No Decrease in Knee Survivorship or Outcomes Scores for Patients With HIV Infection Who Undergo TKA

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Abstract

Background HIV is prevalent worldwide and numerous patients with this diagnosis ultimately may become candidates for TKA. Although some studies have suggested that complications are more common in patients with HIV who undergo TKA, these studies largely were done before the contemporary era of HIV management; moreover, it is

unclear whether patients with HIV achieve lower patient-reported outcome scores or inferior implant survivorship.

Questions/purposes We asked whether there were any differences in the outcomes of patients with HIV without hemophilia who undergo TKA compared with a matched control cohort in terms of: (1) patient-reported outcomes; (2) implant survivorship; and (3) complication rates.

Methods Forty-five patients with HIV who had undergone 50 TKAs at three institutions with a minimum followup of 4 years between 2005 and 2011 were identified. An additional three patients were lost to followup before the fourth-year annual visit. All patients with HIV underwent thorough preoperative optimization with their primary care physician and infectious disease specialist. There were 31 men and 14 women with a mean age of 57 years and mean followup of 6 years (range, 4–10 years). These patients were compared with a matched cohort of 135 patients (one-to-three ratio) who did not have HIV and who had undergone a primary TKA by the same surgeons during this same period using the same implant. Matching criteria included patient age (within 2 years), BMI (within 2 kg/m²), surgeon performing TKA, followup (within 6 months), minimum followup of 4 years, sex ratio, and primary diagnosis (degenerative joint disease versus osteonecrosis). Approximately 10% of patients in the matching group had not returned for followup after their sixth annual visit. Outcomes evaluated included The Knee Society objective and function scores, University of California, Los Angeles (UCLA) activity scores, overall implant survivorship (free of revision) using Kaplan-Meier analysis, and complications. With the numbers available, there were no differences in preoperative Knee Society score or UCLA activity scores among the cohorts.

Results With the numbers available, there were no differences in the mean Knee Society objective scores between

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Each author certifies that his institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

This work was performed at Sinai Hospital of Baltimore, Baltimore, MD, USA.

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patients with HIV (89 ± 11 points) and the matching cohort (91 ± 14 points) (95% CI, -7 to 3 ; $p = 0.38$). There were no differences among the Knee Society functional component as well (88 ± 12 points versus 90 ± 13 points; 95% CI, -6 to 2 ; $p = 0.36$) at latest followup. Similarly, there were no differences with the numbers available in the UCLA activity scores (6 ± 5 points [range, $4-7$] versus 6 ± 7 points [range, $4-8$]; $p = 0.87$) between the cohorts. With the numbers available, Kaplan-Meier analysis showed no significant difference in the overall implant survivorships between patients with HIV (98%; 95% CI, 94%–99%) compared with the matching group (99%; 95% CI, 98%–100%; $p = 0.89$). Postoperative complications were also comparable between the two groups.

Conclusions With the numbers available, we found that patients with HIV had no differences in clinical scores and implant survivorship compared with patients without the disease at mid-term followup. We believe practitioners should not be reluctant to perform TKA on this patient population. However, we believe the preoperative optimization process is crucial to achieving good outcomes and minimizing the risk of complications. Future comparative studies should have longer followup and a larger sample size with greater power to determine if there are differences in complications and implant survivorship.

Level of Evidence Level III, therapeutic study.

Introduction

Worldwide, approximately 35 million individuals are living with HIV of whom more than 1 million are estimated to live in the United States [7, 9]. Patients diagnosed at an early stage of disease, and who are compliant with contemporary highly active antiretroviral therapy (HAART), have life expectancies approaching that of the general population [3, 4] and therefore are susceptible to numerous chronic illnesses such as degenerative joint disease (DJD) [3, 20]. HIV infection is also a reported risk factor for osteonecrosis (ON) [2–4, 14]. Therefore, DJD and ON may be the underlying diagnoses for end-stage knee arthritis. Although there are numerous nonoperative treatments that can be attempted, many of these patients may progress to having end-stage arthritis and undergo TKA to improve function and reduce knee pain.

However, there is great concern that these patients may be at greater risk when they undergo any elective surgical procedures, including lower extremity total joint arthroplasty [12, 14]. Numerous studies have reported a higher risk of perioperative complications including myocardial infarction, acute renal failure, and surgical site infection [6, 11–13, 15]. Furthermore, some studies have

reported lower implant survivorship after total joint arthroplasty in patients with HIV compared with those without the virus [17, 21]. Conversely, some studies showed that these patients have outcomes comparable to their counterparts without the virus, with a similar risk of complications [10, 18, 22].

In our practices, we observed that patients with HIV were experiencing similar clinical outcomes compared with other patients. However, we thought that careful analysis needed to be done, given the disagreement among published studies on this population [11, 15, 17]. Furthermore, there is a paucity of comparative studies regarding the outcomes after TKA in patients with HIV at mid-term followup. Therefore, we performed a case-control study to assess if there were any differences in (1) patient-reported outcomes based on The Knee Society and University of California, Los Angeles (UCLA) activity scores; (2) implant survivorship; and (3) complications in primary TKA in patients with HIV who do not have hemophilia compared with a matching cohort of patients undergoing TKA who did not have HIV.

Patients and Methods

Institutional review board approval was sought and obtained before initiation of this study. We conducted a retrospective chart review of all patients who underwent primary TKA between January 1, 2005, and December 31, 2011 who also had a diagnosis of HIV. All procedures were performed at three high-volume arthroplasty institutions by fellowship-trained joint reconstruction surgeons (MAM, SFH, AJS). In identifying our cohort, we excluded patients with a diagnosis of hemophilia (two patients). All remaining patients had contracted HIV through sexual contact or nonblood-transfusion methods. An additional three patients (6%) with HIV who had undergone TKA were lost to followup after their second-year visit and were not included in this study because they did not meet the minimum followup criteria. We identified 45 patients (50 TKAs) who had an established HIV diagnosis. This cohort consisted of 31 men (69%) and 14 women (31%) with a mean age of 57 years (range, 38–72 years) and mean followup of 6 years (range, 4–10 years). There were no deaths in the cohort during this study period. These patients were compared with a matched cohort of 135 patients (one to three) without HIV who underwent TKA by the same surgeons during the same period. Matching criteria included patient age (within 2 years), BMI at the time of surgery (within 2 kg/m^2), surgeon performing the TKA, followup (within 6 months), minimum followup of 4 years, sex ratio (men to men and women to women), primary diagnosis (DJD versus ON), and operating surgeon. In both

Table 1. Summary of demographics and clinical outcomes in HIV and matching groups

Metrics	HIV group	Matching group	p Value
Number of patients (TKAs)	45 (50)	135 (145)	–
Mean age in years (range)	57 (38–72)	57 (49–81)	–
Mean followup in years (range)	6 (4–10)	6 (4–10)	–
Diagnosis, DJD; %	94	94	–
Diagnosis, ON; %	6	6	–
Kaplan Meier survivorship* (95% CI)	98 (94–99)	99 (98–100)	0.89
Deep periprosthetic infection rate (%)	0	0	–
Superficial infection; % (number)	4 (2)	0	0.06
Mean preoperative KSS objective score in points (range)	41 (30–55)	42 (30–62)	0.31
Mean preoperative KSS functional score in points (range)	45 (32–58)	44 (32–58)	0.33
Mean postoperative KSS objective score in points (range)	89 (65–100)	91 (72–100)	0.38
Mean postoperative KSS functional score in points (range)	88 (50–100)	90 (65–100)	0.36
Mean preoperative UCLA score in points (range)	4 (3–5)	4 (3–5)	0.63
Mean postoperative UCLA score in points (range)	6 (4–7)	6 (4–8)	0.54

DJD = degenerative joint disease; ON = osteonecrosis; KSS = The Knee Society; UCLA = University of California, Los Angeles; *failure in survivorship defined by revision for any reason.

groups, all patients had a minimum of 4 years followup and the majority had 6 years or more followup. If a patient was lost to followup in the comparison group before their fourth-year visit, they were not included in the study. Approximately 70% of patients were seen during the past 4 years and approximately 10% of patients in the comparison group had not followed up after their sixth-year visit. All patients received the same cemented implant—the cruciate retaining Triathlon™ Knee System (Stryker® Orthopaedics, Mahwah, NJ, USA) with a highly crosslinked polyethylene tibial insert. Antibiotic-impregnated cement was not used in either of the groups. For infection prophylaxis, both cohorts of patients received 1 g intravenous cefazolin 30 minutes before incision followed by two additional doses every 8 hours for a total of 24 hours of antibiotic coverage.

Before surgery, all patients with HIV had a detailed and complete preoperative clearance workup and optimization with their primary care internist, cardiologist, and infectious disease physicians. All patients in the HIV cohort were actively receiving HAART medications throughout their preoperative course and were more than 90% compliant with the therapy. More specifically, each patient was receiving at least two nucleoside reverse transcriptase inhibitors and one medication of either an integrase inhibitor or a protease inhibitor. This therapy was continued during the perioperative and postoperative periods. Postoperatively, patients received 1 g intravenous cefazolin every 8 hours for 24 hours, and medical and infectious disease consultations were obtained for ideal optimization. In all of these patients, the CD4 cell count was greater than 200 at the time of surgery. In nine patients, the surgery was

delayed from 4 to 24 weeks for further medical optimization and to reach the appropriate CD4 cell count. No surgery was performed in patients with a CD4 count less than 200.

All patients were followed up at 2, 6, 12, 26, and 52 weeks, and then annually thereafter. To assess for radiographic loosening, all radiographs were assessed for any evidence of progressive radiolucencies, loosening, fracture, or changes in alignment based on the standardized grading system that has been formulated by The Knee Society [8]. The radiographic hallmarks of component loosening were a wide or progressive zone of radiolucency at the interfaces around the components and an interval change in position of the components [1]. All radiographs were evaluated blinded by two of the authors (MAM, SFH), and kappa value for inter- and intraobserver reliability were 0.88 and 0.83 respectively. For the purposes of this study, failure was defined as exchange of any of the components for any septic or aseptic reasons. To investigate any potential complications, all medical records and radiographs were evaluated for medical and surgical complications throughout the entire followup.

Clinical outcomes were measured using The Knee Society objective and functional scores. In addition, activity levels were assessed using the UCLA activity scale. These scores were assessed at each followup, and the latest scores were used to assess final outcome in this study. The cohorts had no differences in preoperative Knee Society objective and functional scores and UCLA activity scores (Table 1).

All deidentified data were tabulated in an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA)

for statistical analyses. Kaplan-Meier analyses were performed for assessment of implant survivorship. Kappa coefficient was used to assess inter- and intraobserver reliability of data. The statistical software GraphPad Prism Version 5.01 (GraphPad Software Inc, La Jolla, CA, USA) was used for all statistical calculations. Statistical comparisons between both cohorts were performed using population Z-tests or t-tests to determine if there was a difference in proportions or means, respectively. A *p* value less than 0.05 was considered significant.

Results

With the numbers available, there were no differences in mean Knee Society objective (89 ± 11 versus 91 ± 14 points; 95% CI, -7 to 3 ; *p* = 0.38) or functional scores (88 ± 12 points versus 90 ± 13 points; 95% CI, -6 to 2 ; *p* = 0.36) at final followup between the two cohorts (Table 1). The mean Knee Society objective and functional scores in the HIV group had improved from 41 ± 6 points (range, 30–55 points) and 45 ± 6 points (range, 32–58 points) to 89 ± 11 points (range, 65–100 points) and 88 ± 12 points (range, 60–100 points), respectively. There were no differences compared with the matching group who had improved from 42 ± 6 points (range, 30–62 points) and 44 ± 6 points (range, 32–58 points) to 91 ± 14 points (range, 72–100 points) and 90 ± 13 points (range, 65–100 points), respectively. In addition, there were no differences in the UCLA self-reported activity levels between the two cohorts (6 ± 2 points versus 6 ± 2 points; *p* = 0.54) (Table 1). In the HIV cohort, the mean UCLA activity scores had improved from a mean 4 ± 2 points (range, 3–5 points) to 6 ± 2 points (range, 4–7 points). This did not differ from the matching group that improved from a mean 4 ± 3 points (range, 3–5 points) to 6 ± 2 points (range, 4–8 points).

With the numbers available, Kaplan-Meier analysis showed no significant differences in overall implant survivorship for the patients with HIV (98%; 95% CI, 94%–99%) compared with the matching groups (99%; 95% CI, 98%–100%) (*p* = 0.89) (Fig. 1). There was one aseptic revision in the HIV cohort in a 55-year-old woman who required a revision 2 years after her initial TKA for pain and instability. In addition, there was one revision in the matching cohort in a 66-year-old man attributable to aseptic loosening 3-years after his primary TKA. There were no other instances of radiographic loosening in either cohort. There were no revisions resulting from deep periprosthetic infection in either of the cohorts.

Postoperative complications were comparable between the two groups. In the HIV group, two patients had surgical site superficial skin infections develop; both were treated

Fig. 1 A Kaplan-Meier survivorship curve for the HIV (red) and control (blue) cohorts up to 10 years is shown

successfully with antibiotics. One patient in this group had knee stiffness develop limiting his activities, therefore he underwent manipulation under anesthesia at 8 weeks postsurgery. Another medical complication in the HIV cohort was in a 52-year-old woman who had a urinary tract infection develop during the hospital stay; she was treated successfully with antibiotics. The final medical complication was in a 67-year-old man with no previous history of arrhythmias or kidney disease in the HIV group. He had bradycardia and kidney failure develop after surgery and was treated successfully by the cardiology and nephrology services. Each of the patients who experienced a complication had CD4 counts greater than 400 and undetectable viral loads before surgery. In the matching group, a 53-year-old woman had a urinary tract infection develop which was treated successfully with antibiotics. Three patients in the matching group had knee stiffness develop after surgery and underwent manipulation under anesthesia 6 to 9 weeks postoperatively, achieving flexion ROM greater than 105° at final followup. All patients with complications in both groups had achieved mean Knee Society scores greater than 80 points with no evidence of implant loosening at their final followup.

Discussion

Paccou et al. [16] stated that, according to the WHO, the annual incidence of HIV remained at 2 million cases per year in 2014 and 2015, with an increasing prevalence noted. This increasing global prevalence of patients with HIV is most likely attributable to improved medical management leading to increased survival rates [16]. Therefore, it is critical that practitioners be familiar with the potential risks and complications associated with these patients

when considering TKA. Some studies have suggested that patients with HIV may have a higher risk of complications after undergoing a TKA [11, 12] and less satisfactory implant survival [11, 15, 17], however, a recent database study showed no significant differences in overall perioperative complications [5]. Therefore, we aimed to determine if patients with HIV had comparable clinical outcomes and complication rates as matched counterparts. Our results showed that with the numbers available, patients with HIV had no differences in implant survivorship and patient-reported outcomes compared with their counterparts. Additionally, complications were comparable and relatively infrequent between the two groups.

This study has some limitations. This was a retrospective study with some of the obvious gaps in knowledge that this entails. For example, because many of our patients were referred after preoperative medical management, we did not have access to the cohort's exact viral loads or CD4 counts on a routine basis, nor did we have complete information regarding the actual disease state, length of time from diagnosis, type of HAART therapy and actual compliance, or other factors that might help further distinguish this heterogeneous population. Thus, we could not assess if there was an association of these measures of the disease with patient-reported outcomes, complications, or implant survivorship. Additionally, when assessing for complications, some patients may have had postoperative complications that were treated at outside institutions, which were not assessed in this study. Furthermore, although we did match for many variables, we were unable to match for other factors that may influence postoperative outcomes such as preoperative knee ROM, American Society of Anesthesiologists comorbidity scores, SF-36 scores, preoperative narcotic use, blood loss, duration of surgery, or length of stay during the perioperative period. Although large for the nature of the study, the HIV cohort is small, which may have limited our ability to detect differences in certain parameters owing to decreased statistical power. The followup is still relatively short and outcomes may vary with more long-term followup. Moreover, because our surgeons practice in large urban settings with wide availability of medical specialists, the generalizability of our optimization process may be questioned. Despite these limitations, we believe the results of our study are valuable because, to our knowledge, this is the largest comparative study with a matched cohort performed on this patient population.

We found that The Knee Society scores and UCLA activity scores were not different with the numbers available between the groups at latest followup. Good functional outcomes have been reported in patients with HIV. Silva and Luck [21] evaluated a series of 33 patients with HIV and hemophilia (n = 43 arthroplasties). After a mean

followup of 8 years (range, 1–26 years), the cohort achieved excellent Knee Society clinical and functional scores (81 and 89 points, respectively). Although they did not have a comparison cohort, their finding agree with our finding that patients with HIV can achieve good functional outcomes. However, their cohort differs from ours in that their patients also had hemophilia. Therefore, this is a particular subset of patients with HIV who also can achieve optimal outcomes after TKA.

We also noted no differences with the numbers available in terms of implant survivorship between the groups at mid-term followup. By contrast, some older studies have shown high early implant failure rates in patients who are HIV positive. Parvizi et al. [17] evaluated implant failure rates in patients who underwent THA (n = 8) and TKA (n = 13). After a mean 10-year followup (range, 2–23 years), eight arthroplasties in that series required revision, four for periprosthetic joint infection and four owing to aseptic loosening. In addition, some older studies regarding patients with HIV after TKA have been in patients with hemophilia (Table 2) [18, 19, 21]. Silva and Luck [21] performed a retrospective review of all patients who underwent TKA between 1975 and 2001 and who were diagnosed with hemophilia (n = 90 knees). They found no difference in the infection rates between patients with hemophilia with and without HIV after a mean 8-year followup (range, 1–26 years). Similarly, Powell et al. [18], in a study involving patients undergoing THA and those undergoing TKA with hemophilia (n = 51 arthroplasties), found no increased risk of infection in patients with HIV. The infection rate among these patients is much higher than what we found in our study; however, their results must be interpreted cautiously in light of baseline differences with our study. The implants that were used in these studies were also different from more-recent designs. Additionally, the majority of patients with HIV in these older studies had hemophilia and had contracted HIV through blood transfusions. At the time of these studies, such patients were highly susceptible to infection and were reported to achieve inferior clinical outcomes [17–19]. Moreover, these studies were performed before the use of HAART therapy and thus may represent a noncomparable group that was not medically optimized by today's standards. In our study, none of the patients in the HIV cohort had a diagnosis of hemophilia and all had acquired their disease through nontransfusion methods.

There were relatively few complications among both of our study cohorts, and similar findings have been seen in several studies (Table 2). Recently, Boylan et al. [5] evaluated the risk of short-term adverse events after TKA in patients with HIV using the Nationwide Inpatient Sample (NIS) (n = 2772 patients) and compared it with a control cohort of patients who did not have this disease (n =

Table 2. Studies on complications and clinical outcomes after primary TKA in patients with HIV

Study	Number of patients	Mean followup (years; range)	OR infectious complications (95% CI; p value)	OR all complications (95% CI; p value)	Latest followup KSS clinical score (points; range)	Latest followup KSS functional score (points; range)	Implant survivorship (%)
Boylan et al. [5], 2015*	2772	NR	2.78 (1.15–6.72; p = 0.024)	1.21 (0.83–1.77; p = 0.321)	NR	NR	NR
Capogna et al. [6], 2013*	69	NR	6.22 (0.64–61.0; p = 0.11)	NR	NR	NR	NR
Lin et al. [11], 2013*	1730	NR	NR; p = 0.02	0.78 (0.49–1.25; p = 0.76)	NR	NR	NR
Silva and Luck [21], 2005	90	8 (1–26)	NR	NR	81.3 (50–99)	88.7 (15–100)	87
Rodriguez-Merchan and Wiedel [19], 2002	37	NR	NR	NR	NR	NR	89
Current study	47	6 (4–10)	NR	3.9 (1–15; p = 0.048)	89 (65–100)	88 (50–100)	98

*Nationwide Inpatient Sample database studies only containing information regarding hospital stay complications; OR = odds ratio; KSS = The Knee Society; NR = not reported

5.67 million) between 1998 and 2010. They found that patients with HIV were not at an increased risk of all postoperative complications during inpatient stays. Furthermore, there was no difference in the risk of medical or surgical complications. However, they found that patients with HIV had a higher risk of wound infection (OR, 2.8; 95% CI, 1.15–6.72; p = 0.024). Similarly, in a study performed by Lin et al. [11] using the same NIS database (n = 1730 TKAs), but with a different time (2000–2008), no difference was found in the risk of perioperative complications after TKA between patients who were HIV positive or HIV negative. Furthermore, they found no difference in wound infection rates after TKA between the cohorts. In our study, we found comparable infectious complications and no patients had deep periprosthetic infections. However, in NIS studies, patients were followed for complications strictly during their inpatient hospital stay. Furthermore, given the limited followup, it is difficult to make conclusions regarding the role of preoperative optimization.

Our study showed that patients with HIV can achieve satisfactory and comparable clinical outcomes compared with a matched cohort without HIV after TKA at a mean 6-year followup. Furthermore, complications appeared to be minor and comparable to those in the matching group. Given the improvement in life expectancy for patients with HIV, it is important that these patients continue to be followed to ensure that their outcomes remain positive. As such, surgeons must work in close consultation with medical and infectious disease specialists to ensure that each patient is optimized preoperatively. Future comparative studies should be larger for improved statistical power, have longer followup, and assess the role of various medication regimens and their compliance rates to better determine the effect on functional outcomes and implant survivorship.

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