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Metabolic Syndrome Predicts All-Cause Mortality in Persons with Human Immunodeficiency Virus

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Abstract

We examined the association between metabolic syndrome (MS) and its individual defining criteria on all-cause mortality in human immunodeficiency virus (HIV)-infected persons. We used data from 567 HIV-infected participants of the Nutrition for Healthy Living study with study visits between 9/1/2000 and 1/31/2004 and determined mortality through 12/31/2006. MS was defined using modified National Cholesterol Education Program guidelines. Cox proportional hazards for all-cause mortality were estimated for baseline MS status and for its individual defining criteria. There were 83 deaths with median follow-up of 63 months. Baseline characteristics associated with increased risk of mortality were: older age in years (univariate hazard ratio [HR] 1.04, $p < 0.01$), current smoking (HR 1.99, $p = 0.02$), current heroin use (HR 1.97, $p = 0.02$), living in poverty (HR 2.0, $p < 0.01$), higher mean HIV viral load (HR 1.81, $p < 0.01$), and having a BMI < 18 (HR 5.84, $p < 0.01$). For MS and its criteria, only low HDL was associated with increased risk of mortality on univariate analysis (HR 1.84, $p = 0.01$). However, metabolic syndrome (adjusted HR 2.31, $p = 0.02$) and high triglycerides (adjusted HR 3.97, $p < 0.01$) were significantly associated with mortality beyond 36 months follow-up. MS, low HDL, and high triglycerides are associated with an increased risk of mortality in HIV-infected individuals.

Introduction

Metabolic syndrome, a syndrome of dyslipidemia, insulin resistance, and abdominal obesity, has long been recognized as an important metabolic complication associated with human immunodeficiency virus (HIV) disease and its treatment. Many studies have reported a high prevalence of metabolic syndrome in HIV-infected populations from different countries, ranging between 18–52.2%.[1–6] In HIV-negative populations, metabolic syndrome has been shown to increase the risk of cardiovascular events, cardiovascular mortality, and all-cause mortality.[7–13] The potential health impact of metabolic syndrome on HIV-infected populations is not as clearly understood. Studies have shown that HIV-infected patients with metabolic syndrome are more likely to have subclinical carotid artery atherosclerosis, a surrogate marker of cardiovascular disease, than those without metabolic syndrome.[14–16] However, there have been few published reports to date that have explored the impact of metabolic syndrome on mortality in HIV-infected populations.

It is important to understand the impact of metabolic syndrome in HIV-infected populations better, as it may lead to intensification of current screening and treatment recommendations for metabolic abnormalities in HIV. In this study, we assess the impact of metabolic syndrome and its individual components (dyslipidemia, insulin resistance, hypertension, and abdominal obesity) on all-cause mortality in a cohort of HIV-infected adults.

Subjects and Methods

We analyzed data from 567 subjects who were participants in the Nutrition for Healthy Living study (NFHL), a prospective study of nutrition and metabolic outcomes in HIV-infected adults from 1995–2005. Participants provided written informed consent, and the study was approved by the Institutional Review Boards of Tufts Medical Center, Massachusetts, and Miriam Hospital, Rhode Island. Subjects used in this analysis had study visits between 9/1/2000 and 1/31/2004, when metabolic measurements pertinent to the diagnosis of

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metabolic syndrome were collected. Mortality was ascertained by periodic review of the Massachusetts death registry, Rhode Island death registry, and the National Death Index. We reviewed these registries for all participant deaths occurring through December 31, 2006. To assure that all deaths through the end of 2006 were captured, the last review of the registry data was done in June 2008. Causes of death were determined by a panel of physicians (authors 1, 2, 4–6) using available medical records and/or death certificates, when no records were available. Cases were classified as 'unknown' when no records could be obtained to establish cause of death.

Demographic information was obtained from interviewer-administered questionnaires. Height, weight and waist circumference were measured in a standardized manner.[5,10] Plasma triglycerides, HDL, and glucose levels were obtained after a minimum 8-h fast and measured using standard enzymatic methods.[17] Hepatitis C virus (HCV) antibody was measured by enzyme immune-assay (EIA) followed by HCV RNA detection if antibody was positive. Participants were determined to have chronic hepatitis C if both antibody and RNA were positive. CD4 counts were measured using flow cytometry, and HIV RNA level was measured by reverse transcriptase polymerase chain reaction (PCR) assay (Roche Diagnostics; limit of detection 400 copies/mL). Further information regarding patient selection and data collection for the NFHL has been previously described.[5,10,18]

Metabolic syndrome was defined using the modified National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP III) guidelines, if at least three of the following five metabolic abnormalities were present: (1) abdominal obesity: waist circumference >102 cm for men, >88 cm for women; (2) high triglycerides: triglyceride level >150 mg/dL; (3) low high-density lipoprotein (HDL) cholesterol level: <40 mg/dL for men, <50 mg/dL for women; (4) hypertension: blood pressure ≥130/85 mm Hg (to which we included the prescription of hypertensive medications); and (5) impaired glucose metabolism: fasting glucose level: ≥100 mg/dL.[19] We included participants diagnosed with diabetes or receiving diabetes treatment in this category.

Analysis was performed using SAS 9.2 for Windows (SAS Institute, Cary, NC). Patient characteristics were compared based on survival status, and univariate survival models were determined using Cox Proportional Hazards. Final multivariate (adjusted) Cox models were constructed for metabolic syndrome and separately for each of its individual defining criteria. Baseline data was used in both unadjusted and adjusted Cox models for metabolic syndrome, its individual components, and all covariates included in the final models, as we are interested in determining which baseline metabolic characteristics are predictive of future mortality in HIV-infected individuals. Baseline was defined as the first visit on or after 9/1/2000. Observation time was from the baseline visit through 12/31/2006. Potential covariates for the adjusted analyses included a range of factors that were known or suspected of impacting survival in HIV-infected individuals (see Table 2). These baseline characteristics were considered as potential covariates for the final Cox models if the univariate hazard ratio was significant to $p < 0.2$ and final covariate selection was determined using stepwise regression modeling. Statistical significance for the multivariate hazard models was defined as $p < 0.05$. These retained covariates were used in the final multivariate Cox models for metabolic syndrome and its individual components and statistical significance for the final multivariate models was defined as $p < 0.05$.

The Cox proportional model assumes that hazard ratio for a predictor is constant over time, which is not always true. Of concern in this study was that impact of some covariates of interest might take time before a clinical impact would be observable. The assumption of proportional hazards was evaluated using Shoenfeld's residuals for all variables in the final model and found not to be supported for metabolic syndrome and high triglycerides (Test of proportional hazards, $p = 0.058$ and $p = 0.055$, respectively). Based on the shape of the smoothed Shoenfeld's residuals over time, we reparameterized these variables in the statistical model. We found the best model fit using a cutoff of 36 months and estimating two separate hazard ratios for each of these variables, one for early clinical impact (before 36 months) and one for late clinical impact (after 36 months). The p values for the both the global test of proportional hazards from the reparameterized models for metabolic syndrome and triglycerides were >0.2 ($p = 0.33$ and 0.60, respectively) and the individual terms tests were $p > 0.10$ for metabolic syndrome and $p > 0.2$ for triglycerides. These values are well above conventional $p \leq 0.05$ threshold of significance, indicating that these new models no longer violated the assumption of proportional hazards.

Results

There were 83 deaths (14.6%) in the cohort by the time of censorship on December 31, 2006. Median follow-up time in the cohort was 63 months. Table 1 lists the primary causes of death. Acute/subacute infection was the most common cause of death (16.9% HIV-related and 8.4% non-HIV related). Overall, more deaths were non-HIV related (54.2% non-HIV related vs. 36.1% HIV related). Of the non-HIV related deaths, four were due to a cardiovascular event (1 cardiac event and 3

Table 1. Primary Cause of Death (N = 83) Among 567 Study Participants

HIV related	N (%)	Non-HIV related	N (%)
AIDS[a]	8 (9.6)	Cardiac	2 (2.4)
Opportunistic infection[b]	3 (3.6)	Stroke	3 (3.6)
Pneumonia/sepsis[a]	11 (13.3)	Chronic liver disease	3 (3.6)
Lymphoma	4 (4.8)	Other chronic condition	2 (2.4)
Wasting/diarrhea	3 (3.6)	Malignancy	9 (10.8)
Other	1 (1.2)	Infection/ ARDS	7 (8.4)
		Substance abuse	12 (14.5)
Total HIV related	30 (36.1)	Trauma[c]	4 (4.8)
		Other	3 (3.6)
Sudden, unexplained	4 (4.8)		
Unknown	4 (4.8)	Total non-HIV related	45 (54.2)

[a]Not otherwise specified. [b]One case each of *Pneumocystis jirovecii* pneumonia, central nervous system fungal infection, and progressive multifocal leukoencephalopathy; [c]Includes accidents, homicide, and suicide.

Table 2. Baseline Characteristics of the Nutrition for Healthy Living Cohort by Survival Status as of 12/31/2006 and Univariate Hazard Ratios for Mortality (=567)

	Dead	*Alive*	*Univariate hazard ratio*	p *Value*[a]
Number (%)	83 (14.6)	484 (85.4)		
Demographics[b]				
Mean age, years[c]	46.2 ± 8.7	43.3 ± 7.2	1.24	< 0.01
Female	26 (31.3)	157 (32.4)	0.98	0.92
Race				
African American	29 (34.9)	167 (34.5)	Referent	—
White	44 (53.0)	245 (50.6)	1.01	0.97
Hispanic/other	10 (12.1)	72 (14.9)	0.77	0.48
Smoking history				
Never smoked	14 (16.9)	130 (26.9)	Referent	—
Prior smoker	15 (18.1)	106 (21.9)	1.28	0.51
Current smoker	54 (65.1)	248 (51.2)	1.99	0.02
Drug use history				
IDU ever	37 (44.6)	188 (38.8)	1.31	0.23
Current heroin use	14 (16.9)	44 (8.7)	1.97	0.02
Current cocaine use	19 (22.9)	90 (18.6)	1.29	0.33
Living in poverty	54 (66.7)	227 (49.1)	2.00	< 0.01
Chronic Hepatitis C infection	35 (50.7)	129 (33.3)	1.97	< 0.01
HIV related[b]				
Mean CD4 cells, $\times 10^9$/L[d]	323 ± 299	471 ± 291	0.81	< 0.01
Log_{10} HIV viral load, copies/ml	3.8 ± 1.2	3.0 ± 1.0	1.81	< 0.01
HIV transmission				
MSM	28 (33.3)	218 (45.6)	0.67	0.04
Heterosexual	37 (45.7)	207 (43.3)	1.09	0.70
IDU	32 (39.5)	148 (31.0)	1.49	0.08
On HAART therapy	55 (66.3)	350 (72.6)	0.76	0.23
Protease-inhibitor	40 (48.2)	211 (43.8)	1.16	0.49
NNRTI	27 (32.5)	167 (34.5)	0.96	0.87
Metabolic[b]				
BMI, kg/m^2				
Low (< 18)	7 (8.4)	4 (.8)	5.84	< 0.01
Normal (18.5 to < 25)	38 (45.8)	216 (44.6)	Referent	—
High (≥ 25)	38 (45.8)	264 (54.6)	0.83	0.43
Serum albumin, g/dL	3.7 ± 0.6	4.0 ± 0.4	0.27	< 0.01
Metabolic syndrome[e]	37 (45.7)	193 (40.8)	1.29	0.26
Abdominal obesity	28 (33.7)	144 (29.8)	1.20	0.44
Waist circumference, cm	92.3 ± 13.7	91.4 ± 12.6		
High triglycerides	46 (57.5)	240 (50.5)	1.35	0.19
Triglyceride level, mg/dL	195 (113–294)	151 (86–234)		
Low HDL	57 (71.3)	280 (59.1)	1.84	0.01
HDL level, mg/dL	35 (28-48)	39 (32-52)		
Hypertension	32 (40.0)	172 (36.3)	1.18	0.46
Systolic BP, mm Hg	122 ± 19	121 ± 17		
Diastolic BP, mm Hg	76 ± 12	77 ± 11		
High fasting glucose	9 (11.4)	51 (11.7)	1.03	0.94
Glucose level, mg/dL	78 (69–86)	79 (72–87)		
Lipid lowering drugs	4 (5.4)	26 (4.8)	0.97	0.87

Sample size varied based on missing data but no more than 5% data missing, except for serum albumin (n = 534), fasting serum glucose and fasting glucose > 100 mg/dL (n = 514 for both), and hepatitis C infected (n = 457). [a]p Value for univariate hazard ratio for mortality. [b]Values represent n (%), median (Q1–Q3), or mean ± SD. [c]Hazard ratio for 5-year increase in age. [d]Hazard ratio for 100 cells, x 10^9/L increase in mean CD4. [e]The cutoffs for components of metabolic syndrome are as follows: high triglycerides > 150 mg/dL, low HDL < 40 mg/dL (M) or < 50 mg/dL (F), high fasting glucose > 100 mg/dL, waist circumference > 102 cm (M) or > 88 cm (F), blood pressure ≥ 130/85 mm Hg.

strokes) and three were due to chronic liver disease. Of note, a total of 16 participants (19.3 %) had liver disease as either the primary or contributing cause of death, with most deaths due to a complication of cirrhosis such as infection or malignancy (hepatocellular carcinoma).

Characteristics of the cohort by survival status are shown in Table 2. The mean age of the cohort was 43.7 years of age, with those who died being on average 3 years older than those who survived at time of censorship. Approximately 30% of the cohort were women, and most identified themselves as White (50%) or African American (35%). Chronic hepatitis C infection (HR 1.97), current smoking (HR 1.99), heroin use (HR 1.97), and living on < $10,000 annually (HR 2.00) were associated with an increased risk of mortality.

Table 3. Adjusted Cox Proportional Hazards of Mortality for Metabolic Syndrome and its Components

	n	*Deaths*	*Adjusted hazard ratio (95%CI)*[a]	p *Value*
High triglycerides	512	73	1.52 (0.94, 2.48)	0.09
Low HDL	511	73	1.42 (0.82, 2.48)	0.22
High fasting glucose	477	73	1.06 (0.50, 2.23)	0.89
High waist circumference	515	74	1.23 (0.74, 2.03)	0.42
High blood pressure	504	71	0.92 (0.55, 1.53)	0.73
Metabolic syndrome[b]	511	74	1.17 (0.72, 1.91)	0.53

[a]Adjusted for age, current heroin use, albumin, BMI < 18.5, and HIV viral load. [b]The cutoffs for components of metabolic syndrome are as follows: high triglycerides > 150 mg/dL, low HDL < 40 mg/dL (M) or < 50 mg/dL (F), high fasting glucose > 100 mg/dL, waist circumference > 102 cm (M) or > 88 cm (F), blood pressure ≥ 130/85 mm Hg.

Neither gender nor race was associated with mortality in the cohort.

Decedents had a significantly lower mean CD4 count (323 vs. 471×10^9 cells/L,) and higher mean HIV viral loads (3.8 vs. 3.0 $\log_{10}$ copies/mL) at baseline, and both were associated with an increased risk of mortality ($p < 0.01$). Transmission of HIV through sexual activity by men-who-have-sex-with-men (MSM) was associated with a decreased risk of mortality (HR 0.69, $p = 0.04$), while there was a trend toward increased risk of mortality among those who contracted HIV through intravenous drug use (IDU) (HR 1.49, $p = 0.08$) Being on highly active antiretroviral therapy (HAART) at the time of inclusion was not associated with a risk of mortality in the cohort ($p = 0.23$) irrespective of protease inhibitor-based ($p = 0.49$) or non-nucleoside reverse transcriptase inhibitor-based (NNRTI) ($p = 0.87$) regimens.

Of the cohort, 41.5% met the criteria for the presence of the metabolic syndrome. The presence of metabolic syndrome in our cohort was primarily defined by the presence of high triglycerides, low HDL, and hypertension. On univariate analysis, no increased risk of mortality was seen with the presence of metabolic syndrome ($p = 0.26$). Of the components of metabolic syndrome, only the presence of low HDL was associated with an increased risk of mortality (HR 1.84, $p = 0.01$). Having a low body mass index (BMI) consistent with malnutrition ($< 18.5\,kg/m^2$) or lower albumin at baseline were also associated with a higher risk of mortality in the cohort ($p < 0.01$). Only 5% of the cohort reported being on lipid lowering drugs and this had no impact on survival in the cohort.

Results from the multivariate Cox models for metabolic syndrome and its components are shown in Table 3. Due to missing data, the median sample size and deaths included in the multivariate analysis were 511 and 73, respectively. Of the individual criteria for the metabolic syndrome, only high triglycerides approached significance for association with all-cause mortality (HR 1.52, $p = 0.09$) when adjusted for age, current heroin use, albumin, low BMI, and HIV viral load. Low HDL, while significantly associated with an increased risk of mortality in the univariate analysis, no longer remained significant in the adjusted analysis. Metabolic syndrome was also found not to be significantly associated with mortality in the initial adjusted analysis (HR 1.17, $p = 0.53$).

Table 4. Adjusted Cox Proportional Hazards of Mortality for High Triglycerides and Metabolic Syndrome Before and After 36 Months Follow-Up

	Adjusted hazard ratio (95%CI)[a]	p *Value*
High triglycerides ≤ 36 months	0.84 (0.43, 1.63)	0.61
High triglycerides > 36 months	3.97 (1.45, 6.50)	< 0.01
Metabolic syndrome ≤ 36 months[b]	0.65 (0.33, 1.28)	0.21
Metabolic syndrome > 36 months	2.31 (1.13, 4.69)	0.02

[a]Adjusted for age, current heroin use, albumin, BMI < 18.5, and HIV viral load. [b]The cutoffs for components of metabolic syndrome are as follows: high triglycerides > 150 mg/dL, low HDL < 40 mg/dL (M) or < 50 mg/dL (F), high fasting glucose > 100 mg/dL, waist circumference > 102 cm (M) or > 88 cm (F), blood pressure ≥ 130/85 mm Hg.

However, as stated in the methods section, high triglycerides and metabolic syndrome failed the assumption of proportional hazards over time. Based on Schoenfeld residuals, they demonstrated changing hazards after 36 months of follow-up. Therefore, we further explored the relationship of high triglycerides and metabolic syndrome with mortality using reparameterized models in which we determined the risk of mortality before and after 36 months (Table 4). We found that the risk of death from high triglycerides or metabolic syndrome was significant when participants with metabolic syndrome were tracked for 36 months of follow-up. In a reparameterized model, allowing for early (≤ 36 months) and late (> 36 months) clinical effects, the adjusted hazard ratio for high triglycerides was 0.84 prior to 36 months of follow-up ($p = 0.61$), and 3.97 after 36 months of follow-up ($p < 0.01$). Similarly, the adjusted hazard ratio for metabolic syndrome was 0.65 prior to 36 months of follow-up ($p = 0.21$), and 2.31 after 36 months of follow-up ($p = 0.02$).

Discussion

This is the first study to explore the impact of metabolic syndrome and its individual criteria on all-cause mortality in an HIV-infected population. We found that when mortality was examined as a function of the time of follow-up, metabolic syndrome and high triglycerides were both associated with an increased risk of death after 36 months of follow-up (adjusted HR 2.31 and 3.97, respectively). We also found that low HDL was associated with an increased risk of mortality in univariate analysis, though this did not remain significant in the adjusted model.

Our finding of an increased risk in all-cause mortality from metabolic syndrome is in agreement with previous studies in HIV-negative populations.[9,11–13] However, many of these studies in HIV-negative populations had a much longer follow-up time, and studied older individuals or persons with known or suspected cardiovascular disease. The finding of an increased risk of mortality in a younger HIV population suggests that there may be an accelerated risk of death associated with metabolic syndrome and its components in HIV disease. In addition, the change in hazard from no risk to greater than twofold risk seen for metabolic syndrome after 36 months of follow-up suggests a threshold effect of metabolic syndrome on mortality risk in HIV-infected individuals. To our knowledge, this

threshold effect has not been noted in studies of metabolic syndrome and mortality in HIV-negative populations.

We have previously shown in the NFHL cohort that metabolic syndrome is defined differently in HIV-infected individuals compared to the general population.[5] We found that dyslipidemia (99.1%), as represented by low HDL and/or high triglycerides, was the most prevalent criteria of metabolic syndrome in HIV-positive individuals. while insulin resistance (85.5%), for which abdominal obesity and/or high glucose may be considered surrogate markers, was the most prevalent criteria in the general population. The high prevalence of dyslipidemia in HIV-infected individuals with metabolic syndrome has been supported in multiple other studies.[1,3,4,20–22] This is not surprising since low HDL and high triglycerides are metabolic abnormalities that have long been associated with HIV disease prior to the use of highly active antiretroviral therapy.[23,24] Our study shows that, consistent with prior research, low HDL is associated with an increased risk of mortality, although after adjusting for age, heroin use, albumin, BMI, and HIV viral load, the association was not significant at the $p < 0.05$ level. The study also shows a threshold effect for high triglycerides, where there is an association with long-term mortality, but not short-term mortality, and the same threshold effect seen in metabolic syndrome may be a reflection of that risk.

In HIV-negative populations, metabolic syndrome has been associated with increased death from cardiovascular disease (34–44% of all deaths) as well as all-cause mortality.[9,11] In our HIV-infected population, death related to cardiovascular disease represented only 6% of all deaths and most common cause of death was due to acute/subacute infection (25.3%). The low proportion of cardiovascular deaths seen in this study may be due to several factors, including: (1) the differences in the components that typically define metabolic syndrome in HIV-infected versus -uninfected populations as outlined above; (2) relatively short duration of follow-up in our analysis, (3) the higher percentage of HIV-related deaths (36.1%) and death secondary to acute intoxication from substance abuse (14.5%). It is possible that cardiovascular causes were responsible for additional deaths in the "Sudden, unexplained" and "Unknown" categories.

Metabolic syndrome may be associated with increased mortality in the setting of HIV disease by several mechanisms. Metabolic syndrome may increase systemic inflammation in a host already beset by the on-going inflammation of HIV and opportunistic infections. Increased systemic inflammation, as defined by elevated C-reactive protein (CRP), has been shown to independently predict mortality in HIV positive and negative cohorts.[25–27] Falasca et al. reported increased serum levels of IL-18 in HIV-infected individuals with metabolic syndrome.[28] However, no consistent relationship has been found between metabolic syndrome and inflammatory markers, such as high-sensitivity-CRP, in other studies of HIV-infected cohorts and further studies are needed to explore the relationship between cytokines, metabolic syndrome, and mortality in HIV infection.[15,21]

Metabolic syndrome may also be a marker of a greater burden of accumulated HIV disease, which results in higher mortality. Prior studies have shown that high triglycerides and low HDL are associated with advanced HIV disease.[29,30] In the NFHL cohort, we have previously shown that metabolic syndrome is associated with progression of HIV disease with ≥ 0.5 log increase in viral load between follow-up visits being associated with a 1.8 relative risk of developing metabolic syndrome.[5] Similarly, other studies have shown a higher prevalence of metabolic syndrome among HIV-infected individuals with detectable viremia and an increased risk of metabolic syndrome in those with advanced HIV disease (CDC class C, VL > 100,000 or CD4 < 100).[22,31] Therefore, an increased risk of all-cause mortality from metabolic syndrome seen in our cohort may be a reflection of the inter-relationship of systemic inflammation, metabolic abnormalities, and HIV disease.

A limitation of our study was the relatively small size of our cohort and short follow-up time (63 months or 5.25 years) compared to previous studies in HIV-negative population.[8,9,11–13] The association between metabolic syndrome and mortality found in this study, despite a shorter follow-up period, adds strength to our conclusions. We chose our baseline assessment as the earliest period in which we had data to diagnose metabolic syndrome in the NFHL cohort, although participants may have met the criteria for metabolic syndrome and its individual components prior to that date. This is similar to clinical practice in which patients may have metabolic syndrome for some time before a formal diagnosis is made. Therefore, the true time period for an increase in the hazard for mortality due to metabolic syndrome or high triglycerides may be longer than the 36 months reported in our study. It should also be noted that the high prevalence of metabolic syndrome in our cohort may have been due, in part, to the antiretroviral regimens common in 1995–2005 and, with decreased use of protease-inhibitor-based regimens today, the incidence of metabolic syndrome may decrease over time. However, this would not impact the association found in our study between the presence of metabolic syndrome in HIV-infected individuals and an increased risk of mortality. The strengths of this study are the prospective design of the cohort, the detailed assessment of metabolic risk factors in this population, and the rigorous surveillance for deaths in the cohort.

In summary, we present evidence that metabolic syndrome, low HDL, or high triglycerides are associated with an increased risk of mortality in HIV-infected patients. While low HDL is associated with an increased risk of mortality in a univariate model, in adjusted models, the association was not significant. However, there is a clear threshold effect for high triglycerides and metabolic syndrome, which are associated with long-term mortality after 36 months of follow-up. Early screening for these metabolic abnormalities may be an important tool to identify HIV-infected persons who may be at increased risk of death over time.

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Author Disclosure Statement

The authors declare no conflict of interest including any financial, personal, or other relationships with other people or organizations that could inappropriately influence the results.

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