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Midterm Results of Total Hip Arthroplasty for Osteonecrosis of the Femoral Head in Human Immunodeficiency Virus-Infected Patients in South Korea

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Background: Studies have reported that osteonecrosis of the femoral head (ONFH) is more prevalent in patients with human immunodeficiency virus (HIV). Total hip arthroplasty (THA) is considered reasonable management of ONFH. However, only scarce data exist on the outcomes of THA for HIV-infected patients in South Korea. The purpose of this study was to evaluate the midterm results of HIV-positive patients who underwent THA for ONFH.

Methods: We performed a retrospective review of HIV-infected patients with ONFH who underwent THA in our institution from 2005 to 2021. Twenty-two hips in 15 patients underwent THAs with cementless implants. The clinical and radiographic evaluation was performed at each follow-up, and any complication was recorded.

Results: The mean follow-up period was 5.2 years (range, 1.0–16.0 years). The mean age of the HIV infected patients with osteonecrosis at the time of surgery was 44.7 ± 11.6 years. ONFH occurred 9.8 ± 3.7 years after the initial diagnosis of HIV infection. The average modified Harris hip score improved from 58.3 ± 14.8 to 95.2 ± 11.3 at the latest follow-up. Surgical complications such as infection, nerve injury, or dislocation were not present. The radiographic evidence of stable fixation by bone ingrowth without migration was seen in all implants.

Conclusions: Our data suggest that THA is a safe and valid option of treatment for ONFH in well-controlled HIV-infected patients in Korea. Further large-scale nationwide studies are warranted.

Keywords: *Total hip arthroplasty, HIV*

Despite increasing efforts to prevent, diagnose, and treat human immunodeficiency virus (HIV) infection, HIV/acquired immune deficiency syndrome (HIV/AIDS) remains a major global public health issue.[1] First reported in the 1980s, HIV infection is a relatively recent health issue in South Korea compared to tuberculosis, which has been a major threat to public health of the country for a long time. Yet, Korea Disease Control and Prevention Agency has annually reported more than 1,000 newly diagnosed HIV-infected cases, with 13,857 HIV-infected people still alive in 2019.[2] As the socioeconomic burden of HIV/AIDS

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escalates gradually, careful attention needs to be drawn to the treatment and care of HIV-infected individuals.

Studies have reported a higher prevalence of osteonecrosis of the femoral head (ONFH) in patients with HIV.[3,4] Besides, owing to the development of highly active anti-retroviral therapy (HAART), the life expectancy of HIV-infected individuals is improving.[5] Thus, the total number of ONFH patients among the HIV-infected population is expected to grow due to the aging of the cohort. While total hip arthroplasty (THA) is widely acknowledged as a reasonable treatment of ONFH, little data exist on the outcomes of THA for HIV-infected individuals in South Korea.[6] The aim of this study was to evaluate the clinical and radiological outcomes of HIV-infected patients who underwent THA for ONFH in South Korea.

METHODS

The study was conducted upon approval of the Institutional Review Board of Seoul National University Hospital (No. H-2105-109-1219). Informed consent was waived due to the retrospective nature of the study. We retrospectively enrolled HIV-infected ONFH patients who underwent THA with cementless components in our institution from 2005 to 2021. The medical records, laboratory results, and radiographs of the patients were reviewed. The infection of HIV was confirmed by western blot, and the patients without confirmed HIV-infection were excluded. HIV-infected patients who had not undergone HAART prior to THA were excluded as well. The demographic data of the included patients are shown in Table 1.

The HIV-infected patients had undergone regular check-ups at the internal medicine outpatient clinic at our institution. The HAART regimen used in the included patients consisted of six different classes, including nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors, protease inhibitors, integrase strand transfer inhibitors (INSTIs), fusion inhibitors, and chemokine receptor antagonists. The most commonly used regimen was a combination of two NRTIs and one non-NRTI or INSTI. We followed the definition of "well-controlled HIV infection" as a CD4 count > 350 cells/uL and undetectable viral load (< 200 copies/mL), as defined by the World Health Organization and recent literatures.[1,7,8]

Two surgeons (JJY and HJK) at our institution performed all index surgeries, which were performed with either a posterolateral approach or a modified direct lateral approach. To protect the medical staff from virus transmission, all procedures were performed abiding by the HIV infection control guidelines, provided by the Korea Disease Control and Prevention Agency and the internal biosafety protocols.[2,6] All surgeons involved in the surgery wore waterproof gowns, caps, masks, head gear, two pairs of sterilized gloves, and protective boots. To avoid needle stick injuries or stabbing injuries, all sharp devices were handed over indirectly through a space set up between the surgeons and nurses. All instruments in the operating room were covered with vinyl and disposable linen. Postoperatively, all surgical instruments and tissues were tagged with an HIV infection mark to ensure that they were easily recognized by other personnel at our institution. Cefazolin was injected once before surgery and three times throughout the first 24 hours after surgery for surgical infection prophylaxis. The stem reviewed in this study was a Bencox M stem (Corentec), which is a type 1 stem made of titanium alloy.[9] In 8 cases, third generation alumina-alumina bearing system (BIOLOX Forte, CeramTec AG) was used, and fourth generation alumina-alumina bearing system (BIOLOX Delta, CeramTec AG) was used in 14 cases. Crutch gait with partial weight-bearing to the operated hip was recommended for 6 weeks. The patients were followed up at 6 weeks, 6 months, and 12 months af-

Table 1. Demographics and Baseline Characteristics of 15 HIV-Infected Patients Who Underwent Total Hip Arthroplasty

Parameter	Value
Age (yr)	44.7 ± 11.6
Sex	
Female	0
Male	15 (100)
BMI (kg/m^2)	21.8 ± 3.3
Right : left	12 : 10
ASA physical status classification	
1	3 (13.6)
2	19 (86.4)
Anesthesia	
Spinal anesthesia	18 (81.8)
Combined spinal and epidural anesthesia	3 (13.6)
General anesthesia	1 (4.5)
Operative duration (min)	127.3 ± 59.8

Values are presented as mean ± standard deviation or number (%).
HIV: human immunodeficiency virus, BMI: body mass index, ASA: American Society of Anesthesiologists.

ter surgery and annually thereafter.

Postoperative evaluation of the patients was based on the radiologic findings and clinical improvements. For radiologic assessment, fixation, migration, component loosening, and degree of stress shielding were evaluated as described by Engh et al.[10] In addition, other abnormal radiologic findings, including radiolucency, focal osteolysis, heterotopic ossification, and notching of the femoral stem, were examined. Osteolysis was defined as a periprosthetic cystic or scalloped lesion, larger than 2 mm in diameter that had not been observed on the immediate postoperative radiographs. Whether osteolysis or component loosening took place during follow-up was evaluated, as it is critical in suspicion for periprosthetic joint infection (PJI).[11] In addition, serological evaluation of white blood cell (WBC) count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) was performed.[12,13]

Clinical outcomes were evaluated with modified Harris hip score and the questions were asked in person at the follow-up visits (18 hips) or through telephone interviews (4 hips). Other medical complications, such as infection, pulmonary embolism, or morbidity, were checked as well.

RESULTS

HIV Infection Management and ONFH

The typical symptoms of ONFH, including pain and limping, occurred 9.8 ± 3.7 years after the initial diagnosis of HIV infection. The patients underwent HAART 8.0 ± 5.1 years before hip surgery and the average CD4 count of the patients before surgery was 476.3 ± 238.7 cells/uL. Preoperative HIV viral load revealed less than 200 copies/uL in 15 patients (68.2%). Three (13.6%) showed 420 copies/mL before surgery.

Clinical Outcome

The mean follow-up period of the patients was 5.2 years (range, 1.0–16.0 years). The mean modified Harris hip score improved from 58.3 ± 14.8 to 95.2 ± 11.3 at the latest follow-up. During the follow-up, no wound or PJI was reported. One case of postoperative pneumonia was reported, but the operated hip was intact (Table 2).

Radiologic Outcome

All implants showed no radiologic evidence of implant loosening, focal osteolysis, and femoral neck notching. Stress shielding or heterotopic ossification was not observed in all cases.

Laboratory Outcome

The WBC count, CRP, and ESR for each patient were analyzed. They increased immediately after the index surgery, with gradual decrease throughout the follow-up period as in uninfected patients.

DISCUSSION

To the best of our knowledge, this study is the first to report the outcome of arthroplasty in HIV-infected patients in South Korea. All 22 THA cases investigated in this study showed satisfactory clinical and radiologic outcomes as conventional THA cases, with much improved modified Harris hip scores and minimal radiological aberrations throughout the follow-up period. There was no noted complication such as surgical site infection and all-cause revision along with the agreeable clinical and radiologic outcomes. Even though 1 case of pneumonia was reported, no other medical complication was reported.

HIV infection is an emerging concern in South Korea, along with other chronic viral infections, such as hepatitis B virus and hepatitis C virus.[2] Yet, the lifespan of the HIV-infected population was greatly improved, owing to the advent of HAART.[5,14] As a result, the total number of HIV-infected patients undergoing elective primary joint

Table 2. Follow-up and Complication Details

Follow-up detail	Value
Follow-up (yr)	5.2 ± 4.7 (0.1–16.0)
Follow-up > 1 yr (case)	18 (81.8)
Surgery-related complication	
Periprosthetic joint infection	0
Revision surgery	0
Dislocation	0
Stem subsidence, cup migration	0
Loosening	0
Medical complication	
Pneumonia	1
Pulmonary embolism	0
Acute kidney injury	0
Death	0

Values are presented as mean ± standard deviation (range) or number (%).

arthroplasty has gradually escalated as well.[15] Not only the increasing number of senile HIV-infected population but also multiple factors contribute to the mounting incidence of ONFH in patients with HIV.

Despite a limited understanding of its etiology, a higher incidence of ONFH in infected patients has been reported in many studies.[4,16,17] While controversy remains, HAART itself is pointed out in many literatures as the culprit of ONFH in HIV-infected patients. HAART may produce autoantibodies predisposing patients to thrombosis as well as infection-related vasculitis, which Stahl et al.[18] suggested as a possible mechanism of ONFH. Gutierrez et al.[19] and Scribner et al.[20] accused protease inhibitors, including saquinavir, of precipitating ONFH in those who had undergone HAART. As the total number of HIV-infected ONFH patients accumulates, we face a growing need to comprehend the outcomes of THA as a treatment of ONFH in HIV-infected patients.

There have been concerns about the early failure of THA in HIV-infected patients, mainly due to postoperative infection. Lehman et al.[21] and Parvizi et al.[22] reported an alarming rate of postoperative infection of 14%–28.6% among HIV-infected patients. Yet, following the advent of HAART in 1997, which improved the medical management of HIV-infected patients, recent studies challenged the vulnerability and hazard of THA procedures in those living with HIV. Lin et al.[15] reviewed 6,499 cases of THA performed from 2000 to 2008 and found that wound infection occurred in 0.6% of postoperative HIV-infected patients. Though the uninfected group showed a significantly lower infection rate of 0.3% in the same study, they concluded that HIV was not an independent risk factor for complications in THA. Dimitriou et al.[23] reviewed 6.5 million joint surgeries included in 21 articles and found that the survival rate of THA in HIV-infected patients was comparable to that of non-HIV-infected patients at 1 and 5 years postoperatively. In accordance with recent literature, postoperative infection is becoming less common in total joint arthroplasty among HIV-infected patients. This trend is also reflected in our study, which reported no surgery-related infection after 22 cases of THA in HIV-infected patients. All patients also showed elevation of serological parameters, including leukocyte count, CRP, and ESR, immediately after surgery, while those values returned to preoperative levels throughout the follow-up period without abnormal spikes. Along with the absence of osteolysis and component loosening, this recovery reflected little chance of PJI after surgery during the follow-up period. We attribute our low incidence of complications to thorough evaluation and management of HIV infection prior to elective THA.

CD4 cell count and viral load were the two parameters we used for perioperative evaluation of HIV infection. We defined well-controlled HIV-infection as a CD4 count > 350 cells/uL and undetectable viral load (< 200 copies/mL).[1,7,8] In the current study, 63.6% (14/22) of the index patients showed CD4 count greater than 350 cells/uL, and 86.3% (19/22) showed viral load less than 200 copies/mL. The patients with CD4 cell count lower than 350 cells/uL had undergone HAART for a mean of 6.4 years (range, 2.0–13.1 years) before the arthroplasty surgery, and the stable level of CD4 cell count was confirmed preoperatively. CD4 cell count and viral load were followed up postoperatively, and no case showed an abrupt decrease of CD4 cell count or a drastic increase of viral load within 1 year after surgery (Table 3). It should be noted that Lin et al.[24] found that CD4 counts at the time of index surgery did not correlate with the development of deep implant infection. Instead, they added that the patients who showed precipitous drops in CD4 counts were more prone to greater risk for deep implant infection. Our data were consistent with those in previous reports that perioperative medical optimization for elective arthroplasty and regular postoperative follow-up can reduce complications, despite preoperatively low CD4 cell counts.

Table 3. Detailed Perioperative Medical History of Treatment for Human Immunodeficiency Virus

Variable	Value
Onset of ONFH from initial diagnosis of HIV infection (yr)	9.8 ± 3.7
HAART before surgery (yr)	8.0 ± 5.1
Preoperative CD4 count (cell/uL)	476.3 ± 238.7
Preoperative viral load (copy/mL)	
Negative	15 (68.2)
Less than 200	4 (18.2)
More than 200	3 (13.6)
Postoperative CD4 count (cell/uL)	490.8 ± 177.85
Postoperative viral load (copy/mL)	
Negative	20 (90.9)
Less than 200	-
More than 200	2 (9.1)

Values are presented as mean ± standard deviation or number (%).
ONFH: osteonecrosis of the femoral head, HIV: human immunodeficiency virus, HAART: highly active antiretroviral therapy.

Yet, we reported one case of pneumonia that occurred postoperatively, and the preoperative CD4 cell count of the case was 262 cell/mL and the postoperative CD4 cell count was 271 cell/μL. Though the rate of surgical complications might not correlate with the absolute value of preoperative status of HIV control, this suggests that we should take caution in patients who do not meet the criteria of "stable HIV infection" before arthroplasty in terms of medical complications.

Another possible reason for the low incidence of postoperative complications in our study is the low proportion of intravenous drug users and hemophiliacs among the HIV-infected population in South Korea. Recent studies have shown non-hemophiliac HIV-infected patients have revision rates comparable to those in previous reports on HIV-negative patients of similar ages.[25,26] The fact that all cases in this study were non-hemophiliac patients with no history of intravenous drug abuse could have contributed to reducing the complication rate.

There are some limitations in our study. Since the study was based on a retrospective review of the cases, a well-designed comparative study would be required to determine the clinical efficacy and safety of THA in HIV-infected patients. Secondly, as this study was based on the data of 22 hips of 15 patients from a single center, further investigation with a larger sample size from multiple institutions would provide more chance to observe the complications and increase credibility to generalize the clinical findings.

The advancement of highly active antiretroviral therapy and optimization of underlying comorbidities appeared to lower the rate of complications of THA in HIV-infected ONFH patients. Our follow-up data suggest that THA can be a safe and valid option of treatment for ONFH in well-controlled HIV-infected patients in South Korea. In particular, under the current circumstance with a low proportion of hemophiliac and intravenous drug abuse among the HIV-infected population in South Korea, THA can provide significant clinical improvements in HIV-infected patients with ONFH through meticulous perioperative evaluation and follow-up of HIV infection.

CONFLICT OF INTEREST

The corresponding author (JJY) has patent arrangement from Corentec company manufacturing Bencox M stem. The other authors certify that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

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