# Clinical Predictors of Acute Kidney Injury in HIV Infected Patients Treated with Tenofovir Disoproxil Fumarate (TDF)

Rachel Wagers[1]; Alice Thornton, MD[2]; Donald Holleman, MD[2]

[1]University of Kentucky,; [2]Division of Infectious Diseases, Department of Internal Medicine, Lexington, KY

## Background

TDF is a nucleotide reverse transcriptase inhibitor used for treating HIV and hepatitis B and for HIV pre-exposure prophylaxis (PrEP). TDF is potentially toxic to renal proximal tubules leading to overt nephrotoxicity in some recipients of the drug.

Previous studies have identified risk factors for TDF-associated renal dysfunction. However, these studies have been limited by narrow demographics (male veterans or Asian countries), using only univariate analyses, having short follow-up times, or having small sample sizes.

We evaluated whether routinely available clinical variables could predict risk of TDF-associated acute kidney injury (AKI) in patients treated for HIV infection at the University of Kentucky (UK).

## Methods

**Setting:** The Bluegrass Care Clinic (BCC), a Ryan White funded ID clinic at UK providing HIV treatment to approximately 1600 HIV infected patients from central and eastern Kentucky.

**Subjects:** ≥ 18 years old; HIV infected; and initiated first TDF containing ART regimen at the BCC between 1/1/2012 and 12/31/2016.

**Design:** Retrolective cohort study. Data source was the electronic medical record.

**Outcomes:** Time to acute kidney injury (AKI), defined as ≥ 50% rise in serum creatinine compared to value at initiation of TDF.

**Analyses:** Kaplan-Meier survival curves (KM) for univariate analyses and Cox Proportional Hazards model (CPH) for multivariable analysis. Schoenfeld Test was used to evaluate the proportional hazards assumption.

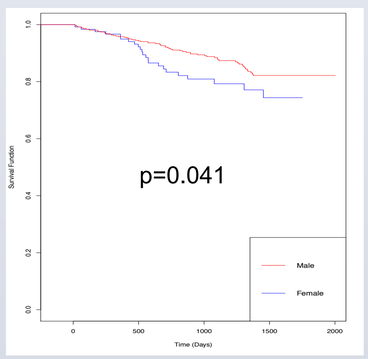
**Ethics:** The study was approved by the UK Medical IRB including waiver of informed consent.

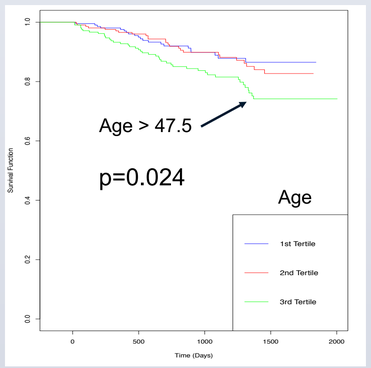
## Results

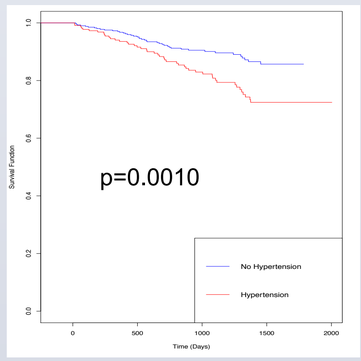
**Subject Characteristics (n = 660)**

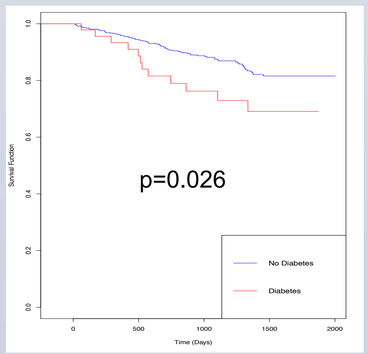
| Characteristic | |
|---|---|
| Sex | N (%) |
| Male | 527 (79.8) |
| Female | 126 (19.1) |
| Transgender (Male-to-Female) | 7 (1.1) |
| Ethnicity | N (%) |
| White | 460 (69.7) |
| African American | 149 (22.6) |
| Hispanic | 45 (6.8) |
| Other | 6 (0.9) |
| Age at TDF Initiation | Years |
| Average + Std Dev. | 41.2 + 11.9 |
| Median | 41.6 |
| Developed AKI | N (%) |
| | 88 (13.3) |

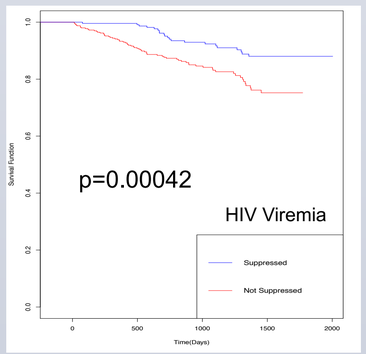
KM Curves

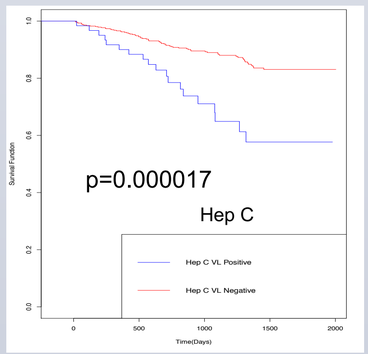


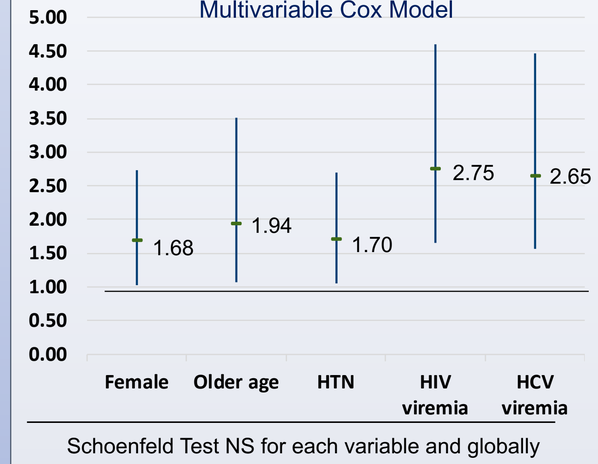




Schoenfeld Test NS for each variable and globally

## Discussion

- We studied the relationship between routinely available clinical and demographic factors and the risk of developing AKI during TDF therapy for HIV infection.
- Because we could not determine the cause of AKI, the extent that the risk factors reflect risk of AKI due to TDF vs general AKI risk is unclear.
- We could not determine the reason that TDF was stopped in subjects without AKI (right censoring). The extent that risk factors influenced those decisions could bias the HR estimates toward the null.
- Female sex, age > 47.5 years, HTN, and HIV or HCV viremia significantly predicted risk of TDF-associated AKI.
- Except for female sex, our results are similar to those of previous studies.
- HIV or HCV viremia was associated with the greatest AKI risk.
- We conclude that AKI risk can be estimated before initiating ART and might be useful in choosing an appropriate regimen.
- It is unclear whether these results will generalize to other populations, such as those receiving PrEP.
- It is also unclear whether closer monitoring of high-risk TDF treated patients can mitigate nephrotoxicity.