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Thigh circumference and low ankle brachial index in US adults: Results from the National Health and Nutrition Examination Survey 1999–2004

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ABSTRACT

Objective: Recent studies have suggested that smaller thighs are a disadvantage for health and survival, but the association of thigh circumference with atherosclerosis remains uncertain. The purpose of this study was to investigate the association between thigh circumference and peripheral arterial disease (PAD), as measured by ankle brachial index (ABI).

Methods: This study used data from the National Health and Nutrition Examination Survey (1999–2004), in which participants' ABI and thigh circumference were measured simultaneously. A total of 5716 participants (2959 men and 2757 women) were included in the final analysis. A diagnosis of PAD was determined on the basis of ABI<0.9.

Results: The overall prevalence of PAD in this sample was 6.6%. Thigh circumference of those with PAD was 50.1 cm compared to 52.2 cm for those without PAD ($p<0.0001$). After adjusting for potential covariates, the prevalence of PAD generally decreased as thigh circumference increased up to 55 cm. In the first quantile (smallest thigh circumference), men and women had as much as a 4.8-fold (95% CI, 2.28–10.29) and a 3-fold (95% CI, 1.45–6.18) increased risk of PAD, respectively. Above 55 cm, PAD was no longer related to thigh circumference.

Conclusions: Small thigh circumference may be associated with PAD, as measured by ABI.

1. Introduction

Obesity is a major risk factor for cardiovascular diseases [1]. Several studies have noted a J- or U-shaped association between body mass index (BMI) and cardiovascular morbidity and mortality [2,3]. Consequently, alternative indices such as waist circumference, hip circumference, and waist-to-hip ratio have been suggested to predict cardiovascular events [4–6]. Recent studies posit the specific contribution of thigh fat or circumference to disease risk. In a population-based cohort study of diabetes, larger thigh circumference was associated with lower glucose metabolism markers such as fasting and post-load glucose, HbA1c, and insulin in women [7] and reduced risk of type 2 diabetes [8]. A study of the Danish MONICA (monitoring trends in and determinants of cardiovascular disease) project showed independent inverse associations between thigh circumference and total death and morbidity from cardiovascular disease in both men and women [9].

Peripheral arterial disease (PAD) is a common circulatory problem in which arterial blood flow is limited by atherosclerotic changes of the arteries. The importance of PAD as a public health issue is due to its high prevalence and its prediction of future vascular complications, such as carotid atherosclerosis, myocardial infarction, or stroke [10–12]. The disease also causes functional impairment in older adults [13]. Currently, only limited evidence is available on the potential relationship between thigh muscle mass and atherogenesis [14–16].

The purpose of this study was to determine whether thigh circumference is independently associated with PAD, as measured by ankle brachial index (ABI), in the general population. We hypothesized that smaller thigh circumference is associated with a higher incidence of PAD. Using a representative sample from the National Health and Nutrition Examination Survey (NHANES) 1999–2004, we compared thigh circumference between persons with and without PAD.

2. Methods

2.1. Study population

The NHANES, conducted by the Centers for Disease Control and Prevention, is a national representative survey of non-institutionalized civilian people in the US. The NHANES study protocols (1999–2004) were approved by the National Center for Health Statistics Institutional Review Board. Oral and written consents were obtained from all participants.

This study used data collected from 1999 to 2004 that concurrently measured participants' ankle brachial index (ABI) and thigh circumference. Among the 31,126 participants we initially selected 6726 participants≥40 years of age for whom ABIs could be measured with values<1.4. Among these subjects, 5716 (85% of those eligible) had a valid thigh circumference and responded to all covariate variables.

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2.2. Peripheral arterial disease

A diagnosis of PAD was made on the basis of an ABI below 0.9. Participants with no bilateral amputation of the feet or toes and weight under 181 kg underwent systolic blood pressure measurements over the right brachial artery and bilateral posterior tibial arteries with a Doppler device (Parks Mini-Lab IV, model 3100; Parks Medical Electronics, Inc., Aloha, Oregon). Participants aged 40 to 59 years underwent two measurements on each site, whereas those older than 60 years of age were measured once on each site. If a participant had a condition precluding blood pressure measurement on the right arm, the left brachial blood pressure was taken. ABI was calculated as the ratio of the systolic pressures in the ankle to the simultaneously measured systolic blood pressure in the brachial artery. An ABI of less than 0.9 in at least one lower extremity was regarded as a sign of PAD. Details of ABI measurement procedures are available at http://www.cdc.gov/nchs/data/nhanes/le.pdf [17].

2.3. Thigh circumference

For thigh circumference measurement, a standardized position was used: standing with most of the weight on the left leg with the right leg forward, knee slightly flexed, and soles of both feet flat on the floor. The measurements of thigh circumference were made on the right side of the mid thigh. If an examinee had an amputation, a medical condition, or a medical appliance, such as a cast, that prevented measurements from being taken on the right side of the thigh, measurements were taken on the left side. For the purpose of analysis, thigh circumference was categorized into six quantiles. The sextile containing thigh circumference of 55 cm was chosen as the reference point based on earlier findings of a two-fold increase of heart disease and death in subjects with thighs<55 cm [9].

The measurement of thigh circumference was conducted by trained health care technicians. General guidelines on standard procedures were followed for the anthropometric measures [18].

2.4. Other variables of interests

The potential confounders analyzed in this study were based on known relevance to thigh circumference and PAD. The socio-demographic variables were age (40–49 years, 50–59 years, 60–69 years, 70–79 years vs. 80 years and over), gender (male vs. female), race/ethnicity (White, Black, Hispanic and others), education (less than high school vs. high school vs. college or more), and family income (less than $20,000 vs. over $20,000). For cigarette smoking, current smoking status was categorized into three groups: never smoked, former smoker, and current smoker; serum cotinine levels were stratified into quartiles (less than 0.028 ng/mL, 0.029–0.061 ng/mL, 0.062–3.6 ng/mL vs. over 3.7 ng/mL). Current alcohol consumption was divided into drinkers and non-drinkers. History of diabetes mellitus was defined based on a physician's diagnosis. BMI was calculated as weight in kilograms divided by the height in meters squared and included three categories: underweight (BMI<18.5 kg/m^2), healthy (18.5≤BMI<25 kg/m^2), overweight (25≤BMI<30 kg/m^2), and obese (BMI≥30 kg/m^2). Physical activity included two categories (yes vs. no) based on whether participants performed moderate physical activity. Central obesity was based on waist circumference>102 for men and >88 for women (NCEP-ATP III criteria). History of diabetes was defined as a fasting plasma glucose level of at least 126 mg/dL, current insulin use, or a prior physician diagnosis of diabetes. History of coronary heart disease was defined as a prior physician diagnosis of coronary heart disease. Classification of hypertension was based on systolic blood pressure≥140, and/or diastolic blood pressure>90 (JNC-7 criteria), anti-hypertensive drug use, or a prior physician diagnosis of hypertension. Hypercholesterolemia was defined as a serum total cholesterol level of at least 240 mg/dL, current medication use, or a self-reported diagnosis by a physician. For females, the variable of menopausal status (post-menopause vs. pre-menopause) was included.

2.5. Statistical analysis

To account for the complex sampling design, the weighted estimates of the population parameters were computed using the NHANES Analytic and Reporting Guidelines. All of the analyses were performed using the PROC SURVEY procedures in SAS 9.2 (SAS Institute, Cary, NC, USA) and R (R Foundation for Statistical Computing, Vienna, Austria). The statistical significance level was set at $\alpha = .05$ (two-sided).

The percentage of prevalence of general characteristics among participants with and without prevalent PAD was summarized. The mean value of thigh circumference was compared between subjects with and without PAD according to these characteristics. To estimate the association of PAD with increasing thigh circumference, the cubic spline function with four knots was applied and plotted for both men and women (Fig. 2). Logistic regression was conducted to compute the odds ratio (OR) of PAD and the corresponding 95% confidence interval (95% CI) for the sextiles (the six quantiles) in the distribution of thigh circumference.

We fitted three models with increasing degrees of adjustment and in both men and women. Model 1 was adjusted for age and Model 2 was adjusted for Model 1 + race/ethnicity, education, income, physical activity, BMI, and menopause status (for females). Model 3 was further adjusted for Model 2 + cigarette smoking, serum cotinine level, alcohol consumption, and history of diabetes.

3. Results

Males constituted 51.8% of the subjects. The mean age was 59.2 years (range, 40 to 85). The overall prevalence of PAD in this sample was 6.6% (375/5716). The mean ABI was 1.11 (range, 0.4 to 1.4).

The thigh circumference of those with PAD was 50.1 (range, 36 to 83.6) compared to 52.2 (range, 29.2 to 87) for those without PAD ($p<0.0001$).

Table 1 summarizes the general characteristics of subjects with and without PAD, as classified by ABI. Subjects with PAD were more likely to be older, Black, of lower educational levels and family income, smokers, currently non-drinkers, diabetic, hypertensive patients, have higher levels of serum cotinine, have lower levels ;of physical activity, and have a history of coronary heart disease compared with those without PAD. There were no significant differences in terms of gender, BMI, central obesity, and hypercholesterolemia between the two groups. However, female PAD patients were more likely to be in menopause. The mean values of thigh circumference in subjects with and without PAD are shown in Table 2. In general, male and female subjects with PAD had smaller thigh circumference than those without PAD. There were significant differences in thigh circumference, except for alcohol consumption, history of diabetes, hypertension, serum cotinine (for only females), and hypercholesterolemia (for only females), between subjects with and without PAD.

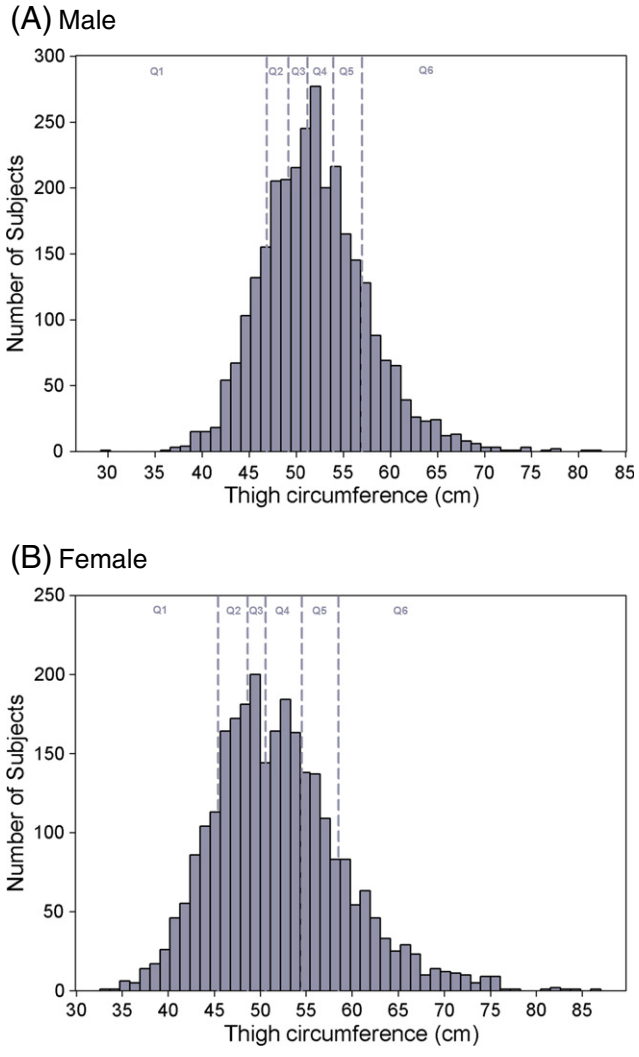

Fig. 1. Distribution of male and female thigh circumferences per each quintile. Each quintile (Q) has a similar number of subjects.