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The Relationship of Peripheral Arterial Disease and Metabolic Syndrome Prevalence in Asymptomatic US Adults 40 Years and Older: Results from the National Health and Nutrition Examination Survey (1999-2004)

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The Relationship of Peripheral Arterial Disease and Metabolic Syndrome Prevalence in Asymptomatic US Adults 40 Years and Older: Results From the National Health and Nutrition Examination Survey (1999–2004)

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Peripheral arterial disease (PAD) is a subclinical marker of coronary artery disease and identifies asymptomatic individuals at high risk for cardiovascular disease (CVD) events. The metabolic syndrome (MetS) is a constellation of clinical factors that increases the risk of developing diabetes and CVD. The authors' objectives were to estimate the prevalence of MetS in patients with PAD and to determine the prevalence of PAD in the population of asymptomatic US adults 40 years and older with MetS. The authors analyzed data from 3 National Health and Nutrition Examination Surveys (NHANES, 1999–2004). Prevalence of MetS as defined by the Third Report of the Adult Treatment Panel criteria and prevalence of associated cardiac risk factors were determined in 5376 asymptomatic participants 40 years and older. Presence of PAD was defined as ankle-brachial index <0.9. Estimates were weighted with the sample weights accounting for the unequal selection probability of complex NHANES sampling and over sampling of selected population subgroups. Prevalence of PAD in asymptomatic US adults 40 years and older was 4.2%. PAD prevalence in persons with MetS was 7.0% compared with 3.3% in persons without MetS. A total of 38% of the population with PAD also had MetS. High rates of abdominal obesity, hypertension, hyperglycemia, and low high-density lipoprotein cholesterol are significant contributors to both MetS and PAD. Persons with MetS have twice the risk of having PAD. Of persons with PAD, almost 40% have MetS. The presence of either PAD or MetS should warrant screening for both conditions so that risk stratification and management of risk factors may be performed. *J Clin Hypertens (Greenwich).* 2012;14:144–148. ©2012 Wiley Periodicals, Inc.

The ankle-brachial pressure index (ABI), the ratio of ankle to brachial systolic blood pressure (BP), is a simple noninvasive test that is used in the assessment of lower extremity arterial obstruction and for screening of patients with suspected peripheral arterial disease (PAD). An ABI <0.9 is diagnostic of PAD and is associated with an increased risk of coronary heart disease, stroke and transient ischemic attack, and all-cause mortality in both men and women.[1–6] For these reasons, even asymptomatic patients with PAD should be treated with aggressive risk factor reduction.[6]

The metabolic syndrome (MetS) is defined by the clustering of at least 3 of the following 5 interrelated metabolic factors: abdominal obesity, hypertriglyceridemia, low levels of high-density lipoprotein (HDL), hyperglycemia, and hypertension. Patients with MetS have a 2- to 3-fold increased risk of having an adverse cardiovascular event.[7–10]

Because PAD and MetS are independently associated with a high incidence of future cardiovascular disease (CVD) events, identifying the respective prevalence of PAD in those patients with MetS and vice versa could identify a group of patients at especially high risk for further cardiovascular events. To this end, the purpose of this present study was to determine the prevalence of: (1) MetS in patients with PAD and (2) PAD in the population of asymptomatic US adults 40 years and older with MetS.

METHODS

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the US civilian noninstitutionalized population conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. Since 1999, NHANES has conducted continuous interviews and physical examinations. This study is based on 6 years of the continuous NHANES survey data (1999–2004).

NHANES participants are interviewed in their homes to obtain information on health history, health behaviors, and risk factors. Those participants then undergo a physical examination at a mobile examination center. The procedures followed to select the representative sample and conduct the interview and examinations are carefully outlined in the National Center for Health Statistics Analytic Guidelines (2006) and informed consent is obtained from all participants. All data, including that used in this study, are available online through the NHANES Web site.

NHANES participants 40 years and older were asked to participate in the ABI section of the lower extremity disease examination. Persons were excluded from the examination if they had a bilateral amputation or weighed more than 400 pounds (due to equipment limitations). Some participants who were eligible for the assessment might not have received the examination due to multiple reasons (eg, casts, ulcers, dressings, or other conditions that interfered with testing, equipment failure, participant refusal). The lower extremity disease examination was performed by trained health technicians in a specially equipped room in the mobile examination center and following a prescribed protocol.

The NHANES ABI is automatically calculated by their computer system and verified by the National Center for Health Statistics before data release. The right ABI was determined by dividing the mean systolic BP in the right ankle by the mean systolic BP in the brachial artery of the arm. The left ABI was computed in the same way using only measurements from the left extremities. The mean BP value for the arm and ankles are computed based on the first and second readings at each site. Since the second reading for all persons older than 60 were missing, the mean values are in fact the first recorded BP readings at a site. The presence of PAD was defined as an ankle-brachial index <0.9.

MetS, as defined by the National Cholesterol Education Program (NECP) Third Report of the Adult Treatment Panel (ATP III), is present when any 3 of the following 5 traits exist in the same individual: abdominal obesity (waist circumference >102 cm [40 in] in men and >88 cm [35 in] in women); serum triglycerides ≥150 mg/dL; HDL cholesterol <40 mg/dL in men and <50 mg/dL in women; BP ≥130/85 mm Hg; and a fasting blood glucose ≥110 mg/dL.

Demographic variables including age and race/ethnicity were assessed in this study using data from the NHANES demographic questionnaire. Race/ethnicity was classified as non-Hispanic white, non-Hispanic black, and Hispanic. Individuals were classified as asymptomatic if they answered "no" to all of the following: Has a doctor told you that you have had a myocardial infarction? Has a doctor told you that you have had a stroke? Has a doctor told you that you have coronary heart disease? Has a doctor told you that you have had angina?

All estimates were weighted, with the sample weights accounting for the unequal selection probability of the complex NHANES sampling and the oversampling of selected population subgroups. Weights are created in NHANES to account for the complex survey design (including oversampling), survey nonresponse, and post-stratification. When a sample is weighted in NHANES II it is representative of the US Census civilian noninstitutionalized population. A sample weight is assigned to each sample person. It is a measure of the number of people in the population represented by that sample person.

RESULTS

MetS Prevalence in Persons With PAD
The prevalence of MetS in asymptomatic US adults 40 years and older during the 3 NHANES survey periods

TABLE II. Prevalence of the MetS in Asymptomatic US Adults 40 Years and Older With a Prior Diagnosis of PAD: Sex, Race/Ethnicity, and MetS Components

NHANES	MetS(+)/PAD(+)			
	1999–2000, %	2001–2002, %	2003–2004, %	Total, %
Women	48.8	37.3	48.6	43.9
Men	24.0	35.0	24.3	28.6
Non-Hispanic black	40.4	17.5	17.3	24.5
Non-Hispanic white	37.2	39.0	50.0	41.5
Mexican American/other Hispanic	40.9	46.1	27.0	38.9
[a]Abdominal obesity	54.8	51.6	56.0	53.8
Men	41.9	58.2	40.7	50.2
Women	58.6	48.55	59.7	55.1
Triglycerides >150 mg/dL	87.8	74.2	76.5	78.8
HDL cholesterol	79.1	68.5	77.8	74.7
<40 mg/dL (men)	66.4	58.9	57.9	61.2
<50 mg/dL (women)	84.8	76.1	83.0	81.5
[b]Hypertension	45.7	47.1	47.0	46.7
[c]Fasting glucose	81.3	74.2	74.1	76.2

Abbreviations: HDL, high-density lipoprotein; MetS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; PAD, peripheral arterial disease. [a]Abdominal obesity: waist circumference ≥102 cm (men) or ≥88 cm (women). [b]Hypertension: blood pressure ≥130/85 mm Hg or treatment for hypertension. [c]Fasting plasma glucose >110 mg/dL.

TABLE I. Prevalence of MetS in Asymptomatic US Adults 40 Years and Older With and Without PAD

NHANES	MetS(+) and PAD(−) (N=43,720,682)				MetS(+) and PAD(+) (N=3,287,736)			
	1999–2000	2001–2002	2003–2004	Total	1999–2000	2001–2002	2003–2004	Total
MetS, %	22.9	20.8	23.3	22.2	38.3	36.5	41.4	38.4

Abbreviations: MetS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; PAD, peripheral arterial disease.

was 22.8%, while the prevalence of MetS in individuals with and without PAD was 38.4% and 22.2%, respectively (Table I).

Women with PAD had a higher prevalence of MetS than do men. Non-Hispanic black patients with PAD had a lower incidence of MetS than either non-Hispanic white or Mexican American/other Hispanic individuals (Table II). Women with MetS also had a higher prevalence of abdominal obesity and had a generally higher prevalence of low HDL cholesterol in each of the 3 NHANES surveys (Figure).

PAD Prevalence in Persons With MetS

The prevalence of PAD in asymptomatic US adults 40 years and older during the 3 NHANES survey periods was 4.2%. Overall, the prevalence of PAD in individuals with the MetS was 7.0% (Table III). In persons with MetS, women had a higher prevalence of PAD than men. Non-Hispanic black individuals with MetS had a higher prevalence of PAD than did non-Hispanic white or Mexican American/other Hispanics (Table IV).

Prevalence of MetS Clinical Factors

Individuals with PAD had a significantly higher prevalence of MetS and its associated clinical factors (Figure). In the total population studied, all MetS clinical factors were more prevalent in persons with PAD compared with persons without PAD. When stratifying the prevalence of MetS clinical factors by sex, the prevalence of abdominal obesity and low HDL was higher in women with PAD than those without, but was similar in men with and without PAD.

DISCUSSION

In this observational study of asymptomatic US adults 40 years and older, we found that (1) individuals with PAD had a significantly higher prevalence of MetS than did those without PAD and (2) individuals with MetS have a higher prevalence of PAD.

In the literature, estimates of the prevalence of MetS have differed depending on the definition (NCEP/ATP III, World Health Organization, International Diabetes Federation, European Group for the Study of Insulin Resistance) used to categorize individuals, study
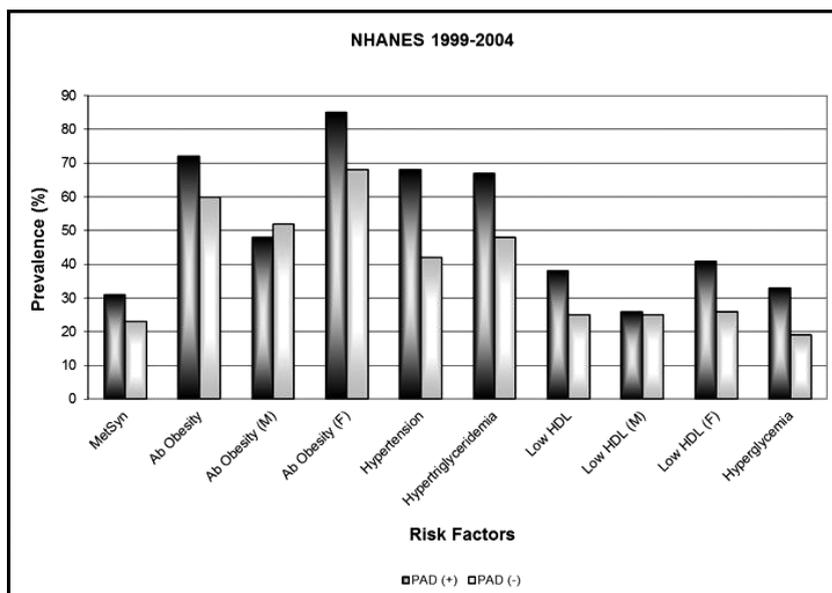

FIGURE. Metabolic syndrome (MetS) factors in individuals by peripheral arterial disease (PAD) diagnosis.

TABLE III. Prevalence of PAD in Asymptomatic US Adults 40 Years and Older With and Without MetS							
	PAD(+) and MetS(−) (N=5,263,043)				PAD(+) and MetS(+) (N=3,287,7360)			
NHANES	1999–2000	2001–2002	2003–2004	Total	1999–2000	2001–2002	2003–2004	Total
PAD, %	3.0	3.4	3.6	3.3	6.0	7.2	8.0	7.0
Abbreviations: MetS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; PAD, peripheral arterial disease.								

TABLE IV. Prevalence of PAD in Asymptomatic US Adults 40 Years and Older With a Prior Diagnosis of MetS: Sex, Race/Ethnicity, and MetS Components

NHANES	PAD(+)/MetS(+)			
	1999–2000, %	2001–2002, %	2003–2004, %	Total, %
Women	7.6	9.3	11.8	9.4
Men	3.8	5.0	3.1	4.1
Non-Hispanic black	17.0	6.8	13.2	12.0
Non-Hispanic white	5.6	7.8	8.0	7.2
Mexican American/other Hispanic	17.0	6.8	4.8	4.6
[a]Abdominal obesity	4.9	7.1	8.0	6.6
Men	2.2	5.6	2.7	3.7
Women	6.7	8.4	11.9	8.8
Triglycerides >150 mg/dL	6.4	6.0	8.1	6.7
HDL cholesterol	6.8	6.4	8.0	6.9
<40 mg/dL (for men)	4.4	5.2	3.0	4.4
<50 mg/dL (for women)	8.5	7.4	11.5	8.9
[b]Hypertension	5.8	9.0	8.0	7.6
[c]Fasting glucose	8.0	7.3	7.6	7.6

Abbreviations: HDL, high-density lipoprotein; MetS, metabolic syndrome; NHANES, National Health and Nutrition Examination Survey; PAD, peripheral arterial disease. [a]Abdominal obesity: waist circumference ≥102 cm (men) or ≥88 cm (women). [b]Hypertension: blood pressure ≥130/85 mm Hg or treatment for hypertension. [c]Fasting plasma glucose >110 mg/dL.

population, and measurement methods.[11–14] Prevalence estimates have increased over time across 2 NHANES cohorts from approximately 24.1% (1988–1994 cohort) to 27% (1999–2000 cohort). The cause of this increase is thought to be due to differences in the compositions of the cohorts.[15] Our estimate of MetS prevalence is nearly identical to that from NHANES III, which reported an age-adjusted MetS prevalence of 24% among US adults.[16]

In the present study, we found that MetS was present in a higher number of individuals with PAD as compared with those without PAD. These results are consistent with the findings of Gorter and colleagues[17] who found that in PAD, MetS is highly prevalent. Other cross-sectional studies have reported an even higher prevalence of MetS in patients with PAD (57%–60%).[18,19] The highest prevalence of 97% was reported by Qadan and associates,[20] but their investigation included patients with clinically advanced PAD. These different estimates of PAD prevalence are likely due to differences in study size and population.

It is interesting to note that the Edinburgh Artery Study did not find a significant association between MetS and incident PAD (hazard ratio, 0.89; 95% confidence interval, 0.57–1.38).[21] This lack of association between MetS and PAD may be due to differences in the study population. The Edinburgh cohort was older (mean age, 65 years), had a high prevalence of baseline smoking status (25.3%), and represented a cohort of patients with symptomatic PAD. Moreover, components of MetS were measured differently relative to our study. The Edinburg Artery Study did not use waist circumference measurement for evaluating body mass index. Instead, it used a proxy measure of body mass index.[21]

In the current study, we also found that the prevalence of MetS in a person with PAD varied between women and men, with a higher prevalence of MetS in women with PAD than in men. Other researchers have reported similar findings, observing a higher prevalence of MetS in women with PAD than men.[17,22] We also found that women with MetS have a higher prevalence of asymptomatic PAD than do men. This finding adds to the existing data of Conen and colleagues[23] who found that MetS was associated with a higher risk of developing future symptomatic PAD in women. The researchers in that study suggested that the risk appears to be largely mediated by the effect of inflammation and endothelial activation especially since women with MetS in that study had a higher level of C-reactive protein than did those without MetS. Other researchers have described an association between inflammation and PAD.[22,23] Our data put into context the public health significance of this association within a representative sample of the total US population.

Abdominal obesity was the most prevalent component of the MetS in our PAD population. When stratified by sex, the prevalence of abdominal obesity was higher in women with PAD, but was similar in men with and without PAD. Hypertension was the second most prevalent MetS component in our study. In the Secondary Manifestation of ARTerial disease (SMART) study and the work of Brevetti and colleagues,[17,22] hypertension was the MetS component observed most commonly in patients with PAD. This difference in MetS component prevalence is likely due to the fact that those were smaller studies (1117 patients and 154 patients, respectively) and represented an older cohort. This difference in prevalence of risk factors for MetS may be important because abdominal obesity plays an important role in insulin resistance, which is regarded as the primary etiologic process of MetS.[24] Epidemiologic and pathophysiologic data indicate that visceral obesity is a main factor in the occurrence of the MetS.[25,26] We also found that all of the MetS clinical components were more prevalent in the PAD population compared with the population without PAD.

In terms of race and ethnicity, we found that non-Hispanic black individuals with MetS had a higher prevalence of PAD than did non-Hispanic whites or Mexican Americans/other Hispanics. We also found that non-Hispanic whites with PAD have a higher incidence of MetS than either non-Hispanic blacks

or Mexican Americans/other Hispanic individuals. Our data represent the first assessment of race and ethnicity as a stratifying factor for examining the relationship between PAD and MetS prevalence.

LIMITATIONS

The present study should be interpreted in the context of several potential limitations. First, our study did not include data on markers of subclinical inflammation such as high-sensitivity C-reactive protein or markers of endothelial injury or activation. Second, data regarding cigarette smoking were not collected. Third, our study assessed the prevalence of MetS in a population of patients with PAD and vice versa, but did not evaluate a causal relationship between the presence of MetS and PAD. Fourth, our data do not evaluate the effect of MetS and PAD on clinical outcomes.

CONCLUSIONS

Our findings indicate a high prevalence of PAD in asymptomatic US adults 40 years and older with MetS and also a high prevalence of MetS in the population of asymptomatic persons with PAD. These findings support screening patients with PAD for MetS, and vice versa, so as to identify a group of patients at potentially high cardiovascular risk.

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