The Impact of Antiretroviral therapy on the incidence of Avascular Necrosis in Patients with Human Immunodeficiency Virus

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Background:

- Patients with HIV have higher rates of avascular necrosis (AVN).
- Previous studies suggest that antiretroviral therapy may increase risk of AVN development among the HIV population.

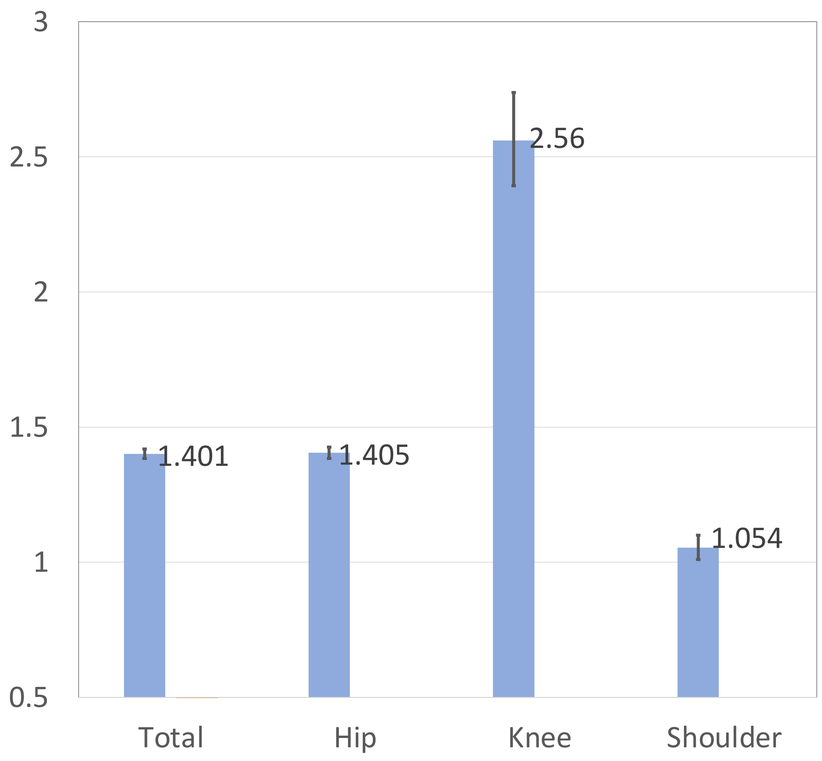
Purpose:

- To identify if ART increase the risk of development of AVN in the HIV population.

Methods:

- A **retrospective cohort analysis** was performed using the **PearlDiver Technologies** Mariner dataset.
- Over **122 million records** for all payer sources from **2010-2019** .
- **ICD-9** and **10 codes** for **AVN**, **HIV**, and **ART** were used ensuring AVN occurred after HIV diagnosis or ART treatment.
- **Cohorts: HIV+/ART+ vs HIV+/ART-**
- Univariate analysis was used to identify confounding factors (age, gender, etc), and comorbidities (Elixhauser).
- **Multivariate analysis** of outcomes controlling for significant univariate factors.

Figure 1: Multivariate analysis by location of AVN. Presented with Odds Ratios and 95% Confidence Interval.



Results:

- 219,853 HIV+ patients; **123,710 on ART**, and **96,143 not receiving ART**.
- **Table 1: All univariate factors** analyzed were statistically **significant** and included in the multivariate analysis, **except coagulopathy**. (**p-value <0.2**)
- **All AVN locations** were statistically **significant**. (p-value <0.2)
- **Figure 1:** Multivariate analysis results for each AVN location presented as **OR with 95% CI** as error. (**p-value <0.05** considered significant)

Table 1: Demographic difference of prevalence in HIV+/ART+ vs HIV+/ART-

CATEGORY	% Difference	P-value
TOTAL	12.54%	**<0.001**
SEX		
Male	19.80%	
Female	-18.18%	**<0.001**
COMORBIDITIES		
Alcohol Abuse	-0.68%	**<0.001**
Arrhythmias	-2.15%	**<0.001**
Blood Loss Anemia	-1.90%	**<0.001**
Chronic Kidney Disease	1.49%	**<0.001**
Chronic Pulmonary Disease	-1.30%	**<0.001**
Coagulopathy	0.00%	0.365
Congestive Heart Failure	-2.52%	**<0.001**
Defiency Anemia	-5.34%	**<0.001**
Depression	3.82%	**<0.001**
Diabetes Mellitus	-11.07%	**<0.001**
Drug Abuse	1.48%	**<0.001**
Fluid/Electrolyte disorders	1.87%	**<0.001**
Hyperlipidemia	-5.91%	**<0.001**
Hypertension	-3.78%	**<0.001**
Hypothyroidism	-9.98%	**<0.001**
Leukopenia	2.06%	**<0.001**
Liver Disease	-2.75%	**<0.001**
Long-term steroids	-0.33%	**<0.001**
Lymphoma	0.83%	**<0.001**
Obesity	-4.49%	**<0.001**
Other Neurological Disorders	-0.84%	**<0.001**
Paralysis	-0.20%	**<0.001**
Peptic Ulcer Disease	-0.23%	**<0.001**
Peripheral Vascular Disease	0.00%	**<0.001**
Psychoses	-1.14%	**<0.001**
Pulmonary Circulatory Disorders	-0.24%	**<0.001**
RA /Collagen Vascular Disease	-5.10%	**<0.001**
Sickle Cell Disease	-0.43%	**<0.001**
Smoking	3.37%	**<0.001**
Valvular Disease	-2.26%	**<0.001**

Discussion:

- Our study supports and provides statistical evidence of ART increasing the rate of AVN among the HIV population.
- Joints that are weight baring have higher rates of AVN.
- Outcomes of THA for HIV+ patients have improved and are comparable to those with HIV.
- As AVN effects patients at younger ages, considerations should be made of management.
- Patients with HIV should still be treated with ART.

Conclusion:

- ART appears to play a role in the development of AVN among the HIV population.
- Physicians should be aware of the risks of developing AVN, which ART appears to increase the likelihood for those with HIV.
- Further studies are needed to provide insight as to the offending agent within ART.

References:

- Bayard C, Ledergerber B, Flepp M, et al. Associations between antiretroviral treatment and avascular bone necrosis: The swiss HIV cohort study. *Open Forum Infectious Diseases*. 2017;4(4). doi:10.1093/ofid/ofx177
- Ready R, Daftary MN, Delapenha R, Dutta A, Oliver J, Frederick W. Avascular necrosis and protease inhibitors. *Journal of the National Medical Association*. 2005;97(11).
- Valencia ME, Barreiro P, Soriano V, Blanco F, Moreno V, González Lahoz J. Avascular necrosis in HIV-infected patients receiving antiretroviral treatment: Study of seven cases. *HIV Clinical Trials*. 2003;4(2). doi:10.1310/8EW3-GYJ9-08NA-6D5H
- Mehta P, Nelson M, Brand A, Boag F. Avascular necrosis in HIV. *Rheumatology International*. 2013;33(1). doi:10.1007/s00296-011-2114-5
- Pietrzak JRT, Maharaj Z, Mokete L, Sikhauli N. Human immunodeficiency virus in total hip arthroplasty. *EFORT Open Reviews*. 2020;5(3). doi:10.1302/2058-5241.5.190030
- Issa K, Pierce TP, Harwin SF, Scillia AJ, Festa A, Mont MA. No Decrease in Knee Survivorship or Outcomes Scores for Patients With HIV Infection Who Undergo TKA. *Clinical Orthopaedics & Related Research*. 2017;475(2). doi:10.1007/s11999-016-5122-7
- Leibold CS, Schmaranzer F, Siebenrock KA, Steppacher SD. Femoral osteotomies for the treatment of avascular necrosis of the femoral head. *Operative Orthopadie und Traumatologie*. 2020;32(2). doi:10.1007/s00064-019-00642-x