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Metabolic Abnormalities and Coronary Heart Disease Risk in Human Immunodeficiency Virus–Infected Adults

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Abstract

Background: Metabolic syndrome is a combination of risk factors for cardiovascular disease and diabetes, It has been reported to be increased in human immunodeficiency virus (HIV)–infected individuals.
Methods: In a cohort of HIV-infected adults we examined parameters that contribute to defining the metabolic syndrome and to estimating the 10-year risk of coronary heart disease (CHD). The study group consisted of 296 participants (217 men and 79 women) of mixed ethnicity with a mean age of 45.3 years.
Results: There was an appreciable prevalence of metabolic syndrome (30.0%), with the frequency increasing to 42.5% in those over 50 years of age. Those with the metabolic syndrome had a lower viral load. More women had abdominal obesity (59.5%) than men (20.7%, $P < 0.001$). The frequency of elevated plasma glucose was higher in females (37.2%) compared to males (16.9%, $P = 0.004$). High frequencies of decreased high-density lipoprotein cholesterol (HDL-C) and elevated blood pressure were seen in both sexes. Hypertriglyceridemia was less prevalent in African Americans. In those under 50 years of age, the 10-year CHD risk score for men was double that for women (6.2% vs 2.7%, $P < 0.001$). In older participants, the risk was similar between the sexes, with a third having scores over 10%.
Conclusions: The prevalence of metabolic syndrome was higher than in most other HIV cohorts. Those with the syndrome had significantly lower viral loads. Mean 10-year Framingham Cardiovascular Risk (FCR) scores were nearly doubled for those with metabolic syndrome. Both researchers and clinicians should consider age as well as sex when assessing patients with HIV infection for risks associated with metabolic syndrome.

Introduction

It is well established that dyslipidemia is a common metabolic hallmark of human immunodeficiency virus (HIV) infection and antiretroviral therapy (ART).[1] Fat maldistribution (previously known as lipodystrophy) is a common comorbidity in HIV infection,[2] and it is also associated with insulin resistance, dyslipidemia, and cardiovascular disease.[3] Numerous reports have confirmed that ART is associated with changes in body fat. Studies have indicated some drug combinations to be more strongly associated with these changes.[4] Body image is an important part of one's self-esteem, quality of life, and adherence to treatment.[5] Some people may normally prefer a larger body size to avoid any possible hint of HIV infection and stigma, whereas others may strive for an underweight body size and even refuse therapy to maintain their weight. Either scenario, being overweight or underweight, has negative health effects.

Metabolic syndrome is a constellation of risk factors for cardiovascular disease. In addition to dyslipidemia and central obesity, the other risk factors are hypertension and insulin resistance. Assessment of metabolic syndrome risk factors and risk of coronary artery disease (CAD) in the context of

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HIV is important for optimum clinical management and quality of life. Metabolic perturbations of ART impacting glucose homeostasis and atherogenic profiles include: Elevated plasma glucose, decreased insulin sensitivity, elevated total cholesterol (TC), very-low-density lipoprotein cholesterol (VLDL-C), and low-density lipoprotein cholesterol (LDL-C), lower high-density lipoprotein cholesterol (HDL-C), and elevated plasma triglycerides.[6] Furthermore, sex differences have been reported.[7] Problems associated with these metabolic abnormalities are numerous and pose life-compromising and -threatening conditions, including CAD , stroke, diabetes mellitus, and renal failure.

The presence of metabolic syndrome is a risk factor for the development of nonalcoholic fatty liver disease (NAFLD).[8] NAFLD can progress to the more severe nonalcoholic steatohepatitis, and is itself an independent risk factor for cardiovascular disease (CVD).[8] In the context of HIV, individuals have been shown to be at greater risk for NAFLD, probably due to use of ART and coinfection with hepatitis C.[9,10]

There is no consistent definition of metabolic syndrome. The World Health Organization (WHO) guidelines were originally proposed in 1999 as a working definition intended as a starting point for further refinement.[11] One commonly used definition is that of the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP),[12] and this is the definition we use. The WHO and National Heart, Lung, and Blood Institute have recently issued an interim statement[13] with the ultimate aim of a unified criteria. In this statement, the waist circumference cut off has country-specific definitions and the fasting glucose cut point has been lowered. In addition to waist circumference, we have used the ratio of waist to thigh, which is strongly associated with type 2 diabetes.[14]

Adeyemi and co-workers[15] recently reported on the prevalence of metabolic syndrome in a cohort of HIV-infected individuals aged over 50 years. They also calculated the 10-year Framingham Cardiac Risk (FCR) score and found that women had much lower FCR scores than men.

Previously, we have described our cohort of HIV-infected adults participating in the Symptoms and Genetics Study of HIV-infected adults.[16] In that report, we described personal characteristics and symptom prevalence in our sample of individuals living with HIV. In this report, we determine how our cohort compares with other samples of HIV infection in regard to parameters that define the presence of metabolic syndrome. We have assessed whether these parameters associated with the metabolic syndrome are associated with age, sex, viral load, CD4 count, or HIV medication use. We stratified our cohort to look at the prevalence of metabolic syndrome and FCR score in both younger and older patients, enabling a comparison with the previous study.[15]

Methods

Study design

This is a cross-sectional analysis of factors related to metabolic syndrome in the previously described Symptoms and Genetics Study cohort of 350 HIV-infected adults.[16] Eligible participants were English-speaking adults at least 18 years of age who had been diagnosed with HIV at least 3 months prior to enrollment. They were recruited using flyers posted at approved local HIV clinics and approved community sites. Data were collected at the baseline study visit between April, 2005, and December, 2007. Study visits were conducted at the University of California San Francisco (UCSF) General Clinical Research Center. In addition to completing the demographic and symptom questionnaires, the baseline assessment included a fasting blood sample for genetic and metabolic analysis, and obtaining anthropometric measures of height, weight, and circumference of neck, waist, hips, and thighs. Participants also provided urine samples for toxicology screening using RediCup® (Redwood Toxicology Laboratory, Inc, Santa Rosa CA). Written informed consent was obtained for all participants, and the UCSF Committee of Human Research approved the study protocol.

The study sample was not limited to self-identified men and women, but also included transgender adults. The criteria for metabolic syndrome are different for men and women; no guidelines are available for transgender individuals. Given that most of the transgender participants were taking hormone therapy that could influence lipid metabolism, categorizing them by sex would be inaccurate. Therefore, the 23 self-identified transgender adults were excluded from this analysis. Participants who tested positive for cocaine or methamphetamine by urine toxicology screening (RediCup,® Redwood Toxicology Laboratory, Inc, Santa Rosa CA) during data collection were also excluded. Inclusion of these individuals might have led to an overdiagnosis of metabolic syndrome because these drugs are known to elevate blood pressure. We failed to get a blood sample from 1 participant.

Measures

Participants reported demographic information, health and HIV history, and current HIV medication regimen. Medication regimens were subsequently coded into one of five categories: (1) Nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) only; (2) non NRTI-based regimen with an NRTI backbone; (3) protease inhibitor (PI) based with an NRTI backbone; (4) other regimens; or (5) no HIV medications. Most recent CD4, viral load, and fasting glucose values were obtained from the subject's medical record. Trained research staff obtained anthropometric and blood pressure measurements. Body mass index (BMI) was calculated as the weight in kilograms divided by squared height in meters.

A fasting blood sample was also collected at the study visit. The cholesterol and triglyceride (TG) content of plasma and lipoproteins was measured by automated chemical analysis using standards provided by the Centers for Disease Control.[17] HDL-C was determined after precipitation of apoliprotein B (apoB)-containing lipoproteins with dextran sulfate and magnesium.[18] LDL-C was calculated as total cholesterol (TC) minus HDL-C plus VLDL-C or by using the Friedewald equation when the TG was <400 mg/dL.[19]

Metabolic syndrome was defined according to theNCEP ATP III guidelines.[12] Three metabolic abnormalities out of a possible total of five were required: (1) Waist circumference >102 cm for men or >88 cm for women; (2) plasma triglycerides ≥ 150 mg/dL; (3) HDL-C <40 mg/dL for men or <50 mg/dL for women; (4) blood pressure $\geq 130/85$ mmHg; (5) fasting glucose ≥ 110 mg/dL. The FRC score was calculated for each participant as described in the Framingham Heart Study.[20]

Statistical analysis

Anthropometric, demographic, and clinical characteristics were summarized by descriptive statistics. Data are presented throughout as means ± standard deviation (SD). Group differences were assessed using chi-squared tests, Mann–Whitney tests, *t*-tests, or analysis of variance (ANOVA), as appropriate. CD4 counts were square root–transformed prior to analysis. Logistic regression analysis was conducted to identify predictors of metabolic syndrome while controlling for other factors. For all analyses, $P < 0.05$ was considered statistically significant. Statistical tests were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL) and STATA (StataCorp LP, College Station, TX).

Results

After exclusion of 23 transgender individuals and 31 of those who tested positive for cocaine or methamphetamines, the sample for this analysis included a total of 296 HIV-infected participants. The demographic and clinical characteristics are described in Table 1. A total of 267 individuals had sufficient data to enable an evaluation of presence or absence of metabolic syndrome. Compared to the 187 participants without metabolic syndrome, those categorized as having metabolic syndrome ($n = 80$) were older, had a lower viral load, and fewer were taking NRTI ART. There were no differences in CD4 count. A third of participants had been diagnosed with hepatitis C, but there was no difference in the prevalence of metabolic syndrome. The percentage of those taking hormone or steroid therapy was also similar. Although almost twice as many participants with metabolic syndrome were taking lipid-controlling medication, this was not a statistically significant finding. The overall frequency of reported alcohol use was similar. Those with metabolic syndrome were at almost twice the risk of developing coronary heart disease (CHD), as assessed using the Framingham 10-year percentage risk scores compared to those without (see Table 1), with a mean difference in

Table 1. Demographic Characteristics of Study Participants, HIV Status, and Medication History

			Metabolic syndrome		
	n	*Total 296*	*+80*	*−187*	*P value*
Female (%)		26.7	30.0	23.5	0.266
Age (years)		45.3 ± 8.3	47.0 ± 9.3	44.5 ± 7.6	0.032
Range		22–77	26–77	22–64	
Race					0.457
Caucasian (%)		42.6	37.5	43.3	
African American (%)		37.2	36.2	38.5	
Mixed/Asian/Other (%)		10.5	15.0	9.1	
Hispanic/Latino (%)		9.8	11.2	9.1	
Time since HIV diagnosis (years)		12.1 ± 6.9	12.0 ± 7.1	12.2 ± 6.8	0.805
Ever diagnosed with AIDS (%)		53.7	55.0	54.5	0.946
Time since AIDS diagnosis (years)		7.8 ± 5.8 (157)	6.9 ± 5.8 (45)	8.4 ± 5.8 (100)	0.135
Hepatitis C diagnosis (%)		33.8 (281)	36.8 (76)	33.5 (176)	0.611
CD4 count (cells/mL)		455 ± 267 (281)	478 ± 260 (76)	447 ± 266 (179)	0.324
Range		4-1740	27-1088	4-1740	
CD4 <200 (%)		16.7	14.5	17.3	0.575
Viral load (VL, copies/mL)					
Detectable VL (≥50; %)		47.6 (275)	43.2 (74)	47.4 (175)	0.545
VL ≥10,000 (%)		18.9 (275)	10.8 (74)	21.1 (175)	0.053
Median detectable VL		4529 (131)	2990 (32)	5533 (83)	0.045
HIV medications					0.331
NRTI based (%)		5.1	1.2	7.5	
NNRTI based (%)		19.3	18.8	18.7	
Protease inhibitor based (%)		42.2	46.2	42.8	
Other regimen (%)		3.7	2.5	3.7	
No current HIV medication (%)		29.1	31.2	27.3	
Taking hormones or steroids (%)		16.6	15.0	16.6	0.748
Taking lipid-controlling medication (%)		11.8	15.2	8.6	0.115
Framingham 10-year % CHD risk[a]		6.7 ± 5.5 (278)	10.0 ± 7.6 (74)	5.6 ± 4.1 (183)	<0.001
Relative risk		0.92 ± 0.58	1.25 ± 0.71	0.79 ± 0.46	<0.001

Values are percentages or means ± standard deviation (SD) with the numbers of subjects in parentheses (except median is provided for viral load). Differences between those with or without metabolic syndrome tested by chi-squared test or *t*-test, with the exception of viral load where the MannWhitney test was used. CD4 count was square root–transformed prior to testing.

[a]As previously defined [20].

Abbreviations: HIV, Human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; NRTI, nucleoside/nucleotide reverse trancriptase inhibitor; NNRTI, non-NRTI; CHD, coronary heart disease.

the scores of 4.43 [95% confidence interval (CI) 2.99–5.88; $P < 0.001$]. If we had used the new interim guidelines for defining metabolic syndrome,[13] with the cut point of 100 mg/dL for fasting glucose, 5 additional participants would have met the criteria.

There were significant differences in the racial/ethnic composition between male and female participants (Table 2) . Women had a higher mean BMI than men, which was reflected in a higher percentage of men with normal weight (48.4%) compared to women (29.1%), and a higher frequency of obesity among women (39.2%) compared to men (15.7%). The percentages of those who were overweight (BMI values, 25–29.9 kg/m^2) were similar between men and women (Table 2). Both waist-to-hip ratio, and waist-to-thigh ratio were higher in men than women. We found, in men, that the waist-to-thigh ratio was strongly associated with the presence of diabetes. The ratios in diabetics and nondiabetics were 2.14 ± 0.21 ($n = 13$) and 1.87 ± 0.20 ($n = 203$), respectively ($P < 0.001$). There was a less pronounced effect in women with the ratio in diabetics being 1.91 ± 0.25 ($n = 9$) and nondiabetics 1.75 ± 0.22 ($n = 70$) ($P = 0.041$).

Although there was no difference in systolic blood pressure, diastolic blood pressure was higher in men (Table 2). There was no sex difference in the frequency of diabetes or smoking. Although the prevalence of metabolic syndrome was similar for men (28.1%) and women (35.3%), there were significant differences in the underlying parameters that define this disorder. Women were more likely to have metabolic syndrome than men because of relatively high waist circumference or raised levels of glucose, whereas men were more likely to have elevated TGs. The prevalence of low HDL-C was similar between the sexes. Overall, 63.3% of participants had a total of two or more metabolic abnormalities; 59.9% of men and 72.5% of women ($P = 0.064$). Similarly, 11.0% had a total of four or more metabolic abnormalities—9.5% of men and 15.3% of women ($P = 0.180$). Men reported a higher alcohol use than women, but this difference was not significant (15.2% among men and 7.6% among women, $P = 0.087$; data not shown).

Both male and female participants had similar levels of TC [191 ± 52 vs. 190 ± 45 mg/dL, respectively; not significant]. These values are lower than those of comparable age

Table 2. Characteristics of Study Participants by Sex: All Participants

	n	*Males 217*	*Females 79*	*P value*
Age (years)		45.1 ± 8.3	46.0 ± 8.2	0.390
Race				<0.001
Caucasian (%)		49.8	22.8	
African American (%)		28.1	62.0	
Mixed/Asian/Other (%)		11.5	7.6	
Hispanic/Latino (%)		10.6	7.6	
BMI (kg/m^2)		26.0 ± 4.8	29.1 ± 6.3	<0.001
BMI <25		48.4	29.1	0.003
BMI 25–29.9		35.9	31.6	0.492
BMI ≥30		15.7	39.2	<0.001
Neck circumference (cm)		38.4 ± 2.8	34.5 ± 3.0	<0.001
Waist circumference (cm)		93.9 ± 12.2	93.8 ± 14.4	0.946
Waist-to-hip ratio		0.92 ± 0.07	0.86 ± 0.08	<0.001
Waist-to-thigh ratio		1.89 ± 0.21	1.77 ± 0.23	<0.001
Central obesity(%)[a]		61.3	64.6	0.608
Systolic blood pressure (mmHg)		126 ± 16	124 ± 19	0.248
Diastolic blood pressure (mmHg)		75.6 ± 10.3	71.7 ± 11.2	0.005
Diabetes (%)		6.0 (216)	11.4	0.12
Current smoker (%)		54.9 (213)	54.5 (77)	0.954
Metabolic syndrome(%)[b]		28.1 (199)	35.3 (68)	0.266
Glucose > 110 mg/dL (%)		16.9	37.2	0.004
Waist circumference >102 cm men; >88 cm women (%)		20.7	59.5	<0.001
TG ≥150 mg/dL (%)		49.1	32.1	0.01
HDL-C <40 mg/dl men; <50 mg/dl women (%)		40.7	42.3	0.805
Blood pressure ≥130/85 mmHg (%)		53.5	45.6	0.23
Framingham 10-year CHD risk (%)[c]		7.6 ± 5.4 (201)	4.6 ± 5.4 (77)	<0.0001
Relative risk[d]		0.87 ± 0.52	1.03 ± 0.71	0.077

Values are percentages or means ± standard deviation (SD) with the numbers of subjects in parentheses.

Post hoc analysis (Bonferonni-adjusted) showed a significant difference between Caucasians and African Americans ($P < 0.01$) and African Americans versus Mixed/Asian/Other ($P = 0.024$).

[a]As defined by the WHO.[11]

[b]As defined by the ATP III guidelines.[12]

[c]As defined by ref.[20]

[d]The relative 10-year CHD risk was calculated by dividing an individual's risk score by the average value for a person of the same sex and age in the Framingham population.

Abbreviations: BMI, Body mass index; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; CHD, coronary heart disease; WHO, World Health Organization.

and sex in the U.S. population at large[21]; TC was 10% lower in our sample of men and 8% lower in our sample of women. Male and female participants also have similar levels of LDL-C (110 ± 37 vs. 114 ± 35 mg/dL, respectively; N.S.). These values are lower than the U.S. population at large[21]; LDL-C was 23% lower in our sample of men and 12% lower in our sample of women.

We calculated the 10-year Framingham CHD risk scores[20] (Table 2) and found a difference, as expected, between men (7.6 ± 5.4%) and women (4.6 ± 5.4%; $P < 0.001$). Occurrence of smoking, one of the major factors influencing the score, was similar between men and women. The relative risk was calculated by dividing an individual's risk score by the average value for a person of the same sex and age in the Framingham population.[20] We found that men had somewhat lower relative risk (0.87 ± 0.52) than women (1.03 ± 0.71), but this was not statistically different (Table 2).

The occurrence of metabolic syndrome was not significantly different among the four ethnic/racial groups: Caucasians = 27.0%; African Americans = 28.7%; Hispanic/Latinos = 34.6%; others = 41.4% ($P = 0.457$). The overall 10-year CHD risk was also similar: Caucasians = 7.4 ± 5.8%; African Americans = 6.0 ± 5.4%; Hispanic/Latino = 5.8 ± 3.5%; others = 7.6 ±6.1% ($P = 0.162$).

Logistic regression analysis showed that with men age was the only significant and strong predictor of odds for having metabolic syndrome. The model only explained 3.5% of the variance for having metabolic syndrome. For women, age was not a predictor. Regression analysis allowed an examination of the extent to which ethnicity confounded the differences seen between men and women. With the exception of frequency of elevated TGs, the differences in parameters between the sexes seen in Table 2 were still highly significant after accounting for ethnicity. The waist-to-thigh ratio was lower among African Americans, in both men and women, compared to all other ethnicities. The waist-to- hip ratio was also lower, but only in African-American men when compared to men of other ethnicities. Diastolic blood pressure was higher among African-American women compared to women of other ethnicities. The frequency of elevated TGs was lower among African Americans compared to other ethnicities, and within each ethnic group there were no sex differences.

To compare the prevalence of metabolic syndrome and CHD risk scores in younger and older participants, the sample was dichotomized to less than 50 years of age and 50 years of age or older. The differences in ethnic/racial origin were more pronounced in the younger group (Table 3) compared to the older group (Table 4). The relative sex

Table 3. Characteristics of Study Participants by Sex: Participants under 50 Years of Age

	n	*Males 151*	*Females 54*	*P value*
Age (years)		40.8 ± 5.6	42.0 ± 6.0	0.200
Race				<0.001
Caucasian (%)		46.4	13.0	
African American (%)		27.2	66.7	
Mixed/Asian/Other (%)		11.9	9.3	
Hispanic/Latino (%)		14.6	11.1	
BMI (kg/m^2)		26.0 ± 4.9	29.1 ± 6.2	0.001
Neck circumference (cm)		38.3 ± 2.6	34.6 ± 3.2	<0.001
Waist circumference (cm)		92.4 ± 12.2	93.5 ± 14.3	0.627
Waist-to-hip ratio		0.90 ± 0.07	0.85 ± 0.07	<0.001
Waist-to-thigh ratio		1.83 ± 0.19	1.74 ± 0.22	0.008
Central obesity (%)[a]		55.0	59.3	0.585
Systolic blood pressure (mmHg)		126 ± 15	122 ± 18	0.141
Diastolic blood pressure (mmHg)		75.4 ± 9.9	72.2 ± 11.4	0.052
Diabetes (%)		2.6	9.3	0.057
Current smoker (%)		60.4 (149)	61.5 (52)	0.885
Metabolic syndrome (%)[b]		22.5 (138)	30.6 (49)	0.255
Glucose >110 mg/dL (%)		12.5	36.4	0.002
Waist circumference >102cm men; >88 cm women (%)		17.2	55.6	<0.001
TG ≥150 mg/dL (%)		46.7	26.4	0.01
HDL-C <40 mg/dL men; <50 mg/dL women (%)		42.1	37.7	0.583
Blood pressure ≥130/85 mmHg (%)		50.3	42.6	0.329
Framingham 10-year CHD risk (%)[c]		6.2 ± 4.1 (143)	2.7 ± 1.7 (52)	<0.001
Relative risk[d]		0.94 ± 0.55	1.10 ± 0.66	0.099

Values are percentages or means ± standard deviation (SD). If the number of subjects differs from that at the top of the column, the correct number is in parentheses.

Post hoc analysis (Bonferonni-adjusted) showed a significant difference between Caucasians and African Americans ($P < 0.01$).

[a]As defined by the WHO.

[b]As defined by the ATP III guidelines.[12]

[c]As previously defined.[20]

[d]The relative 10-year CHD risk was calculated by dividing an individual's risk score by the average value for a person of the same sex and age in the Framingham population.

Abbreviations: BMI, Body mass index; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; CHD, coronary heart disease; WHO, World Health Organization; ATP III, Adult Treatment Panel III.

Table 4. Characteristics of Study Participants by Sex: Participants 50 Years of Age or Over

	n	*Males 66*	*Females 25*	*P value*
Age (years)		54.8 ± 4.5	54.7 ± 4.3	0.917
Race				0.235
Caucasian (%)		57.6	44.0	
African American (%)		30.3	52.0	
Mixed/Asian/Other (%)		10.6	4.0	
Hispanic/Latino (%)		1.5	0.0	
BMI (kg/m^2)		26.2 ± 4.6	29.3 ± 6.7	0.044
Neck circumference (cm)		38.5 ± 3.2	34.2 ± 2.7	<0.001
Waist circumference (cm)		97.4 ± 11.5	94.5 ± 14.9	0.326
Waist-to-hip ratio		0.95 ± 0.07	0.87 ± 0.09	<0.001
Waist-to-thigh ratio		2.03 ± 0.21	1.82 ± 0.23	<0.001
Central obesity (%)[a]		75.8	76.0	0.981
Systolic blood pressure (mmHg)		127 ± 17	127 ± 20	0.98
Diastolic blood pressure (mmHg)		76.0 ± 11.0	70.5 ± 10.9	0.035
Diabetes (%)		13.6	16.0	0.774
Current smoker (%)		42.2 (64)	40.0	0.851
Metabolic syndrome(%)[b]		41.0 (61)	47.4 (19)	0.623
Glucose >110 mg/dL (%)		26.0	40.0	0.37
Waist Circumference >102cm men; >88cm women (%)		28.8	68.0	0.001
TG ≥150 mg/dL (%)		54.8	44.0	0.36
HDL-C <40 mg/dL men; <50 mg/dL women (%)		37.3	52.0	0.211
Blood pressure ≥130/85 mm Hg (%)		60.6	52.0	0.457
Framingham 10-year CHD risk (%)[c]		10.9 ± 6.7 (57)	8.5 ± 7.8	0.159
Relative risk[d]		0.70 ± 0.41	0.89 ± 0.80	0.266

Values are percentages or means ± standard deviation (SD) with the numbers of subjects in parentheses.

[a]As defined by the WHO.[11]

[b]As defined by the ATP III guidelines.[12]

[c] As previously defined.[20]

[d]The relative 10-year CHD risk was calculated by dividing an individual's risk score by the average value for a person of the same sex and age in the Framingham population.

Abbreviations: BMI, Body mass index; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; CHD, coronary heart disease; WHO, World Health Organization; ATP III, Adult Treatment Panel III.

differences in BMI, neck circumference, waist-to-hip ratio, and waist-to-thigh ratio observed in the total population were seen in both the younger and older groups. The higher diastolic blood pressure among men was more pronounced among older participants. There was a trend toward a higher occurrence of diabetes in younger women (9.3%) compared to younger men (2.6%; $P = 0.057$). The prevalence of diabetes in men and women was similar in the older group of participants. The proportion of those who smoked was higher in younger men (60.4%) compared to older men (42.2%; $P = 0.014$), and there was a similar trend among women (61.5% vs 40.0%; $P = 0.076$). Although there was no significant difference in the prevalence of metabolic syndrome between males and females in either age group, the occurrence in older men was nearly doubled (41.0%) compared to younger men (22.5%, $P = 0.007$). In older women, although the prevalence was higher than in younger women (47.4% vs 30.6%), it was not significantly so ($P = 0.194$).

There were some differences between the two age groups in the parameters that define the metabolic syndrome. As in the total population, more women had elevated levels of glucose than men of a similar age. In the younger group, there was a pronounced effect, with three times more women affected than men (36.4% vs. 12.5%, $P = 0.002$) (Table 3). However, there was no significant sex difference in the older group. Whereas the percentage of participants, both male and female, with a high waist circumference increased with age, the large sex disparity was maintained, with three times as many women in the younger group and over twice as many in the older group affected (Tables 3 and 4). There were more men in the under 50-year-old group with raised TGs (46.7%) than women (26.4%; $P = 0.010$). There was no significant sex difference in the older group. As with the overall cohort, in the two age groups, there were no significant sex differences in the prevalence of decreased levels of HDL-C or of elevated blood pressure, nor were there changes in these parameters with age.

The FCR CHD score in younger men was double that seen in younger women (Table 3). This sex difference was not seen in the older age group, but the score increased in older versus younger men (10.9 ± 6.7 vs. 6.2 ± 4.1; $p < 0.001$) and older versus younger women (8.5 ± 7.8 vs. 2.7 ± 1.7; $P < 0.001$). The occurrence of high CHD risk scores (over 10%) in younger men compared to younger women was particularly striking; whereas 8.4% of men were in this category, there were no women in this category ($P = 0.031$). In older participants, both males and females, the proportion with risk scores over 10% had risen sharply and there was no longer any difference by sex (32.8% vs. 32.0%). Virtually absent in the younger age group, the frequency of individual risk

scores over 20% was similar in older men (10.3%) and older women (12.0%).

Discussion

In this sample of HIV-infected adults, there was an appreciable occurrence of metabolic syndrome, which confers an increased risk of developing type II diabetes and symptoms of CVD. Our population was ethnically diverse, with fewer Caucasians and more African Americans among the women. There was no significant difference in the occurrence of metabolic syndrome among the four ethnic groups.

Women were significantly more overweight than men, as indicated by their higher mean BMI values. Interestingly, as others have shown,[14] waist-to-thigh ratio was associated with diabetes especially in men. Women, particularly those under 50 years of age, had a higher prevalence of diabetes and elevated levels of glucose than men, and had (in both age groups) a higher frequency of increased waist circumference. With men, notably those under 50 years of age, the prevalence of elevated TGs was higher than for women. Higher TGs might, in part, be explained by the trend toward a higher prevalence of reported alcohol use among men, The pattern of metabolic syndrome differed between the sexes, a reflection of differences in the occurrence of metabolic abnormalities.

Those with metabolic syndrome were slightly older than those without, had a lower viral load, but had a similar CD4 count, similar frequency of acquired immunodeficiency syndrome (AIDS) diagnosis, and similar time since HIV or AIDS diagnosis. The two groups showed no difference in the percentage receiving ART, similar to a previous study,[22] although fewer of those with metabolic syndrome were taking NRTI-based medication, probably reflecting targeted clinical management of their metabolic abnormalities.

In total, 30.0% of participants had metabolic syndrome, with more women (35.3%) affected than men (28.1%), This high prevalence in women is slightly higher than the 33% in the Women's Interagency Study.[23] In one report, a higher frequency in HIV-positive women was observed compared to men,[24] whereas in other studies there was no difference.[25–28] The prevalence we found is higher than reported in other studies of HIV patients. Pao et al.[29] cataloged of 12 studies of metabolic syndrome in HIV cohorts. Three reports, from Pavia, Italy, cited frequencies above 30.0%. The prevalence in the other nine studies ranged from 11.4% to 25.5%, In comparison, the frequency in the general U.S. population reported in 2002 was 21.8%.[30] However, in a more recent study, 34% of U.S. adults were reported to meet the criteria.[31] There is considerable disparity in the literature concerning whether the prevalence of metabolic syndrome is indeed higher among HIV-infected individuals. Two reports, both using matched control groups, demonstrate this conundrum: One found a similar frequency in patients (25.5%) compared to controls (26.5%),[27] whereas the other found a higher occurrence in patients (15.8%) than controls (3.2%).[32]

We also examined the frequency of two or more, and four or more metabolic abnormalities 63.3% had at least two abnormalities, This is somewhat more than the 49% in a multicenter study of HIV-infected patients.[33] For those with four or more metabolic abnormalities, men had a slightly lower frequency (9.5%) than reported for the male population at large (11.1%),[30] but for women it was higher (15.3% vs. 9.6%).

Older men (>50 years) had nearly double the prevalence of metabolic syndrome compared to younger men, and there was a trend toward a higher frequency in women. The percentages of men (41.0%) and women (47.4%) affected is somewhat higher than reported for a similar population of where the respective values were 34% and 36%.[15] We found a much higher percentage of older women with elevated waist circumference compared to men. However, Adeyemi and colleagues observed a much higher frequency of low HDL-C in men (61%) compared to women (21%), whereas our study showed a trend toward a higher frequency in women. Despite a similar high frequency of raised glucose levels in older women, in both studies we saw a nearly three-fold higher prevalence of diabetes (16% vs. 6%). Adeyemi et al.[15] reported a low mean 10-year cardiac risk scores (FCR) for the older female participants (3.1%) compared to 11.8% for the men. We found much higher mean scores in older women (8.5%), closer to what might be expected for this age group in the general population.[20]

In conclusion, we examined the parameters that define metabolic syndrome in a sample of HIV-infected men and women. The prevalence was higher than in most other studies, with the frequency increasing to 42.5% in those over 50 years of age. Those with the syndrome, and detectable HIV virus, had significantly lower median viral loads. Mean 10-year FCR scores were nearly doubled for those with metabolic syndrome. Both researchers and clinicians should consider age as well as sex when assessing patients with HIV-infection for risks associated with metabolic syndrome.

Author Disclosure Statement

No competing financial interests exist for any of the authors.

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