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Predictors of Change in the Ankle Brachial Index with Exercise

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WHAT THIS PAPER ADDS

It is well known that the ankle brachial index (ABI) has good sensitivity and specificity as a marker for peripheral artery disease (PAD). Less well known is that persons with PAD but normal ABIs can frequently be identified by a simple exercise test involving heel rises. This study is the first to evaluate multiple predictors of a decrease in the ABI with exercise, and shows that age, cigarette smoking, and a history of chronic obstructive pulmonary disease are independent markers of masked PAD. Thus, an exercise ABI test can identify persons who would benefit from aggressive risk factor modification.

Objective: A 20% or greater decrease in the ankle brachial index (ABI) with exercise is suggestive of peripheral artery disease (PAD), and could identify patients with an increased mortality risk. The predictors of a change in the ABI with exercise have received little attention.
Methods: This was a cross-sectional analysis. Two hundred and sixty five participants of the San Diego Population Study with a resting ABI between 0.90 and 1.10 performed 50 heel raises and immediately had their ABIs measured again. The relationship between the change in the ABI with exercise and multiple potential risk prediction variables were examined using linear regression. In addition, the categorical percent change in the ABI with exercise was analysed by multinomial logistic regression.
Results: The mean age of participants was 71.8 years, and 80.4% were female. At rest, the average ABI was 1.04 (SD 0.04) before and 0.94 (SD 0.13) after exercise; a mean decrease of 9.5%. In analyses of ABI change as a continuous variable, higher age, any smoking history, and a diagnosis of chronic obstructive pulmonary disease (COPD) were associated with a significant decrease in the ABI with exercise ($p = .01$, .04, and .03, respectively). Categorical analyses of the risk factors associated with a 20% or greater ABI decrease with exercise confirmed these results. Congestive heart failure was associated with an increased ABI with exercise ($p = .04$) in continuous ABI change analyses only.
Conclusions: Older age, a positive history of smoking, and a history of COPD were independently and significantly associated with a greater ABI decrease with exercise. These risk variables may help identify persons with subclinical PAD.

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INTRODUCTION

Peripheral artery disease (PAD), obstructive atherosclerosis of large to medium sized arteries that supply blood to the legs, is estimated to affect at least 8 million adults in the United States.[1] PAD can present clinically with symptoms including exercise leg pain (intermittent claudication), and physical findings including slow or non-healing wounds, but it is often asymptomatic. Moreover, PAD is associated with increased cardiovascular morbidity and mortality.[2] Although it has a relatively high prevalence, PAD is under-recognised in primary care practices.[3] The 2017 European Society of Cardiology (ESC) Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS) have recently been published.[4]

The ankle brachial index (ABI) is a well validated diagnostic test used to identify patients with PAD.[5] Using a cutoff point of $\leq .90$,[6] the ABI shows excellent specificity ($\approx .95$) and a good sensitivity ($\approx .80$) for arterial stenosis of $\geq 50\%$ when compared with angiography.[7] This level of sensitivity indicates that the .90 criterion results in a false negative rate of about 20%. Peripheral resistance decreases

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during exercise resulting in increased blood flow to the peripheral musculature. However, flow across a significant atherosclerotic plaque causes a pressure decrease, which may be exacerbated by exercise. Thus, some persons may have false negative ABIs only at rest, and measuring the ABI after exercise may "unmask" significant obstructive disease in persons with a normal resting ABI. Prior studies have shown an average decrease of 5% in the ABI with exercise ABI among normal individuals, while those with PAD had an average decrease of 20%.[8] These data indicate that the exercise ABI may be a useful adjunct in PAD evaluation.

Prior studies on the exercise ABI have largely been limited to subjects referred to vascular specialists or laboratories, rather than a free living population.[9,10] In addition, prior studies have not fully elucidated the demographic and cardiovascular risk factors of subjects who have decreases in ABI with exercise.[11] The present study reports the prevalence and the predictors of a decrease in ABI with exercise in a free living population. To the authors' knowledge, this is the first study to evaluate the predictors of a decrease in the ABI with exercise.

MATERIALS AND METHODS

Study population

From 1994 to 1998, the San Diego Population Study (SDPS) enrolled 2408 adults from current and retired employees of the University of California, San Diego (UCSD). Random selection was stratified by age, sex, and ethnicity to ensure an adequate representation of these groups. Women and certain ethnic minorities (Hispanic, African American, and Asian) were oversampled to preserve statistical power in subgroup analysis. Spouses and significant others were also invited to participate in the study and did not necessarily meet pre-specified inclusion criteria for age. Details of the SDPS methodology have been published previously.[12]

Surviving subjects who could be located from the SDPS were contacted to participate in an incidence visit 11 years later. Of these, 1103 agreed to participate, representing 46% of the original cohort. Study participants completed a resting ABI. Participants with ABIs in the range of 0.90—1.10 were deemed possible borderline PAD, and immediately underwent a standardised exercise protocol, involving 50 heel raises, followed by an ABI measurement.[13]

Prior to participating in the study, all subjects received a detailed introduction and description of the study procedures and signed informed consent documents. The Institutional Review Board Committee on Investigations Involving Human Subjects at University of California—San Diego approved the study.

Data collection

Subjects were interviewed by trained study staff using standardised questionnaires to obtain demographic information, past medical history including myocardial infarction (MI), angina, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting (CABG), congestive heart failure (CHF), stroke, transient ischaemic attack, diabetes mellitus, hypertension, and chronic obstructive pulmonary disease (COPD), as well as family history, and symptoms possibly related to PAD.

Ethnicity, education, and occupation were self reported. Smoking history was assessed and pack years were calculated as average packs of cigarettes smoked daily multiplied by number of smoking years. A blood sample was drawn, and total and high density lipoprotein (HDL) cholesterol were measured with standardised laboratory assays (Beckman Coulter analyser), as well as creatinine. Demographic variables, cardiovascular risk factors, and comorbidities were considered as potential risk predictor variables for an abnormal ABI with exercise.

Resting and the exercise ankle brachial index

Certified vascular technologists conducted a physical examination using standardised protocols that included obtaining systolic blood pressures (SBP). In brief, with the subject resting in the supine position, continuous wave Doppler ultrasound was used to measure the SBP twice at the same setting in both brachial arteries, and twice in both the dorsalis pedis and posterior tibial arteries of each leg. The ABI for each leg was calculated as the higher average SBP of the posterior tibial or dorsalis pedis divided by the highest average arm SBP. The index ABI was the lower of the left and right ABI.

If the resulting index ABI fell within the range of 0.90—1.10, subjects were immediately asked to perform 50 consecutive heel raises while standing.[13] Subjects stood 1—2 feet from a wall and were allowed fingertip support for balance. Immediately following exercise, the SBP in the ankle artery that was used for the index ABI numerator (posterior tibial or dorsalis pedis) was measured once. After measuring the ankle pressure, the SBP in the brachial artery used for the index ABI denominator was also measured once. The ankle SBP was divided by the arm SBP to calculate the exercise ABI.

The primary endpoint of this study was the ABI change with exercise, which was calculated by subtracting the ABI with exercise from ABI at rest. Also, the relative categorical change in the exercise ABI percent was calculated as follows: [(Exercise ABI - Resting ABI)/Resting ABI] $\times$ 100%. Group 1 ($n = 136$) had a $<$10% ABI decrease, Group 2 ($n = 77$) had a decrease between 10% and 20%, and Group 3 ($n = 52$) had a $>$20% decrease. Thus, Group 3 met the standard clinical criteria for an ABI decrease.[11] In initial analyses Group 1 was split into two subgroups: an exercise ABI percent increase ($n = 55$) and an exercise ABI decrease between 0 and -10% ($n = 81$). Analyses showed that these subgroups did not differ with respect to demographic and clinical predictors, so they were combined in these analyses.

Statistical analysis

Potential risk predictor variables were summarised using mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables. Predictors of exercise ABI change were determined in univariate and multivariate analyses using the linear regression