there was an increased risk of death and admission to a rehab facility in the transplant cohort.

Conclusion: Overall, this study demonstrates that solid organ transplant alone does not increase the risk of peri-operative complications in patients who underwent hip and knee replacement. However, it should be expected that these patients have a higher mortality rate and that many of them will need to be discharged to a post-acute care facility.

1. Introduction

Both the incidence of solid organ transplant and survival of these patients are increasing with improved perioperative protocols and immunosuppressant regimens.[1] However, the immunosuppressant medication regimens and medical complexity of these patients increases their need for arthroplasty, often due to avascular necrosis (AVN) or osteoporotic fractures. Studies have demonstrated an overall 5% rate of AVN in transplant patients.[2–4] Additionally, many of these patients now live long enough to develop osteoarthritis treated with subsequent joint replacement.[5] For these reasons, it has been estimated that transplant patients have a fivefold increased incidence of joint replacement when compared to the general population.[6,7]

While joint replacement is now relatively common in the transplant population, the risk of complications is also theoretically higher in this population for a number of reasons. The immunosuppressant medications create concern for infection and wound complications. Many of these patients are thrombocytopenic and/or anemic, and patients with a cardiac or lung transplant are especially sensitive to decreases in hemoglobin. Additionally, poor bone density is common as a result of a combination of factors including renal osteodystrophy, vitamin D metabolic dysfunction, poor nutrition, and medication related osteopenia.[8] These conditions can lead to periprosthetic fracture, poor bone ingrowth, and decreased construct durability.[9–11] Finally, these patients are typically more medically complex and often have medical issues beyond just the transplanted organ.

Despite the theoretical increased risk of complications, the published results are heterogeneous in terms of complication rates and outcomes.[12–18] Many of these studies are older and do not

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reflect advances in the fields of solid organ transplant including improved patient and donor selection, perioperative care, and better optimized immunosuppressant regimens with a decreased reliance on steroids. The purpose of this study was to evaluate the recent outcomes of TJA in solid organ transplant patients as compared to non-organ transplant controls at one academic medical center.

2. Materials and methods

Following institutional IRB approval, a retrospective review was performed to identify all patients who had a primary hip or knee replacement following solid organ transplantation. All procedures were performed by one of four fellowship-trained arthroplasty surgeons between September 2006 and December 2016 at one academic institution. These were compared to a consecutive series of patients who underwent primary joint replacement during this same time period.

A total of 55 patients undergoing 71 arthroplasty procedures following their transplantation and 3161 non-transplanted control patients undergoing 3695 arthroplasty procedures were identified (Table 1). The transplant cohort included 34 males and 21 females who underwent 30 Total Knee Arthroplasties (TKAs) and 41 Total Hip Arthroplasties (THAs) (Table 1). Among these 55 patients, there were a total of 74 transplanted organs including 28 kidneys, 20 hearts, 18 lungs, and 8 livers. Of the 71 procedures, 43 were for osteoarthritis, 18 for osteonecrosis, 5 for fracture, 4 for inflammatory arthritis, and 1 was for post-traumatic arthritis. Regarding the control group, there were a total of 1218 males and 1943 females undergoing 2029 TKAs and 1666 THAs (Table 1). Indications for surgery included 3115 cases for osteoarthritis, 198 for osteonecrosis, 146 for fracture, 131 post-traumatic, 72 inflammatory, and 33 listed as other.

The mean BMI in the transplanted group (29.18, SE = 1.18) was lower when compared to the control cohort (32.07, SE = 0.15; $p = .02$) (Table 2). Similarly, patients undergoing transplantation were younger ($M = 61.15$, SE = 1.63) than those in the control cohort ($M = 65.30$, SE = 0.21; $p = .01$) (Table 2). Thirty (55%) patients in the transplant group were diabetic as compared to 496 (16%) in the control group ($p < .001$).

2.1. Statistical analysis

Univariable and multivariable generalized linear mixed effects models were used to compare the odds of readmission, infection, mortality, and being discharged home between transplanted (cases) and non-transplanted (control) patients (Table 3). In these models, a binomial distribution with logit link was specified for each outcome. Further, because patients could contribute multiple procedures to the analysis, random intercepts were allowed for each patient to account for their within-subject correlation.

For readmission, separate models were estimated for 30-day

Table 2
Summary statistics for age and BMI.

	Control			Case			Total		
	n	*M*	SD	n	*M*	SD	N	*M*	SD
BMI	3566	32.07	8.48	68	29.18	5.56	3634	32.12	8.44
Age	3695	65.30	12.15	71	61.15	9.37	3766	65.07	12.12

Note: N = Number of valid procedures. *M* = Mean. SD = Standard Deviation. BMI = Body Mass Index.

Table 1
Summary frequencies.

		Control		Case		Total	
		n	Col%	n	Col%	N	Col%
Diabetes	No	3093	83.7%	34	47.9%	3127	83.0%
	Yes	602	16.3%	37	52.1%	639	17.0%
Sex	Female	2292	62.0%	26	36.6%	2318	61.6%
	Male	1403	38.0%	45	63.4%	1448	38.4%
Race	Black	493	13.3%	8	11.3%	501	13.3%
	White	2931	79.3%	60	84.5%	2991	79.4%
	Other	271	7.3%	3	4.2%	274	7.3%
Ethnicity	Non-Hispanic	3371	91.6%	69	97.2%	3440	91.7%
	Hispanic	309	8.4%	2	2.8%	311	8.3%
Admission Type	Routine	3533	95.6%	65	91.5%	3598	95.5%
	Urgent	162	4.4%	6	8.5%	168	4.5%
Procedure Type	Hip	1666	45.1%	41	57.7%	1707	45.3%
	Knee	2029	54.9%	30	42.3%	2059	54.7%
Readmission 30 Days	No	3525	95.4%	66	93.0%	3591	95.4%
	Yes	170	4.6%	5	7.0%	175	4.7%
Readmission 90 Days	No	3440	93.1%	61	85.9%	3501	93.0%
	Yes	255	6.9%	10	14.1%	265	7.0%
Infection 30 Days	No	3666	99.2%	70	98.6%	3736	99.2%
	Yes	29	0.8%	1	1.4%	30	0.8%
Infection 90 Days	No	3647	98.7%	70	98.6%	3717	98.7%
	Yes	48	1.3%	1	1.4%	49	1.3%
Infection 1 Year	No	3626	98.1%	69	97.2%	3695	98.1%
	Yes	69	1.9%	2	2.8%	71	1.9%
Infection 5 Years	No	3604	97.5%	67	94.4%	3671	97.5%
	Yes	91	2.5%	4	5.6%	95	2.5%
Overall Infection	No	3601	97.5%	67	94.4%	3668	97.4%
	Yes	94	2.5%	4	5.6%	98	2.6%
Mortality	No	3533	95.6%	52	73.2%	3585	95.2%
	Yes	162	4.4%	19	26.8%	181	4.8%
Discharged Home	No	1378	37.3%	29	40.8%	1407	37.4%
	Yes	2317	62.7%	42	59.2%	2359	62.6%

Note: N = Number of valid procedures. Col% = Column percent.

Table 3
Unadjusted and adjusted effect sizes for cases versus controls.

	Valid N	Odds Ratio (95% CI)	*p*	Valid N	Adjusted Odds Ratio (95% CI)	*p*
Infection						
Overall	3766	2.16 (0.68–6.84)	.19	3634	2.36 (0.72–7.73)[a]	.16
90-day	3766	1.10 (0.15–8.25)	.93			
1-year	3766	1.56 (0.36–6.81)	.55			
5-year	3766	2.23 (0.71–7.00)	.17			
Readmission						
30-day	3766	1.59 (0.62–4.08)	.33	3766	1.08 (0.41–2.85)[b]	.87
90-day	3766	2.25 (1.12–4.53)	.02	3766	1.55 (0.75–3.20)[c]	.23
Mortality	3766	7.55 (3.77–15.12)	<.001	3619	7.42 (3.37–16.32)[d]	<.001
Discharged Home	3766	0.90 (0.52–1.54)	.69	3619	0.54 (0.30–0.97)[e]	.04

Valid N = The number of procedures used to compute the estimates.
[a] Adjusted for age, body mass index, and diabetes status.
[b] Adjusted for age, procedure type, admission type, race, and diabetes status.
[c] Adjusted for procedure type, admission type, race, diabetes status, and sex.
[d] Adjusted for age, body mass index, infection status, diabetes status, sex, ethnicity, admission type, and procedure type.
[e] Adjusted for age, body mass index, diabetes status, sex, ethnicity, admission type, and procedure type.

and 90-day readmission and were adjusted for patients' age, sex, diabetes status, race, admission type (urgent versus routine), and procedure type (hip versus knee). These covariates were selected because of their importance on univariable analysis and improvement in model fit statistics. A similar approach was used to compare the odds of infection between cases and controls while controlling for patients' age, body mass index (BMI), and diabetes status.

Regarding mortality, we compared the odds (rather than risk) of mortality between transplanted and non-transplanted patients because time-to-event data was unavailable for this analysis. This model adjusted estimates for patients' age, BMI, infection status, diabetes status, sex, ethnicity, admission type, and procedure type. The same approach was used to compare the odds of being discharged home between transplanted and non-transplanted patients. As before, these covariates were selected because of their importance on univariable analysis and improvement in model fit statistics. All analyses were completed using SAS version 9.4 (Cary, NC).

3. Results

Ten of 71 (14%) arthroplasty procedures among transplanted patients required readmission. This included five within 30-days of the procedure and another five within 90-days of the procedure (Table 1). Two hundred fifty-five (6.9%) of the 3695 arthroplasty procedures in the control cohort were re-admitted. This included 170 complications within 30-days and another 85 within 90-days of the procedure (Table 1). Reasons for re-admission in the transplant group included one for wound drainage, one DVT, one dislocation, and the remainder were medical complications. In the control group there were 69 wound issues (drainage, hematoma, superficial infection, dehiscence), 10 periprosthetic fractures, 5 deep infections, 4 dislocations, 4 isolated DVTs and another 4 with DVT/PE, and the remainder were medical complications. Four (5.6%) of the 71 arthroplasty procedures among transplanted patients resulted in an infection as compared to 94 (2.5%) of the 3695 procedures among non-transplanted patients (Table 1). Fourteen (25%) of the 55 patients in the transplant group died compared to 141 (4.5%) of the 3161 control participants. Death occurred at an average of 3.83 years following surgery (range 19 days to 8.94 years). These patients were followed for a mean 7.18 years (range 2–12). Twenty-nine (41%) of the 71 arthroplasty procedures among transplanted patients and 1378 (37%) of 3695 procedures of non-transplanted patients required discharge to an acute rehab or skilled nursing facility (Table 1).

In this sample of data, there was no statistical difference in the odds of 30-day ($OR = 1.08$, 95% CI: 0.41–2.85; $p = .87$) or 90-day ($OR = 1.55$, 95% CI: 0.75–3.20; $p = .23$) readmission between transplanted and non-transplanted patients undergoing arthroplasty – even after controlling for patients' age, sex, diabetes, race, urgency of their index admission, and procedure type (Table 3). Further, controlling for patients' age, BMI, and diabetes status, there remained no statistical difference in the odds of infection between transplanted and non-transplanted patients ($OR = 2.36$, 95% CI: 0.72–7.73; $p = .16$) (Table 3). Univariable sensitivity analyses confirmed the infection rate was comparable between transplanted and non-transplanted patients 90-days post arthroplasty ($OR = 1.10$, 95% CI: 0.15–8.25; $p = .93$) as well as 1 year after the procedure ($OR = 1.56$, 95% CI: 0.36–6.81; $p = .55$) and 5 years post-procedure ($OR = 2.23$, 95% CI: 0.71–7.00; $p = .17$) (Table 1).

Transplanted patients undergoing arthroplasty were far more likely to die when compared to their non-transplanted peers. That is, controlling for patients' age, BMI, infection status, diabetes status, sex, ethnicity, urgency of their index admission, and procedure type, transplanted patients were 7.42 (95% CI: 3.37–16.32) times more likely to die ($p < .001$) (Table 3). Conversely, they were only 0.54 (95% CI: 0.30 to 0.97) times as likely to be discharged home when compared to non-transplanted patients ($p = .04$) (Table 3).

4. Discussion

This study of patients who underwent primary hip or knee arthroplasty following solid organ transplantation at one academic center overall demonstrated no difference in readmission or infection rates as compared to a non-transplant control cohort. The transplant patients were younger, had a lower BMI, but a higher incidence of diabetes. When controlling for these factors, there continued to be no statistically significant difference in infection rate between the cohorts ($OR = 2.26$, $p = .16$) (Table 3). However, the transplant patients were less likely to be discharged home versus rehab ($OR = 0.54$, $p = .04$) and had a higher risk of post-operative death ($OR = 7.42$, $p < .001$) Table 3.

The published data is mixed on whether the presence of a solid organ transplant dramatically increases the risk of complications following primary total hip or knee arthroplasty.[13–17] The reason for the variability in outcomes is unknown. Many of these procedures are performed at high volume tertiary centers, which potentially may lead to a higher level of care and lower complications. Conversely, these centers also may attract more complicated patients, which could result in a higher complication rate. Angermeier, et at found a 6.8% infection rate in transplant patients versus

a 1.8% rate overall.[19] Diabetic patients were at particularly high risk, which is consistent with the non-transplant arthroplasty literature. While rates of infection have been reported as high as 50%,[20] a systematic review by Nowicki et al. demonstrated the incidence of infection to be closer to 4.5%[21] and a large study by Goffin et al. had a similar 4.3% rate.[22] This is consistent with the 4.6% of patients in this study with a post-operative infection. However, Chang et al. had no infections at 10 year follow-up in 74 THAs performed for AVN after kidney transplant.[9]

Data on discharge to a rehab facility is also mixed.[6,13,19,23] Some studies have found higher rates of discharge to rehab facilities in the transplant population, presumably due to higher medical complexity and desire for closer monitoring. In contrast, others have shown decreased rates likely due to relatively younger patient age and longer inpatient admissions. Despite the younger age of transplant patients in this study (61 years versus 65 years, $p = .01$) (Table 2), there was a lower likelihood of discharge home as compared to the control cohort ($p = .04$) (Table 3).

The higher rate of mortality in the transplant cohort is expected given the nature of the transplant population in general. These patients are typically more medically complex, and the presence of a transplanted organ increases the risk for a variety of medical complications including infection, malignancy, medication side effects, and many others.[24–29] While organ transplant has a clear survival benefit, these patients do have a higher risk of mortality than the general population.[30] Despite the higher mortality rate, we feel that joint replacement is safe in the transplant population. The deaths occurred at an average of 3.83 years post op, and the cause of mortality was related to the transplanted organ rather than the joint replacement in most cases.

This study was limited by the fact that it was a retrospective review. The patient cohorts and complications were identified based on a query of ICD 9/10 and CPT codes in the electronic medical record system. Therefore, it is possible that complications were under or over-reported. However, the search criteria were standardized to be consistent between the groups. Additionally, there were a limited number of patients in the transplant cohort. This precluded the analysis of risk factors specific to a transplanted organ or immunosuppressant regimen. Finally, these outcomes are not necessarily generalizable as all cases were performed by fellowship trained arthroplasty surgeons at a high-volume transplant center.

Overall, this study demonstrated that there was no statistically significant difference in infection or readmission rates between the transplant and control cohorts after total joint arthroplasty when controlling for covariate factors. Therefore, the presence of a solid organ transplant is not a contraindication to total joint arthroplasty. However, it is critical to note that transplant patients often have multiple co-morbidities that also increase their risk of complication and these must be taken into account along with age and BMI when determining whether a patient is a candidate for the procedure. Further, the transplant patients were more likely to require discharge to a post-acute care facility. Additionally, they had a higher rate of death, but this is likely independent of the joint replacement status and more related to the lower overall health status of the organ transplant population.

Author contribution

Nicholas Brown, MD (Contribution: study design, analysis, data interpretation, manuscript preparation).

Steven Ralles, MD (Contribution: study design, analysis, data interpretation, manuscript preparation).

Ellen Kroin, MD (Contribution: study design, data acquisition, critical manuscript revision).

William Adams, PhD (Contribution: data acquisition, analysis, critical manuscript revision).

Karen Wu, MD (Contribution: study design, data acquisition, manuscript preparation).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcot.2019.07.018.

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