



# Metabolic Syndrome and Markers of Early Atherosclerosis in a Cohort of HIV Infected Subjects from Nutrition for Healthy Living (NFHL)

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## Introduction:

•Metabolic Syndrome (MXS) is characterized by abdominal obesity, hypertriglyceridemia, low HDL-cholesterol, hypertension and insulin resistance (1).

•Those with MXS have a higher incidence and progression of carotid and coronary atherosclerosis and increased CV morbidity and mortality (2,3).

•Metabolic and morphologic abnormalities in HIV infection include dyslipidemia (low HDL, high TG), insulin resistance, fat atrophy and visceral fat deposition, some of which overlap with the components of MXS.

•Measurements of common (CCA) and internal (ICA) carotid intima-media thickness (IMT) and calculation of coronary artery calcium (CAC) scores are non-invasive techniques to evaluate for early signs of atherosclerosis.

•We evaluated the relationship of MXS with subclinical carotid and coronary atherosclerosis in HIV infected subjects by B-mode ultrasound and computed tomography.

## Methods:

•Cross-sectional analysis of 327 participants in the NFHL study, a cohort study that examines nutritional and metabolic issues in patients infected with HIV.

•MXS was defined as having at least 3 of the following: 1) Abdominal obesity: waist circumference > 102 cm for men, > 88 cm for women; 2) Hypertriglyceridemia: > 150 mg/dL; 3) Low high-density lipoprotein (HDL) cholesterol: < 40 mg/dL for men, < 50 mg/dL for women; 4) High blood pressure: ≥ 130/85 mm Hg; 5) High fasting glucose: ≥ 110 mg/dL.

•For the IMT measurements, multiple images were obtained of the right and left CCA and ICA by high-resolution B ultrasound. The mean of the maximum of near- and far-wall IMT measurements were used for the final analysis (4).

•For the CAC score analysis, high-resolution, ECG synchronized computed tomography of the heart was obtained with attention to the four main coronary arteries. CAC score was computed with standardized scoring techniques (5).

•Analyses were performed with SAS/Windows statistical software Version 9.0.

## Results:

### Prevalence of MXS and its components (N=327)

	N	(%)
Metabolic Syndrome	72	23
Components:		
Abdominal Obesity	94	28.8
High Triglyceride	138	44.2
Low HDL-cholesterol	186	59.6
High Blood Pressure	82	25.6
High Glucose	19	6.0

### Characteristics of Participants with and without MXS

	N (%) or Mean ± SD		p-value
	MXS (N=72)	No MXS (N=242)	
Mean Age, yrs	45.3 ± 7.4	43.9 ± 7.1	0.135
Gender			
Male	46 (63.9)	188 (77.7)	<b>0.018</b>
Female	26 (36.1)	54 (22.3)	
Race			
African American	28 (38.9)	79 (32.6)	0.770
Latino/Hispanic	17 (8.3)	10 (7.9)	
White	144 (48.6)	28 (54.1)	
Other	11 (4.1)	6 (5.4)	
Current smoker	35 (48.6)	120 (49.6)	0.989
Ever smoked	54 (75.0)	183 (75.6)	0.915
Systolic BP, mm Hg	126 ± 16.8	116 ± 15.8	<b>&lt;0.0001</b>
Diastolic BP, mm Hg	81 ± 9.9	74 ± 9.9	<b>&lt;0.0001</b>
BMI, kg/m <sup>2</sup>	31 ± 5.7	25 ± 3.9	<b>&lt;0.0001</b>
Triceps skinfold, mm	18 ± 4	11 ± 9	<b>&lt;0.0001</b>
Cholesterol, mg/dl			
Total	188 ± 55.2	187 ± 49.1	0.907
HDL	33 ± 11.3	45 ± 18.4	<b>&lt;0.0001</b>
LDL	100.5 ± 43.5	112 ± 37.0	<b>0.027</b>
Triglycerides, mg/dl	279 ± 169.8	155 ± 163.6	<b>&lt;0.0001</b>
ApoA1, mg/dl	120 ± 25.6	131 ± 29.8	<b>0.005</b>
ApoB, mg/dl	89 ± 20.0	83 ± 20.9	0.067
ApoE, mg/dl	6 ± 3.3	4 ± 2.0	<b>&lt;0.0001</b>
Lp(a), mg/dl	27 ± 28.5	28 ± 30.2	0.859
RLPC, mg/dl	22 ± 21.4	13 ± 18.5	<b>0.001</b>
Glucose, mg/dl	94 ± 31.3	81 ± 16.1	<b>&lt;0.0001</b>
Insulin, mU/l	24 ± 30.2	11 ± 9.1	<b>&lt;0.0001</b>
QUICKI	0.32 ± 0.04	0.35 ± 0.03	<b>&lt;0.0001</b>
CRP, mg/l	3.9 ± 8.4	2.6 ± 3.4	0.06
Homocysteine	9.1 ± 4.4	8.9 ± 3.6	0.559

## Results (cont'd):

### HIV and Treatment History of Participants with and without MXS

	Mean ± SD or N (%)		p-value
	MXS (N=72)	No MXS (N=255)	
Duration of HIV, yrs	9.8 ± 4.9	9.9 ± 4.7	0.878
Duration of HAART, mo	30 ± 27	25 ± 26	0.068
CD4 count, cells/mm <sup>3</sup>	505 ± 384	441 ± 257	0.103
Log HIV-RNA, copies/mm <sup>3</sup>	3.3 ± 1.2	3.0 ± 1.0	0.070
Currently on HAART	55 (76.4)	175 (72.3)	0.493
Current NRTI use	54 (75.0)	176 (72.7)	0.702
Current NNRTI use	24 (33.3)	80 (33.1)	0.965
Current PI use	35 (48.6)	106 (43.8)	0.471

### Unadjusted Association between MXS and Surrogate Markers

Carotid Arteries	Mean ± SD or N (%)		p-value
	MXS (N=72)	No MXS (N=255)	
<b>Mean IMT, mm</b>			
CCA	0.66 ± 0.24	0.59 ± 0.16	<b>0.005</b>
ICA	0.80 ± 0.45	0.69 ± 0.31	0.072
<b>IMT cut-offs (mm)</b>			
CCA >0.6	32 (44.4)	87 (36.3)	0.209
>0.8	12 (16.7)	17 (7.1)	<b>0.014</b>
>1.0	5 (6.9)	5 (2.1)	<b>0.040</b>
ICA >0.6	38 (53.5)	115 (48.1)	0.423
>0.8	20 (28.2)	48 (20.1)	0.148
>1.0	14 (19.7)	30 (12.6)	0.129
<b>Coronary Artery Calcium</b>			
Mean log CAC Score	1.99 ± 1.92	1.11 ± 1.77	<b>0.0003</b>
<b>CAC Score cut-offs</b>			
0	14 (19.7)	127 (53.3)	<b>&lt;0.0001</b>
1-100	48 (67.6)	95 (39.6)	
>100	9 (12.7)	17 (7.1)	

### Odds Ratio (95% CI) of abnormal surrogate markers comparing those with and without MXS

	Unadjusted	p-value	Adjusted for Age, Sex, Smoking, Race	
			Adjusted OR	p-value
CCA IMT, mm				
>0.6	1.3 (0.7-2.4)	0.385	1.4 (0.8-2.4)	0.193
>0.8	2.8 (1.3-6.3)	<b>0.011</b>	2.9 (1.2-7.1)	<b>0.020</b>
>1.0	4.4 (1.2-16.9)	<b>0.029</b>	3.5 (0.8-15.5)	0.092
ICA IMT, mm				
>0.6	1.2 (0.7-2.1)	0.425	1.8 (0.7-2.1)	0.572
>0.8	1.5 (0.8-2.8)	0.164	1.5 (0.8-2.9)	0.250
>1.0	1.7 (0.8-3.4)	0.152	1.6 (0.7-3.4)	0.255
CAC Score				
Detectable 0.9 (0.3-2.3)	0.917		1.0 (0.4-2.9)	0.941
>100 0.5 (0.2-1.2)	0.140		0.6 (0.2-1.7)	0.348

## Summary of Results:

•23% of HIV+ individuals fulfilled the diagnostic criteria for the MXS.

•Most of those with MXS had low HDL-cholesterol and elevated triglycerides, but very few had hyperglycemia.

•BMI, triceps skinfolds, ApoB, ApoE, remnant lipoprotein cholesterol (RLPC) and hs-CRP were higher in those with MXS than those without MXS.

•There was a trend for those with MXS to have higher HIV viral loads and to have been on HAART for longer time than those without MXS, but there was no difference in current HAART, PI or NNRTI use between the two groups.

•Those with MXS had significantly greater common carotid IMT than those without MXS. There was a trend for internal carotid IMT to be higher in those with MXS than those without MXS. More participants with MXS had common carotid IMT greater than 0.8 mm and greater than 1.0 mm. More participants had internal carotid IMT greater than 1.0 mm, but this was not statistically significant.

•The mean log CAC score was significantly higher in those with MXS compared to those without MXS. The prevalence of a detectable calcium score was significantly higher in those with MXS compared to those without the condition. A score of 0 was more prevalent in those without MXS than those with MXS.

•The odds ratio of common carotid IMT greater than 0.8 mm and 1.0 mm was significantly higher among those with MXS. These relations persisted after adjusting for age, gender, smoking and race. The odds ratios of internal carotid IMT and CAC scores were not significantly higher among those with MXS.

## Conclusions:

•Our results suggest a concerning prevalence of subclinical carotid and coronary atherosclerosis among HIV-infected individuals defined to have MXS.

•The concurrent presence of MXS and subclinical atherosclerosis in HIV infection may help identify those at greater risk of CV disease and direct therapy to prevent future CV events in this population.

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