

Total Joint Arthroplasty in HIV-Positive Patients in Malawi

Outcomes from the National Arthroplasty Registry of the Malawi Orthopaedic Association

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Background: In this observational study, we describe the medium-term outcomes of total joint arthroplasty (TJA) in human immunodeficiency virus (HIV)-positive patients in Malawi, a low-income country. With a high prevalence of HIV and increasing arthroplasty rates in low and middle-income countries, understanding the outcomes of TJA in this unique cohort of patients is essential to ensure that surgical practice is evidence-based.

Methods: Data for all HIV-positive patients who had TJA from January 2005 to March 2020 were extracted from the National Arthroplasty Registry of the Malawi Orthopaedic Association (NARMOA). From January 2005 to March 2020, a total of 102 total hip arthroplasties (THAs) and 20 total knee arthroplasties (TKAs) were performed in 97 patients who were HIV-positive and without hemophilia or a history of intravenous drug use. The mean length of follow-up was 4 years and 3 months (range, 6 weeks to 15 years) in the THA group and 4 years and 9 months (range, 6 weeks to 12 years) in the TKA group. The mean patient age was 50 years (range, 21 to 76 years) and 64 years (range, 48 to 76 years) at the time of THA and TKA, respectively.

Results: The primary indication for THA was osteonecrosis (66 hips). In the THA group, the mean preoperative Oxford Hip Score and Harris hip score were 14.0 (range, 2 to 33) and 29.4 (range, 1 to 64), respectively, and improved to 46.6 (range, 23 to 48) and 85.0 (range, 28 to 91) postoperatively. The primary indication for TKA was osteoarthritis (19 knees). The mean preoperative Oxford Knee Score was 14.9 (range, 6 to 31) and increased to 46.8 (range, 40 to 48) postoperatively. In patients who underwent THA, there was 1 deep infection (1 of 102 procedures), and 6 patients developed aseptic loosening (6 of 102). There was 1 postoperative superficial infection following TKA (1 of 20 procedures), and 1 patient developed aseptic loosening (1 of 20). Postoperative 6-week mortality among all patients was zero.

Conclusions: To our knowledge this is the largest medium-term follow-up of HIV-positive patients, without hemophilia or a history of intravenous drug use, who have had TJA in a low-income country. This study demonstrated good medium-term results among HIV-positive patients undergoing TJA, low complication rates, and improvements in patient-reported outcome measures.

Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Worldwide, it is estimated that there were 38 million people living with the human immunodeficiency virus (HIV) at the end of 2019, representing 0.7% of all adults aged 15 to 49 years¹. The number of people living with the disease is increasing globally. Although the rate of infection is decreasing across Africa², it is estimated that within sub-

Saharan Africa, 1 in 25 adults are living with the disease¹. The prevalence of HIV in Malawi is one of the highest in the world, with 8.9% of adults aged 15 to 49 being HIV-positive³.

The prognosis of patients with HIV has changed dramatically since the introduction of antiretroviral therapy (ART) in 1997^{2,4,5}. ART has dramatically reduced the mortality and

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morbidity of patients living with HIV and reduced the incidence of HIV-associated infection, with the number of acquired immune deficiency syndrome (AIDS)-related deaths in Eastern and Southern Africa having fallen by 44% since 2010^{2,4-8}. The introduction of ART has meant that total joint arthroplasty (TJA) has become more common among people living with HIV internationally and in sub-Saharan Africa because of the increase in life expectancy⁹. Furthermore, HIV and ART are risk factors for the development of osteonecrosis of the femoral head¹⁰⁻¹², and osteoporotic fractures are also associated with ART^{12,13}.

Previous studies¹⁴⁻²³ have suggested that HIV is an independent risk factor for the development of postoperative joint infection in patients undergoing TJA. However, these studies have included HIV-positive patients with hemophilia and/or a history of intravenous drug use, which are independent risk factors for joint infection^{16,24}. Our previous studies^{9,25-27} have demonstrated low complication rates in HIV-positive patients without hemophilia or intravenous drug-use history, and outcomes that are not substantially different than those of HIV-negative patients.

In January 2005, the National Arthroplasty Registry of the Malawi Orthopaedic Association (NARMOA) was established. This records all TJAs performed in Malawi for the purposes of research and clinical governance. Ethical approval has been given to the NARMOA from the Research Ethics Committee of the College of Medicine of the University of Malawi since its inception in 2005. Previous studies by our group using data from the NARMOA of all patients with known HIV status have shown low complication rates and good functional outcomes^{9,25-27}.

We aimed to study whether TJA in HIV-positive patients increased the risk of complications or of poorer functional outcome. In the present study, we describe our medium-term findings on the prevalence of complications, including infection, and the functional outcomes of a group of HIV-positive patients, without hemophilia or a history of intravenous drug use, who underwent TJA in a low-income country. These data include patients from 4 of our previous studies^{9,25-27} in which we reviewed complication rates and functional outcomes following TJA. While we have previously reported on HIV-positive TJA patients in the NARMOA, the current report contains additional patients who more recently have undergone surgery, giving a larger cohort, and providing longer follow-up than previously reported. With a high prevalence of HIV and increasing arthroplasty rates in low and middle-income countries (LMICs), understanding the outcomes of TJA in this unique cohort of patients is essential to ensuring that surgical practice is evidence-based.

Materials and Methods

All patients in Malawi undergoing TJA since 2005 were approached to give consent to be included in the NARMOA and have their data included in this study. These data were obtained prospectively via a set protocol at preoperative assessment and routine follow-up points as detailed in Figure 1. All HIV-positive patients who had undergone either total hip

arthroplasty (THA) or total knee arthroplasty (TKA) in Malawi from January 2005 to March 2020 were identified through the NARMOA (Table I) for inclusion in this observational study.

Exclusion criteria were the presence of any AIDS-defining illness, or revision arthroplasty for which the primary surgery had not been performed in Malawi. We identified 102 THAs in 85 HIV-positive patients (with 17 having bilateral procedures) and 20 TKAs in 12 HIV-positive patients (with 8 having bilateral procedures). No patients were excluded from this study.

Patients included in this study were seen by an orthopaedic surgeon and research nurse prior to the decision to operate. All patients were aware of their positive HIV status prior to surgery and all had been taking ART at the time of surgery and during follow-up, although exact therapy was not recorded. Preoperatively, patients undergoing THA had taken ART for a mean period of 5 years and 7 months (range, 1 to 18 years) and had a mean CD4 count of 529 cells/mm³ (range, 365 to 807 cells/mm³). Patients undergoing TKA had been taking ART for a mean period of 8 years and 2 months (range, 3 to 14 years) and had a mean CD4 count of 659 cells/mm³ (range, 448 to 800 cells/mm³). Patients were assessed clinically, and the absence of AIDS-defining illness was confirmed. CD4 count measurement and viral load were not used as definitive parameters to determine whether a patient was medically fit enough for their procedure, but they were used in combination with a general medical assessment.

Patient-reported outcome measures (PROMs) were used to assess functional outcomes of TJA. Preoperatively and at each follow-up evaluation, the modified Oxford Knee Score (OKS) was recorded for the TKA patients and the modified Harris hip score (HHS) and modified Oxford Hip Score (OHS) were recorded for the THA patients. Informed consent was obtained for the operative procedure and inclusion in the registry. Thirteen surgeons performed the TJAs at 4 hospital sites in Malawi, with the largest proportion at Beit CURE International Hospital (BCIH) (72 of 122 procedures, 59%).

For THA, the principal indication for surgery was osteonecrosis (66 hips), followed by osteoarthritis (21 hips). TKA indications were different, with the majority being for osteoarthritis (19 knees), with osteonecrosis being the indication for 1 knee. Indications are shown in Table II. No operating theaters had a laminar flow system. Most operations were performed using regional spinal anesthesia; 5 THAs which were performed using general anesthesia.

A Charnley prosthesis (DePuy Orthopaedics) with either a flanged or round-backed femoral stem and a standard long posterior wall or Ogee acetabular component (DePuy) was used in 42 hips. Stanmore implants with modular stems and 28-mm cobalt-chromium heads (Biomet) were used in 35 hips. An uncemented modular stem (Polarstem) with a Reflection uncemented acetabular cup system (Smith & Nephew) was used in 25 hips. A PFC cruciate-retaining prosthesis (DePuy Orthopaedics) with a

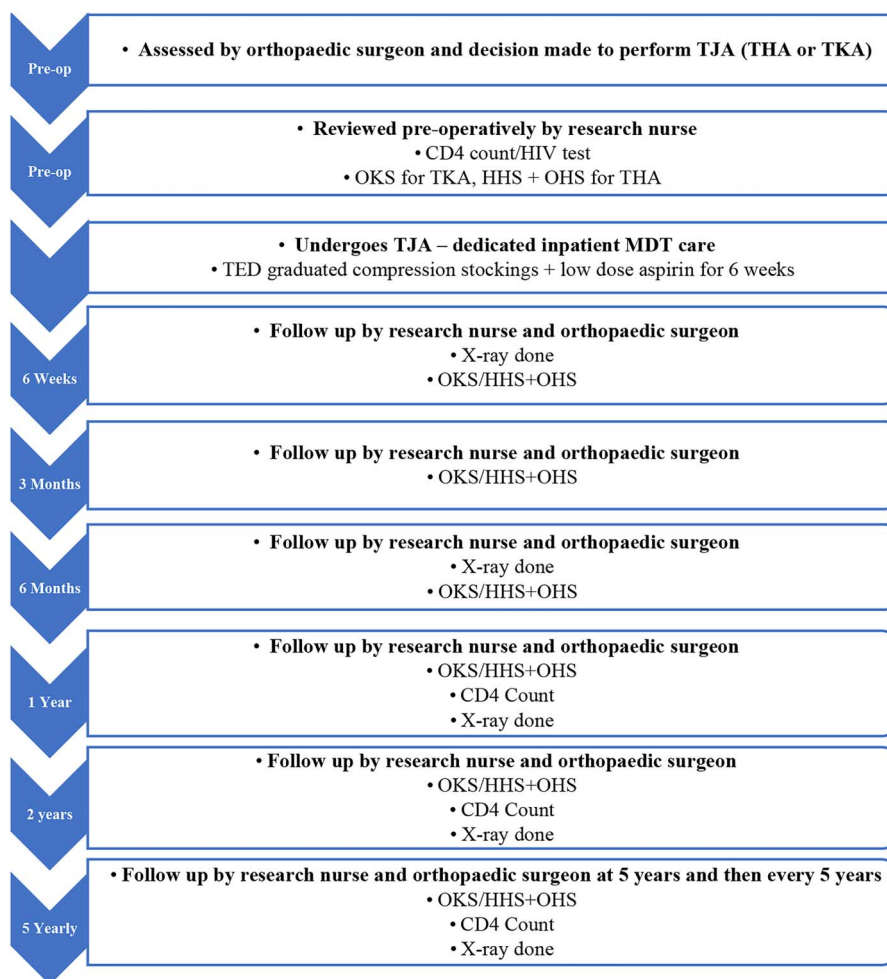


Fig. 1 Patient flow protocol for the management of patients undergoing total joint arthroplasty (TJA) and entry onto the National Arthroplasty Registry of the Malawi Orthopaedic Association (NARMOA). THA = total hip arthroplasty, TKA = total knee arthroplasty, OKS = Oxford Knee Score, HHS = Harris hip score, OHS = Oxford Hip Score, MDT = multidisciplinary team, and TED = thromboembolism deterrent.

metal tray and polyethylene insert was used in 11 knees, and an AGC prosthesis (Biomet) was used in 9 knees. All cemented implants were secured with SMARTSET GHV gentamicin cement (DePuy). Prosthetic choice was directed by availability at the operating hospital.

All patients received a prophylactic dose of cefuroxime or gentamicin (if allergic to penicillin) at the start of surgery. Post-operatively, patients were mobilized on the day following surgery. For venous thromboembolism prophylaxis, all patients were given thromboembolism-deterrent (TED) graduated stockings and given either low-dose aspirin for 6 weeks or low-molecular-weight heparin for 5 days (this varied by center as per preexisting local policies).

A research nurse and orthopaedic surgeon reviewed all patients at regular intervals preoperatively and postoperatively (6 weeks, 3 months, 6 months, 1 year, 2 years, 5 years, and then every 5 years) (Fig. 1). The majority of follow-up appointments were face-to-face; however, some later follow-ups (>12 months) were performed via telephone (17 hip patients, 5 knee patients). All patients had radiographic imaging and were assessed for postoperative complications, pain, and functional scoring. Wounds were assessed with the ASEPSIS (Additional treatment, the presence of Serous discharge, Erythema, Purulent exudate, and Separation of the deep tissues,

| TABLE I Patient Demographics and Procedures Performed for HIV-Positive Patients in the NARMOA Who Underwent TJA During the Study Period | | |
|---|------------|------------|
| | TKA | THA |
| No. of patients | 12 | 85 |
| No. of procedures | 20 | 102 |
| No. of patients with bilateral procedures | 8 | 17 |
| Mean age (range) (yr) | 64 (48-76) | 50 (21-76) |
| No. (%) of procedures in male patients | 3 (15%) | 59 (58%) |
| No. (%) of procedures in female patients | 17 (85%) | 43 (42%) |

TABLE II Cohort Sizes *

| Demographic and Surgical Data | No. of Patients (Hips) | No. of Patients (Knees) |
|-------------------------------|------------------------|-------------------------|
| Entered in registry | 85 (102) | 12 (20) |
| Lost to follow-up | 2 | 0 |
| ≥10-yr follow-up in registry | 12 | 3 |
| Died | 12 | 0 |
| Indication for surgery | | |
| Osteonecrosis | (66) | (1) |
| Osteoarthritis | (21) | (19) |
| Fractured neck of femur | (7) | NA |
| Failure of internal fixation | (2) | (0) |
| Previous infection | (2) | (0) |
| Legg-Calvé-Perthes | (2) | NA |
| Other | (11) | (0) |
| Type of implant | | |
| Charnley | (42) | NA |
| Stanmore | (35) | NA |
| Polarstem + Reflection | (25) | NA |
| PFC cruciate-retaining | NA | (11) |
| AGC prosthesis | NA | (9) |

*NA = not applicable.

the Isolation of bacteria, and the duration of inpatient Stay) wound scoring system²⁸, which has been validated and shown to be reproducible²⁹. A low threshold score of 10 was used to define wound infection. An independent orthopaedic surgeon who had not performed the operation assessed anteroposterior and lateral radiographs of the joints to assess for loosening, positioning, and radiolucent lines.

Statistical Analysis

Parametric data were analyzed using a Student t test. A p value of <0.05 was considered significant.

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Results

We identified 102 THAs in 85 HIV-positive patients (59 hips in male patients hips and 43 hips in female patients) with a mean age of 50 years (range, 21 to 76 years). Twenty TKAs in 12 HIV-positive patients (3 knees in male patients, 17 knees in female patients) were identified, with a mean patient age of 64 years (range, 48 to 76 years).

All 85 patients who underwent THA were seen at 6 weeks postoperatively. Two were lost to follow-up after 6 weeks; both patients were from outside of Malawi. These 2 patients had no complications at the 6-week follow-up. Twelve patients who underwent THA died during the study period, which began in 2005; all of these deaths were at least 6 weeks after the operation, and there is no evidence indicating that the deaths were related to the surgery. No patient who underwent TKA was lost to follow-up at 6 weeks, and none died. All 85 patients with THA and 12 with TKA were included in the final analysis. The total numbers of patients included at each follow-up point are shown in Table III.

Patients who underwent THA were followed for a mean period of 4 years and 3 months (range, 6 weeks to 15 years), with a mean age at the time of surgery of 50 years (range, 21 to 76 years). The mean body mass index (BMI) at the time of surgery was 24.7 kg/m² (range, 18 to 42 kg/m²). The mean follow-up for patients who underwent TKA was 4 years and 9 months (range, 6 weeks to 12 years), with a mean age at the time of surgery of 64 years (range, 48 to 76 years) and BMI of 32.2 kg/m² (range, 26 to 38 kg/m²).

The mean preoperative OHS was 14.0 (range, 2 to 33) of a maximum 48 points and increased to a mean of 46.6 (range, 23 to 48) postoperatively, an improvement of 32.6 (p ≤ 0.001). The mean preoperative HHS was 29.4 (range, 1 to 64) of a maximum 100 points and increased to a mean of 85.0 (range, 28 to 91) postoperatively, an improvement of 55.6 (p ≤ 0.001). The mean preoperative OKS was 14.9 (range, 6 to 31) of a maximum 48 and increased to a mean of 46.8 (40 to 48) postoperatively, an improvement of 31.9 (p ≤ 0.001).

In patients who underwent THA, there were 7 recorded complications. One patient had a complication within less than 6 weeks of surgery: a deep infection treated successfully with debridement, antibiotics, and implant retention (DAIR). This patient was not reachable as of 5 years postoperatively but was infection-free prior to this (4 years postoperatively). Six THA patients (6 hips) had aseptic loosening at varying time points: 2 patients at 10 years, 1 at 9 years, and 3 at 5 years of follow-up. Of the 6 patients, 1 is awaiting revision surgery and 5 have had

TABLE III Total No. of Patients Included at Each Follow-up Point for THA and TKA

| Follow-up | No. of Patients (Hips) | No. of Patients (Knees) |
|-----------|------------------------|-------------------------|
| Preop. | 85 | 12 |
| 6 wk | 85 | 12 |
| 3 mo | 18 | 4 |
| 6 mo | 29 | 3 |
| 1 yr | 23 | 6 |
| 2 yr | 42 | 3 |
| 5 yr | 43 | 4 |
| 10 yr | 11 | 2 |
| >10 yr | 1 | 1 |

TABLE IV Harris Hip Score (HHS) and Oxford Hip Score (OHS) for HIV-Positive Patients Undergoing THA in the NARMOA*

| Follow-up | No. of Patients | HHS | OHS |
|-----------|-----------------|-----|-----|
| Preop. | 85 | 29 | 14 |
| 3 mo | 18 | 71 | 41 |
| 6 mo | 29 | 83 | 46 |
| 1 yr | 23 | 85 | 45 |
| 2 yr | 42 | 87 | 46 |
| 5 yr | 43 | 89 | 46 |
| 10 yr | 11 | 83 | 47 |
| >10 yr | 1 | 91 | 48 |

*Maximum possible score of 100 for the HHS and 48 for the OHS.

revision surgery, with culture samples taken intraoperatively showing no evidence of infection.

There was 1 complication within 6 weeks of surgery among the patients who underwent TKA. This was a superficial surgical site infection that was examined and cleaned in the theater and healed with no exchange of the prosthesis. There was 1 patient with evidence of aseptic loosening at 2 years who is awaiting revision surgery.

Discussion

To our knowledge, this is the largest study in the literature to date reporting outcomes of TJA performed in patients who are HIV-positive in a low-income country. The results of this study are encouraging and show reassuringly low complication rates and good functional outcomes for HIV-positive patients undergoing both THA and TKA in the medium term. It is also encouraging that the observed low complication rates were seen across 4 hospitals now undertaking arthroplasty; this is compared with our earlier reports based primarily on a single center (BCIH).

We believe this study to be unique in that, unlike the majority of previous reports looking at TJA in HIV-positive patients, this relatively large cohort of HIV-positive patients did not include patients with a history of hemophilia and/or intravenous drug use. This is important because hemophilia can increase the risk of infection resulting from regular injections of Factor VIII (a possible source of bacteria)¹⁶ and bleeding around the joint. Intravenous drug use is a risk factor for infection as it can cause bacteremia²⁴. Higher complication rates in HIV-positive patients with hemophilia and/or intravenous drug-use history versus HIV-negative patients have been reported in several studies^{14,18-21,30}, although others have found TJA in these patients to be safe in terms of infection rates and have shown functional outcomes similar to HIV-negative patients^{15,17}. Other studies^{22,23} have shown complication rates among patients who are HIV-positive without a history of intravenous drug use and/or hemophilia versus HIV-negative patients to be similar, but cohort numbers of these patients are low.

International registries of TJA in high-income countries have shown consistent deep-infection rates of approximately 1% across all patients undergoing TJA³¹. The current study shows a similar rate of deep infection of 0.8% (1 of 122). Capogna et al.³⁰ showed an infection rate of 4.4% among 69 HIV-positive patients compared with 0.72% among 138 HIV-negative patients; some patients in that study had a history of intravenous drug use. In a retrospective review of a center in the U.S., Lin et al.³² found a total deep-infection rate of 9.1% among 22 HIV-positive patients, although this included patients with notable liver disease and previous intravenous drug use. A larger review by Lin et al.³³ that included 8,229 HIV-positive patients within a cohort of >5.6 million patients showed no significant difference in early complications (8.3% compared with 7.8%; $p = 0.52$); data were not available for deep-infection rates.

In the current study, the mean age at the time of surgery in the THA group (50 years) was lower than that of patients in the national registry in the U.K. (median age, 69 years)³⁴. This is likely because of early HIV/ART-related osteonecrosis of the femoral head¹⁰⁻¹². This early osteonecrosis of the femoral head is also likely to be the reason that 22% of THAs (102 of 456 hips) in the NARMOA were performed on HIV-positive patients compared with 7% of TKAs (20 of 285 knees). Mean age at the time of TKA in Malawi (64 years) was more similar to U.K. data (median age, 69 years)³⁴, which is in keeping with the main indication being osteoarthritis. Given the prolonged life expectancy of HIV-positive patients in the ART era, there is a need for medium and, indeed, long-term follow-up studies.

The most common indication for THA in the U.K. is osteoarthritis, in 92% of patients³⁴. In this Malawian cohort of patients, the most common indications for surgery were different: the main indications were osteonecrosis (66 of 102 hips, 65%) followed by osteoarthritis (21 of 102, 21%). The most common indication for TKA in this cohort was osteoarthritis (19 of 20 knees, 95%), which is similar to the U.K. rate, with the indication for 97% of TKAs being osteoarthritis³⁴. In Malawi, the mean national BMI is 22 kg/m² among men and 24.5 kg/m²

TABLE V Oxford Knee Score (OKS) for HIV-Positive Patients Undergoing TKA in the NARMOA*

| Follow-up | No. of Patients | OKS |
|-----------|-----------------|-----|
| Preop. | 12 | 15 |
| 3 mo | 4 | 42 |
| 6 mo | 3 | 36 |
| 1 yr | 6 | 47 |
| 2 yr | 3 | 48 |
| 5 yr | 4 | 48 |
| 10 yr | 2 | 48 |
| >10 yr | 1 | 48 |

*Maximum possible score of 48 for the OKS.

among women³⁵. Our cohort of patients undergoing TKA was generally overweight, with a mean BMI of 32.2 kg/m² (range, 26 to 38 kg/m²), contributing to their risk of osteoarthritis³⁶.

All PROMs for TJAs improved significantly postoperatively and are similar to results from high-income countries and are above thresholds that would indicate the requirement for early revision surgery^{37,38}. Improved PROMs in this cohort were sustained throughout the study period (Tables IV and V).

The post-TJA revision rate for HIV-positive patients in this study was 5.9% in the THA group (6 hips, including 1 listed that has not yet undergone surgery) across 15 years of the NARMOA. This rate is lower than the total revision rate for the U.K. (7.2%) over 15 years of data collection in its national joint registry³⁴. The absence of revision surgery for instability is reassuring with regard to the standard of surgery and aftercare in this low-income-country context.

Despite this being, to our knowledge, the largest cohort of HIV-positive patients undergoing TJA in a low-income country in a report published to date, the main limitation of this study was the relatively small number of patients included, particularly in the TKA group. The follow-up rate for this study is remarkably high (85.6%) given that patients have to travel extremely long distances for medical consultation and Malawi is a low-income country with poor transport infrastructure. Despite these long distances, the majority of last follow-up appointments were face-to-face (68 of 85 THA patients, 7 of 12 TKA patients).

Given increasing life expectancy, use of ART, and the number of people living with HIV, TJA is becoming more common among HIV-positive patients across high- and low-income countries. Currently, 26% of patients undergoing TJA in Malawi in the NARMOA are HIV-positive. This study adds evidence to the literature that TJA can be safely undertaken in patients with HIV and that excellent patient-reported outcomes

with low complication rates can be sustained in the medium term. ■

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