Risk Factors for Peripheral Arterial Disease in United States Asymptomatic Patients Aged 40 – 69 and Asymptomatic Patients Aged ≥ 70: Results from NHANES 1999-2004

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Citation

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Abstract

Our purpose was to establish the prevalence of PAD using National Health and Nutrition Examination Surveys (NHANES) data from 1999-2004 in men and women ages 40-69 and 70+ without history of coronary heart disease, MI, stroke or TIA, or angina.Results: Females aged 40-69 were 1.77 times more likely to have PAD than men.Diabetics were 3.07 times more likely to have PAD than non-diabetics. Class 2 and Class 3 hypertension patients were 3.08 and 2.47 more likely, respectively to have PAD than patients with blood pressure of <140/90. Overall, diabetes in addition to another risk factor increased odds of having PAD more than three fold. For individuals aged 70 or older, similar patterns of risk were identified. Conclusions: PAD is highly prevalent among asymptomatic individuals. Diabetes mellitus, moderate and low kidney function, hypertension (treated but not controlled and untreated), and smoking are all independently associated with greater prevalence of PAD.

INTRODUCTION

Peripheral arterial disease (PAD) is an occlusive vascular disease resulting from progressive narrowing and hardening of the arteries that deliver blood flow to the limbs. With the presence of PAD one's extremities, often the legs, do not receive enough oxygenated blood to keep up with the demand. The most common symptom of PAD is intermittent claudication (IC) which is pain or discomfort felt in the legs while walking or exercising that disappears during rest. PAD is associated with many of the same causal factors as other related atherosclerotic cardiovascular and cerebrovascular diseases including hypertension, hypercholesterolemia, diabetes mellitus, decreased kidney function, smoking, age, and race/ethnicity.

According to estimates by the American Heart Association as many as 8 to 12 million Americans have PAD, predominantly those who are of 50 years of age or older. Nearly 75% of these people are either asymptomatic or mistake their symptoms of PAD for something else. Both symptomatic and asymptomatic PAD are associated with a greater risk of functional decline and are often subclinical markers for coronary artery disease which identifies individuals at high risk for future cardiovascular events such as myocardial infarctions or strokes (1-3).

The estimates of the prevalence of PAD in the United States based on an ankle-brachial index (ABI) < 0.90 vary substantially. Using similar diagnostic criteria, estimates of PAD prevalence have ranged from 3% to 30% in US adult populations (4-7). Based on the first 2 years of the National Health and Nutrition Examination Survey (NHANES), the reported PAD prevalence among U.S. adults aged 60 to 69 was 4.8%, 12.0% in 70 to 79 year olds, and 22.0% prevalence in octogenarians (8). A more recent report also indicated that the prevalence of lower extremity disease increases with age: 7.0% for those aged 60-69, 12.5% for those aged 70 to 79, and 23.2% for those aged 80 and older (5).

As the population of the United States continue to age and the prevalence of risk factors such as hypertension, hypercholesterolemia, and diabetes increase, the public health burden of PAD will also continue to increase, having a dramatic effect on the U.S. healthcare industry.

The aim of this study was to establish the prevalence of PAD

using National Health and Nutrition Examination Surveys (NHANES) data from 1999-2004 in men and women ages ≥ 40 without a history of coronary heart disease, MI (heart attack), stroke or TIA, or angina.

METHODS AND MATERIALS

The National Health and Nutrition Examination Surveys (NHANES) is a nationally representative survey of the U.S. civilian non-institutionalized 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 six years of the continuous NHANES 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 those used in this study, are available online through the NHANES website.

NHANES participants 40 years of age and older were asked to participate in the ABI Section of the Lower Extremity Disease examination. Persons were excluded from the exam if they had a bilateral amputation or weighed over 400 pounds (due to equipment limitations). Some participants who were eligible for the exam might not have received the exam for multiple reasons {e.g. casts, ulcers, dressings, or other conditions 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 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 blood pressure in the right ankle by the mean systolic blood pressure in the brachial artery of the arm. The left ABI was computed in the same way only using measurements from the left extremities. The mean blood pressure value for the arm and ankles are computed based on the first and second reading at each site. Since the second reading for all persons 60+ are missing, the mean values are in fact the first recorded blood pressure readings at a site.

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 Mexican American.

Brachial blood pressure was categorized into four groups: normal BP (<140/90 mmHg taking no prescription drugs for hypertension); untreated hypertension (≥ 140 or ≥ 90 mmHg and not taking blood pressure medication); treated, uncontrolled hypertension (currently taking prescription for high BP and BP ≥ 140 mmHg or ≥ 90 mmHg); and treated controlled hypertension (currently taking prescription for high BP and BP < 140/90). Individuals were defined as diabetic if they reported ever having had a doctor tell them that they had diabetes mellitus. Height and weight measures were used to compute body mass index (BMI kg/m2). BMI was then categorized into < 25.0 kg/m2, 25.0 – 29.9 kg/m2, and ≥ 30.0 kg/m2.

A measure of kidney filtration function, glomerular filtration rate (GFR), was calculated using the abbreviated Modification of Diet in Renal Disease (MRDR) Study formula based on serum creatinine, age, sex, and race. A GFR > 90 (mL• min-1 • 1.73m-2) was defined as normal, mildly decreased kidney function was defined as 60 to 90 (mL• min-1 • 1.73m-2), and a low kidney function was defined as a GFR < 60 (mL• min-1 • 1.73m-2).

RESULTS

In the 40-69 year olds, females were 1.77 times more likely to have PAD than men (CI 1.27 -2.48), and diabetics were 3.07 times more likely to have PAD than non-diabetics (CI 2.11 - 4.46). Non-Hispanic blacks were 2.25 times more likely to have PAD than non-Hispanic whites (CI 1.56 - 3.23). Both Class 2 and 3 hypertension patients were 3.08 and 2.47 times more likely to have PAD than Class 1 patients (CI 2.03 – 4.66 and 1.66 - 3.69, respectively). Smokers and patients with a low glomerular filtration rate (GFR) were 1.90 and 2.34 times more likely than non-smokers and those with a normal GFR to have PAD (CI 1.35 – 2.65 and 1.10 – 4.99, respectively). Overall, diabetes increased the odds of having PAD more than three fold in some cases. For example, diabetic smokers are 6.61 times more likely to have PAD than non-diabetic non-smokers (CI 3.76 - 11.6). Female diabetics were 5.02 times more likely to

have PAD than non-diabetic males (CI 2.84 – 8.87). Further, diabetics with low GFR were almost twice as likely to have PAD than non-diabetics with normal GFR (OR = 1.88, CI 1.08-3.30).

Figure 1

Table 1. Univariate Odds Ratios (95% Confidence Intervals) for Peripheral Arterial Disease (Ankle Brachial Index < 0.90) in Selected Risk Factors in Adults without Cerebrovascular Disease

	Adults 40-69		Adults 70+	
	%	OR (95% CI)	%	OR (95% CI)
Gender				
Male	2.7%	1.00 (reference)	17.2%	1.00 (reference)
Female	4.6%	1.77 (1.27 – 2.48) †	19.3%	1.15 (0.86 – 1.55)
Diabetes mellitus				
No	3.0%	1.00 (reference)	17.1%	1.00 (reference)
Yes	8.8%	3.07 (2.11 – 4.46)†	27.3%	1.82 (1.20 – 2.75) †
Race/Ethnicity				
NH White	3.2%	1.00 (reference)	16.4%	1.00 (reference)
NH Black	6.9%	2.25 (1.56 – 3.23) †	27.4%	1.92 (1.29 - 2.96) †
MA/Other Hispanic	2.6%	0.79 (0.51 – 1.23)	18.7%	1.17 (0.80 – 1.72)
Hypertension[1]				
Class 1	2.5%	1.00 (reference)	15.0%	1.00 (reference)
Class 2	7.4%	3.08 (2.03 – 4.66) †	24.5%	1.84 (1.30 – 2.59) †
Class 3	6.0%	2.47 (1.66 – 3.69) †	18.5%	1.29 (0.87 – 1.90)
Class 4	5.71%	2.05 (0.81 – 5.20)	24.2%	1.81 (0.80 – 4.14)
Hypercholesterolemia				
No	3.7%	1.00 (reference)	17.1%	1.00 (reference)
Yes	3.7%	0.99 (0.77 – 1.38)	18.8%	1.12 (0.82 – 1.53)
BMI				
<25	3.4%	1.00 (reference)	20.2%	1.00 (reference)
25-30	2.8%	0.82 (0.53 – 1.26)	16.6%	0.79 (0.56 – 1.10)
>30	4.6%	1.34 (0.89 – 2.01)	16.8%	0.80 (0.53 – 1.20)
Smoking status				
Former/never	3.1%	1.00 (reference)	16.5%	1.00 (reference)
Current	5.6%	1.90 (1.35 – 2.65)†	35.5%	2.78 (1.81 – 4.26)
Glomerular filtration rate (mL/min)				
Normal (GFR > 90)	3.0%	1.00 (reference)	13.3%	1.00 (reference)
Mildly decreased (60 ≤ GFR ≤ 90)	4.1%	1.38 (0.97 – 1.95)	16.7%	1.31 (0.89 – 1.93)
Low (GFR < 60)	6.8%	2.34 (1.10 – 4.99) †	28.9%	2.65 (1.71 – 4.12) †
CRP (mg/dL)				
<1.0	3.1%	1.00 (reference)	16.7%	1.00 (reference)
1.0 – 2.3	7.1%	2.39 (1.49 – 3.84)	28.3%	1.97 (1.22 – 3.20)
≥ 2.4	11.9%	4.26 (2.15 – 8.47)	28.6%	2.00 (0.94 – 4.25)

† P-value < 0.05

[1] Hypertension: Class 1: BP < 140/90
Class 2: Treated and SBP ≥ 140 mmHg or DBP ≥ 90 mmHg,
Class 3: Treated and BP < 140/90,
Class 4: Untreated and SBP ≥ 140 mmHg or DBP ≥ 90 mmHg

In the 70+ year olds, diabetics were 1.82 times more likely to have PAD than non-diabetics (CI 1.20 - 2.75). Non-Hispanic blacks were 1.92 times more likely to have PAD than non-Hispanic whites (CI 1.29 - 2.86). Both Class 2 hypertension patients and Class I hypertension patients were more likely to have PAD than Class 1 patients. Smokers were 2.78 more likely than non-smokers have PAD (CI 1.81 - 4.26). Diabetes also increased the risk of having PAD. For example, diabetic smokers are 6.16 times more likely to have PAD than non-diabetic non-smokers (CI 2.20 - 17.2). Female diabetics were 1.90 times more likely to have PAD than non-diabetic males (CI 1.03 - 3.52) and diabetic patients with low GFR were 2.54 times more likely to have PAD than non-diabetics with normal GFR (CI 1.23 – 5.24).

Figure 2

Table 2. Univariate Odds Ratios (95% Confidence Intervals) for Peripheral Arterial Disease (Ankle Brachial Index < 0.90) in Selected Risk Factors in Adults without Cerebrovascular Disease

	Adults 40-69		Adults 70+	
	%	OR (95% CI)	%	OR (95% CI)
Gender				
Male w/o Diabetes	1.9%	1.00 (reference)	15.7%	1.00 (reference)
Male w Diabetes	8.6%	4.83 (2.74 – 8.53) †	28.2%	2.18 (1.19 – 3.70) †
Female w/o Diabetes	4.1%	2.20 (1.47 – 3.30) †	18.5%	1.22 (0.86 – 1.67)
Female w Diabetes	8.9%	5.02 (2.84 – 8.87) †	26.2%	1.90 (1.03 – 3.52) †
Race/Ethnicity				
NH White w/o Diabetes	2.9%	1.00 (reference)	15.8%	1.00 (reference)
NH White w Diabetes	7.9%	2.90 (1.48 – 5.67) †	23.7%	1.66 (0.88 – 3.12)
NH Black w/o Diabetes	5.7%	2.04 (1.35 – 3.10) †	25.4%	1.81 (1.16 – 2.84) †
NH Black w Diabetes	14.2%	5.61 (3.14 – 10.0) †	35.5%	2.93 (1.37 – 6.28) †
MA/Other w/o Diabetes	1.8%	0.63 (0.37 – 1.07)		
MA/Other w Diabetes	6.8%	2.41 (1.27 – 4.59)		
Hypertension[1]				
Class 1 w/o Diabetes	2.3%	1.00 (reference)	13.7%	1.00 (reference)
Class 1 w Diabetes	5.9%	2.72 (1.47 – 5.04) †	31.3%	2.87 (1.49 – 5.51) †
Class 2 w/o Diabetes	6.1%	2.79 (1.71 – 4.57) †	23.7%	1.96 (1.35 – 2.85) †
Class 2 w Diabetes	12.8%	6.35 (3.29 – 12.2) †	29.7%	2.70 (1.27 – 5.61) †
Class 3 w/o Diabetes	4.7%	2.12 (1.30 – 3.46) †	17.8%	1.37 (0.88 – 2.12)
Class 3 w Diabetes	10.9%	5.29 (2.93 – 9.56) †	21.3%	1.71 (0.82 – 3.56)
Smoking status				
Former/never w/o Diabetes	2.6%	1.00 (reference)	15.7%	1.00 (reference)
Former/never w Diabetes	6.7%	2.68 (1.66 – 4.35) †	23.9%	1.69 (1.07 – 2.68)†
Current w/o Diabetes	4.4%	1.73 (1.16 – 2.56) †	32.6%	2.31 (1.63 – 4.17) †
Current w Diabetes	15.0%	6.61 (3.76 – 11.6) †	53.3%	6.16 (2.20 – 17.2) †
Glomerular filtration rate (mL/min)				
Normal GFR w/o Diabetes	3.5%	1.00 (reference)	15.9%	1.00 (reference)
Normal GFR w Diabetes	10.6%	3.22 (1.70 – 6.15) †	24.2%	1.69 (0.90 – 3.15)
Decreased GFR w/o Diabetes	3.3%	0.92 (0.28 – 3.02) †	28.4%	2.10 (1.42 – 3.11) †
Decreased GFR w Diabetes	20.0%	6.83 (2.46 – 18.9) †	32.1%	2.50 (1.10 – 5.71) †
Low GFR w/o Diabetes	2.6%	0.72 (0.49 – 1.08)	10.8%	0.64 (0.41 – 0.99) †
Low GFR w Diabetes	6.5%	1.88 (1.08 – 3.30) †	32.4%	2.54 (1.23 – 5.24) †

† P-value < 0.05

[1] Hypertension: Class 1: BP < 140/90
Class 2: Treated and SBP ≥ 140 mmHg or DBP ≥ 90 mmHg,
Class 3: Treated and BP < 140/90,
Class 4: Untreated and SBP ≥ 140 mmHg or DBP ≥ 90 mmHg

DISCUSSION

These results confirm that PAD is highly prevalent among asymptomatic individuals. Our results show that diabetes mellitus, moderate and low kidney function measured by GFR, hypertension (treated but not controlled and untreated), and smoking are all independently associated with greater prevalence of PAD.

PAD is characterized by arterial stenosis and occlusion in the peripheral arterial bed and can be symptomatic or asymptomatic. Symptomatic PAD ranges in severity from intermittent claudication to critical limb ischemia. In symptomatic or asymptomatic patients, PAD is an indicator of diffuse and significant atherothrombotic disease and may lead to increased risk of myocardial infarction and strokes.

Intermittent claudication is the primary and often only clear symptom of PAD. However, an estimated 16.5 million of PAD patients do not experience any symptoms of the disease (9). Additionally, one-third of patients with symptomatic PAD do not report their symptoms to their doctor believing

symptoms to be a natural manifestation of the aging process Compounding this under-reporting is the report that clinicians who rely on a classic history of claudication alone to detect PAD will miss 85% to 90% of their patients with this high-risk atherothrombotic disease (10).

The ankle-brachial pressure index, the ratio of ankle to brachial systolic blood pressure, is a simple non-invasive test that can be performed in the primary care setting without expensive or elaborate equipment, extensive training or experience. This test is used in the assessment of lower extremity arterial obstruction and for screening of patients with suspected peripheral arterial disease. Studies have shown that a low ABI (ABI < 0.90) as an indicator of PAD is associated with an increased risk of all-cause mortality, cardiac events, stroke, and kidney failure in both symptomatic and asymptomatic individuals (2, 11-13). In other studies, subjects with borderline PAD (0.90 ≤ ABI ≤ 0.99) or with low-normal ABI (1.00 ≤ ABI ≤ 1.09) implied an increased risk of coronary and carotid atherosclerosis with an associated increased risk of premature death adverse cardiovascular events (1-2, 14-15).

The Prevention of Atherothrombotic Disease Network (16) outlined a five-item action plan to improve the current unmet need with respect to the treatment and diagnosis of PAD: (1) increase awareness of PAD and its consequences (myocardial infarction, stroke, vascular disease), (2) improve the identification of patients with symptoms of PAD, (3) Initiate screening for patients at high risk for PAD especially smokers, people with diabetes and with a history of myocardial infarction and/or stroke, (4) improve treatment rates among for symptomatic PAD patients, and (5) increase the rate of early detection of among the high-risk population without PAD.

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