

# Relationship Between Neck Circumference and Cardiometabolic Parameters in HIV-Infected and Non-HIV-Infected Adults

KATHLEEN V. FITCH, MSN  
TAKARA L. STANLEY, MD  
SARA E. LOOBY, PHD

ALISON M. ROPE, AB  
STEVEN K. GRINSPOON, MD

**OBJECTIVE**—Upper body fat is associated with increased cardiometabolic risk. More recently, neck circumference (NC) and/or neck fat have been associated with hyperlipidemia, impaired glucose homeostasis, and hypertension. The objective of this study was to determine whether this relationship is evident in HIV-infected individuals, who often exhibit changes in relative fat distribution, and to determine whether NC is independently associated with carotid intima-media thickness (cIMT) in HIV and non-HIV-infected patients.

**RESEARCH DESIGN AND METHODS**—Body composition, including anthropometrics, visceral adipose tissue assessment by CT, and metabolic parameters, including lipids, cIMT, and oral glucose tolerance test, were measured in 174 men and women with HIV infection and 154 non-HIV-infected subjects. NC was measured in triplicate inferior to the laryngeal prominence.

**RESULTS**—In univariate analysis, NC was significantly and positively related to blood pressure, hemoglobin A<sub>1c</sub>, glucose, and insulin and significantly and negatively related to HDL cholesterol in HIV-infected individuals and HIV-negative control subjects. NC was significantly associated with cIMT in univariate regression analysis among HIV-infected ( $r = 0.21$ ,  $P = 0.006$ ) and non-HIV-infected ( $r = 0.31$ ,  $P = 0.0001$ ) patients. This relationship remained significant among non-HIV-infected patients ( $R^2 = 0.45$ ,  $P < 0.001$ ) but not HIV-infected patients in multivariate modeling controlling for age, sex, race, smoking hypertension, glucose, and lipids.

**CONCLUSIONS**—Among both HIV and non-HIV-infected patients, increased NC is strongly associated with decreased HDL and impaired glucose homeostasis. Among non-HIV-infected subjects, NC also predicts increased cIMT when controlling for traditional risk factors.

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**C**ardiovascular disease (CVD) is a leading cause of morbidity and mortality in the U.S.. In HIV disease, CVD is more prevalent than in the general population (1). Adiposity is a well known risk factor for cardiovascular morbidity, and recent research highlights the cardiovascular risk conferred by specific patterns of fat distribution, particularly visceral and upper body adiposity (2,3).

The role of body fat distribution is of particular importance in HIV infection, because over half of infected individuals experience peripheral fat atrophy and/or increased central adiposity. Body fat redistribution may be related to HIV itself but is more commonly related to antiretroviral (ARV) medications, traditional CVD risk factors, and poor lifestyle habits (4,5). The cardiometabolic risk conferred

by increased visceral fat in HIV infection has been well characterized (6,7). Upper trunk fat has also been identified as a strong determinant of insulin resistance in this population (8); however, neck circumference (NC) has not been investigated. In the non-HIV-infected population, a recent study looking at NC concluded that NC is associated with CVD risk factors even after adjustment for visceral adipose tissue (VAT) and BMI (9). In the current study, we sought to examine NC among HIV-infected and non-HIV-infected men and women to determine whether NC independently relates to cardiometabolic risk controlling for BMI and more sophisticated measurements of adiposity. Furthermore, we sought for the first time to investigate the association of NC to subclinical atherosclerosis as measured by carotid intima-media thickness (cIMT).

## RESEARCH DESIGN AND METHODS

Data were collected from 2000 to 2007 in 174 HIV-infected subjects at the Massachusetts General Hospital (MGH) and the Massachusetts Institute of Technology (MIT), and 154 HIV-negative subjects simultaneously were recruited from the community as control subjects. The subjects in this study comprise a convenience cohort for the purposes of the current analysis, consisting of baseline data collected for two observational studies, in which NC and cIMT data were available in HIV-infected and BMI, age, and race-matched non-HIV-infected control subjects recruited based on similar criteria. The first cohort recruited consisted of HIV-infected women and female control subjects, whereas the second cohort consisted of HIV and non-HIV-infected men and women. For each study, consecutive HIV-infected subjects between 18 and 65 years of age were enrolled without regard to fat distribution. Subjects in both the HIV and non-HIV groups were excluded if they had a known history of diabetes; were receiving insulin, antidiabetic agents,

From the Program in Nutritional Metabolism and Neuroendocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.

Corresponding author: Steven K. Grinspoon, [sgrinspoon@partners.org](mailto:sgrinspoon@partners.org).

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K.V.F. and T.L.S. contributed equally to this work.

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glucocorticoids, growth hormone, supra-physiologic testosterone replacement, or anabolic steroids; or were pregnant or breastfeeding within the past year. Partial data on 199 patients were published previously (10) but did not include an analysis of NC. All participants provided informed consent. The studies were approved by the Institutional Review Boards at both the MGH and MIT.

### Body composition

Weight and anthropometric measurements were determined before breakfast. All measurements were obtained using a nonelastic tape; measurements were obtained in triplicate and then averaged. NC was obtained with the subject sitting with head in the Frankfort Horizontal Plane position. A measuring tape was applied around the neck inferior to the laryngeal prominence and perpendicular to the long axis of the neck, and the minimal circumference was measured and recorded to the nearest 0.1 cm. Intrasubject variability in the NC measurement was examined, and the difference between maximal and minimal measures averaged 0.3%. Waist, hip, arm, and chest circumferences were determined. To assess abdominal visceral and subcutaneous adipose tissue area (VAT and SAT, respectively), a cross-sectional abdominal CT scan at the level of the L4 pedicle was performed (11). Dual X-ray absorptiometry to assess body fat composition was performed using a Hologic densitometer (Hologic, Waltham, MA). In one of the cohorts, physical activity was assessed using the Modifiable Activity Questionnaire (12).

### cIMT

Imaging was conducted using a 7.5-MHz phased-array transducer (SONOS 2000/2500; Hewlett-Packard, Andover, MA) as described previously (13). The published reproducibility of the technique is excellent with a SD of 0.007 mm (13). The cIMT over the length of the left and right segments was averaged. Although there were no statistical differences between left and right cIMT measurements, with a good univariate correlation between the two sides ( $r = 0.65$ ,  $P < 0.001$ ), there was some intraindividual variability of left and right cIMT measurements because of the focal nature of atherosclerosis. Average cIMT was used to reduce variability of this measurement, as reported in prior studies, such as the Atherosclerosis Risk in Communities Study (ARIC) cohort (14). To determine whether increasing

neck size affected the variability of the cIMT measurement, we assessed the variance of cIMT across quartiles of NC. The SEM for the lowest quartile was 0.014, and the SEM for the highest quartile was 0.014, suggesting minimal change in variance in our cIMT data with increasing NC.

### Biochemical indexes

Fasting insulin, glucose, triglycerides, cholesterol, HDL cholesterol, LDL cholesterol, and CD4 were measured using standard techniques. HIV testing was performed by chemiluminometric immunoassay and confirmed by Western blot. HIV viral load was measured using ultrasensitive assay.

A 75-g oral glucose tolerance test (OGTT) was performed after a 12-h overnight fast.

### Statistical analysis

Comparison of demographic variables was made using Student *t* test for continuous variables and the  $\chi^2$  test for noncontinuous variables. Pearson correlation coefficients were assessed in univariate analysis. Multivariate regression analysis using standard least squares was performed. All multivariate analyses controlled for age, sex, race, and HIV status. Cumulative exposure to ARVs by class, e.g., nucleoside reverse transcriptase inhibitor (NRTI), was used when examining the effect of ARVs. In multivariate modeling for cIMT, there was not an interaction between NC and HIV status, permitting use of a combined model. For clinical relevance, we also provided separate models of the relationship between NC and cIMT. The study was able to detect an approximate 9- $\mu$ m change in cIMT for each 1-cm change in NC, with power of 0.8 in the HIV and non-HIV groups. All analyses were performed using SAS JMP (SAS Institute, Cary, NC). Results are means  $\pm$  SEM.

## RESULTS

### Demographic data

HIV-infected and control subjects were similar in age and sex (Table 1). There was no difference in racial composition of the groups (HIV, 36% Caucasian, 43% black, 16% Hispanic, 5% other; non-HIV, 38% Caucasian, 47% black, 10% Hispanic, 5% other;  $P = 0.18$ ). The HIV group had a significantly higher percentage of current smokers (52 versus 26%) and previous smokers (16 versus 12%) and a higher number of lifetime

pack-years (Table 1). Although known diabetes was an exclusion criterion for entry into the study, a small percentage of subjects had a fasting glucose or 2-h glucose in diabetic range (Table 1).

Among the HIV-infected group, 84% of HIV-infected subjects were currently being treated with combination ARV therapy: 45% currently on protease inhibitors (PIs), 82% on NRTIs, and 25% on non-nucleoside reverse transcriptase inhibitors (NNRTIs). See Table 1 for duration of use of each class of antiretroviral therapy.

### Metabolic parameters

Two-hour glucose, fasting insulin, and triglycerides were all significantly higher among HIV-infected subjects compared with control subjects. In contrast, HDL cholesterol was significantly lower among HIV-infected subjects. These differences persisted when controlling for sex (see adjusted *P* value; Table 1).

### Anthropometric measurements

Waist-to-hip ratio (WHR) and VAT were significantly higher among HIV-infected subjects, whereas SAT and arm circumference were significantly lower among HIV-infected subjects. These differences persisted when controlling for sex between the groups (Table 1). NC was similar between groups and was not significantly affected by HIV status when controlling for age, race, and sex ( $P = 0.67$  for HIV status). By design, BMI was not different between the two groups (Table 1).

### Univariate regression analysis relating cardiometabolic parameters to NC

In univariate regression analysis among all subjects, NC was significantly related to numerous body composition measures and metabolic parameters (Table 2). In a subset for which exercise data were available ( $n = 199$ ), physical activity was not related to NC ( $P = 0.38$ ). In the HIV group, with the exception of triglycerides, NC was related to the same parameters as the entire cohort. Among non-HIV-infected subjects, NC was also related to the same parameters as in the entire cohort. Duration of HIV infection ( $r = 0.16$ ,  $P = 0.03$ ) and cumulative exposure to NRTIs ( $r = 0.15$ ,  $P = 0.05$ ) did show an association with NC in univariate analysis, but neither was significant when controlling for age. NC was not significantly associated with cumulative exposure to PIs ( $P = 0.25$ ) or NNRTIs ( $P = 0.10$ ). CD4 count was not

Table 1—Demographic and clinical characteristics of the study population

Parameter	Group		P value	Adjusted P value*
	HIV-infected	HIV-negative		
N	174	154		
Demographics				
Age (years)	44 ± 1	43 ± 1	0.43	
Sex (n [%])			0.08	
Male	43 (25)	26 (17)		
Female	131 (75)	128 (83)		
Race (n [%])			0.12	
Caucasian	89 (51)	92 (60)		
Non-Caucasian	85 (49)	62 (40)		
Current smoking (n [%])	90 (52)	40 (26)	<0.0001	
Lifetime smoking (pack-years)	12.1 ± 1.0	4.6 ± 1.1	<0.0001	
Diabetes (n [%])†	9 (6)	3 (2)	0.10	
HIV parameters				
Duration HIV (months)	121 ± 5	N/A		
CD4 (n/mm <sup>3</sup> )	510 ± 21	N/A		
HIV viral load (copies/mL)	6,075 ± 1,320	N/A		
Duration PI use (months)	30 ± 3	N/A		
Duration NRTI use (months)	59 ± 4	N/A		
Duration NNRTI use (months)	16 ± 2	N/A		
Metabolic parameters				
Blood pressure (mmHg)				
Systolic	116 ± 1	114 ± 1	0.24	0.43
Diastolic	74 ± 1	72 ± 1	0.05	0.12
Fasting glucose (mg/dL)	87 ± 1	84 ± 1	0.04	0.07
2-h glucose (mg/dL)	128 ± 4	108 ± 3	<0.0001	<0.0001
Fasting insulin (μU/mL)	8.9 ± 0.7	5.7 ± 0.3	0.0002	<0.0001
Cholesterol (mg/dL)				
Total	183 ± 3	176 ± 3	0.12	0.07
LDL	109 ± 3	105 ± 3	0.32	0.27
HDL	46 ± 1	56 ± 1	<0.0001	<0.0001
Triglycerides (mg/dL)	149 ± 11	79 ± 3	<0.0001	<0.0001
Average cIMT (mm)	0.68 ± 0.01	0.66 ± 0.01	0.26	0.48
Body composition parameters				
BMI (kg/m <sup>2</sup> )	26.6 ± 0.4	27.5 ± 0.4	0.11	0.10
WHR	0.93 ± 0.01	0.86 ± 0.01	<0.0001	<0.0001
SAT area (cm <sup>2</sup> )	251 ± 10	284 ± 11	0.02	0.04
VAT area (cm <sup>2</sup> )	109 ± 5	87 ± 5	0.001	0.004
Arm fat by DEXA (kg)	2.6 ± 0.1	3.0 ± 0.1	0.005	0.01
Trunk fat by DEXA (kg)	11.6 ± 0.4	11.6 ± 0.4	0.91	0.94
Iliac waist (cm)	94 ± 1.0	91 ± 1.1	0.09	0.15
NC (cm)	37.0 ± 0.3	36.4 ± 0.3	0.50	0.80
Arm circumference (cm)	31.0 ± 0.4	32.1 ± 0.3	0.03	0.008

Data are reported as means ± SEM or percentage. N/A, not applicable. \*P value for effect of HIV infection controlling for sex. †Diabetes diagnosed by 2-h OGTT, fasting blood glucose ≥126, and/or 2-h blood glucose ≥200.

significantly associated with NC on univariate analysis ( $P = 0.17$ ). HIV viral load was also not associated with NC ( $P = 0.89$ ).

#### Univariate regression analysis relating cardiometabolic parameters to cIMT

In univariate regression analysis among all subjects, cIMT was significantly related to age, BP, hemoglobin A<sub>1c</sub>, fasting glucose,

waist circumference, WHR, BMI, VAT, smoking pack-years, and NC. It is noteworthy that dual-energy X-ray absorptiometry (DEXA) measurements of upper arm fat and trunk fat were not significantly associated with cIMT, in contrast with the highly significant relationship seen between NC and cIMT in all groups. Subgroup analysis among HIV and HIV-negative subjects is shown in Table 3.

#### Multivariate analysis of NC in relationship to lipid and glucose parameters

In multivariate modeling among the entire cohort, controlling for age, sex, race, HIV status, and VAT, NC was no longer a significant predictor of BP, LDL, or triglyceride (data not shown). However, NC remained a strong independent predictor of HDL ( $P = 0.001$ ), glucose ( $P = 0.02$ ), and insulin ( $P = 0.0002$ ). There was no relationship between NC and 2-h glucose (Supplementary Table 1). When BMI was used in the model instead of VAT, results were similar (Supplementary Table 2). In subanalyses, multivariate modeling was performed separately for the HIV-infected and HIV-negative groups (Supplementary Tables 1 and 2). For the HIV-negative cohort, NC remained a significant predictor of HDL but did not significantly predict glucose or insulin. In the HIV-infected group, NC remained a significant independent predictor of HDL ( $P = 0.02$ ) and fasting insulin ( $P = 0.002$ ). When cumulative exposure to PI, NRTI, and NNRTI was added to the models, results were similar.

#### Multivariate analysis of NC in relationship to cIMT

Among the entire group of subjects, NC was also a significant predictor of average cIMT in multivariate modeling controlling for HIV status and traditional cardiovascular risk factors, including age, sex, race, pack-years of smoking, hypertension or use of antihypertensive medications, glucose, and LDL ( $P = 0.02$  for NC; for model,  $R^2 = 0.41$ ,  $P < 0.0001$ , Table 4). In this model, each 1-cm increase in NC was associated with a 5-μm increase in cIMT. This association remained significant when additionally controlling for VAT ( $P = 0.001$  for NC; for model,  $R^2 = 0.42$ ,  $P < 0.0001$ ) but was no longer significant with BMI in the model rather than VAT ( $P = 0.90$  for NC). In sensitivity analysis using only women, NC remained significantly associated with cIMT. In the subset for which physical activity was available, adding activity to the model did not change the significance of NC in relationship to cIMT ( $P = 0.02$ ).

In a separate analysis among non-HIV control subjects, NC was significantly associated with cIMT, controlling for traditional risk factors, including age, sex, race, smoking, hypertension, glucose, and lipids ( $P = 0.005$  for NC; for model,  $R^2 = 0.45$ ,  $P < 0.0001$ , Table 4) and in a model controlling for traditional risk factors and VAT ( $P = 0.005$  for NC;

**Table 2—Univariate associations between cardiometabolic parameters and NC in HIV- and non-HIV-infected individuals**

Parameter	Group					
	Entire cohort		HIV-infected		HIV-negative	
	<i>r</i> *	<i>P</i>	<i>r</i> *	<i>P</i>	<i>r</i> *	<i>P</i>
Age (years)	0.22	<0.0001	0.20	0.008	0.23	0.004
Blood pressure (mmHg)						
Systolic	0.25	<0.0001	0.16	0.04	0.37	<0.0001
Diastolic	0.30	<0.0001	0.23	0.002	0.38	<0.0001
Cholesterol (mg/dL)						
Total	−0.001	0.98	0.002	0.98	−0.02	0.84
LDL	0.10	0.09	0.07	0.38	0.13	0.11
HDL	−0.35	<0.0001	−0.25	0.002	−0.48	<0.0001
Triglycerides (mg/dL)	0.13	0.02	0.10	0.18	0.30	0.0002
Hemoglobin A <sub>1c</sub> (%)	0.20	0.0004	0.16	0.04	0.28	0.0006
Fasting glucose (mg/dL)	0.27	<0.0001	0.27	0.0004	0.27	0.0008
Fasting insulin (μU/mL)	0.21	0.0005	0.18	0.03	0.26	0.003
2-h glucose (mg/dL)	0.02	0.73	−0.04	0.62	0.09	0.31
Iliac waist circumference (cm)	0.68	<0.0001	0.67	<0.0001	0.70	<0.0001
WHR	0.51	<0.0001	0.49	<0.0001	0.60	<0.0001
BMI (kg/m <sup>2</sup> )	0.57	<0.0001	0.58	<0.0001	0.57	<0.0001
SAT area (cm <sup>2</sup> )	0.35	<0.0001	0.36	<0.0001	0.35	<0.0001
VAT area (cm <sup>2</sup> )	0.60	<0.0001	0.53	<0.0001	0.69	<0.0001
Arm fat by DEXA (kg)	0.37	<0.0001	0.41	<0.0001	0.35	<0.0001
Trunk fat by DEXA (kg)	0.53	<0.0001	0.54	<0.0001	0.52	<0.0001
Smoking history (pack-years)	0.08	0.17	0.10	0.21	0.03	0.76

\**r* is Pearson correlation coefficient.

for model,  $R^2 = 0.45$ ,  $P < 0.0001$ ). In contrast, in the analysis of the HIV-infected cohort, NC was not a significant predictor of cIMT in models controlling for traditional risk factors with or without the addition of VAT (Table 4). Similar results were seen when cumulative exposure to PI, NRTI, and NNRTI was included in the modeling (data not shown). Neither CD4<sup>+</sup> count nor viral load was significantly associated with cIMT (data not shown).

**CONCLUSIONS**—Although the association between visceral obesity and cardiometabolic abnormalities is well established (2), less is known about the metabolic relevance of other upper body subcutaneous fat stores. Upper body adipose tissue is an important contributor to circulating free fatty acids (FFA) and is more lipolytically active than lower body adipose tissue (15). Because FFA concentrations are directly associated with insulin resistance (16), hepatic VLDL production (17), and endothelial dysfunction (18), upper body adipose tissue may have important cardiovascular and metabolic consequences (19). NC, as a surrogate measure of upper body

adiposity, has been associated with numerous cardiovascular risk factors in the general population (20,21). Moreover, a recent analysis of the Framingham Heart Study demonstrated that NC is associated with insulin resistance, elevated BP, and dyslipidemia, independent of visceral adiposity (9).

An important and novel aspect of the current study is the significant relationship observed between NC and cIMT. Our data extend the observations of the Framingham Heart Study (9) by demonstrating that NC is associated with a direct measure of subclinical atherosclerosis, cIMT, in the general population. To our knowledge, this is the first study to assess the relationship between NC and cIMT. The relationship between NC and cIMT was independent of traditional risk factors, including smoking, hypertension, LDL, glucose, and visceral adiposity. The significant independent relationship between cIMT and NC seen among all subjects held in a multivariate regression analysis limited to HIV-negative patients. However, the relationship did not remain significant when controlling for BMI instead of VAT, which may be the result of significant covariance of NC and BMI.

These data suggest that NC may indicate a high-risk adipose depot in relationship to atherosclerotic indexes.

In subanalysis of the HIV-infected cohort alone, NC was not a significant predictor of cIMT after controlling for traditional risk factors. The risk factors for CVD in HIV infection are numerous and include traditional factors as well as lifestyle factors and inflammatory and immune status as characterized by markers such as D-dimer (22), monocyte chemoattractant protein (MCP)-1 (23), and decreased CD4<sup>+</sup> count (24). The nontraditional factors contributing to CVD in this population may explain the lack of association between cIMT and NC, in contrast with the significant relationship seen in the HIV-negative group. Moreover, NC may be a more stable fat depot, less affected by exposure to chronic ARVs than other fat depots; changes in these other depots, such as VAT, might drive cIMT changes to a greater degree in the HIV population.

In HIV infection, an association between upper trunk fat and insulin resistance has been described (8), but the relationship between NC per se and metabolic variables has not been characterized. We now show that among both HIV and non-HIV groups, NC is strongly associated with cardiometabolic risk factors, including HDL and fasting insulin. It is noteworthy that NC remains strongly and significantly associated with these risk factors in models controlling for VAT or BMI, demonstrating the importance of upper body fat, distinct from visceral fat, as a contributor to dyslipidemia and insulin resistance. The lipolytic activity of upper body fat may mediate this relationship with lipid metabolism and glucose homeostasis. Studies of regional lipolysis have demonstrated that, in the postabsorptive state, ~50% of circulating FFA is from nonsplanchnic upper body fat stores (15). Of note, arm circumference did not demonstrate the same associations with lipid and glucose parameters as NC in our cohort (data not shown), possibly because arm circumference may be more reflective of lean mass as well as adiposity.

Our study has limitations. First, NC is a measure of both adipose and lean tissue, thus not a direct measure of adiposity, although our data suggest that it is a good surrogate measure of adiposity and, in fact, much more significantly related to cIMT than other measures of upper body adiposity. There is variability

**Table 3—Univariate associations between cardiometabolic parameters and cIMT in HIV- and non-HIV-infected individuals**

Parameter	Group					
	Entire cohort		HIV-infected		HIV-negative	
	r*	P	r*	P	r*	P
Age (years)	0.53	<0.0001	0.57	<0.0001	0.49	<0.0001
Blood pressure (mmHg)						
Systolic	0.35	<0.0001	0.35	<0.0001	0.33	<0.0001
Diastolic	0.30	<0.0001	0.25	0.0009	0.34	<0.0001
Cholesterol (mg/dL)						
Total	0.06	0.32	-0.03	0.69	0.18	0.03
LDL	0.07	0.22	-0.06	0.47	0.24	0.003
HDL	-0.04	0.50	0.14	0.07	-0.21	0.01
Triglycerides (mg/dL)	-0.006	0.92	-0.08	0.32	0.17	0.04
Hemoglobin A <sub>1c</sub> (%)	0.22	<0.0001	0.22	0.004	0.26	0.0014
Fasting glucose (mg/dL)	0.20	0.0005	0.15	0.06	0.25	0.003
Fasting insulin (μU/mL)	0.03	0.63	0.004	0.96	0.01	0.88
2-h Glucose (mg/dL)	0.10	0.10	0.08	0.35	0.10	0.22
Iliac waist circumference (cm)	0.24	<0.0001	0.19	0.01	0.30	0.0002
WHR	0.21	0.0001	0.09	0.26	0.34	<0.0001
BMI (kg/m <sup>2</sup> )	0.16	0.004	0.15	0.05	0.19	0.02
SAT area (cm <sup>2</sup> )	0.10	0.07	0.05	0.48	0.17	0.03
VAT area (cm <sup>2</sup> )	0.16	0.005	0.04	0.64	0.30	0.0001
Arm fat by DEXA (kg)	0.05	0.36	0.04	0.57	0.09	0.29
Trunk fat by DEXA (kg)	0.08	0.13	0.03	0.66	0.15	0.06
Smoking history (pack-years)	0.39	<0.0001	0.39	<0.0001	0.38	<0.0001
NC (cm)	0.25	<0.0001	0.21	0.006	0.31	0.0001

\*r is Pearson correlation coefficient.

in measurement of NC, but we have shown this to be small. There are limited data on the effects of racial differences and lifestyle factors on measurements of NC, and further data are needed in this regard. Inclusion of patients with known diabetes might have enhanced our ability to describe associations between body

composition and glucose parameters across a broader disease spectrum. However, by excluding subjects with known diabetes, we avoided recruiting subjects in whom our ability to see a strong relationship with NC might have been confounded by a high prevalence of diabetes. A small number of subjects met

**Table 4—Multivariate modeling of the relationship of traditional risk factors and NC to average cIMT**

Parameter	Group					
	Entire cohort		HIV-infected		HIV-negative	
	β-Estimate	P value	β-Estimate	P value	β-Estimate	P value
Age	0.006	<0.0001	0.008	<0.0001	0.004	0.0002
Sex (male)	0.000	1.00	0.004	0.77	-0.011	0.41
Race (Caucasian)	-0.013	0.04	-0.015	0.11	-0.013	0.11
HIV (HIV negative)	0.008	0.20	N/A	N/A	N/A	N/A
Smoking pack-years	0.002	<0.0001	0.002	0.008	0.003	<0.0001
Hypertension or antihypertensive use	0.031	0.0001	0.019	0.09	0.048	<0.0001
LDL (mg/dL)	0.000	0.53	0.000	0.98	0.000	0.14
Fasting glucose (mg/dL)	0.000	0.74	0.000	1.00	0.000	0.69
NC (cm)	0.005	0.02	0.003	0.39	0.009	0.005

For entire cohort, R<sup>2</sup> = 0.41 and P < 0.0001. For HIV-infected group, R<sup>2</sup> = 0.41 and P < 0.0001. For HIV-negative group, R<sup>2</sup> = 0.45 and P < 0.0001.

criteria for diabetes on glucose tolerance testing, and these data were included in the analysis. Further studies examining these specific relationships in large populations with diabetes are now needed. NC may be a strong predictor of obstructive sleep apnea (25). We cannot exclude the possibility that the metabolic consequences of obstructive sleep apnea may confound the relationship between NC and metabolic parameters. Longitudinal data relating change in NC to cardiovascular risk will be useful. Finally, cIMT may be more difficult to measure in subjects with increasing neck girth, but we show similar variance in the measure of cIMT across NC quartiles, suggesting that our results were not affected in this way.

Overall, our data highlight the metabolic importance of upper body adiposity, as measured by NC, in both HIV-infected and HIV-negative individuals. In particular, NC is a strong predictor of measures of insulin resistance and HDL cholesterol, and, in HIV-negative individuals, is also significantly associated with cIMT. These data reinforce the notion that upper body fat is particularly and uniquely linked to metabolic abnormalities, independent of other measures of abdominal adiposity such as VAT.

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K.V.F. researched data, performed the analysis, and wrote the manuscript. T.L.S. performed data analysis and wrote the manuscript. S.E.L. researched data and reviewed the manuscript. A.M.R. researched and compiled data and reviewed the manuscript. S.K.G. obtained funding, reviewed data analysis, and edited and reviewed the manuscript.

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