Reduced Kidney Function and Preclinical Atherosclerosis in HIV-Infected Individuals: The Study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM)

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Key Words

Cystatin C • Intima-medial thickness • HIV • Atherosclerosis • Cardiovascular disease • Kidney

Abstract

Background/Aims: Reduced kidney function and albuminuria are associated with higher risk for cardiovascular disease (CVD) and mortality in HIV-infected individuals. We investigated whether reduced estimated glomerular filtration rate (eGFR) and albuminuria are associated with subclinical vascular disease, as assessed by carotid intima-medial thickness (cIMT). **Methods:** Cross-sectional analysis of 476 HIV-infected individuals without clinical evidence of CVD enrolled in the Fat Redistribution and Metabolic Change in HIV infection (FRAM) study, using multivariable linear regression. eGFR_{Cys} and eGFR_{Cr} were calculated from cystatin C and creatinine levels. Albuminuria was defined as a positive urine dipstick ($\geq 1+$) or urine albumin-to-creatinine ratio ≥ 30 mg/g. Common and internal cIMT were measured by high-resolution B-mode ultrasound. **Results:** In unadjusted analyses, eGFR_{Cys} and eGFR_{Cr} were strongly associated with common and internal cIMT. Each 10 ml/min/1.73 m² decrease in eGFR_{Cys} and eGFR_{Cr} was associated with a 0.008 mm higher

common cIMT ($p = 0.003$, $p = 0.01$) and a 0.024 and 0.029 mm higher internal cIMT ($p = 0.003$), respectively. These associations were eliminated after adjustment for age, gender, and race. Albuminuria showed little association with common or internal cIMT in all models. **Conclusions:** In HIV-infected individuals without prior CVD, reduced kidney function and albuminuria were not independently associated with subclinical vascular disease, as assessed by cIMT. These results suggest that research should focus on searching for novel mechanisms by which kidney disease confers cardiovascular risk in HIV-infected individuals. Copyright © 2011 S. Karger AG, Basel

Introduction

Cardiovascular disease (CVD) is an important cause of morbidity and mortality in HIV-infected patients. Previous studies have demonstrated that HIV-infected patients have a higher prevalence and incidence of CVD when compared with age-matched uninfected controls

Andy Choi is deceased.

[1]. Carotid intima-medial thickness (cIMT) is an established measure of subclinical vascular disease that is strongly associated with future CVD events in the general population [2]. In the study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM), HIV-infected patients without clinical CVD had substantially higher cIMT compared with uninfected individuals, even after adjustment for traditional CVD risk factors [3]. This finding suggests that HIV infection may promote the development of atherosclerosis or vessel hypertrophy, though its mechanisms remain unclear.

A potential contributor to vascular disease in the setting of HIV infection is kidney disease. Early in the HIV epidemic, HIV-associated nephropathy (HIVAN) was an important cause of HIV-related kidney disease [4]. Although the prevalence of clinically significant cases of HIVAN has decreased considerably with the advent of antiretroviral therapy [5], HIV infection remains associated with a higher prevalence of microalbuminuria [6] and risk for end-stage renal disease (ESRD) [7]. For instance, in the first FRAM examination, HIV-infected individuals had higher levels of microalbuminuria and significantly worse renal function, as measured by cystatin C, compared to uninfected controls [6, 8]. Furthermore, cystatin C-based estimated glomerular filtration rate (eGFR_{Cys}) and albuminuria were strong and independent risk factors for mortality among individuals with HIV [9]. In the general population, both chronic kidney disease (CKD) and albuminuria are well established and independent risk factors for cardiovascular events, including myocardial infarction, heart failure, stroke and cardiovascular mortality [10]. A recent study from the Veterans Administration's National HIV Registry found that CKD and albuminuria are independently associated with CVD and mortality in HIV-infected individuals as well [11].

Despite these strong associations, the mechanisms by which CKD may contribute to cardiovascular risk in the setting of HIV infection remain unclear. Accelerated vascular disease could be a common pathway linking CKD and CVD given their shared risk factors and the adverse effects of reduced kidney function on blood pressure control, inflammation, insulin resistance, and dyslipidemia. We hypothesized that albuminuria and reduced kidney function would be associated with subclinical vascular disease in HIV-infected individuals. To this end, we determined the association of eGFR_{Cys}, creatinine-based eGFR (eGFR_{Cr}), and prevalence of albuminuria with cIMT as measured in the second examination of FRAM.

Methods

Study Participants and Design

FRAM was originally designed to evaluate the association of HIV infection and its treatment with changes in body composition and metabolic abnormalities. The methods of FRAM have previously been described in detail [12]. Between June 2000 and September 2002, 1,183 HIV-infected individuals were recruited from 16 geographically diverse HIV or infectious disease clinics. The demographics of the FRAM cohort were similar to those of a national random sampling of HIV-infected individuals in the United States [12]. Exclusion criteria for FRAM included: age less than 18 years, pregnancy or plan for pregnancy within 3 months of enrollment, and contraindication to magnetic resonance imaging or dual-energy x-ray absorptiometry scanning. Between October 2004 and August 2007, a second examination was conducted which included ultrasonographic assessment of cIMT. The current cross-sectional study used data collected at this 5-year follow-up visit of FRAM. FRAM year 5 retention outcomes for participants initially enrolled have been reported [13]. Of the 581 HIV-infected participants examined at this visit, we restricted our analysis to the 476 participants who had IMT measurements available and were free of self-reported clinical CVD at the time of the ultrasound scan [3]. Institutional review board approval was obtained at each participating center, and informed consent was obtained from all participants.

Predictors

Cystatin C was measured by a BNII nephelometer (Siemens, Inc., Deerfield, Ill., USA) that used a particle-enhanced immunonephelometric assay (N Latex Cystatin C) in serum specimens previously frozen and stored at -70°C [14]. The coefficient of variation for between-run precision was less than 2% for cystatin C [14]. eGFR_{Cys} was estimated from serum cystatin C levels using the CKD Epidemiology Collaboration equation ($\text{eGFR}_{\text{Cys}} = 76.7 \times \text{cysC}^{-1.19}$) [15]. eGFR_{Cys} was capped at 120 ml/min/1.73 m², as higher estimates are unlikely to be accurate or precise. Creatinine level was measured by the enzymatic method at Covance Laboratories (Indianapolis, Ind., USA); eGFR_{Cr} was calculated using the abbreviated (4-variable) Modification of Diet in Renal Disease (MDRD) equation [16], as in prior FRAM studies, and also capped at 120 ml/min/1.73 m². A random urine sample was used to assess for albuminuria. Albuminuria was defined as the presence of a positive result on a urine dipstick ($\geq 1+$), or the presence of a spot albumin-to-creatinine ratio >30 mg/g on laboratory examination.

Covariates

Age, sex, race, personal and family medical history, smoking history, current medication use, and drug use were assessed by standardized questionnaires [12]. Height, weight and blood pressure were measured by standardized protocols. Hypertension was defined as a systolic blood pressure >140 mm Hg, a diastolic blood pressure >90 mm Hg, or antihypertensive medication use. Diabetes was defined as a fasting blood glucose level of 126 mg/dl or higher or reported use of insulin or oral hypoglycemic medication. All laboratory measurements of lipid levels, glucose metabolism and other markers from blood specimens were performed at Covance Laboratories. Total and regional subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and lean body mass

Fig. 1. Mean common cIMT by quartile of $eGFR_{Cys}$. Bars represent 95% confidence intervals. IMT levels were calculated for each eGFR quartile using LS-means from a linear GEE regression model with the dependent variable cIMT. Common cIMT model adjusts for age, gender, race, antihypertensive use, systolic blood pressure, diastolic blood pressure, current smoking, skeletal muscle, CD4 lymphocyte count, and tenofovir duration. * $p < 0.05$ compared with quartile 4.

Fig. 2. Mean internal cIMT by quartile of $eGFR_{Cys}$. Bars represent 95% confidence intervals. IMT levels were calculated for each eGFR quartile using LS-means from a linear GEE regression model with the dependent variable cIMT. Internal cIMT model adjusts for age, gender, race, antihypertensive use, hypolipidemic use, HDL, current smoking, HIV RNA, and indinavir duration. * $p < 0.05$ compared with quartile 4.

were measured by magnetic resonance imaging as described previously [12]. HIV-related covariates included CD4 lymphocyte count, HIV RNA levels, duration of antiretroviral use (self-reported and on the basis of abstracted medication information at the HIV clinic sites) and duration of HIV infection (defined as time since first positive HIV diagnosis). Hepatitis C virus (HCV) RNA levels were measured using the Bayer Versant 3.0 (bDNA) assay (Bayer Diagnostics, Berkeley, Calif., USA); values ≥ 615 IU/ml were defined as HCV-positive.

Outcomes

High-resolution B-mode ultrasonography was performed to capture images of the right and left, near and far walls of the common carotid and internal carotid arteries [17]. The assessment of cIMT in FRAM has been described previously [3]. Ultrasound images were analyzed centrally at the Ultrasound Reading Center (Department of Radiology, Tufts Medical Center, Boston, Mass., USA) to calculate the maximum near-wall and far-wall cIMT at each arterial site. The maximal cIMT of the common carotid artery was calculated as the mean of the maximum cIMT of the near and far walls of the right and left sides. Maximal wall thickness of the internal carotid artery was computed by the same method but also included measurements of the bulb region. A subset of patients ($n = 77$) had replicate readings, the same ultrasound scan read by two different readers. As in previous analyses [3], we included these replicates in our analysis using generalized estimating equations (GEEs), adjusting for IMT reader to account for the repeated measures.

Statistical Analysis

We compared demographic and clinical characteristics across quartiles of $eGFR_{Cys}$, using Fisher's exact test for categorical variables, and the Kruskal-Wallis test for continuous variables, because many measures were non-normally distributed. To account for replicate cIMT readings in a subset of participants ($n = 77$) as noted above, we used linear GEEs with robust standard errors [18] to evaluate the association of $eGFR_{Cys}$, $eGFR_{Cr}$, and albuminuria with common and internal/bulb cIMT. The semi-parametric GEE method is useful for correlated data when the normality assumption may not be valid. All analyses were adjusted for IMT reader. Multiple imputation was performed for missing covariates using the Markov chain Monte Carlo method for arbitrary missing data [19]. We evaluated the associations between predictor and outcome variables in stages: unadjusted analysis; adjusted for demographic characteristics (age, sex and race); and, multivariate-adjusted analyses incorporating demographics and selected CVD risk factors and HIV-related covariates that were associated with $eGFR_{Cys}$. The final multivariate-adjusted models were built separately for each outcome (common and internal cIMT) using a stepwise regression with a p value of 0.05 or less for entry and retention of covariates. We also conducted a sensitivity analysis to account for those with missing cIMT, adjusting estimates using an inverse probability weighting approach by modeling the participant's probability of having non-missing cIMT [20]. The inverse of this probability was then used as a weight applied to persons with non-missing cIMT in the linear GEE regression analysis of cIMT.

IMT levels in figures 1 and 2 were calculated for each eGFR quartile using least-squares means (LS-means) from a linear GEE

Table 1. Demographic and clinical characteristics of participants by quartile of eGFR_{Cys}

	Quartile of eGFR _{Cys}				p value
	1 (n = 117)	2 (n = 118)	3 (n = 118)	4 (n = 118)	
Range of eGFR _{Cys} , ml/min/1.73 m ²	<71.8	71.8–88.2	88.3–107.5	>107.5	
Age, years	50 (46, 55)	48.5 (42, 54)	46 (42, 51)	45 (39, 50)	<0.001
Female	32 (27%)	34 (29%)	30 (25%)	48 (41%)	0.05
Race					
African-American	49 (42%)	54 (46%)	46 (39%)	40 (34%)	0.3
Caucasian	55 (47%)	47 (40%)	61 (52%)	58 (49%)	
Other	13 (11%)	17 (14%)	11 (9%)	20 (17%)	
Smoking Status					
Current	47 (40%)	52 (44%)	40 (34%)	24 (21%)	0.007
Past	26 (22%)	28 (24%)	26 (22%)	33 (28%)	
Never	44 (38%)	38 (32%)	52 (44%)	60 (51%)	
Total cholesterol, mg/dl	179 (150, 215)	183 (154, 214)	180 (155, 217)	187 (162, 215)	0.7
High-density lipoprotein, mg/dl	39 (32, 52)	41 (33, 54)	43 (37, 54)	47 (39, 59)	<0.001
Diabetic	10 (9%)	16 (14%)	7 (6%)	5 (4%)	0.06
Fasting glucose, mg/dl	92 (84, 104)	95 (85, 101)	94 (85, 100)	93 (86, 100)	0.9
Insulin, μ U/ml	17 (11, 27)	16 (10, 27)	14 (10, 20)	14 (10, 20)	0.03
Systolic blood pressure, mm Hg	123 (114, 135)	128 (116, 140)	119 (113, 134)	121 (113, 129)	0.03
Diastolic blood pressure, mm Hg	78 (70, 86)	79 (73, 84)	77 (71, 84)	76 (70, 83)	0.3
Family history of MI					
Father	25 (22%)	26 (22%)	18 (16%)	19 (17%)	0.8
Mother	21 (19%)	17 (15%)	13 (12%)	16 (14%)	0.6
Body mass index	25 (22, 27)	25 (22, 29)	25 (22, 28)	25 (23, 28)	0.8
Lipid-lowering medication	19 (16%)	31 (27%)	30 (26%)	29 (25%)	0.2
Antihypertensive medication	36 (31%)	34 (29%)	31 (27%)	23 (20%)	0.3
ACE use	16 (14%)	17 (15%)	12 (10%)	10 (8.7%)	0.5
ARB use	2 (1.7%)	2 (1.7%)	2 (1.7%)	3 (2.6%)	0.9
ART	109 (93%)	112 (95%)	110 (94%)	112 (96%)	0.8
CD4 lymphocyte count	356 (198, 526)	372 (240, 622)	441 (339, 599)	463 (336, 656)	0.001
Detectable HIV RNA	47 (41%)	37 (32%)	29 (25%)	19 (17%)	<0.001
HIV RNA, copies/ml					
Below detectable	68 (59%)	78 (68%)	88 (75%)	96 (84%)	0.003
400–10,000	20 (17%)	12 (10%)	15 (13%)	10 (8.7%)	
>10,000	27 (24%)	25 (22%)	14 (12%)	9 (7.8%)	
HIV duration, years	14 (10, 17)	12 (10, 16)	13 (10, 17)	12 (9, 15)	0.009
HCV RNA+	42 (36%)	28 (24%)	24 (21%)	12 (10%)	<0.001
Heroin	28 (24%)	26 (22%)	23 (20%)	18 (15%)	0.4
eGFR _{Cr} , ml/min/1.73 m ²	78 (62, 96)	90 (76, 109)	97 (86, 113)	108 (95, 120)	<0.001
Presence of albuminuria	47 (52%)	28 (35%)	30 (30%)	20 (21%)	<0.001

Continuous variables are displayed as median (IQR). Dichotomous variables are displayed as number (%).

ACE = Angiotensin-converting enzyme; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate; ART = antiretroviral therapy; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IQR = interquartile range; MI = myocardial infarction.

regression model with the dependent variable cIMT, adjusting for covariates included in table 2. LS-means are within-group means adjusted for other effects in the model and are also known as population marginal means [21]. All analyses were conducted using the SAS system, version 9.2 (SAS Institute, Inc., Cary, N.C., USA).

Results

The cIMT was measured in 476 HIV-infected individuals without clinical evidence of CVD. The demographics of the slightly smaller subset (n = 471) with cystatin C

Table 2. Association of eGFR and albuminuria with cIMT in HIV-infected individuals

	Unadjusted analysis			Demographic-adjusted analysis ¹			Multivariable-adjusted analysis ²		
	Estimate (per mm)	95% CI	p value	Estimate (per mm)	95% CI	p value	Estimate (per mm)	95% CI	p value
<i>Common cIMT</i>									
eGFR _{Cys} ³	0.008	0.003, 0.013	0.003	−0.003	−0.007, 0.002	0.3	−0.004	−0.008, 0.001	0.1
eGFR _{Cr} ³	0.008	0.002, 0.014	0.01	−0.002	−0.007, 0.004	0.5	−0.003	−0.008, 0.003	0.3
Presence of albuminuria	0.021	−0.007, 0.049	0.1	−0.008	−0.036, 0.019	0.6	−0.006	−0.042, 0.030	0.8
<i>Internal cIMT</i>									
eGFR _{Cys} ³	0.024	0.008, 0.039	0.003	0.000	−0.015, 0.015	0.9	0.003	−0.012, 0.019	0.7
eGFR _{Cr} ³	0.029	0.010, 0.047	0.003	−0.003	−0.021, 0.016	0.8	0.001	−0.020, 0.021	0.9
Presence of albuminuria	0.005	−0.087, 0.097	0.9	−0.045	−0.137, 0.047	0.3	−0.01	−0.107, 0.086	0.8

Estimates are from linear GEEs with robust standard errors, as described in the Methods section.

cIMT = Carotid intima-medial thickness; eGFR_{Cys} = cystatin C-based estimated glomerular filtration rate; eGFR_{Cr} = creatinine-based estimated glomerular filtration rate; 95% CI = 95% confidence interval.

¹ Adjusted for age, gender, and race. ² Common cIMT model adjusts for age, gender, race, antihypertensive use, systolic blood pressure, diastolic blood pressure, current smoking, skeletal muscle, CD4 lymphocyte count, and tenofovir duration. Internal cIMT model adjusts for age, gender, race, antihypertensive use, hypolipidemic use, HDL, current smoking, HIV RNA, and indinavir duration. ³ Per 10 ml/min/1.73 m² decrease.

measurements are shown in table 1. The mean age of the study participants was 48 years. Females comprised 31% of the study sample. The overall median values for eGFR_{Cys} and eGFR_{Cr} among study participants were 88 ml/min/1.73 m² (interquartile range (IQR), 72, 108) and 94 ml/min/1.73 m² (IQR, 79, 113), respectively. Of the 369 patients with urine albumin measured, the prevalence of albuminuria was 34%.

Participants with lower eGFR_{Cys} were older and more often men compared to those with higher eGFR_{Cys}. There were no statistically significant differences in race across quartiles of eGFR_{Cys}. Participants in the lower quartiles of eGFR_{Cys} had higher prevalence of smoking, lower HDL levels, and higher systolic blood pressures. The prevalence of diabetes appeared higher in the lower quartiles of eGFR_{Cys}, but did not reach statistical significance ($p = 0.06$). Insulin levels were modestly higher in patients with lower eGFR_{Cys}. There were no statistically significant differences in the use of lipid-lowering medications, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers across quartiles of eGFR_{Cys}. As previously reported [8], patients with lower eGFR_{Cys} had lower CD4 lymphocyte counts, higher prevalence of HIV viremia, longer duration of HIV infection, and higher rates of coinfection with HCV. As anticipated, lower eGFR_{Cys} was strongly associated with lower eGFR_{Cr} and higher prevalence of albuminuria.

Overall mean values of common and internal cIMT were 0.86 ± 0.16 and 1.15 ± 0.49 mm, respectively. In the unadjusted analysis (fig. 1), patients in the lower

two quartiles of eGFR_{Cys} had a significantly higher common cIMT compared to patients in the highest eGFR_{Cys} quartile (mean common cIMT 0.88 ± 0.15 and 0.89 ± 0.16 mm, respectively, in quartiles 1 and 2, compared to 0.83 ± 0.16 mm in quartile 4, $p < 0.05$). However, this association was attenuated by demographic factors alone (age, gender, and race). Multivariate adjustment, which also included traditional CVD risk factors, HIV-related factors, and body composition, had little further effect. Similarly (fig. 2), there was a strong unadjusted association between eGFR_{Cys} and internal cIMT (mean internal cIMT 1.25 ± 0.56 and 1.21 ± 0.52 mm, respectively, in quartiles 1 and 2, compared to 1.04 ± 0.39 mm in quartile 4, $p < 0.01$). This association was also attenuated after adjustment for demographic factors, and little association was present after full multivariate adjustment.

In table 2, we display the multivariable linear regression analyses comparing eGFR_{Cys}, eGFR_{Cr}, and albuminuria with common and internal cIMT. Both eGFR_{Cys} and eGFR_{Cr} were negatively associated with common and internal cIMT in the unadjusted analyses. However, the associations of eGFR_{Cys} and eGFR_{Cr} with common and internal cIMT were largely attenuated after adjustment for demographic factors alone. The presence of albuminuria was associated with an increase in common cIMT of 0.021 mm in the unadjusted analysis, but the association did not reach statistical significance ($p = 0.14$), and was completely attenuated after demographic adjustment. Albuminuria showed little association with internal cIMT.

Results were similar in a sensitivity analysis that used inverse probability weighting to mitigate selection bias (supplemental table 1).

Discussion

In HIV-infected individuals without clinical evidence of CVD, reduced kidney function, as measured by cystatin C and creatinine, showed a statistically significant association with common and internal cIMT in unadjusted analyses. However, this association was accounted for entirely by demographic factors (age, gender, and race). Furthermore, there appeared to be minimal association between albuminuria and common or internal cIMT.

To our knowledge, this is the first study examining the relationship between reduced kidney function and subclinical vascular disease in the HIV-infected population. Contrary to our working hypothesis, our results suggest that accelerated atherosclerosis and vessel hypertrophy may not be the primary pathways by which kidney disease contributes to cardiovascular risk in HIV-infected patients. Interestingly, similar results were found in HIV-uninfected populations. In the Multi-Ethnic Study of Atherosclerosis (MESA), a cohort of healthy individuals free of clinical CVD, Bui et al. [22] did not find an independent association between cystatin C and cIMT. Furthermore, in MESA, there was no independent association between cystatin C and measures of coronary calcification [23]. However, cystatin C was independently associated with a higher prevalence of left ventricular hypertrophy [24]. Similarly, albuminuria was independently associated with the presence of left ventricular hypertrophy, but was not associated with cIMT [25]. These findings suggest that kidney impairment in the general population may confer cardiovascular risk through mechanisms other than atherosclerosis, such as left ventricular remodeling, endothelial dysfunction, susceptibility to plaque rupture, hypercoagulability, or susceptibility to arrhythmia. Similar studies in the HIV-infected population would be of value to better understand the cardiovascular risk of HIV, as well as the contribution of kidney disease.

In the HIV population, few studies to date have examined the relationship between reduced kidney function and CVD. In a national sample of HIV-infected veterans, both albuminuria and $\text{eGFR}_{\text{Cr}} < 60 \text{ ml/min/1.73 m}^2$ were associated with increased incidence of cardiovascular events [11]. From FRAM, a recent publication by Choi et al. [9] found that eGFR_{Cys} and albuminuria were strong

and independent risk factors for all-cause mortality. Unfortunately, the cause of death could not be determined in that study; therefore, it is unknown if these associations were present for cardiovascular-specific deaths. Nevertheless, these findings demonstrate the need to determine the underlying mechanisms by which kidney disease contributes to CVD and mortality in the setting of HIV infection. Although the increased risk of CVD does not appear to be mediated by accelerated atherosclerosis or vessel hypertrophy, as assessed by cIMT, further study is needed to investigate other potential pathways of disease.

There are several limitations to this study. First, its cross-sectional design allowed only one time point for data analysis. We are therefore unable to assess whether mild kidney disease might predict the progression of cIMT over a period of time. Second, of the 1,183 patients initially enrolled in FRAM, only 476 patients were present at the five-year follow-up visit, FRAM2, analyzed in this cross-sectional study. However, results were similar in a sensitivity analysis in which we used inverse probability weighting, suggesting that selection bias did not strongly impact our results. Third, although albuminuria data were available in only 369 of the 476 patients, we accounted for the missing data in our multivariate analyses using multiple imputation [19]. Fourth, in comparison with prior studies evaluating the relationship between kidney disease and CVD, our patient sample had relatively mild impairments in kidney function; the lowest quartile of eGFR_{Cys} represented patients with an $\text{eGFR} < 72 \text{ ml/min/1.73 m}^2$. Given that the majority of our patients had relatively preserved kidney function, we cannot exclude the possibility that more severe kidney impairment might be independently associated with higher cIMT. Other limitations include our use of eGFR_{Cys} and eGFR_{Cr} rather than direct measurements of GFR, as well as our use of cIMT as a surrogate marker of subclinical vascular disease. Our chosen marker for preclinical atherosclerosis, cIMT, is a well-established measure of subclinical CVD, yet it is controversial whether increased cIMT represents true atherosclerosis or arterial wall hypertrophy.

In summary, we did not find an independent association between kidney disease and subclinical vascular disease in HIV-infected individuals. These results suggest that atherosclerosis and vessel hypertrophy may not be the primary pathways linking kidney disease to cardiovascular risk in HIV-infected individuals. Further studies are needed to elucidate the specific mechanisms by which kidney disease contributes to CVD and mortality in the setting of HIV infection.

Appendix

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Disclosure Statement

There are no conflicts of interest to declare.

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