Total hip arthroplasty in patients with human immunodeficiency virus infection

Pathologic findings and surgical outcomes

Craig R Mahoney[1], Marshall J Glesby[2], Edward F DiCarlo[3], Margaret G E Peterson[3] and Mathias P Bostrom[3]

[1]Iowa Orthopedic Center, 411 Laurel St. #3300, Des Moines, IA 50314, [2]Division of International Medicine and Infectious Diseases, Weill Medical College of Cornell University, 525 E. 68th St., Box 566, New York, NY 10021, [3]Hospital for Special Surgery, 535 East 70th St., New York, NY 10021, USA
Correspondence MPB: bostromm@hss.edu
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Background **An increased incidence of osteonecrosis of the femoral head has been reported in patients infected with human immunodeficiency virus (HIV). The purpose of this study was to review the pathologic specimens of HIV-positive patients who had undergone total hip arthroplasty (THA) and compare them with those of THA patients who were HIV-negative. The surgical outcomes of these HIV-positive patients were also reviewed.**

Methods **40 HIV-positive patients who underwent 54 THAs at our institution were identified. The primary pathologic diagnosis for the femoral heads of these patients was osteonecrosis in 35 cases, degenerative joint disease in 11 cases, and other diagnoses in 8 cases.**

Results **There was a higher incidence of osteonecrosis in HIV-positive patients. At the most recent follow-up, 4 patients had died and 1 patient had a significant Staphylococcus aureus infection of the hip.**

Interpretation **There was a significant difference in the pathologic diagnoses of the HIV-positive group and the HIV-negative group, implicating HIV infection as a risk factor for osteonecrosis. Also, the risk of infectious complications is lower in our study than previously reported in other studies of HIV-positive patients who have undergone THA.**

Osteonecrosis of the femoral head associated with human immunodeficiency virus (HIV) infection was first reported in 1990 (Goorney et al.), and has been shown to occur with increased incidence in patients infected with HIV. Recent studies on symptomatic osteonecrosis in HIV-positive individuals have reported an annual incidence of about 1% (Keruly et al. 2001). Osteonecrosis has been reported not only in the hip but also at multiple sites in patients infected with HIV (Gerster et al. 1991). Asymptomatic osteonecrosis as diagnosed by MRI—which has not been extensively studied in the general population—has been estimated to occur in 4% of asymptomatic HIV-positive individuals (Masur et al. 2000). In HIV-positive patients, hyperlipidemia, use of steroids, and protease inhibitor therapy have been implicated as possible etiologies (Brown and Crane 2001).

There have been few reports addressing the pathologic changes of the femoral head in HIV-positive patients who have undergone total hip arthroplasty (THA), and none that focus on the postoperative outcomes of such patients. Thus, the purpose of our study was to review the pathologic specimens of HIV-positive patients after THA and to compare the resulting data with the specimens of HIV-negative, age-matched control patients. We reviewed the risk factors implicated in the development of osteonecrosis in the entire HIV-positive population treated at our hospital, looking for differences between patients with hip symptoms and those without. We also reviewed

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the immediate surgical outcomes of HIV-positive patients after they had undergone THA at our institution.

Patients and methods

HIV-positive cohort

After approval from the Institutional Review Board, the medical records database of the Hospital for Special Surgery was used to identify HIV-positive patients treated at our institution. Our search generated a list of 134 HIV-positive patients who were treated between July 1995 and January 2002. Of those 134 patients, 40 had undergone 54 primary THAs, 34 on the left hip and 20 on the right hip. There were 31 men and 9 women, with a mean age of 44 (28–70) years. Since the pathologic diagnosis in each hip may differ when both hips are operated on in one patient, we analyzed our data by hip rather than by patient. The clinical diagnosis before surgery was avascular necrosis (osteonecrosis) in 35 cases, osteoarthrosis in 11 cases, and other diagnoses in 8 cases. The onset of hip symptoms preceeded the patient's first clinical orthopedic appointment by just over 2 years on average. Patients underwent surgery at a mean of 8 months after the original evaluation. Patients had been diagnosed with HIV at a mean of 8 years before THA.

Of the 54 THAs performed on 40 HIV-positive patients, 25 were completed on patients with acquired immune deficiency syndrome (AIDS). These patients were diagnosed with AIDS an average of 4 years before their surgery. The accepted criterion for being diagnosed with AIDS is a CD4 cell count of < 200 cells/mm3 or the occurrence of an AIDS-defining disease (Centers for Disease Control and Prevention 1993). We obtained patients' viral loads and CD4 cell counts from their charts by looking for the most recent values prior to surgery. These tests were not part of the normal preoperative work-up and did not determine whether the patient underwent surgery or not. Viral loads were available for 23 patients. Values reported as undetectable were assigned values of 400 copies/mL, which is the lower limit of detection of the assay. The mean HIV RNA level was 3.15 log10 copies/mL (SD 0.93). The CD4 cell count was available for 32 patients. The median CD4 cell count was 274 (8–982) cells/mm^3. The clinical characteristics of the HIV-positive patients are listed in Table 1.

Table 1. Characteristics of HIV-positive patients who underwent total hip arthroplasty at our institution

Characteristic	Value
Number of patients	40
with AIDS	25
Number of hips	54
Mean age, years (SD)	44.4 (9.3)
Median CD4 cell count, cells/mm^3 (interquartile range, n = 32 patients)	274 (8–982)
HIV RNA level, log10 copies/mL (SD) (n = 23 patients)	3.15 (0.93)

HIV transmission risk factors were blood product transfusion (5 patients), intravenous drug use (13 patients), and unprotected sex (14 patients), and were unknown for 8 patients. 35 of the 40 patients were taking anti-retroviral medication at the time of surgery. Of those 35 patients, 32 were taking multiple anti-retroviral agents (mean 2.3) at the time of surgery.

Most patients had multiple medical problems: 13 patients had a history of intravenous drug use, 11 were hepatitis C virus seropositive and 6 were hepatitis B virus seropositive. Overall, there was an average of 2.5 comorbidities per patient; only 4 patients had no comorbidities (other than being HIV-positive) at the time of their surgery.

Risk factors implicated in the development of osteonecrosis in this group of patients included protease inhibitor therapy at the time of surgery (14 patients), steroid use (12 patients), alcoholism (7 patients), hypercholesterolemia (9 patients), and previous radiation therapy (1 patient).

All THAs performed on this group of patients were completed through a posterior approach. The acetabular components were cementless in all cases. Based on surgeon preference, the femurs were cemented in 42 cases and cementless in 12 cases. Estimated blood loss averaged 257 (100–1000) mL, and there did not appear to be any predisposing condition that resulted in excessive intraoperative blood loss. 15 patients required blood transfusions while in hospital. The average hospital stay was 6 (3–11) days.

Table 2. Pathologic diagnosis of all HIV-negative patients who underwent total hip arthroplasty at our institution (n= 2129)

Diagnosis	No. of patients
Degenerative joint disease (DJD)	1527
Avascular necrosis of femoral head	235
DJD, hip, secondary, consistent with abnormal growth and development	156
Superficial subchondral fracture	85
Destructive joint disease with lymphoplasmacytic synovitis, consistent with rheumatoid arthritis	45
DJD, consistent with posttraumatic arthropathy	20
Osteoporosis with subcapital pathologic fracture	16
Destructive joint disease, consistent with infectious arthritis	9
Sclerosing bone disease, hypermetabolic state, consistent with renal osteodystrophy	7
Other	29

To analyze the HIV-positive patients for factors implicated in the development of osteonecrosis, we compared the patients treated (treated for what? unclear) at our institution who had no complaints regarding their hips with those patients who were diagnosed with osteonecrosis (by pathology), looking specifically at duration of HIV infection to the time of treatment and history of either steroid or protease inhibitor use.

HIV-negative control groups

To compare the pathologic diagnoses of the HIV-positive cohort with those of an HIV-negative population, we first reviewed the pathology records of all patients treated with THA at our institution over the last 2 years with ages within 2 standard deviations of the mean age of the HIV-positive patients. This search generated a list of 2 129 hips (Table 2). The mean age of these patients was 51 (25–62) years. After further analysis of the list, we determined that since the mean age of the HIV-positive group was statistically lower than that of the HIV-negative group, and since there were more men in the HIV-positive group than in the HIV-negative group, age and sex would have to be controlled for more precisely. The pathology records were searched again and a second group of control patients, matched by sex and exact age, was obtained.

Statistics

The groups were compared using chi-square analysis for categorical data such as sex and steroid use, and diagnosis. Fisher's exact test was used where appropriate. Age was compared using the t test. Duration of HIV infection before the occurrence of THA was analyzed using survival analysis. The p-values were not corrected for multiple comparisons.

Results

In the 54 primary THAs that were performed on HIV-positive patients, the primary pathologic diagnoses of the hips were osteonecrosis (35 cases), degenerative joint disease (DJD) (11 cases), posttraumatic arthritis (2 cases), subchondral fracture (2 cases), subcapital fracture (2 cases), septic arthritis (1 case), and amyloidosis (1 case). Secondary pathologic findings included focal bone necrosis (6 cases), pseudo cyst (5 cases), fibrous proliferation (3 cases), osteoporosis (2 cases), DJD (2 cases), bone marrow necrosis (2 cases), and infarction with secondary extension (1 case).

The mean age of the HIV-positive group at the time of surgery, 44 years, was significantly less than that of the first (broader) HIV-negative control group, 51 years ($p < 0.001$). There was a higher prevalence of osteonecrosis in the HIV-positive group (65%) than in the broader control group (11%) ($p < 0.001$). When we analyzed hips with regard to their diagnoses, the hips that were osteonecrotic in the HIV-positive group were younger (41 years) than the osteonecrotic hips in the control group (45 years) ($p = 0.008$).

Given the significant difference in the mean ages of the HIV-positive THA group and the first (broader) control group, the HIV-positive THA hips were then matched by age and sex to a control group of HIV-negative THA hips. The primary pathologic diagnoses of the age- and sex-matched control group of hips were DJD (38 cases), osteonecrosis (10 cases), developmental dysplasia of the hip (3 cases), posttraumatic arthrosis (1 case), septic arthritis (1 case), and rheumatoid arthritis (1 case). A comparison of the relative percentages of the diagnoses of the 3 groups is included in Table 3. Statistical analysis of the HIV-positive THA

Table 3. Comparison of the pathologic diagnoses of total hip arthroplasty (THA) patients in the HIV-positive group and two different HIV-negative control groups

Diagnosis	HIV-positive THA patients n (%)	HIV-negative THA control patients n (%)	HIV-negative age- and sex-matched control patients n (%)
Avascular necrosis of femoral head	35 (65)	234 (11)	10 (19)
Degenerative joint disease (DJD)	11 (20)	1533 (72)	38 (70)
Superficial subchondral fracture	2 (3.7)	85 (4.0)	0 (0.0)
DJD/posttraumatic arthropathy	2 (3.7)	19 (0.9)	1 (1.9)
Subcapital pathologic fracture	2 (3.7)	17 (0.8)	0 (0.0)
Infectious arthritis	1 (1.9)	9 (0.4)	1 (1.9)
Amyloidosis	1 (1.9)	2 (0.1)	0 (0.0)
DJD/developmental dysplasia of the hip	0	155 (7.3)	3 (5.6)
Rheumatoid arthritis	0	45 (2.1)	1 (1.9)
Other	0	36 (1.7)	0 (0.0)

group against the age- and sex-matched control group showed that there was a higher prevalence of osteonecrosis in the HIV-positive group ($p < 0.001$) and more DJD in the control groups ($p < 0.001$).

A comparison of potential risk factors implicated in the occurrence of osteonecrosis was done by comparing the group of HIV-positive patients who developed osteonecrosis and underwent THAs to a group of HIV-positive patients who had no symptoms pertaining to their hips. The duration of HIV infection in the group with no symptoms pertaining to their hips was available for 46 of 80 patients (mean 10 (1.5–22) years). The duration of HIV infection in the HIV-positive group with osteonecrosis was available for 29 hips (mean 9 (2.4–19) years). This difference was statistically significant ($p < 0.001$).

32 of the 80 patients in the HIV-positive group with no symptoms pertaining to their hips were taking protease inhibitors at the time of surgery, and 21 of 35 hips in the HIV-positive group with osteonecrosis were in patients taking protease inhibitors at the time of surgery. This difference was not statistically significant ($p = 0.07$).

3 of the 80 patients in the HIV-positive group with no symptoms pertaining to their hips had been using or were currently using steroids. 16 of 35 hips in the HIV-positive group with osteonecrosis were in patients who had been using or were currently using steroids. This difference was statistically significant ($p < 0.001$).

Surgical outcome

HIV-positive THA patients were contacted at an average of 2.3 (1–7) years of follow-up. Of 40 patients, 2 were lost to follow-up. Of the remaining 38 patients, 4 patients died within an average of 2.5 years after their surgery. At the time of death, all of their THAs were functioning well, and none of the patients had experienced complications related to their hips.

Regarding infectious complications, 1 patient presented 3 years after his THA with hip pain and fever. An antibiotic-sensitive *Staphylococcus aureus* infection was diagnosed. The patient was arthroscopically debrided; however, the infection did not clear and component removal was ultimately required. The components have not been reimplanted due to the patient's persistent intravenous drug abuse.

Discussion

Previous studies have examined the prevalence of HIV infection in patients treated for osteonecrosis. A study of 38 consecutive patients treated operatively for osteonecrosis examined the prevalence of HIV as an isolated risk factor for osteonecrosis (Ries et al. 2002). 7 patients in the cohort were HIV-positive and 31 were HIV-negative. Of the patients who were HIV-positive, 4 had no known risk factors for osteonecrosis. Of the patients who were HIV-negative, 13% had no known risk factors

for osteonecrosis. The difference was statistically significant

Other studies have compared HIV-positive patients with osteonecrosis and HIV-positive patients without osteonecrosis to look specifically at known and proposed risk factors for osteonecrosis in HIV-positive individuals (Blacksin et al. 1999, Scribner et al. 2000, Glesby et al. 2001). These studies showed an increased number of recognized risk factors in the groups with osteonecrosis and a positive association between both alcohol and glucocorticoid use and the development of osteonecrosis. In two of the studies, the use of glucocorticoids was the most common risk factor (Blacksin et al. 1999, Glesby et al. 2001).

While an association has been described between anabolic steroid use and osteonecrosis in HIV-negative patients (Pettine 1991), testosterone levels in HIV-positive patients have not been found to be similar to those in control patients (Scribner et al. 2000).

Our review focused on the pathologic diagnoses of HIV-positive patients undergoing THA at our institution. For comparison, we used two separate control groups. The first (broader) control group included the hips of all HIV-negative patients who underwent THA and who fell within 2 standard deviations of the mean age of our HIV-positive group. The second control group consisted of a subset of the larger HIV-negative control group; patients in this group were matched to those in the HIV-positive group by exact age and sex. We found an increased prevalence of osteonecrosis in HIV-positive hips when they were compared to hips of HIV-negative control patients in both groups. In the age- and sex-matched control group, we also found an increased rate of degenerative joint disease compared to our HIV-positive cohort.

We also compared all HIV-positive patients who were diagnosed with osteonecrosis to those HIV-positive patients who had no symptoms pertaining to the hip. There was a shorter duration of HIV infection in patients whose hips developed osteonecrosis compared to those whose hips did not develop osteonecrosis. We found an increased prevalence of current or prior use of corticosteroids in the group with osteonecrosis than in the group with no hip symptoms. Although consistent with previously reported data (Mankin 1992), there is potential for bias in this comparison since patients with a clinical diagnosis of osteonecrosis may have been more likely to have been questioned about corticosteroid use.

Protease inhibitor use has been implicated in the development of osteonecrosis in some case series (Brown and Crane 2001), although controlled studies have not confirmed this association (Scribner et al. 2000, Glesby et al. 2001). The data available to us, however, were limited to the number of patients taking protease inhibitors at the time of surgery. Despite this, there was a trend of increased protease inhibitor use in the HIV-positive patients with osteonecrosis.

Surgical outcome in HIV-positive patients

It is well established that orthopedic surgery on patients who are infected with HIV carries with it a higher risk of complications, especially infections (Paiement et al. 1994).

Although joint replacement in HIV-positive patients remains relatively uncommon, it is becoming more frequent. Therefore, as more studies on this subject are published, the frequency and type of complications become more apparent. One retrospective, multicenter study looked at the outcome of replacement arthroplasties at 8 hemophilia centers. At a median follow-up time of 5 years, the overall rate of deep sepsis was 19% for primary procedures and 36% for revisions. Half of the infections resolved fully after medical and/or surgical treatment (Hicks et al. 2001). Another recent study examined the rate of deep periprosthetic infection after total joint arthroplasty in patients with HIV or IVDU (Lehman et al. 2001). Of 28 HIV-positive patients undergoing joint replacement, 4 developed infections. 7 patients with IVDU developed an infection, and 11% of patients with both IVDU and HIV developed a deep infection. Recently, Parvizi et al. (2003) also noted a higher incidence of complications in a diverse group of HIV-positive hip and knee arthroplasty patients.

There have been attempts to correlate preoperative factors such as CD4 cell counts to postoperative infection in HIV-positive patients. Guth et al. (1996) examined the relationship between CD4 cell counts, Injury Severity scores, and bacterial infectious complications in HIV-positive trauma patients and found that only the Injury Severity

score was associated with infections. Studies outside orthopedics have shown that CD4 cell counts are highly associated with postoperative infections, regardless of the type of surgery performed (Emparan et al. 1998).

Although historically, the risk of complications after THA has been high in HIV-positive patients, the incidence of infection in HIV-positive patients treated at our institution was lower than previously reported. We attribute the lower rate of infection to a number of different factors, including advances in the care of the HIV-positive patient in recent years, a lower rate of infection with total joint arthroplasty at our institution as compared to national data, and a relatively low prevalence of patients with IVDU in our series.

In summary, we found that osteonecrosis was more prevalent in HIV-positive patients undergoing primary THA than in HIV-negative control patients. In adult patients having primary THA, osteonecrosis develops at an earlier age in HIV-positive patients than in HIV-negative patients. Also, there is a lower prevalence of osteoarthrosis in HIV-positive patients than in age- and sex-matched HIV-negative controls. The duration of HIV infection in our study was significantly shorter in HIV-positive patients with osteonecrosis who underwent THA than in HIV-positive patients who did not have symptoms pertaining to their hips. Despite the risk of complications, THA in HIV-positive patients is a relatively safe and effective option for treatment of degenerative disorders of the hip.

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