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## Race-Specific Associations of Myeloperoxidase with Atherosclerosis in a Population-Based Sample: The Dallas Heart Study

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### Abstract

**Objective**—Myeloperoxidase (MPO) is a leukocyte-derived enzyme that appears to be directly involved in atherosclerosis development. We evaluated the association of circulating MPO with coronary and aortic atherosclerosis in a large, multiethnic population.

**Methods and Results**—Plasma levels of MPO were measured in 3294 subjects participating in the Dallas Heart Study, a probability-based population sample. Coronary artery calcification (CAC) was measured by EBCT, and abdominal aorta plaque prevalence (AP) and burden (APB), as well as abdominal aorta wall thickness (AWT) were determined by MRI. Associations between MPO and atherosclerosis phenotypes were assessed in multivariable analyses adjusting for traditional atherosclerosis risk factors. MPO levels in the 4<sup>th</sup> compared with 1<sup>st</sup> quartile independently associated with prevalent AP (OR 1.41, 95% CI 1.08–1.84), APB (beta coefficient 0.23,  $p=0.02$ ), and AWT (beta coefficient 0.04,  $p=0.03$ ), but not with prevalent CAC (OR 0.84, 95% CI 0.61–1.17). MPO remained associated with aortic atherosclerosis phenotypes but not coronary calcification after adjustment for other inflammatory biomarkers. A significant interaction was observed between race/ethnicity, MPO and AP ( $p_{\text{interaction}}=0.038$ ), such that MPO levels in the 4<sup>th</sup> vs 1<sup>st</sup> quartile associated with prevalent AP in African Americans, (OR 1.81, 95% CI 1.23–2.65) but not in White or Hispanic participants (OR 0.99, 95% CI 0.68–1.44).

**Conclusion**—Higher levels of MPO associated with aortic but not coronary atherosclerosis, with significant associations limited to African American participants. These findings suggest that MPO might be a novel risk factor contributing to racial disparities in peripheral vascular disease.

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## Keywords

Myeloperoxidase; atherosclerosis; peripheral vascular disease; African American

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## Introduction

Inflammation plays a critical role in the initiation and progression of atherosclerosis. Myeloperoxidase (MPO), a bactericidal enzyme present in neutrophils, monocytes and macrophages, also has pro-inflammatory functions that may contribute to vascular injury. *In vitro*, MPO contributes to peroxidation of low density lipoprotein (LDL) and high density lipoprotein (HDL) as well as consumption of nitric oxide which may contribute to endothelial damage.<sup>1, 2</sup> *In vivo* experimental evidence further supports a potential role of MPO in atherosclerosis development in both animal models<sup>3, 4</sup> and in human studies.<sup>5, 6</sup> MPO has also been investigated as a potential biomarker of coronary atherosclerosis and of the corresponding risk for adverse clinical outcomes. Several studies have reported associations between higher levels of MPO and a greater extent of coronary artery disease,<sup>7-9</sup> and increased risk of adverse cardiac events.<sup>10</sup>

Fewer data are available regarding an association between MPO and peripheral vascular disease (PVD), which affects about 8 million Americans. Although risk factors for PVD overlap with those of CAD, smoking is particularly important as a PVD risk factor; moreover, PVD also disproportionately affects African Americans.<sup>11</sup> Although prior studies have identified several inflammatory biomarkers associated with atherosclerosis in the aorta and peripheral vascular beds,<sup>12-14</sup> little is known about the association of MPO and PVD, and whether MPO may contribute to racial disparities in PVD outcomes. In the present study, we performed a comprehensive evaluation of the association between MPO and atherosclerosis in multiple different vascular beds in a large, multi-ethnic population.

## Methods

### Study Population

The Dallas Heart Study (DHS) is a probability-based population sample of 6101 Dallas County residents.<sup>15</sup> African Americans and women were oversampled intentionally to achieve a final cohort of approximately 50% African Americans and 50% women. Following an initial in-home visit for collection of survey data, body mass index and measurement of blood pressure, participants between the ages of 30 and 65 were invited to participate in a second visit where they provided in-home fasting blood and urine specimens. Those completing visit two were invited to and to a third visit at UT Southwestern Medical Center, where imaging studies including cardiac magnetic resonance imaging and electron beam computed tomography were performed. Demographics, blood pressure and body composition were similar between subjects completing visits 1 and 2, and laboratory data were similar between those completing visits 2 and 3.<sup>15</sup> The present study includes 3294 DHS subjects from visit 2 who underwent measurement of MPO.

### Definition of Variables

Hypertension was defined as an average systolic blood pressure  $\geq 140$  mmHg, diastolic blood pressure  $\geq 90$  mmHg, or use of anti-hypertensive medication. Hypercholesterolemia was defined as a fasting low density lipoprotein  $\geq 160$  mg/dL, a total cholesterol  $\geq 240$  mg/dL, or use of a statin medication. Low high density lipoprotein was defined as HDL-C  $< 40$  mg/dL in men and  $< 50$  mg/dL in women. Diabetes was defined as a fasting blood glucose level of  $\geq 126$  mg/dL, or a non-fasting blood glucose level of  $\geq 200$  mg/dL, or self-reported

diabetes with use of any glucose lowering medication. Body mass index was calculated based on measured body weight and height. Race was self-reported.

### Atherosclerosis Assessment

Personnel who performed atherosclerosis measurements were blinded to all participant data. Coronary artery calcification (CAC) was determined as the average score on two consecutive electron beam computed tomography (EBCT) scans. Agreement between the two scans, as assessed by the intraclass correlation coefficient, was 0.96. Prevalent CAC was defined as >10 Agatston units, which was a data-derived threshold selected to maximize the signal to noise ratio, as previously described.<sup>16</sup> The abdominal aorta was assessed using a 1.5 Tesla whole-body MRI system (Intera, Philips Medical Systems), using a free-breathing, ECG-gated, T2-weighted turbo spin-echo (black-blood) sequence, with 6 transverse slices of the infrarenal abdominal aorta obtained as described previously.<sup>17</sup> Aortic plaque (AP) was defined as a hyper-intense signal volume that protruded  $\geq 1$  mm from the endoluminal surface of the aortic wall, and was manually contoured in each image.<sup>18</sup> Total vascular area (TVA) and total plaque area (TPA) were calculated as the summation of vessel area and plaque area for all 6 slices. Aortic plaque burden (APB) was then calculated by the formula:  $100 \times (TPA/TVA)$ . Aortic wall thickness (AWT) was calculated by dividing the total vessel wall area by the aortic circumference in each slice, as previously described.<sup>19</sup> Mean AWT was then determined by the summation of AWT for each slice divided by number of total slices (n=6). In 70 subjects, an interobserver variability analysis demonstrated an intraclass correlation coefficient between two observers of 0.94 and a mean interobserver difference of  $4.2 \pm 6.6\%$ .<sup>20</sup>

### Measurement of MPO and Other Biomarkers

Venous blood was collected in standard blood collection tubes containing citrate EDTA and samples were maintained at 4°C for  $\leq 4$  hours and then centrifuged (1430g for 15 minutes) at 4°C. Plasma was then removed, aliquoted, and frozen at  $-80^{\circ}\text{C}$  until assays were performed. MPO was measured from thawed frozen plasma at Alere San Diego, Inc (San Diego, CA) Inc using a sandwich assay on a Luminex 200 reader (Austin, TX) and modified paramagnetic Luminex beads from Radix Biosolutions (Georgetown, TX) with minimum and maximum detection limits of 0.2 ng/mL and 250 ng/mL, respectively. The intra-assay coefficient of variation (CV) was 12% and inter-assay CV was 13%. Personnel who performed the assays were blinded to all clinical data.

The following analytes were measured previously and the methods have been described: high sensitivity C-reactive protein (hsCRP)<sup>14</sup>, interleukin-18 (IL18)<sup>12</sup>, osteoprotegerin<sup>13</sup>, Tumor necrosis factor-alpha 1 receptor (TNFR1A)<sup>21</sup>, matrix metalloproteinase-9 (MMP-9)<sup>21</sup>, pulmonary surfactant protein-B (SP-B)<sup>21</sup>, monocyte chemoattractant protein (MCP-1)<sup>22</sup>, and soluble receptor for advanced glycation end products (sRAGE)<sup>23</sup>.

### Statistical Analysis

Participants were divided into quartiles on the basis of MPO levels. Demographic and clinic variables were compared across MPO quartiles using the  $\chi^2$  trend test for categorical variables and the Jonckheere-Terpstra test for continuous variables. Correlations between selected biomarkers and MPO were evaluated by Spearman rank correlation coefficients. Logistic regression was performed to investigate associations between MPO and prevalent CAC and AP in unadjusted models and models adjusted for traditional risk factors including age, sex, race/ethnicity, body mass index, diabetes, current smoking, hypertension, hypercholesterolemia and low HDL. Linear regression was performed to assess associations between MPO and AWT and APB in unadjusted models and models adjusting for the same traditional risk factors. Sensitivity analyses were also performed with MPO entered into the

models as a log-transformed continuous variable. Testing for statistical interaction was performed for MPO  $\times$  race/ethnicity for all the atherosclerosis phenotypes. Because significant race  $\times$  MPO interactions were seen, stratified analyses were performed in subgroups defined by race/ethnicity. All models included only subjects with complete data available for covariates and the phenotype of interest. For all statistical testing, 2-sided probability values were reported and a probability value  $<0.05$  was considered statistically significant. No adjustment for multiple testing was done. All analyses were performed using SAS 9.2 (Cary, NC, USA) and all box-plot figures were created using GraphPad PRISM 5.01 (La Jolla, CA, USA).

## Results

### Associations of MPO with Atherosclerosis Risk Factors and Biomarkers

MPO levels followed a right-skewed distribution and were higher in African American (median 17.5 [13.9, 22.3] ng/mL) compared with non-African American participants (median 16.8 [12.9, 21.0] ng/mL;  $p<0.0001$ ) (Figure 1). Increasing quartiles of MPO were associated with traditional risk factors such as current smoking, diabetes, low HDL higher body mass index, but not with hypertension or hypercholesterolemia (Table 1). In addition, MPO did not differ by age or sex. MPO was significantly correlated with other inflammatory biomarkers, with strong positive associations observed with TNFR 1A and SP-B (Table 1).

### Associations of MPO with Atherosclerosis Phenotypes

MPO was not associated with CAC in either crude or adjusted analyses (Table 2). In contrast, in unadjusted models, MPO was modestly associated with all prevalent aortic atherosclerosis phenotypes, including AP, APB and AWT (Table 2). After adjustment for age, sex, race, BMI, DM, smoking, HTN, hypercholesterolemia, and low HDL, subjects in the 4<sup>th</sup> MPO quartile had a significantly higher prevalence of AP compared with subjects in the 1<sup>st</sup> MPO quartile (OR 1.41, 95% CI 1.08–1.84; Table 2). MPO levels in the 4<sup>th</sup> quartile also independently associated with AWT and APB after multivariable adjustment ( $p<0.05$  for each; Table 2). Similar findings were observed when MPO was entered into the models as a log transformed continuous variable (Table 2). In models additionally adjusting for other inflammatory biomarkers, MPO remained associated with aortic atherosclerosis phenotypes but not coronary calcification (Supplementary Table 4). In sensitivity analyses excluding individuals with self-reported prior myocardial infarction, stroke and revascularization, all results were qualitatively similar (data not shown).

### Race-Specific Association of MPO with Atherosclerosis Phenotypes

Significant interactions were found between race/ethnicity and MPO quartile regarding AP prevalence ( $p_{\text{interaction}}=0.038$ ) and APB ( $p_{\text{interaction}}=0.022$ ) but not AWT ( $p_{\text{interaction}}=0.22$ ). Among African American participants, MPO was significantly associated with prevalent AP (OR 1.81 in quartile 4 versus quartile 1, 95% CI 1.23–2.65, Figure 2) as well as APB and AWT ( $p<0.01$  for each, Table 3) in the fully adjusted models. In contrast, among White or Hispanic participants, there was no association between MPO and prevalent AP (Figure 2), APB or AWT (Table 3). Similar findings were observed when MPO was entered into the stratified analyses as a log-transformed continuous variable (Figure 2, Table 3). Findings were unchanged when White and Hispanic participants were analyzed as separate subgroups.

## Discussion

In this large population-based study, higher MPO levels associated with African American race and with multiple traditional atherosclerosis risk factors. In the overall population, MPO was modestly associated with prevalent aortic plaque, aortic plaque burden and aortic wall thickness after adjusting for traditional risk factors, but not with coronary artery calcification. We found a significant interaction by race, such that MPO independently associated with aortic atherosclerosis in African Americans but not in White or Hispanic participants. These findings suggest that the relationships between MPO and subclinical atherosclerosis may vary across different vascular beds and are modified by race/ethnicity.

## Biology of MPO

MPO is an enzyme found in neutrophils, monocytes and macrophages and plays a crucial role in immune function, producing oxidant species and free radicals that defend against bacterial pathogens.<sup>1</sup> MPO and its byproducts may also cause damage to the endothelial cells, contributing to plaque formation and instability. Several biochemical pathways have been proposed to explain the pathogenic role of MPO in atherosclerosis. MPO acts as an enzymatic catalyst and initiates low density lipoprotein (LDL) peroxidation leading to enhanced LDL uptake and contributing to foam cell development and plaque formation.<sup>2</sup> MPO also selectively oxidizes the apoA1 component of HDL in atherosclerotic lesions, inhibiting ABCA1-mediated cholesterol efflux from macrophages, one of the principal anti-atherosclerotic mechanisms of HDL. In addition, MPO consumes nitric oxide, leading to vasoconstriction and promoting endothelial damage.<sup>24</sup>

Several *in vivo* models provide further support for a role of MPO in atherosclerosis development. Over-expression of the human MPO gene in mice susceptible to atherosclerosis led to a 2.3-fold larger area of aortic atherosclerosis compared with wild type mice without the MPO transgene.<sup>3</sup> In rabbits, MPO activity was increased 3-fold in atherosclerotic compared to normal blood vessels.<sup>4</sup> In human studies, MPO and products of MPO-catalyzed oxidation reactions have been identified in human atherosclerotic lesions.<sup>5, 6</sup>

## MPO as a Biomarker of Atherosclerosis

Although a number of prior studies have reported associations between MPO and the extent of coronary atherosclerosis, these studies focused largely on symptomatic populations with a high burden of disease, contrasted with our population-based sample. In patients presenting with chest pain as well as those with ACS, some prospective studies have confirmed an independent association between higher concentrations of MPO and subsequent adverse coronary events.<sup>7, 10</sup> In previous cross sectional studies, MPO levels have also shown a gradient across coronary disease phenotypes, with lowest levels in patients without coronary artery disease (CAD), intermediate levels in patients with stable CAD and highest levels in patients with acute coronary syndromes (ACS).<sup>8, 9</sup> In contrast, other studies have not confirmed associations of MPO with stable coronary artery disease and or myocardial infarction.<sup>25</sup>

Little is known about the role of MPO as a biomarker of non-coronary vascular disease. One prior study, which enrolled 931 individuals with a strong family history of hypertension, reported that higher MPO levels associated with lower ankle-brachial index and with clinical PVD after adjustment for traditional risk factors.<sup>26</sup> In this study, similar associations were seen in African American and non-African American participants. Additional studies correlating MPO with carotid stenosis measured by duplex ultrasound have been performed, but these were limited to Caucasian subjects or patients with familial

hypercholesterolemia.<sup>27, 28</sup> To our knowledge, no prior study has correlated MPO with coronary and aortic atherosclerosis in the general population.

### Differential Associations of MPO with Atherosclerosis Phenotypes

We report independent associations between MPO and measures of aortic atherosclerosis, but no association with coronary calcification. These discordant observations may reflect biological differences in the role of MPO in different vascular beds, or alternatively may reflect the role of MPO in different stages of atherosclerosis. While coronary calcification is specific for coronary atherosclerosis, calcification is a relatively late manifestation of atherosclerosis, and is more common in stable as compared with vulnerable plaques. Thus, while we observed no association of MPO with calcified plaque, we cannot exclude associations with noncalcified coronary plaque. Although one prior study showed that MPO levels increased according to CAC categories, the increments were marginal, and the association was attenuated after adjustment for risk factors.<sup>29</sup> In contrast to coronary calcification, the aortic measures, and in particular AWT, may represent an earlier phase of atherosclerosis.<sup>19</sup> MPO may contribute more importantly toward earlier than later stages of atherosclerosis, a hypothesis consistent with the known role of MPO in foam cell development.<sup>2</sup>

An alternative hypothesis is that MPO might function differently in non-coronary versus coronary vascular beds. Although risk factors are generally similar between PVD and CAD, some notable differences exist. For example, smoking has a greater impact on non-coronary than coronary vascular disease. In our study, MPO associated with smoking exposure, as well as smoking-related biomarkers such as SP-B. We speculate that the effect of MPO in the peripheral vasculature could represent a pro-inflammatory effect of tobacco exposure, a hypothesis that requires direct testing for confirmation.

Associations of other inflammatory biomarkers with coronary and aortic atherosclerosis phenotypes have previously been reported from the Dallas Heart Study, and several additional analyses were performed for the present study. For example, in risk-factor adjusted models, IL18 and hsCRP were not associated with either coronary or peripheral atherosclerosis,<sup>12,14</sup> while osteoprotegerin significantly associated with atherosclerosis in both vascular beds.<sup>13</sup> MCP-1 had previously been reported to have associations with CAC that attenuated after adjustment for risk factors;<sup>22</sup> new analyses show similar attenuation of associations of MCP-1 with AP and AWT after adjustment (data not shown). Several other biomarkers have shown discordant associations with coronary calcification and aortic atherosclerosis in multivariable models. SP-B<sup>21</sup> and MMP-9<sup>30</sup> were only associated with aortic atherosclerosis while sRAGE (new analyses for aortic measurements, data not shown) associated only with coronary calcification.<sup>23</sup> In aggregate, these findings suggest that some inflammatory pathways may play distinct roles in the coronary and peripheral vascular beds. Further elucidation of the specific roles of these inflammatory contributors to atherosclerosis may help to identify novel treatment approaches.

### Race-specific Associations Between MPO and Atherosclerosis

Based on National Health and Nutrition Examination Survey in 1999–2000, the prevalence of PVD in African Americans was 7.9%, but only 4.4% in white and 3.0% in Hispanics, demonstrating an almost 3-fold excess PVD prevalence in African Americans after adjustment for age and sex.<sup>11</sup> Another prior study reported that African American race was a significant predictor of a lower ankle-brachial index and presence of PVD after adjusting for age and other traditional risk factors.<sup>31</sup> These epidemiological observations suggest that differences in traditional risk factors do not fully explain racial disparities in PVD and that novel risk factors may play a role. In the present study, we found that MPO levels were

higher in African Americans than whites, and that MPO was significantly associated with aortic atherosclerosis only in African Americans. This observation, which requires confirmation in additional studies, suggests that differences in inflammatory pathways may contribute to disparities in PVD between African Americans and other race/ethnicity groups. MPO may be a modifiable target for PVD prevention or treatment, particularly in African Americans, who have the highest burden of PVD.

### Study Limitations

The associations of MPO with peripheral atherosclerosis measures, although statistically significant and independent of traditional risk factors, were quantitatively modest. Associations of this magnitude do not suggest that MPO will have a role in clinical practice to identify individuals with or at risk for aortic atherosclerosis.<sup>32</sup> The cross-sectional nature of this study prevents establishment of any cause-effect relationships, and thus our findings should be considered hypothesis generating. Finally, although reproducibility studies have been performed for CAC and AWT, such studies have not yet been performed for aortic plaque measurements.

### Conclusion

In a large and multi-ethnic population, MPO was independently associated with aortic atherosclerosis but not coronary atherosclerosis. These associations were restricted to African Americans, a finding that suggests differences in inflammation may in part explain ethnic disparities in peripheral vascular disease.

### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

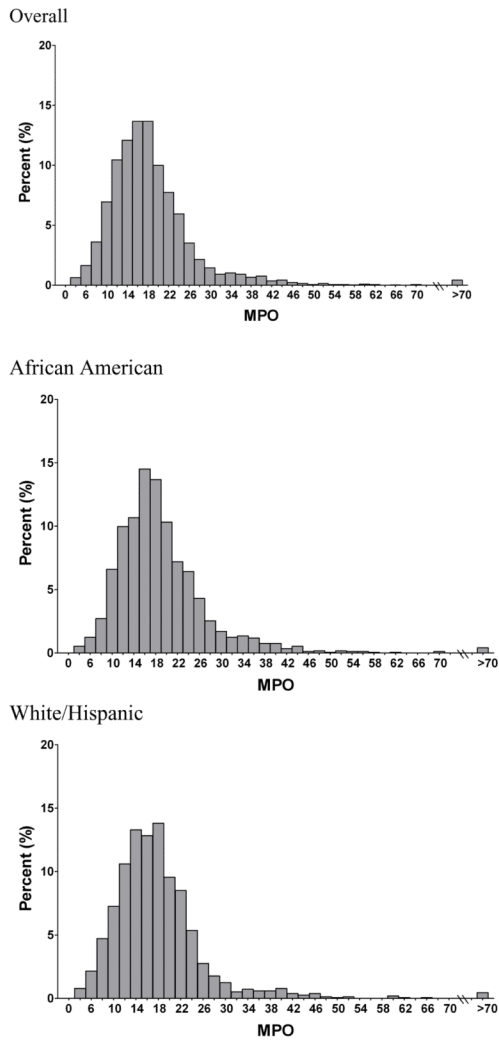
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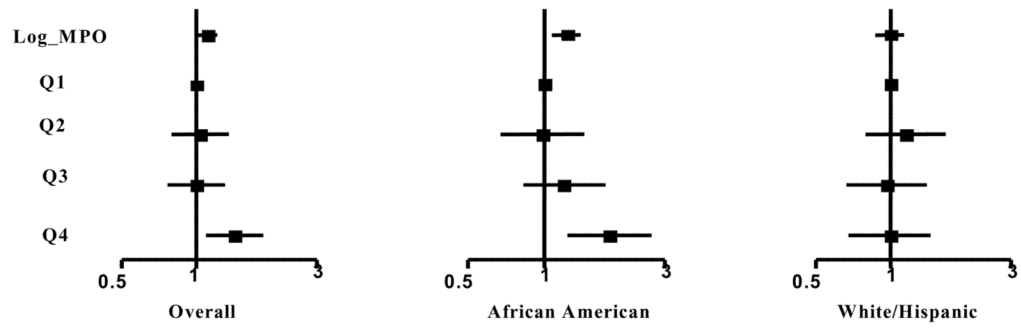
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**Figure 1.**  
Distribution of MPO (ng/mL)



**Figure 2.**

Aortic Plaque Prevalence According to MPO Levels, Stratified by Race/Ethnic Group. All models adjusted for traditional risk factors (age, sex, race, BMI, DM, smoking, HTN, hypercholesterolemia, and low HDL). P-value for interaction of MPO quartile  $\times$  race= 0.038.

Table 1

Demographic and Clinical Variables Across Quartiles of MPO (n=3294)

Variable	Q1 (n=823)	Q2 (n=824)	Q3 (n=824)	Q4 (n=823)	P trend
MPO (ng/mL)	3.7–13.34	13.35–17.12	17.13–21.58	21.59–183.33	
Age (years)	44	43	43	44	0.22
Male	43%	46%	43%	44%	0.77
White	35%	32%	28%	23%	<0.001
African American	46%	51%	52%	57%	<0.001
Hispanic	15%	15%	19%	18%	0.03
Body Mass Index (kg/m <sup>2</sup> )	28.1	29.3	29.6	30.8	<0.001
Hypertension	32%	35%	31%	37%	0.14
Current smoker	27%	27%	29%	34%	<0.001
Hypercholesterolemia	13%	13%	13%	13%	0.80
Low HDL	37%	40%	44%	45%	<0.001
High Triglyceride	12%	12%	12%	13%	0.45
Diabetes Mellitus	9%	12%	12%	14%	0.001
TNFR1A (ng/mL)	0.38	0.55	0.67	0.94	<0.001
SP-B (ng/mL)	1.13	2.21	2.99	6.52	<0.001
MCP-1 (pg/ml)	29.8	34.9	37.9	42.6	<0.001
Osteoprotegerin (pg/ml)	1168	1182	1202	1233	0.001
MMP9 (ng/mL)	3.3	4.8	6.0	10.1	<0.001
IL18 (mg/L)	492.7	501.2	536.9	556.6	0.002
hsCRP (mg/L)	2.4	2.5	2.7	4.2	<0.001
SRAGE (ng/mL)	1.4	1.9	2.1	2.3	<0.001

Values are medians (interquartile range) for continuous variable and proportions for categorical variables. TNFR1A, tumor necrosis factor- $\alpha$  1 receptor; SP-B, pulmonary surfactant protein-B; MCP-1, monocyte chemoattractant protein-1; MMP9, matrix metalloproteinase-9; IL18, interleukin-18; hsCRP, high sensitivity C-reactive protein; SRAGE, soluble receptor for advanced glycation end products.

Table 2

Associations of MPO With Atherosclerosis Phenotypes

	Prevalent CAC (n=2502)		Prevalent Plaque (n=2287)		APB (n=2287)		AWT (n=2300)	
	OR (95% CI)	OR (95% CI)	Beta coeff	P value	Beta coeff	P value	Beta coeff	P value
Age (years)	1.15 (1.13, 1.17)	1.08 (1.07, 1.09)	0.07	<0.01	0.01	<0.01	0.01	<0.01
Male	1.05 (0.82, 1.33)	1.12 (0.93, 1.36)	0.17	0.02	0.15	<0.01	0.15	<0.01
African American	0.92 (0.71, 1.2)	0.89 (0.72, 1.11)	-0.08	0.35	0.003	0.80	0.003	0.80
Body Mass Index (kg/m <sup>2</sup> )	1.02 (1, 1.1)	0.97 (0.95, 0.98)	-0.03	<0.01	0.001	0.34	0.001	0.34
Hypertension	2.73 (2.12, 3.51)	1.44 (1.15, 1.79)	0.33	<0.01	0.06	<0.01	0.06	<0.01
Current smoker	1.99 (1.45, 2.75)	2.13 (1.73, 2.62)	0.69	<0.01	0.12	<0.01	0.12	<0.01
Hypercholesterolemia	1.59 (1.24, 2.05)	1.4 (1.06, 1.84)	0.34	<0.01	0.04	0.01	0.04	0.01
Low HDL	1.57 (1.17, 2.1)	1.15 (0.94, 1.4)	0.16	0.03	0.07	<0.01	0.07	<0.01
Diabetes Mellitus	3.31 (2.59, 4.23)	1.4 (1.03, 1.91)	0.28	0.01	0.05	<0.01	0.05	<0.01
<b>Univariable Model</b>								
Log_MPO	1.01 (0.92, 1.11)	1.06 (0.97, 1.15)	0.06	0.13	0.04	0.03	0.04	0.03
Q1	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Q2	0.95 (0.73, 1.25)	0.96 (0.76, 1.22)	-0.12	0.30	-0.02	0.32	-0.02	0.32
Q3	0.89 (0.68, 1.17)	0.95 (0.75, 1.21)	-0.08	0.51	0.01	0.78	0.01	0.78
Q4	1.02 (0.78, 1.33)	1.29 (1.02, 1.63)	0.24	0.04	0.05	0.02	0.05	0.02
<b>Model Adjusted for Traditional Risk Factors</b>								
Log_MPO	0.98 (0.87, 1.1)	1.1 (1.003, 1.21)	0.07	0.04	0.02	0.01	0.02	0.01
Q1	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Q2	0.86 (0.62, 1.18)	1.03 (0.79, 1.34)	-0.08	0.45	-0.02	0.25	-0.02	0.25
Q3	0.84 (0.61, 1.17)	0.99 (0.76, 1.3)	-0.06	0.52	0.004	0.83	0.004	0.83
Q4	0.84 (0.61, 1.17)	1.41 (1.08, 1.84)	0.23	0.02	0.04	0.03	0.04	0.03

CAC, coronary artery calcification; APB, aorta plaque burden; AWT, aorta wall thickness.

Table 3

Race-specific Association of MPO with Aortic Plaque Burden (APB) and Aortic Wall Thickness (AWT) After Adjustment for Traditional Risk Factors

	APB						AWT					
	African American (n=1097)			White or Hispanics (n=1192)			African American (n=1102)			White or Hispanics (n=1198)		
	Beta coeff	P value		Beta coeff	P value		Beta coeff	P value		Beta coeff	P value	
Age (years)	0.06	<0.01		0.07	<0.01		0.01	<0.01		0.01	<0.01	
Male	0.09	0.39		0.22	0.03		0.13	<0.01		0.16	<0.01	
Body Mass Index (kg/m <sup>2</sup> )	-0.03	<0.01		-0.03	<0.01		0.001	0.58		0.001	0.34	
Hypertension	0.40	<0.01		0.22	0.07		0.07	<0.01		0.04	0.05	
Current smoker	0.58	<0.01		0.82	<0.01		0.11	<0.01		0.12	<0.01	
Hypercholesterolemia	0.20	0.16		0.50	<0.01		0.01	0.74		0.08	<0.01	
Low HDL	0.01	0.95		0.30	<0.01		0.05	0.01		0.08	<0.01	
Diabetes Mellitus	0.23	0.11		0.40	0.03		0.03	0.19		0.07	0.03	
Q1	Reference			Reference			Reference			Reference		
Q2	-0.06	0.67		-0.03	0.81		0.02	0.33		-0.05	0.02	
Q3	0.17	0.24		-0.19	0.18		0.04	0.11		-0.05	0.02	
Q4	0.42	<0.01		-0.06	0.70		0.07	<0.01		-0.01	0.73	
log_MPO (1 stdev)	0.16	<0.01		-0.02	0.73		0.02	<0.01		0.01	0.41	

APB, aorta plaque burden; AWT, aorta wall thickness.