

The Effect of Modern Antiretroviral Therapy on Complication Rates After Total Hip Arthroplasty

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Background: Antiretroviral therapy (ART) remains the cornerstone of decreasing morbidity and mortality in patients with human immunodeficiency virus (HIV), but additional information on its impact on total hip arthroplasty (THA) complication rates is needed to mitigate risks postoperatively. Therefore, we sought to examine patients with HIV who were and were not taking ART compared with a cohort without HIV in the setting of primary THA with respect to the following outcomes: length of stay, readmissions, and postoperative infection.

Methods: A retrospective database review was performed with PearlDiver for patients who underwent THA from 2010 to 2019 (n = 729,101). Patients with HIV who were and were not taking ART were then identified and were matched with patients without HIV at a 1:1:1 ratio based on age, sex, Charlson Comorbidity Index, diabetes, obesity, and tobacco use, resulting in 601 patients in each cohort. Length of stay, 30-day readmissions, and complications at 90 days and 1 year were analyzed. Continuous outcomes were measured via Student t tests, and categorical outcomes were measured via chi-square analyses.

Results: Patients with HIV who were and were not taking ART were found to have similar lengths of stay compared with patients without HIV (range, 4.1 to 4.3 days). Readmission rates were slightly higher in patients with HIV who were taking ART at 4.2% (odds ratio [OR], 1.96 [95% confidence interval (CI), 0.99 to 3.87]) and patients with HIV who were not taking ART at 3.5% (OR, 1.63 [95% CI, 0.81 to 3.30]) compared with patients without HIV at 2.1%. Periprosthetic joint infection rates at 1 year were slightly higher among patients with HIV who were not taking ART at 5.3% (OR, 1.41 [95% CI, 0.82 to 2.45]) compared with patients with HIV who were taking ART at 4.2% (OR, 1.09 [95% CI, 0.61 to 1.94]) and patients without HIV at 3.8%.

Conclusions: Patients with HIV who are and are not taking ART are approaching normalization to the general population in the setting of THA. It is important to note that, although complications may have been mitigated by modern therapy, extreme care should be taken while clinically evaluating these patients prior to the surgical procedure given the complexity of their clinical status. The findings of this study underscore the utility of ART and patient optimization to reduce risk in this patient population.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Human immunodeficiency virus (HIV) has caused a great burden to global health. First clinically recognized in 1981 in the United States, the global impact has been far-reaching, with economic and social disturbances in addition to its direct effect on health. Global incidence has

dropped precipitously as therapies became available¹. The immunosuppressive nature of HIV is the target toward which many treatment modalities are directed, namely, to improve the CD4 cell count. Fortunately, the introduction of antiretroviral therapy (ART) has improved life expectancy such that HIV-

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positive individuals who are taking appropriate therapy have health that is equivalent to that of the general population²⁻⁵. Improved longevity in this population will lead to older HIV-positive patients developing degenerative joint disease and therefore requiring definitive treatments such as total hip arthroplasty (THA). The implementation of ART has been the cornerstone of decreasing morbidity and mortality in patients with HIV, of which success is reflected by an improved CD4 count and viral load. Additional information on its impact on THA complication rates is needed to mitigate the previously reported perioperative complications.

HIV can be especially challenging to orthopaedic surgeons. This infection begets an inflammatory state that involves the dysregulation of skeletal renewal with advanced bone loss⁶. The emergence of ART in 1996 has proven to effectively control viral replication; however, it has been implicated in exacerbating the deleterious, yet ill-defined, effects on bone metabolism. Many studies have highlighted the postoperative complication rate disparities between patients with HIV and those without HIV, but few have reflected current rates. Multiple studies within the last decade have shown increased rates of infection, extended length of hospital stay, and revision in HIV populations⁷⁻¹⁰. This illustrates a broader understanding of HIV-related risks postoperatively, but there is a lack of large samples, homogeneity of reporting, and, therefore, generalizability among these studies. Further, these studies were largely limited to data before 2010 and do not reflect the modern standard of therapy. Newer therapies and a better understanding of evaluating and managing patients with HIV within the past decade beg further examination into this patient population. A larger and updated study is necessary to demonstrate complication differences between patients with HIV and those without HIV undergoing primary THA.

Therefore, the purpose of this study was to compare complication rates between patients with HIV who were and were not taking ART and patients without HIV in a national database. Specifically, we asked if patients with HIV who were and were not taking ART have longer lengths of stay and higher 30-day readmissions rates, and if patients with HIV who were and were not taking ART have a higher incidence of 90-day and 1-year postoperative infection and other complications.

Materials and Methods

Database Selection

A retrospective review was performed using the publicly available, national all-payer Mariner database (PearlDiver). All information was deidentified and U.S. Health Insurance Portability and Accountability Act (HIPAA)-compliant. The Mariner data set contains 122 million patients comprising commercial insurance, Medicare, Medicaid, government insurance, and cash payers from all U.S. states and territories. Research was performed using procedural and diagnosis codes from the International Classification of Diseases, Ninth Revision (ICD-9) and ICD, Tenth Revision (ICD-10), Current Procedural Terminology (CPT), and demographic, prescription, and physician specialty information. The data set contains claims from 2010 to 2019. Providers supplying claims are required to have annual, independent, third-

party audits on validity and reliability of the data. Institutional review board approval was waived for this public database study.

Patient Selection

All patients undergoing primary THA from 2010 to 2019 were identified on the basis of ICD and CPT code definitions ($n = 729,101$). Next, the HIV cohort within THA was identified using the following codes: ICD-9-D-042, ICD-9-D-V08, ICD-9-D-07953, ICD-9-D-79571, ICD-10-D-B20, ICD-10-D-Z21, and ICD-10-D-B9735 ($n = 5,613$). Patients with HIV who were taking ART and who underwent THA were then identified using the following Uniform System of Classification (USC) codes: USC-82110, USC-82120, USC-82130, USC-82140, USC-82180, and USC-82190 ($n = 3,714$). Patients with HIV with no history of taking ART who underwent THA were then identified ($n = 995$). The cohort without HIV who underwent THA was identified by excluding the HIV codes from THA ($n = 710,764$). Groups were matched at a 1:1:1 ratio based on age range, sex, Charlson Comorbidity Index, diabetes, obesity, and tobacco use by corresponding ICD codes. This resulted in 601 matched patients in each of 3 cohorts: no HIV, HIV taking ART, and HIV not taking ART. Lengths of stay, all-cause readmissions at 30 days, and complications at 90 days and 1 year were collected. Length of stay was defined as the mean number of days per inpatient visit. All-cause readmission at 30 days was defined as the total number of readmissions within 30 days since the index THA. Complications were identified using ICD-9 and ICD-10 diagnosis codes and included blood transfusions, deep vein thromboses, hip dislocations, mechanical complications, peri-prosthetic fractures, pneumonia, periprosthetic joint infections (PJIs), pulmonary emboli, respiratory failure, and revision surgical procedures. Over the course of the 1-year study period, 3.8% of patients with HIV who were taking ART and 9.8% of patients with HIV who were not taking ART were lost to follow-up.

Patient Demographic Characteristics

All cohorts were successfully matched on age (range, 55.4 to 55.8 years), sex (69.4% male), Charlson Comorbidity Index, diabetes, obesity, and tobacco use (Table I). Additionally, all cohorts had identical proportions of patients with a Charlson Comorbidity Index score of ≥ 5 , reported to be a significant predictor of 1-year mortality¹¹.

Statistical Analysis

The level of significance of differences in continuous variables, including length of stay, was calculated via Student *t* tests. The level of significance of differences in categorical variables, including readmissions and complications, was calculated via a chi-square analysis. All analysis was performed using R (The R Foundation for Statistical Computing).

Results

Length of Stay and Readmissions

We found a similar mean length of stay when comparing patients who underwent THA in the no-HIV group

TABLE I Demographic Characteristics in Patients Undergoing THA: No HIV, HIV Taking ART, and HIV Not Taking ART

	No-HIV Group (N = 601)	HIV Taking ART Group (N = 601)	HIV Not Taking ART Group (N = 601)
Age* (yr)	55.8 ± 8.4	55.5 ± 8.4	55.4 ± 8.5
Sex†			
Male	417 (69.4%)	417 (69.4%)	417 (69.4%)
Female	184 (30.6%)	184 (30.6%)	184 (30.6%)
Charlson Comorbidity Index ≥5†	337 (56.1%)	337 (56.1%)	337 (56.1%)
Diabetes†	279 (46.4%)	279 (46.4%)	279 (46.4%)
Obesity†	221 (36.8%)	221 (36.8%)	221 (36.8%)
Tobacco use†	324 (53.9%)	324 (53.9%)	324 (53.9%)

*The values are given as the mean and the standard deviation. †The values are given as the number of patients, with the percentage in parentheses.

(4.1 days), the HIV taking ART group (4.3 days), and the HIV not taking ART group (4.3 days) (Table II). There were slightly higher incidences of 30-day, all-cause readmissions in the HIV taking ART group (4.2%) and the HIV not taking ART group (3.5%) compared with the no-HIV group (2.1%). There were also slightly higher odds of 30-day, all-cause readmissions in the HIV taking ART group (odds ratio [OR], 1.96 [95% confidence interval (CI), 0.99 to 3.87]) and the HIV not taking ART group (OR, 1.63 [0.81 to 3.30]) compared with the matched patients without HIV (Table III).

PJI and Other Postoperative Complications

The 90-day PJI incidences were slightly higher in the HIV taking ART group (3.3%) and the HIV not taking ART group (3.3%) compared with the no-HIV group (2.5%). The 90-day PJI odds were also slightly higher in the HIV taking ART group (OR, 1.34 [95% CI, 0.68 to 2.65]) and the HIV not taking ART group (OR, 1.34 [95% CI, 0.68 to 2.65]) compared with the no-HIV group. There was a slightly higher 1-year PJI incidence in the HIV not taking ART group at 5.3% compared with the no-HIV group at 3.8%; the OR was 1.41 (95% CI, 0.82 to 2.45).

TABLE II Outcomes and Complication Rates in Patients Undergoing THA: No HIV, HIV Taking ART, and HIV Not Taking ART

	No-HIV Group (N = 601)	HIV Taking ART Group (N = 601)	HIV Not Taking ART Group (N = 601)	P Value
Length of stay* (days)	4.1 ± 1.9	4.3 ± 3.8	4.3 ± 2.5	0.25
30-day readmissions†	13 (2.2%)	25 (4.2%)	21 (3.5%)	0.14
90-day complications†				
Blood transfusions	15 (2.5%)	—‡	11 (1.8%)	0.55
Deep vein thromboses	28 (4.7%)	27 (4.5%)	22 (3.7%)	0.66
Hip dislocations	20 (3.3%)	22 (3.7%)	21 (3.5%)	0.95
Mechanical complications	11 (1.8%)	—‡	—‡	0.17
Periprosthetic fractures	—‡	—‡	—‡	0.58
Pneumonia	23 (3.8%)	23 (3.8%)	19 (3.2%)	0.77
PJI	15 (2.5%)	20 (3.3%)	20 (3.3%)	0.63
Pulmonary emboli	—‡	11 (1.8%)	—‡	0.10
Respiratory failures	16 (2.7%)	12 (2.0%)	—‡	0.06
1-year complications†				
Hip dislocations	24 (4.0%)	25 (4.2%)	24 (4.0%)	0.99
Mechanical complications	17 (2.8%)	14 (2.3%)	—‡	0.29
Periprosthetic fractures	—‡	—‡	—‡	0.36
PJI	23 (3.8%)	25 (4.2%)	32 (5.3%)	0.42
Revision surgery	25 (4.2%)	26 (4.3%)	14 (2.3%)	0.12

*The values are given as the mean and the standard deviation. †The values are given as the number of patients, with the percentage in parentheses. ‡Data with <11 patients censored in accordance with the PearlDiver confidentiality agreement.

TABLE III Adjusted ORs for Outcomes and Complications in Patients Undergoing THA with HIV Taking and Not Taking ART

Parameter	HIV Taking ART Group*	HIV Not Taking ART Group*
30-day readmissions	1.96 (0.99 to 3.87)	1.63 (0.81 to 3.30)
90-day complications		
Blood transfusions	0.66 (0.29 to 1.48)	0.73 (0.33 to 1.60)
Deep vein thromboses	0.96 (0.56 to 1.65)	0.78 (0.44 to 1.38)
Hip dislocations	1.10 (0.60 to 2.04)	1.05 (0.56 to 1.96)
Mechanical complications	0.91 (0.38 to 2.15)	0.36 (0.11 to 1.13)
Periprosthetic fractures	0.75 (0.17 to 3.36)	1.51 (0.42 to 5.36)
Pneumonia	1.00 (0.55 to 1.80)	0.82 (0.44 to 1.52)
PJI	1.34 (0.68 to 2.65)	1.34 (0.68 to 2.65)
Pulmonary emboli	1.38 (0.55 to 3.46)	0.37 (0.10 to 1.41)
Respiratory failure	0.74 (0.35 to 1.59)	0.31 (0.11 to 0.84)
1-year complications		
Hip dislocations	1.04 (0.60 to 1.80)	1.00 (0.57 to 1.74)
Mechanical complications	0.82 (0.40 to 1.68)	0.52 (0.23 to 1.18)
Periprosthetic fractures	1.20 (0.36 to 4.00)	2.02 (0.69 to 5.94)
PJI	1.09 (0.61 to 1.94)	1.41 (0.82 to 2.45)
Revision surgery	1.04 (0.59 to 1.83)	0.55 (0.28 to 1.07)

*The values are given as the adjusted OR, with the 95% CI in parentheses; patients without HIV undergoing THA served as the reference.

The revision rates at 1 year were slightly lower in the HIV not taking ART group (2.3%) compared with the no-HIV group (4.2%); the OR was 0.55 (95% CI, 0.28 to 1.07). Other medical and surgical complications at 90 days and 1 year were similar among all cohorts.

Discussion

Prior investigations on postoperative complications in patients undergoing primary THA have reported higher incidences of postoperative complications, revisions, and readmissions in patients with HIV^{7-9,12-16}. The deleterious immunosuppressive effects and life-threatening sequelae of HIV have been largely mitigated since the introduction of ART, enabling these patients to live longer^{2-5,17}. Considering the escalating rates of total joint procedures in the United States^{18,19} with a concomitant advancement in HIV medical optimization, this study sought to examine length of stay, readmissions, and complications in patients with HIV who were and were not taking ART and patients without HIV following primary THA. This large study is unique in its ability to investigate these aims in patients with HIV who were and were not taking ART. There were only slight differences among the 3 study cohorts with respect to readmissions and postoperative complications. There is reason to suggest that patients with HIV who were taking ART have approached a similar risk profile relative to the general population in the setting of primary THA.

This study had some limitations. The PearlDiver database is primarily queried via ICD and CPT codes, resulting in grouped data sets. This was limiting because our study could not assess granular information such as race or ethnicity, mortality rates, preexisting medical comorbidities, American Society

of Anesthesiologists (ASA) classification, discharge disposition, and treatment center type. Although clinicians generally initiate ART medication with a CD4 count of ≤ 350 cell/ μL ²⁰, the degree of disease severity either by CD4 count or viral load could not be assessed with this database. However, patients were specifically identified on the basis of using ART or never using ART prior to the surgical procedure. Specific ART formulations were not captured, and use was identified by USC codes to enable large study cohorts. Furthermore, demographic and baseline characteristics of included patients may appear homogenous due, in large part, to matching criteria; however, different risk profiles within each cohort likely exist but could not be captured. The loss to follow-up among patients with HIV who were taking ART (3.8%) and those who were not taking ART (9.8%) may also contribute to the inherent heterogeneity in study cohorts. We did not evaluate operation-specific variables such as surgeon, length of the surgical procedure, and surgical approach. This has the potential to influence complication rates; however, this database draws large cohorts that are validated and generalizable. The factors that could not be accounted for by PearlDiver should not be disqualifying, given our large sample sizes and numerous comorbidities evaluated. This study design is highly valuable because of the opportunity to include a large cohort with robust postoperative data. Despite these limitations, this study is unique and provides the foundation for future studies with regard to patients with HIV taking ART.

Historically, patients with HIV present with a more complex clinical picture than patients without HIV and have disproportionately higher perioperative complication rates, a known driver of health-care costs²¹. Fortunately, today's medical providers

utilize an advanced arsenal of medications to better optimize patients with HIV. Although late diagnosis and delayed initiation of ART continue to predispose patients to higher morbidity and mortality rates, there is much about which to be hopeful. It is reasonable to infer that the optimization of today's patients with HIV has mitigated potential complication risks following THA. The current management guidelines for patients with HIV undergoing a surgical procedure are robust and inclusive with a detailed preoperative assessment, a recommendation to continue ART medications when feasible, and a consideration for opportunistic infection in the postoperative course. Despite the similarities between patients with HIV who were and were not taking ART in our study, it is of paramount importance to recognize the value of ART in the surgical setting.

This study found only slight differences in length of stay, readmissions, and medical or surgical complications among the 3 cohorts. Multiple studies have also demonstrated THA to be an excellent option for patients with HIV²²⁻²⁴. Tornero et al.²² evaluated a group of patients with HIV compared with patients without HIV and found no differences in the duration of hospitalization and postoperative functional outcomes. In a single-center, retrospective study, Rajcoomar et al.²⁴ found low rates of complications and revisions. They singled out the initiation of ART prior to the surgical procedure as an important factor contributing to good outcomes. Despite the favorable results demonstrated, these studies were limited by small sample sizes at single institutions. Our results advance these findings by demonstrating favorable outcomes in patients with HIV who were or were not taking ART and can serve as a framework for future study.

In contrast to the current study with similar medical and surgical complications among our cohorts, previous studies generally demonstrated increased risk of infection and revision in patients with HIV^{7-9,16,25}. Several studies have also demonstrated no increased risk of PJI in patients with HIV. Using the National Inpatient Sample, Lin et al.²⁶ reported that HIV was not an independent risk factor for complications in total joint arthroplasty, including PJI, but they were at higher risk for immediate postoperative wound infection ($p = 0.04$). Kildow et al.²⁷ matched patients with HIV and patients with hepatitis B and C undergoing total joint arthroplasty in another national database study. They found similar risks of PJI among patients with HIV, but increased risk of revision at 90 days in the THA subset ($p = 0.01$). In a small, single-institution study, Falakassa et al.²⁸ identified 24 patients with HIV undergoing primary THA and reported no incidence of PJI. In a systematic review of >700 total joint arthroplasties in patients with HIV, Enayatollahi et al.²⁹ found a PJI rate of 2.28% with follow-up between 1 and 26 years. Although this rate is lower than our 1-year PJI incidence (between 4.2% and 5.3%), it is limited by inclusion of studies with small sample sizes and poor homogeneity. The current literature has provided a framework regarding HIV complications; however, no consensus can be drawn for the risk of infection and revision, specifically in patients with HIV. Our study underscores the utility of ART by providing a more current analysis and advances understanding by utilizing a

national database. To our knowledge, our study is the largest database study to examine THA outcomes among patients with and without HIV, with a total of >1,800 matched patients.

Our study found only slight differences in revision rates between patients without HIV and patients with HIV who were and were not taking ART, aligning with several recent articles. The trend toward lower revision rates among patients with HIV who were not taking ART compared with patients without HIV may be due in large part to the number of patients in this cohort who were considered lost to follow-up (9.8%). Issa et al.³⁰ compared patients with osteonecrosis undergoing THA between those without HIV matched to those with HIV. They found no differences in all-cause revision rates at the 5-year and 10-year follow-up periods ($p = 0.25$). Lin et al.³¹ also found no differences in revision rates in similar cohorts at a single institution. Interestingly, our revision rates at 1 year in patients with HIV and those without HIV were similar. A plethora of large population studies have shown reasons for revision and long-term data; however, to our knowledge, no study has shown all-cause 1-year revision rates for THA in the United States. Early revision rates between 3 and 5 years are estimated to be between 2.1% and 4.1%³²⁻³⁴, but they do not reflect an all-cause, all-age, U.S. demographic characteristic. Our study is unique because it directly examined patients with HIV who were and were not taking ART compared with patients without HIV (i.e., the general population) and can serve as a benchmark for future 1-year revision rate estimates.

The current study suggests that elective THA can be performed in patients with HIV who are actively taking ART or not taking ART, with complication rates similar to patients without HIV. The similarities in length of stay, readmissions, and postoperative complications support these claims. It is important to note that, although complications may have been mitigated by modern therapy, extreme care should be taken while clinically evaluating these patients prior to the surgical procedure, given the complexity of their clinical status. The findings of this study underscore the utility of ART and its ability to reduce postoperative risk in this patient population. Future studies should address factors that may contribute to the success of patients with HIV following THA, namely, CD4 count, viral load, and indications for and formulations of ART. ■

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