



Arthroplasty in patients with rare conditions

Arthroplasty in organ transplant patients

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ABSTRACT

The number of solid organ transplants performed in the United States continues to increase annually as does survival after transplant. These unique patients are increasingly likely to present to arthroplasty surgeons for elective hip or knee replacement secondary to a vascular necrosis from chronic immunosuppression, or even age-related development of osteoarthritis. Transplant recipients have a well-documented increased risk of complications but also excellent pain relief and dramatic improvement in quality of life. A multidisciplinary approach with the assistance of the medical transplant services for risk stratification and perioperative medical optimization is necessary. Prior solid organ transplant is not a contraindication to surgery; however, it is the responsibility of the surgeon to educate patients about the relative risks and benefits of prior to surgery.

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Introduction

The Annual Report of the U.S. Organ Procurement and Transplantation Network demonstrated the increased incidence of all solid organ transplantations (kidney, liver, lung, heart) in recent years [1]. Kidney transplants encompassed the vast majority of solid organ transplants in 2013 with 17,654 procedures performed, a 2.1% increase from the previous year. Additionally, the number of liver transplants increased 3.2% to 6455 and heart transplants increased 6.1% to 2554 procedures. Lastly, the number of lung transplants performed in the United States increased by 9.1% to 1946 procedures in 2013. Aside from the increasing prevalence of transplant procedures performed annually, improved surgical technique, patient selection, perioperative care, and post-transplant immunosuppression regimens has led to improved graft survival and life expectancies for transplant recipients [1].

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Table 1 summarizes the most recently reported five year survivorship, as well as the volume of the four major organ transplants in the United States.

Postoperative medical regimens for transplant recipients influence consideration for elective hip or knee arthroplasty. Newer immunosuppressive regimens including tacrolimus and mycophenolate have decreased the need for corticosteroids, but chronic immunosuppression has lasting consequences beyond infection risk. While immunosuppression is associated with osteonecrosis of the hip and knee, and represents the more traditional indication for consideration of joint replacement surgery, these agents in combination with chronic steroid use may result in poor bone quality and potential for periprosthetic fracture or prosthesis failure. Clearly, improved graft and patient survivorship with modern transplant surgery means that patients are living longer, more active lives. As such, degenerative disease secondary to osteoarthritis is becoming a common indication for joint replacement in this rare population.

Recipients of successful organ transplantation experience substantial gains in functional status and relish the opportunity to regain independence. Degenerative joint disease, as result of avascular necrosis or osteoarthritis, may significantly hinder functional independence and even limit cardiopulmonary rehabilitation. As this unique patient population continues to expand, arthroplasty surgeons will inevitably be faced with patients seeking elective joint replacement. The purpose of this report is to combine

Table 1
Case volume and five year survivorship by organ transplanted in the United States

Organ	# Performed in 2013	5 year patient survivorship
Kidney	17,654	82%
Liver	6455	71%
Heart	2554	75%
Lung	1946	53%

Data from 2012/2013 OPTN/SRTR Annual Data Report and United States Renal Data System 2011 Annual Report.

the current literature with our own experiences to make recommendations regarding perioperative optimization to improve patient outcomes.

Case history

Formal informed consent was obtained from patient (RC) for inclusion in this article as a case example of a typical transplant recipient treated with elective joint replacement at our institution. RC was a 66 year old male that presented to the orthopaedic clinic with end-stage hip osteoarthritis nearly 14 years status-post cardiac transplantation for heart failure (Fig. 1). His hip disease resulted in severe pain aggravated by everyday activity and significantly diminished his quality of life and ability to perform cardiopulmonary exercise. RC was diagnosed with advanced osteoarthritis of the right hip. He was deemed a candidate for arthroplasty with the caveat that he would require a formal consultation with his medical transplant team for risk stratification; if the medical team agreed elective arthroplasty was appropriate, he would then return to orthopaedic clinic for a preoperative appointment. RC wished to proceed with arthroplasty and, as such, he was referred back to his heart transplant medical doctor for preoperative evaluation. Serum levels of his immunosuppression drugs (cyclosporine and mycophenolate) were stable, he had no evidence of graft rejection, and a recent cardiac catheterization was normal. His transplant cardiology team obtained a preoperative echocardiogram, which was also normal, and RC was deemed low risk for cardiovascular complication and cleared for surgery. Recommendations were made to

continue immunosuppression and antihypertensive (amlodipine, labetalol) regimens perioperatively. RC then returned to the orthopaedic clinic for his preoperative visit. After a thorough discussion of the risks, benefits, and appropriate expectations related to elective joint replacement in the setting of chronic immunosuppression and history of solid organ transplantation, RC chose to proceed with total hip arthroplasty (THA), formal operative consent was obtained, and he was given a surgical date.

Right total hip arthroplasty was performed via posterior approach uneventfully. He received three doses of perioperative cefazolin (the standard antibiotic prophylaxis at our institution), and low-molecular-weight heparin was used for deep venous thrombosis (DVT) prophylaxis. RC was discharged home on post-operative day 2 with no complications and did not require perioperative in-hospital consultation with the respective medical transplant service. His recovery was uneventful and without any wound complications. At one year follow up, radiographs were stable (Fig. 2), RC reported zero hip pain and a recent return to recreational golf.

Eighteen months postoperatively, RC was interviewed regarding his THA. When asked his overall impression of hip replacement surgery now that he was 18 months out from surgery he answered, "It was wonderful. I now have a high quality life. Before my hip was replaced I couldn't do anything; I could barely walk in my house. Now I am walking with no pain and golfing as much as I can." When what advice he would you give someone with a transplant considering joint replacement, he responded, "If anyone with a transplant is leery of joint replacement, I would love to persuade them to have it done. My advice would be to have it done as soon as possible. I put it off for a year and looking back I was dumb."

Discussion

An increased rate of complications after hip and knee arthroplasty in organ transplant recipients is well documented [2–8], but with excellent patient satisfaction also described [7,8], surgeons and patients are left to weigh risks and benefits prior to undertaking elective, primary joint replacement. However, a recent study by Cavanaugh et al., which analyzed National Inpatient Sample (NIS) data from 1993 to 2011, revealed that

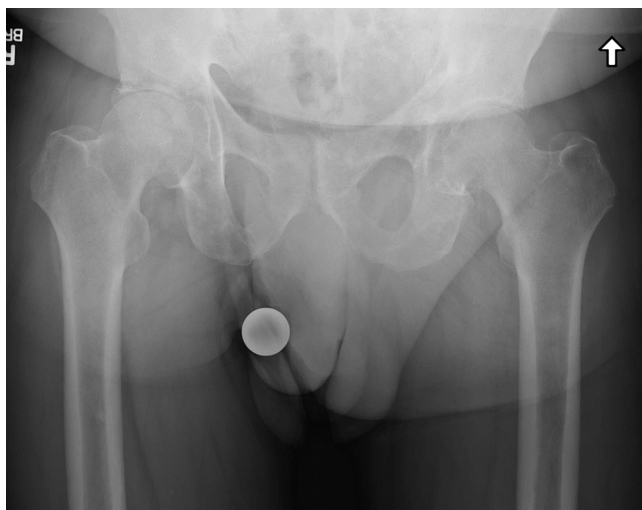


Figure 1. Low AP x-ray of the pelvis demonstrating significant end-stage osteoarthritis of the right hip.

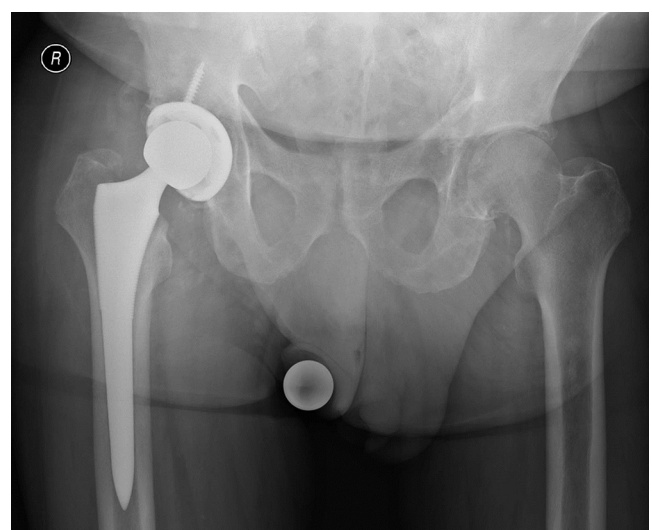


Figure 2. Post-operative x-ray one year following successful right total hip arthroplasty.

revision procedures were more commonly performed in transplant patients than primary procedures [2]. Their study compared in-hospital complications in a total of 4493 patients with a history of at least one organ transplant to non-transplant patients. The study group comprised a mere 0.17% of the NIS patient sample that had undergone hip or knee arthroplasty during the study period. Overall, the most common in-hospital complication in all transplant recipients was acute renal failure (ARF). For comparative analysis, cardiac, lung and pancreas transplant patients were grouped together and collectively found to have a slightly higher risk of respiratory and wound complications when compared to kidney and liver recipients. As could be expected, transplant patients undergoing revision surgery had higher rates of complications than those undergoing primary procedures.

Ledford et al. reviewed 76 patients undergoing primary arthroplasty after solid organ transplantation at a single institution and reported an overall complication rate of 29% in THA and 33% in total knee arthroplasty (TKA), although they included minor complications such as electrolyte abnormalities requiring medical intervention in their analysis [3]. The authors also found ARF to be one of the most common complications following surgery. The etiology of ARF in this population is likely multifactorial depending upon preoperative hemoglobin levels, clotting factors, cardiopulmonary volume capacity, perioperative medication nephrotoxicity, and baseline renal function. Interestingly, this study also found that the rate of symptomatic anemia requiring transfusion was higher in cardiac and lung transplant patients, likely reflecting the fact that these specific transplant populations are unable to tolerate even minor variations in hemoglobin levels in the setting of potentially limited cardiopulmonary reserve.

Infection is perhaps the greatest perioperative and late postoperative concern. There are increased rates of periprosthetic infection (PPI) in all organ recipients with ranges varying in the literature between 3.2 and 17.3% [3–7]. While pathogens are mainly caused by gram positive bacteria, there are reports of opportunistic pathogens such as nontuberculous mycobacteria [6] and *E. coli* [5].

Reoperation for any indication has been investigated by several studies. Beyond infection, the underlying poor bone quality in organ transplant recipients associated with periprosthetic fracture, instability and aseptic loosening contributes to the reoperation rate. Angermeier et al. reported a 13% overall reoperation rate (6.8% noninfectious) in 68 solid-organ transplant patients after hip or knee arthroplasty [3]. This was nearly identical to the 12.9% (7.7% noninfectious) reported by Ledford et al. [3]. Klatt et al. investigated 19 organ recipients undergoing primary hip or knee arthroplasty and reported a reoperation rate of 39.1% [5].

An unpublished study from our institution confirms the increased risk of arthroplasty in organ transplant recipients in the Medicare population. A PearDiver analysis of a comprehensive Medicare database of all enrollees from 2005 to 2011 was performed identifying THA patients with a pre-existing solid organ transplant. There were a total of 3180 patients who underwent THA after one or more various solid OTs (2312 kidney transplants, 561 liver transplants, 196 lung transplants, 428 heart transplants, 149 pancreas transplants). A cohort of 771,498 patients who underwent elective primary THA without prior history of solid organ transplant served as a control. Incidence (IN), odds ratios (ORs) and their respective 95% confidence intervals (CIs) for 30-day, 90-day and overall complications were calculated. The most notable overall increased risks in the transplant cohort include: acute renal failure (IN 76%, OR 13), blood transfusion (IN 48%, OR 1.6), arthrotomy/I&D (IN 2%, OR 1.6), DVT/PE (IN 11%, OR 2.1), mortality (IN 0.6%, OR 1.9), periprosthetic infection (IN 4.3%, OR 1.7), wound complications (IN 2.6%, OR 2.3), and wound infection (IN 16%, OR 2.0).

Based on our experience and the literature, a thorough and frank conversation should be pursued with the patient regarding expectations. Given their underlying systemic illness and chronic immunosuppression, surgical risk is significantly higher, as discussed previously. Anticipated total gain and pain relief after arthroplasty should be considered during preoperative consultation. Referring back to Table 1 the five year patient survivorship after organ transplantation warrants dialogue given the postoperative rehabilitation period. That being said, organ recipients tend to have high satisfaction after arthroplasty with numerous studies reporting good pain relief and functional outcomes [3,6,8]. Ultimately, the decision to undergo an elective procedure lies with the patient, and it is the responsibility of the surgeon to provide realistic expectations regarding risks and potential functional gains in the informed consent process.

Preoperative risk stratification and optimization is of utmost importance. For this reason, it is imperative that patients be seen by the respective medical transplant specialist and undergo appropriate preoperative testing. While the transplant team should also discuss potential complications with patients, their primary function is to risk stratify potential arthroplasty patients to facilitate informed decision making, make necessary preoperative interventions to medically optimize the patient, and provide recommendations for perioperative management. Meriting particular discussion is the lung transplant recipient given their unadjusted median survival rates of 53% at 5 years and only 30% after 10 years [9]. In fact, there are several pulmonary transplant physicians at our institution who request lung transplant patients to be admitted to the pulmonary service postoperatively, with the arthroplasty team to strictly manage orthopaedic issues only. Generally, all immunosuppression regimens should be resumed preoperatively and immediately postoperatively, unless they are taking sirolimus which has been associated with increased infection risk [10]. Postoperatively, there should be a very low threshold, and sometimes automatic trigger for involving the medical specialists once the patient is admitted to the floor. Their expertise on transplant specific medicine reconciliation, fluid management, vital sign abnormality, and inpatient hospital course is superior to that of the orthopaedist and should be utilized.

Anesthesia can play an important role in the transplant recipient's hospital course and outcome. Given their decreased baseline cardiopulmonary and hepatorenal function, avoiding excessive insults is of paramount importance. For that reason, we prefer spinal or regional catheters as they will reduce the patient's systemic load of anesthetic. Postoperatively, we prefer a multimodal pain regimen to limit postoperative discomfort, decrease narcotic intake, and facilitate early ambulation with physical therapy all in an effort to minimize cardiopulmonary complications. Unfortunately, there are contraindications to a multimodal regimen (for example NSAIDs in renal patients) and for that reason we rely upon the coordination among anesthesia and transplant medical specialists. Judicious fluid management is necessary to prevent acute renal failure. In some circumstances, maintenance fluids are contraindicated due to their delicate cardiopulmonary function. Again, we directly involve the medical specialists to determine colloid administration or blood transfusion in any complex case. Our transfusion threshold is quite low in transplant recipients because end organ function is inhibited during anemia, and any small fluctuation in their organ function may result in graft dysfunction. We will typically transfuse a patient for a hematocrit <25 or evidence of end organ hypoperfusion. Our institution has a large lung transplant program and, for this reason, our experience with this specific transplant population is somewhat unique. Our experience with lung transplant recipients has taught us that with their restricted pulmonary function and tenuous volume status,

fluid management can be difficult post-operatively, and aggressive fluid resuscitation can result in pulmonary edema. Blood transfusion thresholds tend to be the lowest with this transplant population for volume repletion. As a result, it is our preference to proactively involve the pulmonary transplant service in post-operative medical management of all lung transplant patients.

While chronically immunosuppressed patients are vulnerable to opportunistic infections, it appears that transplant recipient PJI's are generally the result of the same organisms that infect immunocompetent hosts: gram positive bacteria. Particular attention to infection should be paid to patients a known Cytomegalovirus infection as this will increase susceptibility to bacterial infections [6]. However, when treating PJI's in this population, cultures should be sent for atypical infections as well including anaerobes, fungal, and mycobacteria.

Current controversies and future considerations

With the exception of lung transplant recipients, our standard protocol is to admit kidney, liver, and heart transplant recipients after hip or knee arthroplasty to the orthopaedic service and attempt to primarily manage the patient. If an objective abnormality is encountered during the admission, we have a very low threshold for consulting the respective medical transplant team. There have been no previous studies which randomized patients to either automatically receive interdisciplinary inpatient care (automatic medicine consult) or primarily be managed by the orthopaedic team with consultation after an objective abnormality.

On January 1, 2014 the new Surgical Care Improvement Project (SCIP) measures were announced which included aspirin as acceptable venous thromboembolus prophylaxis following hip and knee replacement. At our institution, our standard practice for DVT prophylaxis in organ transplant recipients has been low-molecular-weight heparin. To our knowledge, no study has been performed evaluating venous thromboembolus prophylaxis this patient population and may be worthy of investigation.

Summary

Hip and knee arthroplasty can be safely performed in solid organ transplant recipients with excellent pain relief and functional outcomes. Proper precautions must be taken to minimize complications including: patient education and expectation delineation, an interdisciplinary approach to care which includes the medical

transplant team, and standardized perioperative protocols to minimize risk.

KEY POINTS

- Surgical risk is increased in organ transplant recipients undergoing total joint replacement, and patients should understand this prior to their intervention.
- Multidisciplinary cooperation is mandatory to minimize complications and maximize outcomes in organ transplant recipients undergoing total joint replacement.
- Perioperative protocols are very helpful for surgical management and may differ from standard total joint protocols (eg transfusion parameters may differ).
- Prosthetic joint infection is more common in organ transplant recipients undergoing total joint replacement, and atypical infections must be considered.

References

- [1] 2013 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of transplant recipients. *Am J Transplant* 2013;13(12):2000–2010.
- [2] Cavanaugh P, Chen A, Rasouli M, et al. Total joint arthroplasty in transplant recipients: In-hospital adverse outcomes. *J Arthroplasty* 2015 May;30(5):840.
- [3] Ledford CK, Watters TS, Wellman SS, et al. Risk versus Reward: total joint arthroplasty outcomes after various solid organ transplantations. *J Arthroplasty* 2014;29(8):1547.
- [4] Angermeier EW, Demos HA, Del Schutte H, et al. Complications of hip and knee joint replacement in solid-organ transplant patients. *J Surg Orthop Adv* 2013;22(3):204.
- [5] Klatt BA, Steele GD, Fedorka CJ, et al. Solid organ transplant patients experience high rates of infection and other complications after total knee arthroplasty. *J Arthroplasty* 2013;28(6):960.
- [6] Vergidis P, Lesnick TG, Kremers WK, et al. Prosthetic joint infection in solid organ transplant recipients: a retrospective case–control study. *Transpl Infect Dis* 2012;14:380.
- [7] Ledford CK, Watters TS, Wellman SS, et al. Outcomes of primary total joint arthroplasty after lung transplantation. *J Arthroplasty* 2014;29(1):11.
- [8] Leonard GR, Davis CM. Outcomes of total hip and knee arthroplasty after cardiac transplantation. *J Arthroplasty* 2012;27(6):889.
- [9] Christie JD, Edwards LB, Kucheryavaya AY, et al. The Registry of the International Society for Heart and Lung Transplantation: 29th adult lung and heart-lung transplant report-2012. *J Heart Lung Transplant* 2012;31(10):1073.
- [10] Fortun J, Martin-Davila P, Pascual J, et al. Immunosuppressive therapy and infection after kidney transplantation. *Transpl Infect Dis* 2010;12(5):397.