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Joint Replacement and Human Immunodeficiency Virus

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Abstract

The incidence of human immunodeficiency virus (HIV) cases that need total joint replacement (TJR) is generally rising. On the other hand, modern management of HIV infected has enabled them longevity while growing the need for arthroplasty procedures due to the augmented degenerative joint disease, fragility fractures, and the risk of osteonecrosis. Although initial investigations on joint replacement in HIV-infected cases displayed a high risk of complications, the recent ones reported acceptable outcomes. It is a matter of debate whether HIV-infected cases are at advanced risk for adverse TJR consequences; however, the weak immune profile has been associated with an increased probability of complications. Likewise, surgeons and physicians should be aware of the complication rate after TJR in HIV-infected cases and include an honest discussion of the probable unwelcoming complication with their patients contemplating TJR. Therefore, a fundamental review and understanding of the interaction of HIV and THA are critical.

INTRODUCTION

The infected case of the Human immunodeficiency virus (HIV) was initially recognized in the early 1980s in humans and documented as the reason for acquired immunodeficiency syndrome (AIDS). With an estimated 37 million affected people in

2015, the pandemic has grown to all corners of the world. Southern and Eastern Africa have tolerated the extreme impact of this problem, with 52% of the total infected people, 19 million cases, and more than 1 million new annual infections. The yearly occurrence of newly infected cases has decreased by 38%, from 2001 (3.4 million) to 2015 (2.1 million), with the successful and advent introduction of antiretroviral therapy (ART) programs in the last years (1, 2). AIDS-related expiries have also dropped from a high in 2005 (2.0 million), distinguished to be the topmost of the epidemic, to 1.1 million yearly in 2015, which means a reduction of about 45% (3).

The etiology varies according to highly active antiretroviral treatment (HAART) and disease-related mechanisms (4).

Femoral head osteonecrosis was initially reported in HIV-infected cases in the early 90s —before the ART time. Several investigations have considered ART drugs as an independent factor for osteonecrosis development (5-7). Therefore, HIV-positive individuals would need TJR at a much earlier age due to the osteonecrosis of the hip, in comparison to their counterparts who are affected by osteoarthritis and mostly are bilaterally involved (8).

Furthermore, a reduction in the density of bone minerals is more frequently seen in HIV-positive cases compared to non-infected controls (9, 10). The stimulation of interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-a) is followed by animbalance of the receptor stimulator of nuclear factor kappa-B (RANK)/RANK ligand (RANKL)/osteoprotegerin (OPG) system, eventually, motivate bone resorption by osteoclast and inhibit osteoclastic action. The cascade mentioned above in thelong term accelerates osteopenia and would augment the probability of fragility fractures, particularly fractures of the femur neck in HIV-infected males (11).

It is controversial whether HIV-infected cases are at advanced menace for adverse TJR consequences; however, the weak immune profile may have been correlated to the increased probability of complications. Although initial investigation on hip and knee arthroplasty in HIV-infected cases displayed a high risk of complications, the recent ones reported acceptable outcomes. (12). Despite the increasing nature of the HIV-

infected population, there is scarce literature investigating outcomes after TJR in infected ones. Periprosthetic joint infection (PJI) is one of the most prevalent causes of revision arthroplasties, and its underlying risk factors could be both non-modifiable and modifiable. Non-modifiable factors include chronic diseases such as cirrhosis, coagulopathies, kidney disease, and obstructive pulmonary as well as race, gender, and age (13, 14). Modifiable issues have been proven to increase early revision rates and complications and prolong the hospital stay. These factors include diabetes, smoking, opioid use, poor dentition, obesity, HIV, and *Staphylococcus aureus* colonization (14). A bunching of risk factors may also have been developed in HIV-positive cases undergoing TJR (15). Initial studies in orthopedic trauma patients infected with HIV displayed a significant rate of postoperative infection rate (16, 17). Parvizi *et al* demonstrated a similar finding in arthroplasty cases (18). However, their study involved patients with hemophilia, which may have been demonstrated as an independent risk factor for PJI (19, 20). Further investigations among non-hemophilic HIV-positive cases have displayed an ample lower rate of infection but a worryingly high total complication (1).

Furthermore, Orthopedic Infections International Consensus in 2018 announced that HIV is an independent factor in increasing the risk of PJI (21). However, the importance was reduced when HAART managed HIV-positive cases, and preoperative optimization was performed for them (21). Therefore, identification and optimization of HIV-positive patients before surgery are mandatory to reduce the burden of already serious healthcare systems.

According to the above, a fundamental approach and understanding of the TJR and HIV interaction are inevitable. Therefore, we conducted a literature review on joint replacement in the HIV-positive group. Moreover, this mini-review highlights the critical aspect of complications and outcomes.

CLASSIFICATION

Clinical staging methods help determine the prognosis and treatment for HIV-positive patients.

Orthopedic surgeons who plan to operate on these patients must understand these systems well. The two most commonly used HIV classification systems were introduced by the Centers for Disease Control (CDC) and the World Health Organization (WHO). In 2014, the CDC released the modified definition of surveillance case for HIV infection (22). This surveillance case explanation for HIV has been revised and combined into a sole case definition for people of every age. New multi-test algorithms, such as HIV-I and HIV-II detection criteria and direct detection of HIV infection, have been added to laboratory criteria to define an approved case. The surveillance case definition refers to monitoring the burden of HIV infection at the population level and planning for care and prevention, not for individual patient treatment decisions. A proven case of HIV infection classifies into five stages (0, 1, 2, 3, or unknown) (Table 1).

The CDC proposes three descriptive classifications based on the presence or absence of specific clinical symptoms (Table 2). The CD4+ T-cell count further subdivides these three types. CD4+ T-cell counts above 500/μL are categorized as types A1, B1, and C1. CD4+ T-cell counts within 200/μL and 400/μL are A2, B2, and C2 categories. infections in patients having CD4+ T-cell numbers lower than 200/μl are classified as A3, B3, or C3.

Orthopedic surgeons mostly use the WHO stage system (23). Patients are divided into four clinical groups using this classification system: stage one is asymptomatic or accompanied by persistent generalized lymphadenopathy; stage two presents with a slight disease along with 10% weight loss and skin exhibition; patients with stage three experienced moderate disease and weight loss of more than 10%, severe bacterial infections, and chronic diarrhea lasting more than a month; and the last stage have a severe disease, AIDS, infected with *cryptosporidiosis*, *toxoplasmosis*, HIV wasting syndrome, *Kaposi's sarcoma*, and *Pneumocystis jirovecii* caused Pneumonia.

PATHOPHYSIOLOGY AND ASSOCIATION BETWEEN HIV AND TJR

In HIV-infected persons, osteonecrosis is still the most common reason for TJR. Since the first case was reported in 1990, the annual osteonecrosis prevalence among HIV-infected ones has consistently grown, ranging from 0.08% to 1.33% (24, 25). Although the specific origin of osteonecrosis in HIV-positive people is unknown, various risk variables have been identified (26, 27).

Alcohol, corticosteroids, hyperlipidemia, anticardiolipin and antiphospholipid, cigarette smoking, antibodies, the course of HIV infection, and antiretroviral therapy are some of the most common risk factors for changes in the bloodstream to the bone (26, 27). Although many researchers believe the multiple effects of several factors that impair bone blood flow would lead to osteonecrosis, some investigators provide evidence that HIV infection alone can cause osteonecrosis (7, 22, 28). According to a study by Ries *et al*, a much higher percentage of HIV-infected individuals with nontraumatic osteonecrosis without any identified risk factors than HIV-negative cases (7). Figure 1 demonestrate factors affecting joint replacement among HIV patients.

Some factors stimulate osteonecrosis in both HIV-positive and negative cases. Steroids alter bone metabolism and the growth of bone marrow stromal cells, resulting in fat penetration into the bone marrow and blockage of the bloodstream inside the bone. The cascade above increases intraosseous pressure. Moreover, steroid use may cause acute fat embolization in capillary arteries (23-26), which are widely used to manage HIV-related diseases, such as pneumocystis pneumonia and also central nervous system (CNS) toxoplasmosis (29-31). Miller *et al* also verified the abovementioned association and determined that even short-term consumption of a corticosteroid drug could significantly raise the incidence of osteonecrosis (29). Hyperlipidemia, a known subsequent [1] of HIV and HAART diets, is substantially implicated in atherosclerotic pathways and is known to be a causative agent in steroid-induced osteonecrosis. Several investigations have linked high serum cholesterol levels and the consumption of fat-reduction drugs to the pathogenesis of osteonecrosis (7, 26, 31).

HIV has a detrimental effect on the density of the bone mineral, and patients with HIV are prone to develop osteoporosis 3.7 times greater than non-infected people (1, 32).

Consequently, there is an augmented fragility fracture risk in HIV-positive cases (1). Low BMD is associated with low CD4+ and long-term HIV infection (1). Another reason for generated osteopenia is the constant inhibition of osteoblasts and activation of osteoclasts which is a result of miss-balanced receptor activation of the nuclear factor kappa-B (RANK)/RANK ligand (RANKL)/osteoprotegerin (OPG) system (11, 33). This pattern is triggered by the virus, which causes activation of tumor necrosis factor-alpha (TNF-a) and interleukin-1 (IL-1) (10).

Increased levels of antiphospholipid antibodies and further thrombophilic factors are correlated with osteonecrosis in HIV-infected cases. Antiphospholipid antibodies are considered a risk factor for venous and arterial thrombosis and are generally found in HIV-infected patients. In a new investigation, the incidence of antiphospholipid antibodies in HIV-infected cases was predicted to be around 44% (34). It is well known that these antibodies are involved in the progress of osteonecrosis in systemic lupus erythematosus patients, and similar processes have been suggested for HIV-infected cases (25, 35).

Recent studies have engrossed the role of antiretroviral therapies, mainly protease inhibitors, in the pathogenesis of osteonecrosis. Even though the precise processes of HAART that may play a role in osteonecrosis are unclear, the association of protease inhibitors and conventional osteonecrosis risk factors has been recognized (8, 22, 26, 29). Hypertriglyceridemia due to HAART treatment has been widely cited as a potential cause of osteonecrosis. Through interactions with cytochrome P450, protease inhibitors may increase the effectiveness of steroid therapy. A study by Penzak et al showed that treatment with ritonavir dramatically amplified the concentration of prednisolone in healthy cases (36). Several HIV-positive cases of osteonecrosis were reported before the introduction of HAART, suggesting that HIV treatment regimens could not be the primary cause of the disease. Osteonecrosis has a complex etiology and is highly prevalent among HIV-positive individuals, thus increasing the need for total joint arthroplasties in this patient population.

As the HIV epidemic spreads, the burden of THA is compounded. While the incidence of HIV is steadily increasing, broad access to HAART has upgraded from 25% in 2010 to 73% in 2021 (37). Increased access to HAART has reduced global AIDS-related mortality by 64% since its peak in 2004 and by 47% since 2010 (37). HIV and HAART are independently associated with joint pathology that ultimately requires joint replacement (4).

HAART should be started in all HIV-positive patients, regardless of clinical stage or CD4+ count (1). This is particularly significant for cases pending elective TJR. First-line of HAART almost always consists of a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) and an agent of a different drug class. Protease inhibitors (PIs) are believed to form the primary drug class that aids AVN in the hip (4). In addition, drugs containing tenofovir have been linked to the progress of osteopenia (1). Remarkably, all first-line regimens in every corner of the world include tenofovir agents.

Due to osteodegenerative and renal complication of tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF) was developed (38). TAF continues to cause renal disease and bone loss, but to a lesser extent than TDF. WHO recommended that integrase strand transfer inhibitors (InSTIs) replace protease inhibitors (PIs) as the ideal first-line regimen. However, more than half of the global HIV prevalence is in East and South Africa, which cannot easily access InSTIs (38).

There are several side effects to HAART drugs, and the patient's diet should be monitored. There are significant drug interactions between anesthetic drugs and NRTIs and PIs that are usually prescribed for induction and sedation. TDF is nephrotoxic, so patients need to be checked for blood urea nitrogen (BUN); the urine protein-to-creatine ratio is sometimes assessed to evaluate their renal function (39). Anemia and neutropenia are side effects of zidovudine (AZT). Thus, these patients need a complete blood count, white cell count, and differential amount (40).

EVALUATION AND PREOPERATIVE OPTIMIZATION

Different studies show how immune system impairment is a key factor in post-operative risk of infection and complications (41). Any major disease which causes impaired immune system like diabetes mellitus, which have impaired leukocyte function (42, 43), and even malnutrition, (44) can be risk factors for PJI (41).

CD4+ is an alternative indicator of immunological status, and the number of CD4+ less than 200 cells/mm^3 confirms the diagnosis of AIDS (39). Optimistic monitoring of the patient's immune status is essential in managing HIV-infected patients undergoing HAART. The opportunistic infections-related prevalence, mortality, and morbidity are higher in patients with CD4+ 200 cells/mm^3 (45). Patients with opportunistic infections and abandoned viral status should be recognized to reduce perioperative and postoperative complications (45). Antibiotic prophylaxis should be initiated for all patients with CD4+ < 200 cells/mm^3 (45). The guidelines recommend trimethoprim-sulfamethoxazole (TMP-SMX) as an effective treatment for opportunistic infections (45). Viral load is a reliable indicator of treatment effectiveness and is influenced by patient adherence to HAART. Elective procedures should be delayed for those with higher viral load (VL) (45). If, after 6 to 8 wk of careful treatment, the VL is greater than 1000 copies/mL or less than one log below starting point, there is a viral failure (45).

Multiple systems can be affected by HIV, and patients should be thoroughly evaluated for perioperative risk classification before TJR. HIV-positive cases often suffer cardiovascular disease, nephropathy, liver disaster, neurological problems, and non-AIDS-related malignancies (46). Evaluation of the patients mentioned before surgery should contain suitable blood work, nutritional status, and immune deficiency syndrome stage (47). In HIV-positive patients, postoperative complications are mainly due to immunodeficiency, not the procedure itself. Therefore, a comprehensive evaluation is required to prevent anesthetic and surgery problems (45).

HIV-infected cases who developed advanced stages of the disease should also have their nutritional status evaluated since their a higher risk for nutritional deficiencies and

wasting (45). Hypoalbuminemia is an independent risk factor for mortality in HIV-infected cases postoperatively compared to the non-infected control group (48).

Malnutrition is related to several problems following THA, such as delayed wound healing and prolonged wound damage, which increases the risk of infection (21). If the diet is inadequate, dietary supplements may be necessary and should be consulted with a nutritionist (45).

On the other hand, compared to the HIV-negative control group, HIV-positive individuals are at higher risk for coronary artery disease, which may be due to persistent chronic inflammation (45). HAART drugs have decreased the risk of perioperative cardiovascular problems (46).

HIV patients treated with HAART have an increased incidence of insulin resistance, diabetes, and hypercholesterolemia. This may increase the risk of AVN in the femoral head and thus upsurge the need for TJR among HIV-infected cases. All HIV-infected patients should undergo a thorough clinical evaluation for lipodystrophy and fasting lipograms, mainly if they consume a HAART diet containing PI (45).

In HIV-positive patients, smoking is approximately 40% more than in the general population, and the probability of quitting is also lower (49). This makes the patients susceptible to atherosclerotic developments, chronic lung disease, and postoperative respiratory infections (45). Before elective surgery, the respiratory function should be evaluated in all HIV-infected smokers to determine their capacity for diffusion (45). In addition, AIDS patients are susceptible to nosocomial invasive bacterial infections, and elective TJR should be delayed to optimize immune system reconstruction (45).

OUTCOMES OF TJR IN HIV

As the global number of HIV-infected cases rises, so does the need to evaluate the results of orthopedic treatment in them. Due to the growing demand for these treatments, the consequences and complications of TJR among them are also receiving particular attention. In addition to functional implications, many of these studies have investigated the incidence of postoperative infections. Previously, HIV was known as

an independent factor for infection after surgery. Therefore, the benefits and safety of elective surgery in these patients have been questioned. However, some recent investigations of TJR in HIV-infected patients have raised doubts about this theory.

The treatment algorithms for HIV-positive patients should be similar to algorithms used for non-infected cases, with two-step revision surgery. We suggest a long course of intravenous antibiotics: up to six months *vs* six weeks. The medical condition of patients, especially their VL and CD4 count, should always be considered.

Several studies focusing on the results of complete joint arthroplasty in HIV-infected cases have focused on hemophilic ones. Due to recurrent periarticular and intra-articular hemorrhage, people with hemophilia are at a much higher risk for joint degeneration. The risk of developing joint arthropathy increased with the higher rates of HIV infection in these people between 1979 and 1985 due to the application of polluted blood products. During that period, injection of infected factor VIII resulted in serum conversion in about 80% of hemophilia patients. Preliminary research, which Gregg-Smith *et al* Field conducted50)) and Weidel *et al* (51), evaluated the infection prevalence in HIV-infected hemophiliac cases who underwent complete knee arthroplasty before the extensive use of HAART. Weidel *et al*, in a 1989 study, found an advanced rise in acute postoperative infections (51). The result, as mentioned earlier, was also confirmed by Gregg-Smith *et al* (50).

Hicks *et al* (52) and several other researchers confirmed that the growing risks are related to TJR in HIV-positive hemophiliacs, linking the probability of these problems to the number of CD4 cells. Hicks *et al* evaluated the results of 102 TJR in 73 hemophiliac patients infected by HIV in a large multicenter retrospective study (52). The incidence of surgical site infection was 18.7% for initial surgeries and 36.3% for revision after an average five-year follow-up. About 62.5% of the infected group had a preoperative CD4 count of less than 0.2 x 109/L, while 16.7% were non-infectious. Ragni *et al* (19) found a similar increase in the rate of postoperative infections in HIV-positive hemophiliac patients with CD4 counts of less than 0.2 x 109/L in patients who underwent knee and hip arthroplasty surgeries. An infection rate of 15% was observed

in a retrospective analysis of 115 hemophilia clinics in the United States in 1995, which the authors highlighted was three times more likely than the risk of infection at surgical sites among HIV-negative arthroplasty patients.

In contrast, many current investigations could not confirm the extensive risk of problems in this population of patients after total joint replacement. For instance, Powell *et al* evaluated the incidence of postoperative infections following total TJR of knee and hip in HIV-negative and HIV-positive hemophilia patients between 1975 and 2002 (53). Three of the 30 joints among HIV-infected cases developed primary joint infections, compared to two of the 21 non-infected groups. The perusal above did not show an elevated relative risk of surgical site infection in HIV-positive patients (RR = 1.49). The researchers concluded that TJR is a viable treatment choice for hemophilic patients with concomitant HIV infection.

The relative safety of the orthopedic procedures in HIV-positive hemophiliac patients was further supported by Unger *et al* they evaluated 26 knee arthroplasties of 15 patients with HIV and type A of hemophilia; all of them experienced an improvement in function after arthroplasty, and also during 6.4 years of follow-up, no infection occurred at the surgical site (54).

Subsequent research has evaluated the outcomes of TJR procedures in HIV-infected adults who are not hemophiliacs. For instance, Parvizi *et al* conducted a study on total hip and knee arthroplasties in 21 infected cases and reported a significant incidence of postoperative complications (18). Twelve of 21 arthroplasties needed to be reconsidered at the subsequent evaluation due to recurrent infection. Furthermore, a significant relationship between the immunological status of patients and the probability of deep infection (six joints). The authors mentioned above discovered a significant prevalence of *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* among deep-seated infections (18).

In parallel to prior investigations, Habermann *et al* have compared the incidence of total complications in non-hemophiliac infected cases and hemophiliac patients after TJR (55). However, they found no significant difference in functional outcomes (55).

Recently Mahoney *et al* conducted a study among non-hemophiliac HIV-infected patients who had total hip arthroplasty, demonstrating favorable functional results (56). Three years afterward, only one in 40 patients with a history of intravenous drug abuse had severe infection with antibiotic-resistant *Aureus*.

Moreover, further comorbidities associated with HIV, including intravenous drug abuse, negatively and significantly influence the clinical outcome of TJR surgery. On the other hand, Lehman *et al* assessed the risk of PJI in HIV- infected and simultaneous infection from IV drug use (IVDU) following TJR (57). In the study mentioned above, patients with co-infection of HIV and IVDU had a more than 40% surgical site infection rate. Infections did not occur in 4 HIV-positive patients without comorbidities (IVDU, hemophilia). The findings of this study suggest an individual-based evaluation of the benefits and risks of TJR.

THA AND HAART IN HIV-INFECTED PATIENTS UNDERGOING TJR

The functional consequences of THA in HIV-positive individuals are controversial in the literature. There is still considerable debate about the relative efficacy and safety of TJR in these patients. It was traditionally believed that HIV infection was associated with an augmented complication risk, particularly infectious adverse effects. In addition, the growing use of HAART has reduced the related complications. HIV-infected patients who do not receive HAART are more prone to unfavorable outcomes. Parvizi *et al* (18) found a substantial complication rate among HIV-infected cases who had undergone total hip arthroplasty; it is worth mentioning that 80% of them did not receive HAART. This amount included 29% of PJIs (58). The mean of CD4+ for those who developed PJI was 239 cells/mm^3, while the mean for the entire study population was 523 cells/mm^3 (58). A similar result was displayed by Lehman *et al* (57); they reported a PJI rate of 14.3% among HIV-infected cases receiving THA. It is worth mentioning that none of them were optimized by HAART.

Several studies have shown ambiguous functional results comparing HIV-positive patients treated with HAART with the HIV-negative control group. Graham *et al* (59)

conducted a survey among 43 THAs which had been performed on 29 HIV-positive patients in 2014; they reported no occurrences of dislocations, deep or superficial infections, or venous thrombotic events (VTE), either in late (> 6 wk) or early (< 6 wk) follow-ups. Significant postoperative functional benefits and tangible progress in the Harris hip scores were recorded. Between 1998 and 2010, Likewise, Naziri *et al* conducted a study among 9,275 HIV-positive patients with THA to evaluate the outcomes of THA and compare it to the results of 2.7 million non-infected cases. The minor and major complications in HIV-infected individuals were 5.2% and 2.9%, respectively, meaningfully higher than the respective rates of 4.8% and 2.7% in non-infected individuals (60). In addition, a longer duration of hospitalization was observed in the HIV-positive group (60).

Sadoghi *et al* (61) analyzed global registration data from New Zealand, Australia, Denmark, Finland, Norway, and Sweden, to show that aseptic loosening is the main reason for revising THAs, which accounts for 55.7% of them. PJI was the third cause of revision (61). The onset of aseptic loosening does not appear to be due to HIV (1, 46).

One and five years survival rate after THA surgery in HIV-positive patients is similar to that of non-HIV-positive patients (1). Issa *et al* (62) evaluated the lifespan of prostheses after ten years; there was no difference in the survival of infected and non-infected cases. Moreover, Novikov *et al* (63) showed that a significant amount of revision THA (80%) happened during the first year after surgery. Still, the revision rate in the long-term analysis was similar to non-infected patients (1). Although functional outcomes of infected cases optimized with HAART are equal to HIV-negative cases, a higher probability of PJI has been reported.

Previously, THA outcomes in HIV-positive individuals with simultaneous hemophilia (19) or IVDUs (57) showed a high proportion of poor outcomes and late deep infections. In a comprehensive assessment of 722 THA out of 25 research studies, Enayatollahi *et al* (58) found that PJI is more prevalent significantly among those with simultaneous HIV infection and hemophilia than in HIV-infected alone. The corresponding PJI rates were

10.98% and 2.28%, respectively. Nevertheless, before HAART, the frequency of PJI was up to 50% (58). The onset of HAART coincided with a reduction in the incidence of THA infections in HIV-positive individuals (46, 58). Also, Youngman *et al* (64) found that the complication rate of HIV-positive patients who did not treat with the HAART and undergone THAs due to femoral head osteonecrosis (FHON) is 12.5% higher than what those who were optimized with HAART.

ELECTIVE SURGERY

Given the increasing need for TJR and the HIV pandemic, it is essential to determine if a threshold should be proposed for elective arthroplasty. King *et al* (48). evaluated 30-day postoperative THA mortality in the United States retrospectively and found that HIV-positive patients had a higher mortality rate (3.4%) than HIV-negative patients (1.6%). Regardless of CD4+, the HIV-positive group had a higher mortality rate than the control group, even though lower CD4+ was correlated with a greater mortality rate (48). There is a hypothesis that a CD4+ threshold of 200 cells/mm^3 is associated with a higher risk of postoperative complications, such as PJI. However, this has not been proven (1, 46).

There is considerable evidence that HIV-positive cases, particularly the poor control ones, are more susceptible to postoperative complications (46). Serum markers should be monitored periodically, as the infection is perilous, mainly if CD4+ counts decrease (46, 65). Many studies have not linked the CD4+ count consistently and accurately. Dimitriou *et al* (1) reported that THA might be safely administered to HIV-positive patients regardless of their CD4+ status, while Shah *et al* (46) suggested a CD4+ count of more than 400 cells/mm^3 was essential for a safe THA. On the other hand, Sax *et al* (66) suggest that elective THA can be done in both groups of HIV patients who are actively taking ART or not, and the complication rates are similar to those not infected by HIV.

Preoperative VL may be more important than CD4+. A higher level of the virus may indicate unsuccessful surgery and require a referral to an infectious disease specialist. Horberg MA *et al* conducted a retrospective study on more than 5,000 HIV-infected

individuals; they believed that In a retrospective study, VL > 30,000 copies/mL was related to a three-fold bigger chance of postoperative complications (47).

In a systematic evaluation, Shah *et al* (46) recommended 50 copies/mL VL before elective procedures. It is suggested that patients continue the HAART regimen, and full compliance is essential. Since the subsequent studies show a decrease in CD4 + or an increase in VL, treatment mismatch or failure should be considered.

CONCLUSION

Currently, reports on HIV-positive patients and TJR afford contradictory information. While some authors reported significant complications and reconsideration rates following TJR on HIV-positive patients, most of these collections include a large proportion of HIV-infected cases with hemophilia. Thus, it is a critical confounder in the results described in prior studies. Future studies should evaluate the results of HIV-positive patients with no simultaneous disease to identify its risks, especially for patients with complete joint arthroplasty. Before surgery, we now examine each patient and try to optimize the general health of HIV-positive patients. Total joint replacement procedures are recommended based on patient-specific factors such as viral load, CD4 count, clinical classification, the history of intravenous drug addiction, and the patient's overall health. The risks and frequency of perioperative problems should be made clear to patients. We expect TJR to improve the quality of life of these patients. In figure 1, we have recommendations for better outcomes of TJR in HIV-positive cases.

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