Published in final edited form as:

Am J Kidney Dis. 2012 May ; 59(5): 628–635. doi:10.1053/j.ajkd.2011.10.050.

Risk Factors for ESRD in HIV-Infected Individuals: Traditional and HIV-Related Factors

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Abstract

Background—Despite improvements in survival with HIV infection, kidney disease remains an important complication. Few studies have evaluated risk factors associated with development of end-stage renal disease (ESRD) in HIV-infected individuals. We sought to identify traditional and HIV-related risk factors for ESRD in HIV-infected individuals, and to compare ESRD risk by eGFR and proteinuria levels.

Study design—Retrospective cohort study.

Setting and Participants—22,156 HIV-infected veterans without preexisting ESRD receiving healthcare in the Veterans' Affairs medical system between 1996 and 2004.

Predictors—Hypertension, diabetes, cardiovascular disease, hypoalbuminemia (serum albumin < 3.5 mg/dL), CD4 lymphocyte count, HIV viral load, hepatitis C virus coinfection, proteinuria, and estimated glomerular filtration rate (eGFR) were identified using the Veterans' Affairs electronic record system.

Outcomes—ESRD was ascertained by the United States Renal Data System.

Results—366 cases of ESRD occurred, corresponding to 3 cases per 1,000 person-years. Hypertension (HR, 1.9; 95% CI, 1.5–2.4), diabetes (HR, 1.7; 95% CI, 1.3–2.2), and cardiovascular disease (HR, 2.2; 95% CI, 1.7–2.7) were independently associated with ESRD risk in multivariate-adjusted models, as were CD4 lymphocyte count < 200 cells/mm³ (HR, 1.5; 95% CI, 1.2–2.0), HIV viral load ≥ 30,000 copies/mL (HR, 2.0; 95% CI, 1.5–2.8), hepatitis C virus coinfection (HR, 1.9; 95% CI, 1.5–2.4), and hypoalbuminemia (HR, 2.1; 95% CI, 1.8–2.5). Compared to persons without chronic kidney disease (CKD), defined as eGFR > 60 mL/min/1.73 m² and no proteinuria, lower eGFR and higher proteinuria categories were jointly associated with exponentially higher

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Financial Disclosure: The authors declare that they have no other relevant financial interests.

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ESRD rates, ranging from 6.6 per 1000 person-years for persons with proteinuria 30–100 mg/dL and eGFR >60ml/min/1.73m², to 193 per 1000 person-years for persons with proteinuria ≥300mg/dL and eGFR <30ml/min/1.73m².

Limitations—Results may not be generalizable to female and nonveteran populations.

Conclusions—In HIV-infected persons, ESRD risk appears attributable to a combination of traditional and HIV-related risk factors for kidney disease. Combining eGFR and proteinuria for CKD staging is most effective for stratifying risk for ESRD.

Keywords

End-stage renal disease; HIV; chronic kidney disease; risk factors

Kidney disease is a well-recognized complication of HIV infection.¹ Early in the HIV epidemic, HIV-associated nephropathy (HIVAN) emerged as the leading cause of HIV-related kidney disease.² This form of HIVAN, seen almost exclusively in black individuals, is characterized by heavy proteinuria and rapid progression to end-stage renal disease (ESRD). After the advent of antiretroviral therapy (ART), the incidence of clinically significant HIVAN declined substantially in parallel with improvements in survival.^{3, 4} However, despite these initial improvements, rates of ESRD in HIV-infected individuals receiving care in the United States have remained stable since 1996.^{5, 6} We and others have previously shown that the burden of kidney disease in HIV infection is disproportionately carried by black individuals,^{7, 8} who are the racial group with the highest HIV prevalence in this country and worldwide. Furthermore, several contemporary cohort studies have demonstrated that the natural history of HIV-related kidney disease is remarkably different from the case histories described early in the course of the HIV epidemic. Currently, HIV-related kidney disease is less characterized by proteinuria⁹ and its progression appears to be influenced by control of viral replication,^{10–12} coinfection with hepatitis C virus,^{10, 13} and comorbid conditions such as diabetes.^{14–16}

Despite the evolving spectrum of HIV-related kidney disease, few studies have evaluated the risk factors associated with progression to ESRD in HIV-infected persons. Prior studies attempting to address this issue have been limited by small numbers of events,⁸ or were restricted to persons of black race¹⁷ or patients undergoing kidney biopsy.¹⁸ The primary objective of this study was to identify traditional and HIV-related risk factors associated with the development of ESRD, and to determine their relative contributions to ESRD risk in a large national cohort of HIV-infected individuals receiving care in the contemporary era of ART. We also aimed to determine whether these risk factors for ESRD differ between black and white patients. Finally, we compared ESRD risk in HIV-infected individuals across chronic kidney disease (CKD) staging categories based jointly on eGFR and proteinuria.

Methods

Data Sources

We conducted a retrospective cohort study of HIV-infected veterans in the Department of Veterans' Affairs HIV Clinical Case Registry¹⁹ between the years 1996 and 2004. The VA HIV Clinical Case Registry is a national database with demographic, clinical, laboratory, pharmacy and vital status information from the VA electronic medical record system. As in prior studies published by our group,^{7, 20, 21} this data source was linked to the VA National Patient Care Database, Medicare claims, and the VA Beneficiary Identification and Records Locator Subsystem Death File for supplemental demographic and clinical data.²² We linked our database to the United States Renal Data System,⁶ a publically funded national registry

of kidney disease, to identify both prevalent ESRD cases at the time of entry into the cohort and incident ESRD cases during the period of follow-up.

Study Population

The target subjects for this study were HIV-infected persons receiving clinical care in the contemporary era of ART. We therefore included all HIV-infected patients in the Veterans Health Administration who had either serum creatinine or urine protein measured between the years 1996 and 2004. Participants entered the study at the time of their earliest measurement of either serum creatinine or urine protein after December 31, 1995. Of the 22,324 HIV-infected veterans identified by serum creatinine or urine protein measurements, 168 patients were excluded due to preexisting ESRD requiring chronic dialysis or kidney transplant. The remaining 22,156 patients were included in the study.

Outcomes

The primary outcome was development of ESRD, defined as the receipt of chronic dialysis treatment or kidney transplant, ascertained by the United States Renal Data System.⁶ Individuals were analyzed from their initial urine protein or serum creatinine assessment until ESRD, and were censored by death or the end of follow-up, December 31, 2004.

Predictors and Covariates

Candidate predictors included: traditional risk factors for advanced kidney disease, including hypertension, diabetes, cardiovascular disease, and dyslipidemia; and HIV-related characteristics, including lower CD4 lymphocyte count, higher HIV viral load, coinfection with hepatitis C virus, and hypoalbuminemia. Most of these factors are considered indications for annual screening for kidney disease according to the Infectious Disease Society of America Guidelines for the Management of Chronic Kidney Disease in HIV-infected patients.¹ Although cardiovascular disease is not mentioned in these guidelines as a risk factor for CKD, it is strongly associated with kidney disease in HIV-uninfected persons.^{23, 24} Additional candidate predictors included age, race, BMI, and use of specific classes of medications including angiotensin-converting enzyme (ACE) inhibitors, statins, and ART.

Demographic characteristics were obtained from the VA or Medicare health plan databases.²⁵ Diabetes, hypertension, cardiovascular disease, and HIV-related characteristics were ascertained by validated algorithms using a combination of ambulatory diagnoses, physician problem lists, hospitalization discharge diagnoses, procedures, laboratory results, and medication prescriptions.^{26–30} Baseline hypertension was defined as the diagnosis of hypertension before or within the first year of follow-up. Hypoalbuminemia was defined as serum albumin <3.5 mg/dL. Proteinuria was measured by spot urine dipstick. Baseline proteinuria was defined by the first urine dipstick measurement during follow-up. eGFR was calculated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation based on age, sex, race, and serum creatinine;³¹ the MDRD Study equation remains in clinical use in the VA laboratory reporting system. Baseline eGFR was defined as either the average of the first two consecutive eGFR measurements separated by at least three months, or the initial eGFR measurement if a subsequent measurement was unavailable. We used medication prescription records to account for exposure to specific classes of medications, including ART, statins, and ACE inhibitors. For all variables, we included a missing indicator category to retain observations in the analysis.

Statistical Analysis

We used a Cox proportional hazards survival analysis to determine the multivariate-adjusted association of each predictor variable with ESRD risk. We used Schoenfeld's residuals³² to test the proportional hazards assumption, and assessed individual risk factors in univariate Cox models. We then built the multivariate model using a p-value of <0.05 for entry and retention of covariates. To account for potential bias due to the competing risk of death before ESRD, we performed a Fine-Gray competing-risks analysis, which extends the Cox proportional hazards model to competing-risks data by simultaneously evaluating hazards for the primary (ESRD) and competing (death) events.³³ Baseline values were used for age, eGFR, proteinuria, and hypertension. All other variables were time-updated using the last-value-carried-forward method.^{26, 34} Analyses were also stratified by white and black race to evaluate for possible effect modification. Finally, we used the C-statistic³⁵ to determine the ability of demographics (age and race), the seven risk factors (hypertension, diabetes, cardiovascular disease, CD4 lymphocyte count, HIV viral load, hepatitis C virus coinfection, and hypoalbuminemia), proteinuria, and eGFR to discriminate risk for ESRD.

We then evaluated the combined ability of baseline eGFR and proteinuria to predict differential ESRD risk in HIV-infected individuals. We stratified the cohort by baseline eGFR (≥ 60 , 30–59, or < 30 mL/min/1.73m²) and baseline proteinuria (0, 30–100, or 300–1000 mg/dL) and determined the ESRD event rate in each group. Using a baseline eGFR > 60 mL/min/1.73m² and negative urine dipstick as the referent group, we calculated the multivariate-adjusted hazard ratio for ESRD in each joint category of baseline eGFR and proteinuria.

All analyses were conducted using Stata version 11.0 (www.stata.com). This study was approved by the Committee on Human Research at the San Francisco VA Medical Center and the VA Public Health Strategic Health Care Group.

Results

We analyzed 22,156 HIV-infected individuals who were followed over a median period of 69 months, during which 366 developed ESRD requiring chronic dialysis. The overall rate of ESRD was 3.1 per 1,000 person-years. Compared to patients who did not develop ESRD, patients who developed ESRD were of similar age and sex, but were overwhelmingly of black race. Despite similar percentages of black and white veterans in the group without ESRD (42% and 36%, respectively), 85% of patients who developed ESRD were black, compared with only 13% who were white (Table 1). As expected, patients who developed ESRD were more likely to have had proteinuria or eGFR < 60 mL/min/1.73m² at baseline, compared to those who did not develop ESRD. Additionally, patients who developed ESRD were more likely to have comorbid conditions at baseline including hypertension, diabetes, and cardiovascular disease, as well as lower CD4 lymphocyte counts and higher prevalence of hypoalbuminemia and coinfection with hepatitis C virus. There was no significant difference in baseline HIV viral load between the two groups. The prevalence of ART use at baseline appeared modestly lower in individuals who developed ESRD, but this difference did not reach statistical significance ($p = 0.06$). Across the entire cohort, the percentage of individuals who ever received ART increased from 25% at baseline to 74% by the end of follow-up, and did not differ between patients who developed ESRD and did not develop ESRD (74% in each respective group; p -value = 0.7).

Several predictors were strongly and independently associated with higher ESRD risk after multivariate adjustment for demographics, traditional risk factors for kidney disease, and HIV-related characteristics (Table 2). Individuals of black race had a 3-fold risk of ESRD compared to non-black individuals. Among the traditional risk factors for kidney disease,

hypertension, diabetes, and cardiovascular disease were each associated with a 2-fold higher ESRD risk. HIV disease severity also predicted the risk of ESRD. Compared to a CD4 lymphocyte count >350 cells/mm³, CD4 lymphocyte counts <200 cells/mm³ were associated with a 50% increase in ESRD risk, whereas CD4 lymphocyte counts of 200–350 cells/mm³ were not independently associated with ESRD risk. Similarly, HIV viral load $\geq 30,000$ copies/mL, hepatitis C coinfection, and hypoalbuminemia each portended a 2-fold increase in ESRD risk. Finally, lower baseline eGFR and higher baseline proteinuria predicted substantially higher ESRD risk in a dose-response fashion.

Modeling demographic characteristics with the seven risk factors (hypertension, diabetes, cardiovascular disease, CD4 lymphocyte count <200 cells/mm³, HIV viral load $\geq 30,000$ copies/mL, hepatitis C coinfection, and hypoalbuminemia) resulted in a C-statistic of 0.87. When combined with baseline eGFR and proteinuria, the C-statistic increased to 0.95.

When the competing risk of death before ESRD was accounted for (Table 2), the multivariate-adjusted associations of CD4 lymphocyte count <200 cells/mm³ and HIV viral load $\geq 30,000$ copies/mL with ESRD were reduced in magnitude and rendered non-significant. All other predictors remained significantly associated with ESRD.

When stratified by race (Figure 1), the adjusted hazard ratios for ESRD for each risk factor were similar between white and black race groups, with the exception of diabetes. Diabetes had a hazard ratio of 4.5 (95% CI, 2.3–9.0) in white individuals compared with 1.6 (95% CI, 1.2–2.1) in black individuals (p-value for interaction = 0.002).

We next stratified the cohort by baseline eGFR and proteinuria and we observed exponential increases in the ESRD event rates with lower eGFR and higher proteinuria (Figure 2). Notably, individuals with a urine dipstick of 300–1000 mg/dL and a preserved eGFR (>60 ml/min/1.73m²) had a greater than 6-fold ESRD rate compared with individuals with a reduced eGFR of 30–59 ml/min/1.73m² but no proteinuria. Additionally, a urine dipstick of 30–100 mg/dL with a preserved eGFR portended similar ESRD risk as a reduced eGFR of 30–59 ml/min/1.73m² without proteinuria. Based on the multivariate-adjusted hazard ratios for ESRD, individuals were categorized as having no, mild, moderate, or severe CKD.

Discussion

In the current era of ART, ESRD remains an important clinical complication of HIV infection. Our observed ESRD rate of 3.1 per 1,000 person-years is nearly as high as the rate of myocardial infarction, 3.5 per 1,000 person-years, observed in the Data Collection on Adverse events of Anti-HIV Drugs (D:A:D) study.³⁶ An important outcome of this study is our finding that traditional risk factors for kidney disease and HIV-related factors had relatively similar associations with ESRD. Furthermore, we found that staging CKD jointly by eGFR and proteinuria resulted in remarkable risk-stratification for ESRD in HIV-infected individuals, and should be utilized broadly in clinical practice.

This is also the first large cohort study in support of the clinical practice guideline published by the Infectious Diseases Society of America, recommending routine screening for kidney disease in specific groups of HIV-infected patients, including black individuals and those with hypertension, diabetes mellitus, low CD4 lymphocyte count, high HIV viral load, and hepatitis C coinfection.¹ Prior studies in support of this recommendation were few in number and limited by their small sample sizes.^{10, 37, 38} We found that the majority of these factors predicted higher risk for ESRD in a large population of HIV-infected veterans, even when the competing risk of death before ESRD was accounted for. The observed reductions in effect sizes of CD4 lymphocyte count and HIV viral load in competing-risks analyses

likely represent the strong association of these factors with death in the HIV-infected patient population.

Our findings also reinforce the dramatic effect of race on the incidence and progression of HIV-related kidney disease, which has been previously reported.^{7, 8} Despite similar risk factors for the development of ESRD and similar access to healthcare in this study, black individuals had a three-fold ESRD risk compared to whites. Unfortunately, biopsy data were not available to us, and we were unable to distinguish cases of HIVAN from other forms of HIV-related kidney disease. However, others have reported that blacks with non-HIVAN histopathology still experience faster progression to ESRD than whites.⁸ This racial predilection for ESRD in HIV infection is consistent with the epidemiology of ESRD in the general population, where the risk of progression from CKD to ESRD has been reported as 4-fold in blacks compared to whites.³⁹ Recent literature suggests there may be genetic polymorphisms that predispose black individuals to kidney disease to a greater degree than white individuals.⁴⁰ Given their disproportionate burden of ESRD, further studies should evaluate the utility of early screening and monitoring of kidney function in black HIV-infected individuals, perhaps with a combination of creatinine, urine protein, and cystatin C.⁴¹

There is concern that long-term exposure to ART may unintentionally promote the development of traditional risk factors for kidney disease, such as hypertension and diabetes.^{14, 15, 42} The present study was not designed to evaluate the long-term effects of ART on the kidney and, in fact, the prevalence of ART exposure by the end of follow-up was similar between patients who developed ESRD and those who did not. However, our findings that high viremia and low CD4 lymphocyte counts remain associated with ESRD suggest that viral suppression and reversal of immunosuppression by ART is beneficial to the kidney. Data from the SMART study also support the concept that continuous use of ART is associated with fewer cardiovascular, renal, and hepatic complications compared with episodic use of ART,⁴³ although the number of renal events in the study was small. Finally, ART-related decreases in mortality rates from infectious complications may have allowed patients to survive long enough to reach ESRD.

The strengths of this study include its large size, national scope, the relatively uniform healthcare system available to United States veterans, and the reliable data source for the outcome of ESRD. There are important limitations to this study. First, as a study of predominantly male veterans receiving care in the Department of Veterans' Affairs healthcare system, the results may not be generalizable to female patients, nonveteran patients, patients without access to healthcare, or other racial and ethnic groups not represented in this cohort. Compared to HIV-infected nonveterans, HIV-infected veterans have previously been shown to have higher CD4 lymphocyte counts and lower prevalence of AIDS-defining conditions.⁴⁴ The incidence of ESRD in this study could therefore be an underestimate of ESRD incidence in the non-veteran HIV population. Second, as noted above, biopsy data were not available for patients who progressed to ESRD, so we were unable to distinguish cases of HIVAN from other forms of HIV-related kidney disease. The presence of biopsy data could have enabled us to differentiate the risk factors specific to HIVAN versus other forms of HIV-related kidney disease. Biopsy data also may have allowed us to evaluate whether proteinuria portends differential risk for HIVAN versus traditional forms of kidney disease. Third, as noted earlier, this study was not designed to evaluate the long-term effects of ART on the kidney. Our data regarding ART use is limited to whether or not patients were exposed to ART during the period of follow-up. We were unable to determine whether exposure to specific classes of ART medications is beneficial or harmful to the kidney. Fourth, we had no knowledge of the veterans' *APOL1* (apolipoprotein L-1) or *MYH9* (nonmuscle myosin, heavy chain 9) genotypes, so we could

not evaluate whether genetic polymorphisms in blacks might interact with clinical risk factors or add to ESRD prediction. Finally, the identified clinical variables may not necessarily be in the causal pathway, and despite our multivariate-adjusted analysis, we cannot exclude the possibility of residual confounding.

In conclusion, in this large, contemporary cohort of HIV-infected veterans, the risk of ESRD appeared to be attributable to a combination of traditional risk factors for kidney disease, such as hypertension and diabetes, and to HIV disease severity. A combined assessment of eGFR and proteinuria constitutes a novel method for CKD staging in HIV-infected individuals, and effectively stratifies individual risk for progression to ESRD. This updated staging method should be further evaluated as a potential framework for targeting renoprotective interventions in this unique population.

Acknowledgments

This paper is dedicated to the memory of Andy I. Choi, MD MAS.

Support: This study was supported by the National Institutes of Health (K23DK080645-01A1 (AIC), 1R03AG034871-01 (AIC), R01 DK066488-01 (MGS)) which were administered by the Northern California Institute for Research and Education, and with resources of the Veterans Affairs Medical Center, San Francisco, California. These funding sources had no involvement in the design or execution of this study.

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Figure 1. Risk Factors for ESRD Stratified by Race

Multivariable model adjusted for baseline age, race, body mass index, baseline eGFR, baseline urine dipstick, baseline hypertension, diabetes, cardiovascular disease, CD4 lymphocyte count, HIV viral load, hepatitis C infection, hypoalbuminemia (serum albumin <3.5 mg/dL), and receipt of ACE inhibitor. Abbreviations: ACE inhibitor (angiotensin-converting enzyme inhibitor); eGFR (estimated glomerular filtration rate); ESRD (end-stage renal disease).

	Proteinuria		
	0 mg/dL	30-100 mg/dL	300-1,000 mg/dL
eGFR ≥ 60 ml/min/1.73m²			
Number of Patients at Risk	15,348	2,390	185
ESRD Rate per 1,000 Person-Years	1.0	6.6	35.4
Hazard Ratio (95% CI)†	Reference	6.3 (4.6-8.6)	24.6 (16.0-37.7)
eGFR 30-59 ml/min/1.73m²			
Number of Patients at Risk	484	350	85
ESRD Rate per 1,000 Person-Years	5.5	31.1	115.6
Hazard Ratio (95% CI)†	7.4 (4.0-13.8)	37.1 (25.3-54.6)	88.7 (56.0-140.5)
eGFR < 30 ml/min/1.73m²			
Number of Patients at Risk	38	106	60
ESRD Rate per 1,000 Person-Years	46.1	111.1	192.9
Hazard Ratio (95% CI)†	42.6 (18.3-99.4)	132.8 (87.1-202.5)	523.0 (323.6-845.4)

Figure 2. CKD Staging by Risk of Progression to ESRD

ESRD rate per 1,000 person-years stratified by baseline eGFR and proteinuria (measured by urine dipstick). Severity of CKD shown by intensity of shading (no CKD vs mild, moderate, and severe CKD). †Multivariate-adjusted hazard ratios for ESRD adjust for baseline age, race, body mass index, baseline eGFR, baseline proteinuria, baseline hypertension, diabetes, cardiovascular disease, CD4 lymphocyte count, HIV viral load, hepatitis C infection, hypoalbuminemia (serum albumin < 3.5 mg/dL), and receipt of ACE inhibitor. Abbreviations: ACE inhibitor (angiotensin-converting enzyme inhibitor); CKD (chronic kidney disease); eGFR (estimated glomerular filtration rate); ESRD (end-stage renal disease).

Table 1Baseline Characteristics by ESRD status^{*†}

	No ESRD (n=21,790)	ESRD (n=366)	P value
Age (y)	45 +/- 10	45 +/- 8	0.9
Female	2.2%	2.2%	0.9
Race			<0.001
White	36%	13%	
Black	42%	85%	
Other	4%	3%	
Unknown	18%	0%	
Body Mass Index (kg/m ²)	24.9 +/- 4.5	24.6 +/- 4.4	0.6
eGFR <60 ml/min/1.73m ²	5%	46%	<0.001
Proteinuria			<0.001
0 mg/dL	84%	32%	
30–100 mg/dL	15%	43%	
300–1000 mg/dL	1%	26%	
Hypertension	30%	67%	<0.001
Diabetes	5%	20%	<0.001
Cardiovascular Disease	5%	8%	0.01
Dyslipidemia	8%	8%	0.7
CD4 Count (cells/mm ³)	285 (289)	236 (243)	0.008
Viral Load (copies/mL)	82,009 (166,484)	96,007 (146,947)	0.5
Hepatitis C Virus Infection	20%	30%	<0.001
Hypoalbuminemia ^{**}	18%	37%	<0.001
Antiretroviral Therapy	25%	21%	0.06
Statin Use	2%	1%	0.09
ACE Inhibitor Use	2%	4%	0.02

* ESRD status defined at end of observation.

† Categorical variables reported as proportion with condition (%); continuous variables reported as mean +/- standard deviation.

** serum albumin <3.5 mg/dL

Abbreviations: ACE (angiotensin-converting enzyme); eGFR (estimated glomerular filtration rate); ESRD (end-stage renal disease).

Table 2**Risk Factors for ESRD in HIV-Infected Veterans**

Risk Factors	Multivariate-Adjusted Model*		Competing-Risks Analysis†	
	HR (95% CI)	P Value	Sub-HR (95% CI)	P Value
Baseline Age Quartile				
<38 y	1.00 (reference)	-	1.00 (reference)	-
38–44 y	0.90 (0.65–1.25)	0.5	0.84 (0.60–1.18)	0.3
45–49 y	0.59 (0.42–0.82)	0.002	0.55 (0.38–0.78)	0.001
≥50 y	0.36 (0.26–0.51)	<0.001	0.33 (0.23–0.48)	<0.001
Race				
White	1.00 (reference)	-	1.00 (reference)	-
Black	3.06 (2.22–4.22)	<0.001	3.24 (2.18–4.82)	<0.001
Baseline Hypertension	1.87 (1.46–2.40)	<0.001	2.04 (1.56–2.68)	<0.001
Diabetes	1.69 (1.32–2.16)	<0.001	1.54 (1.15–2.08)	0.004
Cardiovascular Disease	2.17 (1.72–2.74)	<0.001	1.78 (1.34–2.36)	<0.001
Dyslipidemia	1.16 (0.91–1.49)	0.2	1.46 (1.11–1.94)	0.007
CD4 Count				
>350 cells/mm ³	1.00 (reference)	-	1.00 (reference)	-
200–350 cells/mm ³	0.92 (0.65–1.29)	0.6	0.92 (0.64–1.32)	0.7
<200 cells/mm ³	1.54 (1.17–2.02)	0.002	1.30 (0.97–1.76)	0.08
Viral Load				
<500 copies/mL	1.00 (reference)	-	1.00 (reference)	-
500–3,999 copies/mL	0.89 (0.60–1.32)	0.6	0.81 (0.52–1.27)	0.4
4,000–29,999 copies/mL	1.42 (0.99–2.03)	0.06	1.28 (0.88–1.87)	0.2
≥30,000 copies/mL	2.01 (1.46–2.76)	<0.001	1.44 (1.02–2.03)	0.04
Hepatitis C Virus	1.90 (1.52–2.38)	<0.001	1.95 (1.53–2.50)	<0.001
Hypoalbuminemia**	2.14 (1.80–2.54)	<0.001	1.99 (1.69–2.34)	<0.001
Baseline eGFR				
≥60 mL/min/1.73m ²	1.00 (reference)	-	1.00 (reference)	-
30–59 mL/min/1.73m ²	6.43 (4.81–8.58)	<0.001	5.24 (3.72–7.39)	<0.001
<30 mL/min/1.73m ²	28.09 (20.29–38.88)	<0.001	20.87 (13.73–31.73)	<0.001
Baseline Proteinuria				
0 mg/dL	1.00 (reference)	-	1.00 (reference)	-
30–100 mg/dL	5.63 (4.29–7.38)	<0.001	5.25 (3.88–7.11)	<0.001
300–1000 mg/dL	18.09 (12.96–25.23)	<0.001	18.26 (12.40–26.89)	<0.001

* Proportional hazards multivariate analysis. Adjusted for baseline age, race, body mass index, baseline eGFR, baseline proteinuria, baseline hypertension, diabetes, cardiovascular disease, CD4 lymphocyte count, HIV viral load, hepatitis C infection, hypoalbuminemia (serum albumin <3.5 mg/dL), and receipt of ACE inhibitor.

† Adjustment for the Competing Risk of Death Utilizing Fine-Gray Analysis. Competing-risks model estimates sub-hazard ratio for ESRD accounting for competing risk of death before ESRD.

**
serum albumin <3.5 mg/dL

Abbreviations: ACE inhibitor (angiotensin-converting enzyme inhibitor); eGFR (estimated glomerular filtration rate); HR, hazard ratio; CI, confidence interval.