



Original Research

Total Knee Arthroplasty in Human Immunodeficiency Virus Patients: A Literature Review

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ABSTRACT

Background: Total knee arthroplasty (TKA) has become a common surgical intervention for human immunodeficiency virus (HIV)-positive patients who develop osteonecrosis of the knee. This paper summarized existing literature regarding the outcomes of HIV-positive patients undergoing TKA in 4 subsections: (1) complications; (2) survivorship analyses; (3) patient-reported outcomes; and (4) infections.

Methods: A review of PubMed was performed, searching for articles focused on HIV-positive patients undergoing TKA. There were 6 reports selected, containing 4765 HIV-positive patients, and data regarding the various domains was tabulated and analyzed. To ensure article quality, a methodology score and level of evidence were determined for selected studies.

Results: Complication rates for HIV-positive patients were low, with a larger study reporting that 7.8% of HIV-positive patients developed a complication in comparison to 8% of HIV-negative patients. Survivorship analyses showed similar results, with a study reporting implant survivorship of 98% for HIV-positive and 99% for HIV-negative patients. There were no differences in patient-reported outcomes; HIV-positive patients improved from baseline with respect to the mean Knee Society objective and mean Knee Society functional scores, and the University of California, Los Angeles self-reported activity levels. The infection rate for HIV-positive patients was low, with a larger database study reporting that 0.6% of HIV-positive patients developed a wound infection in comparison to 0.4% of HIV-negative patients.

Conclusions: A TKA is an effective treatment for HIV-positive patients who develop osteonecrosis of the knee. Results showed similar patient-reported outcomes, implant survivorships, revisions, and complication rates when compared to non-HIV patients.

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Introduction

Human immunodeficiency virus (HIV) depresses immune function and is a prevalent disease throughout the world, with increasing survivorship because of the advent of highly active antiretroviral therapy (HAART), which closely monitors and treats HIV patients, allowing them to live active lifestyles and approach a life expectancy similar to that of the general population [1,2]. The HIV

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patients are now presenting with osteonecrosis (ON) of the knee, with the disease being reported as an independent risk factor [3]. Although there are various treatment methods for this disease, including core decompression [4-6] and bone grafting [7,8], many patients will ultimately need a total knee arthroplasty (TKA). Knowledge of the results of HIV-positive patients undergoing TKA is an important topic of research because of the increasing survivorship of patients who have this disease, which leads to an increased number of ON patients who will undergo this procedure.

There is conflicting evidence about the results for HIV-positive patients undergoing total knee arthroplasties. Some studies have reported that this group is more susceptible to perioperative complications [9,10], and other studies have reported lower implant survivorships [11,12]. Also, various studies have shown comparable complication rates between HIV-positive and HIV-negative patients [13,14]. Although previous reports examined the results of HIV-positive patients undergoing TKA, these studies included patients who had hemophilia, patients who were intravenous drug users, and patients who suffered from many comorbidities, all of which can act as potential confounders, thereby influencing the TKA results for this cohort. Furthermore, some of the previously discussed studies did not include a sufficient number of TKA cases to be included in our study.

Due to the variance in results, it appears appropriate to carefully examine the existing literature and collectively assess the difference in TKA results between HIV-positive and negative patients. Therefore, the goal of this study was to perform a literature review to assess various outcome parameters, including: (1) complications; (2) survivorship analyses; (3) patient-reported outcomes; and (4) infections.

Material and methods

We performed an extensive review of the existing literature containing studies that examined the results of HIV-positive patients undergoing TKA. An exhaustive search of PubMed was conducted from September 24, 2023, until October 27, 2023, adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Selection criteria

Two of the authors (D.H. and A.M.) performed the independent searches. The searches of PubMed included the terms “HIV,” “arthroplasty,” “total knee arthroplasty,” and “TKA.” The abstracts were reviewed to ensure article relevancy. Furthermore, we checked the references for each of the selected studies to scan for any additional articles pertaining to our study.

Our inclusion criteria encompassed reports including more than 5 cases that examined at least one of the following 4 domains: (1) complications; (2) survivorship analyses; (3) patient-reported outcomes; and (4) infections. Exclusion criteria included reports that contained patients who had hemophilia, patients who were intravenous drug users, and reports that did not discuss one of the 4 selected outcomes or separate data based on joint arthroplasty.

A total of 209 articles from the years 1989 to 2023 were initially surveyed, with some removed after a title and abstract screening. The remaining articles underwent a full-text screen. This filtering process, shown in Figure 1, left us with a total of 6 articles consisting of 4765 HIV-positive patients undergoing TKA for our review.

Data analyses

The Modified Coleman Methodology Score was used to assess the caliber of each study [15]. This score assesses all aspects of a

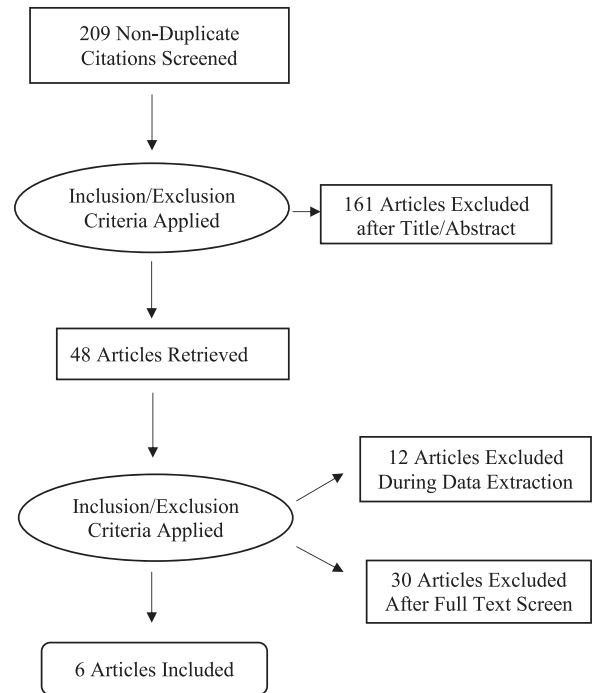


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart displaying the study selection process.

study, including its design, method of data collection, and data analysis. Some of the assessed measures within the score were binary, while others were evaluated along a continuum. The maximum number of points an article can receive is 100. Throughout the literature, many researchers group scores into different levels, where cumulative scores ranging from 85 to 100 are deemed “excellent,” between 70 and 84 are “good,” between 55 and 69 are “fair,” and below 55 are “poor.” Higher scores indicate reduced biases and confounders present in the study.

Furthermore, levels of evidence for each article were determined using criteria from the Oxford Center for Evidence-Based Medicine [16]. There are 4 levels, I to IV, with higher levels corresponding to weaker evidence.

The modified Coleman Methodology Score as well as the level of evidence for each article are shown in Table 1. The 6 articles had a Modified Coleman Methodology Score between 60 and 80. One article contained level II evidence, while 5 had level III evidence.

Outcomes of interest

Studies were separated based on different measures of outcome in the following 4 domains: (1) complications; (2) survivorship analyses; (3) patient-reported outcomes; and (4) infections. Authors, study designs, and sample sizes were included.

Table 1
Level of evidence and modified Coleman methodology score for selected reports.

Article	Level of evidence	Modified Coleman Methodology Score
Boylan et al., 2015 [3]	Level IV	65
Lin et al., 2013 [17]	Level	62
Sakthivelnathan et al., 2022 [18]	Level III	60
Issa et al., 2017 [19]	Level III	80
Akkaya et al., 2022 [20]	Level IV	61
Lin et al., 2014 [21]	Level IV	74

Table 2
Results of total knee arthroplasty in human immunodeficiency virus patients.

Category	Level of evidence	Study population	Study aim	Survivorship analyses	Complications	Infections	Patient-reported outcomes
Boylan et al., 2015 [3]	IV	2772 HIV+ and 5,672,314 HIV- patients from NIS	To assess outcome differences between HIV+ and HIV- patients undergoing TKA	Not reported	Increased risk of perioperative, medical, and surgical complication for HIV+ patients, though not significant ($P = .321$, $P = .579$, and $P = .207$, respectively); HIV+ had a 17% longer stay than HIV- patients in multivariate-adjusted model ($P < .001$)	HIV+ patients are more likely to develop perioperative wound infection ($P = .024$)	Not reported
Lin et al., 2013 [17]	III	1730 HIV+ and 3,847,367 HIV- patients from NIS	Assess complications for HIV+ and HIV- patients undergoing TKA	Not reported	No difference in total complications for HIV+ vs HIV- patients (7.8 vs 8%; $P = .76$); HIV+ patients more likely to have a length of stay ≤ 4 days ($P < .001$); between 5 to 7 days ($P < .001$); >7 days ($P < .001$).	No difference in wound infections (0.6 vs 0.4%; $P = .54$) between HIV+ and HIV- patients; no patients in either group developed an implant infection	Not reported
Sakthivelnathan et al., 2022 [18]	III	203 HIV+ and 558,168 HIV- patients	Assess postoperative complications for HIV+ and HIV- patients undergoing TKA	Not reported	HIV+ patients are more likely to develop acute renal failure (6.4 vs 0.5%; $P = .01$), more likely to require blood transfusion (3.9 vs 0.5%; $P = .018$), longer length of stay (3 vs 2.8 days; $P < .001$)	HIV+ patients are more likely to develop periprosthetic infection (3 vs 1%; $P = .007$) in unmatched analysis; in matched analysis periprosthetic infection rate did not differ ($P = .153$); No cases of superficial surgical site infection or deep surgical site infection in both groups.	Not reported
Issa et al., 2017 [19]	III	45 HIV+ (50 knees) and 135 HIV- patients (145 knees)	To compare outcomes of TKA between HIV+ and HIV- patients	No significant difference in implant survivorship between HIV+ and HIV- patients (98% vs 99%; $P = .89$); one aseptic revision for pain and instability in HIV+ group; one revision for aseptic loosening in HIV- group	No difference between the 2 groups.	Two patients developed superficial surgical site infections (4%). No reports of deep periprosthetic infection.	Mean preoperative KSS objective score: HIV+:41, HIV-:42 $P = .31$; Mean preoperative KSS functional score: HIV+:45, HIV-:44 $P = .33$; Mean postoperative KSS objective score: HIV+:89, HIV-:91 $P = .38$; Mean postoperative KSS functional score: HIV+:88, HIV-:90 $P = .36$; Mean preoperative UCLA score: HIV+: 4 HIV-: 4, $P = .63$; Mean postoperative UCLA score: HIV+: 6 HIV-: 6, $P = .54$
Akkaya et al., 2022 [20]	IV	11 HIV+ patients	To assess complication rate for HIV+ patients undergoing TKA	Not reported	2 patients (18.2%) developed complications such as deep vein thrombosis and acute renal failure.	Not reported	Not reported
Lin et al., 2014 [21]	IV	4 HIV+ and 239 HIV- patients	Assess outcomes for HIV+ and HIV- patients undergoing TKA	No significant difference in Kaplan-Meier survivorship curve between HIV+ and HIV- patients; No significant difference in number of revisions between HIV+ and HIV- patients. $n = 14$, 5.9% vs $n = 1$, $P = .23$)	Not reported	No significant difference in infection rate between HIV+ and HIV- patients ($n = 1$ vs $n = 6$, $P = .11$)	Not reported

NIS, national inpatient sample. ($n = 14$, 5.9% vs $n = 1$, $P = .23$).

Data analyses

The studies provided us with data pertaining to the 4 different outcomes of interest. Articles were assessed and separated based on the differences in targeted outcomes. Data assessing any of the 4 outcomes were analyzed. The data was prepared using a Microsoft Excel spreadsheet (Redmond, Washington) to filter and interpret the data.

Results

Complications

A retrospective review by Boylan et al. [3] utilized the National Inpatient Sample and compared the outcome of 2772 HIV-positive to 5,672,314 HIV-negative patients undergoing TKA. Researchers found no significant difference in rates of perioperative, medical, and surgical complications between the 2 groups [3]. However, HIV-positive patients had increased lengths of stay that were 17% longer than HIV-negative patients in the multivariate-adjusted model ($P < .001$) [3]. Similar results were found by Lin et al. [17] in a study comprising 1730 HIV-positive and 3,847,367 HIV-negative patients from the National Inpatient Sample. The authors reported low complication rates in both cohorts (7.8 vs 8.0%). Furthermore, when comorbidities were accounted for in statistical analyses, abnormal weight loss, fluid and electrolyte imbalance, and chronic kidney disease were more associated with complications than the HIV diagnosis itself [17]. Despite the similar complication rates, HIV-positive patients were more likely to have a length of stay greater than 4 days, between 5 and 7 days, and greater than 7 days ($P < .001$) [17].

Sakthivelnathan et al. [18] reported on 203 HIV-positive and 558,168 HIV-negative patients, both undergoing TKA. Using a matched outcome analysis, findings indicated that HIV-positive patients had an increased risk of developing postoperative acute renal failure (6.4 vs 0.5%; $P = .01$) as well as requiring a blood transfusion (3.9 vs 0.5%; $P = .018$) [18]. Likewise, as seen in previous studies, HIV patients had an increased length of stay (3 vs 2.8 days; $P < .001$), though the relevance of this 0.2 difference would appear to be less meaningful [18]. Issa et al. [19] reported no difference in complication rates between 45 HIV-positive patients (50 knees) and 135 HIV-negative patients (145 knees).

Akkaya et al. [20] included 11 HIV-positive patients undergoing unilateral TKA and found that 2 patients experienced complications, with one encountering deep vein thrombosis and the other developing acute renal failure. However, the authors of this review concluded that the increased complication rate of this study in comparison to existing literature was attributed to the elevated age of their cohort (60.8 ± 16 years) [20].

In summary, 4 of 5 articles showed no difference in complication rates between HIV-positive and HIV-negative patients. Only one report found a statistically significant increase in complication rate for HIV-positive patients (increased incidence of acute renal failure and blood transfusions) (Table 2).

Survivorship analyses

Lin et al. [21] and Issa et al. [19] both reviewed the prosthetic longevity of patients undergoing TKA. Lin et al. [21] included 4 HIV-positive and 239 HIV-negative patients who underwent TKA from 2003 to 2010 in gathering data from billing records using different codes pertaining to TKA. There was no significant difference in the number of revisions between HIV-positive and HIV-negative patients [21]. In Issa et al. [19], one 55-year-old woman in the HIV

group required an aseptic revision with an indication of pain and instability 2 years post-TKA, while one 66-year-old man in the matched control required a revision 3 years post-TKA with an indication of aseptic loosening. In both Lin et al. [21] and Issa et al. [19], the Kaplan-Meier survival analysis displayed no significant difference between the 2 groups.

To summarize, both articles included in this review that examined TKA survivorship showed no difference in revision rates or survivorship curves between HIV-positive and negative patients.

Patient-reported outcomes

Issa et al. [19] include patient-reported outcomes, and at final follow-up, there were no significant differences between HIV-positive and negative patients in their mean Knee Society objective score (KSS objective) (89 ± 11 vs 91 ± 14 points) and mean Knee Society functional score (KSS functional) (88 ± 12 vs 90 ± 13 points) [19].

Both groups saw similar improvements from baseline to post-operative with respect to the mean KSS objective and functional score. The HIV-positive patients had an increase from 41 ± 6 to 89 ± 11 points in the KSS objective score and an increase from 45 ± 6 to 88 ± 12 points in the mean KSS functional score [19]. The HIV-negative patients had an increase from 42 ± 6 to 91 ± 14 points in the mean KSS objective score and an increase from 44 ± 6 to 90 ± 13 points in the mean KSS functional score [19].

There were no significant differences between the 2 groups based on the University of California, Los Angeles (UCLA) self-reported activity levels [19]. The HIV-positive patients increased from 4 ± 2 points to 6 ± 2 points, while the HIV-negative patients improved from 4 ± 3 to 6 ± 2 points, indicating a similar range of improvement between the 2 groups.

To summarize, the singular article included in this manuscript, which presented patient-reported outcomes, found a similar range of improvements from baseline to postoperative with respect to the mean KSS objective score, the mean KSS functional score, and the UCLA self-reported activity levels for HIV-positive and HIV-negative patients [19].

Infections

Boylan et al. [3] found an increase in perioperative wound infection (odds ratio = 2.78) for HIV-positive patients ($P = .024$). Lin et al. [17] reported that no patients developed an implant infection. Furthermore, there was a low rate of wound infection for both groups with no significant difference (0.6 vs 0.4%) [17]. Lin et al. [21] found an increase in infection rate (9.1%) for HIV-positive patients, though there was no statistical significance ($P = .11$).

Sakthivelnathan et al. [18] reported that no patients developed a superficial surgical site infection or a deep surgical site infection. However, HIV-positive patients had an increased rate of periprosthetic infection (3 vs 1%; $P = .007$), though the difference became insignificant ($P = .153$) in the matched outcome analysis [18].

Issa et al. [19] found that none of the patients developed a periprosthetic infection, while 4% ($n = 2$) of HIV-positive patients developed a superficial infection, though the difference between the 2 groups was not significant. Both infected patients were successfully treated with antibiotics [19].

In summary, of the studies included in this manuscript that examined infections, one of the 5 reported a significant increase in infection rates for HIV-positive patients. The others showed a comparatively low infection rate for both groups.

Discussion

A TKA has become an important surgical intervention for HIV-positive patients experiencing ON of the knee because of their increased longevity. However, there is very little literature as well as conflicting evidence pertaining to the results of these patients. Our analyses found similar complication rates, though with an increased length of stay for HIV-positive patients. The survivorship analyses demonstrated excellent results; HIV-positive patients displayed similar Kaplan-Meier curves and comparably low revision rates. Furthermore, HIV-positive patients displayed similar patient reported outcomes as a range of improvements in mean KSS objective, mean KSS functional, and UCLA self-reported activity levels to negative patients. Another encouraging finding was the low infection rate for HIV-positive patients.

There are some potential limitations within our analyses. There were only 6 articles, and some did not cover all 4 domains included in our study, leading to a small sample size. There were 5 studies reporting on complication rates, 2 discussing survivorship analyses, one including patient-reported outcomes, and 5 covering infections. Furthermore, some of the studies are observational level III (3 of 6) and IV (3 of 6) studies and have the associated limitations therein. The results presented are only generalizable based on whether studies specify if patients are on HAART and have well-controlled HIV. Only one study reported on HAART [21], which did not influence the outcomes presented. Although there is a lack of definitive ability to draw definitive conclusions about survivorship with the very low numbers in the studies presented, we feel optimistic about the excellent survivorship (>98%). Due to the lack of heterogeneity in the studies, indications for HIV TKA, such as ON and osteoarthritis, could not be distinguished in the analyses. Even though TKA survivorship and patient-reported outcomes comprise only a few studies, reporting on these outcomes provides an impetus for future studies as well as describing what is known about this topic at the present time. Nevertheless, this is a complete summary of the literature to date on how HIV-positive patients did after TKA.

In our study, we utilized existing literature to assess the results of HIV-positive patients undergoing TKA. This was investigated by deriving data from 6 selected articles regarding complications, survivorship analyses, patient-reported outcomes, and infections. Unfortunately, there are some limitations within our study, and more research is needed on this topic with larger sample sizes and longer follow-ups. Accordingly, findings indicate positive results pertaining to HIV-positive patients undergoing TKA, and we believe that such procedures should be utilized to reduce pain and improve the quality of life for these patients.

Conclusions

The HIV-positive patients have similar results to the general population undergoing TKA. They have improvements in quality of life with a risk of infection or complication similar to the HIV-negative population. With increasing numbers of HIV-positive patients undergoing TKA for ON, our study results lead to optimism for this patient subpopulation.

Conflicts of interest

I. Hong is a paid consultant for Life Net Health. M. Mont receives royalties from Stryker; is a paid consultant for Sage Products, Inc., Stryker, TissueGene, 3M, Centrexion, CERAS Health, Flexion Therapeutics, Johnson & Johnson, Mirror-AR, NXSCI, Pacira, Peerwell, Pfizer-Lily, Skye Biologics, SOLVD Health, Smith & Nephew, and US

Medical Innovations; receives research support from the National Institutes of Health; is a Journal of Arthroplasty Editor in Chief; is an editorial board member of Journal of Knee Surgery, Surgical Technology International, and Orthopaedics; and is a board/committee member of The Knee Society and The Hip Society. All other authors declare no potential conflicts of interest.

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CRediT authorship contribution statement

Asaf Miller: Writing – review & editing, Writing – original draft. **Daniel Hameed:** Software, Methodology, Formal analysis. **Jeremy Dubin:** Writing – review & editing. **Michael A. Mont:** Data curation, Funding acquisition, Validation, Writing – original draft, Writing – review & editing. **Deepak V. Patel:** Investigation, Software. **Christopher Bibbo:** Supervision, Data curation, Software. **Ian S. Hong:** Validation, Supervision, Formal analysis.

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