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# Predictors of Change in the Ankle-Brachial Index with Exercise

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## Abstract

**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 at increased risk of mortality. The predictors of a change in the ABI with exercise have received little attention.

**Design—**Cross-sectional analysis.

**Materials—**Two hundred 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.

**Methods—**We examined the relationship between the change in the ABI with exercise and multiple potential risk prediction variables using linear regression. In addition, the categorical percent change in the ABI with exercise was analyzed by multinomial logistic regression.

**Results—**The mean age of the participants was 71.8 years old, 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 = 0.01, 0.04, and 0.03 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 = 0.04) in continuous ABI change analyses only.

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**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.

### Keywords

Ankle Brachial Index; Peripheral Arterial Disease; exercise

## 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-recognized 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 cut-point of ≤ 0.90,[6] the ABI shows excellent specificity (≈0.95) and a good sensitivity (≈0.80) for arterial stenosis of ≥ 50% when compared to angiography.[7] This level of sensitivity indicates that the 0.90 criterion results in a false negative rate of about 20%. Peripheral resistance decreases 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] Here we report the prevalence and the predictors of a decrease in ABI with exercise in a free-living population. To our knowledge, this is the first study evaluate the predictors of a decrease in the ABI with exercise.

## Materials and Methods

### Study Population

From 1994-1998, the San Diego Population Study (SDPS) enrolled 2 408 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 previously published.[12]

Surviving subjects who could be located from the SDPS were contacted to participate in an incidence visit eleven years later. Of these, 1 103 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 standardized 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 standardized 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, transit ischemic 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 standardized laboratory assays (Beckman Coulter analyzer), as well as creatinine. Demographic variables, cardiovascular risk factors, and co-morbidities 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 standardized protocols that included obtaining systolic blood pressures (SBP). In brief, with the subject resting in the supine position, continuous-wave Doppler ultrasound was utilized to measure the SBP twice at the same setting in both brachial arteries, and twice in both the dorsalis pedis and the 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. We also examined the relative categorical change in the exercise ABI percent, calculated as following: [(Exercise ABI - Resting ABI) / Resting ABI] × 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 summarized using mean and standard deviation (SD) for continuous variables, and frequency and percentage for categorical variables. Predictors of exercise ABI change were determined in univariable and multivariable analyses using the linear regression model. The multivariable analysis initially included all predictors with a p-value < 0.20 in single-predictor analyses. The final multivariable model was determined using backward model selection with a p-value inclusion threshold of < 0.05. Age, gender, and race were retained in the final model irrespective of statistical significance.

For the analysis of categorical change in exercise ABI percent, we used univariable and multivariable multinomial logistic regression. Multivariable analyses initially included all predictors with a p-value < 0.20 in univariate analyses. The final multivariable model was determined using backward model selection with a p-value inclusion threshold of <0.05. Age, gender, and race were retained in the final model irrespective of statistical significance. All analyses were performed using SPSS version 23.

## Results

Of the 1103 study participants, 743 (67.4%) were female and 360 (32.6%) were male and the average age was 70.3 years old. Eight hundred and four (72.9%) had an index ABI >1.10 and 34 (3.1%) had an index ABI < 0.90. The remaining 265 participants (24.0%) had a resting ABI ranging from 0.90 to 1.10 and underwent the standardized exercise protocol.

Table I shows the means for continuous potential risk variables and the ABI measures. The mean age of the 265 participants who completed the exercise ABI measurements was 71.8 years. The average ABI at rest was 1.04, and was 0.94 after exercise, for an average decrease of 0.10, or 9.5%. Table II shows the proportion of participants with each categorical potential risk variable, and the mean ABI decrease for each variable. Groups with an ABI decrease of ≥ 0.14 were Hispanics and current smokers, as well as those with prior stroke, prior CABG, COPD, or chronic kidney disease.

Table III shows the potential risk variables and categorical change in ABI percent with exercise. One hundred thirty-six (51.3%) had an ABI decrease less than 10%, 77 (29.1%) had a decrease between 10% and 20%, and 52 (19.6%) had an ABI that decreased more than 20%. The <10% decrease group was younger than the other two groups (70.5 years old compared to 73.4 years old). (reviewer requests p-values) In general, the ≥ 20% ABI decrease category had the highest level of risk variables.

In the multivariable regression analyses, increasing age was associated with a significant drop in the exercise ABI (beta = - 0.002 per year, p = 0.01) (Table IV). The change in the exercise ABI was not different by gender (p = 0.55). Ethnic differences overall reached statistical significance (p= 0.05), with Hispanics having the largest and Asians the smallest ABI decrease. Former smokers showed a 0.03 and current smokers a 0.08 greater ABI decrease than never smokers (p= 0.04). None of the other traditional cardiovascular risk variables were statistically significantly associated with ABI changes with exercise.

COPD and CHF were both associated with a statistically significant difference in the change of ABI with exercise. Compared to those without COPD, those with COPD demonstrated a 0.10 greater ABI decrease with exercise (p= 0.03). In contrast, participants with a history of CHF actually had no change in ABI post exercise (Table II), which was a difference of 0.10 from those without CHF (p=0.04). All other comorbidities including hypertension, diabetes mellitus, stroke, and myocardial infarction did not independently predict ABI change with exercise.

The categorical analyses using multinomial regression are shown in Table V. Group 1, who had a post-exercise ABI change percent drop <10%, was the reference group. The odds ratio (OR) for increasing age per year for a decrease 10% to 20%, Group 2 (vs. a decrease of < 10%, Group 1) was 1.10 (p = 0.01) and to decrease more than 20%, Group 3, was 1.03 (p = 0.15). Current smokers had a greater ABI decrease compared to never smokers, with an OR of 7.3 (p = 0.03) to decrease 10% to 20%, Group 2, and an OR 12.8 (p = 0.02) to decrease more than 20%, Group 3. For former smokers, the OR for a 10% to 20% ABI decrease, Group 2, was OR= 2.1, p = 0.02, but the OR for a 20% decrease, Group 3, was not significant. Participants with a history of COPD were more likely to have a 20% decrease in the post-exercise ABI, Group 3, OR = 10.4, p = 0.05.

## Discussion

ABI values below 0.90 have been shown to be both sensitive and specific for diagnosing PAD.[7] However, with mild stenosis, the resting ABI could be normal in as many as 56% of PAD cases,[10] suggesting the need of an additional diagnostic testing such as the exercise ABI. We examined a free-living population similar to a primary care practice, and identified a correlation between the ABI change with exercise and several population characteristics.

Age and smoking are significant and independent risk factors for PAD. As expected, these variables had significant associations with the change in the ABI with exercise. COPD also had a significant association with a decrease in the exercise ABI that was surprisingly independent of smoking history. It is possible that COPD, which is strongly associated with smoking history, serves here as a marker of the extent of smoking. The observation that odds ratios for an ABI decrease were increased significantly for both former smokers and current smokers suggests that a >10 percent decrease in the ABI with exercise is suggestive of early atherosclerosis.

An ABI decrease with exercise has been demonstrated previously in patients with symptoms consistent with claudication but with a normal resting ABI.[9] One study of patients referred to a vascular study laboratory demonstrated that 31% had an ABI <0.9 only after exercise.[10] However, a study of 218 patients with PAD demonstrated only a minor benefit in the diagnostic yield of with exercise ABI of 1.6% compared to resting ABI.[8]

The prognostic value of exercise ABI has been shown in different sittings. Diehm and his colleagues showed an increase of the incidence of coronary/carotid revascularization and peripheral revascularization/amputation among patients with low exercise ABI values in a primary care sitting.[14] In a different practice sitting, Hammad, et al. followed 2791 patients for an average of 3.8 years. They showed that an abnormal exercise ABI (a 20% decrease from resting ABI) was associated with increased lower extremity revascularization compared to a normal exercise ABI.[11] These increases in risk indicate the importance of identifying patients at higher risk using the exercise ABI test.

Limitation of our study include that eligible participants were drawn from university employees and their spouses, and the study population may not be representative of the general outpatient population. Other limitations include the relatively small number of subjects studied and the lack of confirmatory studies for PAD, such as additional non-invasive vascular testing or angiography. Finally, this study was conducted in an older population, average age 71.8 years. Future study of these hypotheses in somewhat younger cohorts would be valuable.

Persons who are older, have a history of smoking, or a history of COPD and who have a borderline resting ABI are each independently more likely to have an abnormal exercise ABI. In this study 52 of 265 participants (20%) with an ABI between 0.90 and 1.10 had a >20% ABI decrease with exercise. Such persons could have subclinical PAD and additional confirmation of this diagnosis could lead to interventions to reduce cardiovascular disease morbidity and mortality.

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**What does this study/review add to the existing literature and how will it influence future clinical practice**

It is well known that the ankle-brachial index (ABI) shows 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.

**Table I**

**Continuous potential risk variables for study participants**

| | Mean (SD) |
|---|---|
| **Age, years** | 71.8 (9.4) |
| **Pack-years** | 6.7 (14.3) |
| **Total Cholesterol, mg/dl** | 204.8 (42.3) |
| **HDL, mg/dl** | 62.2 (20.3) |
| **LDL, mg/dl** | 114 (37) |
| **Triglyceride, mg/dl** | 144.7 (86.5) |
| **Creatinine, mg/dl** | 0.87 (0.25) |
| **GFR** | 58.2 (6.9) |
| **Arm Systolic Blood Pressure at rest, mmHG** | 134.69 (18.2) |
| **Ankle Systolic Blood Pressure at rest, mmHG** | 140.21 (19.8) |
| **ABI at rest** | 1.04 (0.04) |
| **Arm Systolic Blood Pressure post-exercise, mmHG** | 142.23 (20.6) |
| **Ankle Systolic Blood Pressure post-exercise, mmHG** | 133.53 (24) |
| **ABI post-exercise** | 0.94 (0.13) |
| **ABI change (at rest – post-exercise)** | 0.10 (0.01) |
| **ABI % change** | 9.5% (11.8) |

**Table II**

**Categorical potential risk variables and mean change in ABI with exercise**

| | N (%) | Mean change in ABI (95% CI) |
|---|---|---|
| **Female** | 213 (80.4) | - 0.10 (-0.12 to -0.09) |
| **Male** | 52 (19.6) | - 0.09 (-0.13 to -0.05) |
| **Non-Hispanic White** | 150 (56.6) | - 0.09 (-0.11 to -0.07) |
| **Hispanic** | 35 (13.2) | - 0.14 (-0.18 to -0.09) |
| **African American** | 49 (18.5) | - 0.12 (-0.16 to -0.09) |
| **Asian** | 31 (11.7) | - 0.05 (-0.09 to -0.01) |
| **Never smoker** | 160 (60.4) | - 0.08 (-0.1 to -0.06) |
| **Former smoker** | 91 (34.3) | - 0.12 (-0.14 to -0.09) |
| **Current smoker** | 12 (4.5) | - 0.16 (-0.22 to -0.08) |
| **Stroke** | 3 (1.1) | -0.17 (-0.63 to 0.3) |
| **MI** | 8 (3) | -0.10 (-0.25 to 0.1) |
| **CABG** | 6 (2.3) | -0.14 (-0.34 to0.06) |
| **Angina** | 7 (2.6) | -0.08 (-0.2 to 0.04) |
| **CHF** | 7 (2.6) | 0.003 (-0.12 to 0.13) |
| **Hypertension** | 162 (61.1) | - 0.11 (-0.12 to -0.09) |
| **Hyperlipidemia** | 98(37) | -0.11 (-0.13 to -0.08) |
| **Diabetes Mellitus** | 31 (11.7) | -0.11 (-0.16 to -0.05) |
| **COPD** | 7 (2.6) | - 0.22 (-0.31 to -0.13) |
| **Kidney Disease** | 11 (4.2) | -0.14 (-0.23 to -0.05) |

## Table III
**Potential risk factors for categorical changes in ABI (as a percent)**

| | Categorical Post-exercise ABI Decrease | | |
|---|---|---|---|
| | **Group 1** | **Group 2** | **Group 3** |
| | **<10% Decrease** | **10-20% Decrease** | **>20% Decrease** |
| ***N (%)*** | 136 (51.3%) | 77 (29.1%) | 52 (19.6%) |
| ***Continuous Mean (SD)*** | | | |
| **Age, years** | 70.5 (±9.7) | 73.4 (±8.9) | 73.4 (±9) |
| **Pack-year** | 4.8 (±4.8) | 9.5 (±9.5) | 7.9 (±7.9) |
| **Total Cholesterol, mg/dl** | 203 (±43.8) | 208.2 (±36.9) | 204.3 (±46.3) |
| **HDL, mg/dl** | 63.2 (±22.4) | 62.3 (±17) | 59 (±21.2) |
| **LDL, mg/dl** | 112.1 (±36.9) | 118.4 (±37.6) | 112.1 (±36.8) |
| **Triglyceride, mg/dl** | 139.7 (±83.2) | 150.8 (±91.1) | 149.1 (±89) |
| **Creatinine, mg/dl** | 0.84 (±0.23) | 0.9 (±0.28) | 0.88 (±0.22) |
| **GFR** | 57.7 (±6.4) | 57.7 (±7.8) | 58.2 (±6.9) |
| ***Categorical N (%)*** | | | |
| **Female** | 107 (78.7%) | 65 (84.4%) | 41 (78.8%) |
| **Male** | 29 (21.3%) | 12 (15.6%) | 11 (21.2%) |
| **Non-Hispanic White** | 80 (58.8%) | 43 (55.8%) | 27 (51.9%) |
| **Hispanic** | 15 (11.0%) | 11 (14.3%) | 9 (17.3%) |
| **African American** | 20 (14.7%) | 15 (19.5%) | 14 (26.9%) |
| **Asian** | 21 (15.4%) | 8 (10.4%) | 2 (3.8%) |
| **Never smoker** | 95 (69.9%) | 37 (48.1%) | 28 (53.8%) |
| **Former smoker** | 38 (27.9%) | 33 (42.9%) | 20 (38.5%) |
| **Current smoker** | 2 (1.5%) | 6 (7.8%) | 4 (7.7%) |
| **Stroke** | 1 (0.7%) | 1 (1.3%) | 1 (1.9%) |
| **MI** | 4 (2.9%) | 1 (1.3%) | 3 (5.8%) |
| **CABG** | 2 (1.5%) | 1 (1.3%) | 3 (5.8%) |
| **Angina** | 3 (2.2%) | 3 (3.9%) | 1 (1.9%) |
| **CHF** | 5 (3.7%) | 1 (1.3%) | 1 (1.9%) |
| **Hypertension** | 80 (58.8%) | 46 (59.7%) | 36 (69.2%) |
| **Hyperlipidemia** | 49 (36.0%) | 28 (36.4%) | 21 (40.4%) |
| **Diabetes Mellitus** | 15 (11.0%) | 6 (7.8%) | 10 (19.2%) |
| **COPD** | 1 (0.7%) | 2 (2.6%) | 4 (7.7%) |
| **Kidney Disease** | 3 (2.2%) | 4 (5.2%) | 4 (7.7%) |

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## Table IV

Multivariable risk factor associations with the change in continuous exercise ABI.

| | **Multivariable analysis** | |
|---|---|---|
| | **Mean change in ABI (95% CI)** | **P-value** |
| ***Age, years*** | -0.002 (-0.004 to -0.0005) | 0.01 |
| ***Gender*** | | |
| **Female** | Reference | |
| **Male** | 0.01 (-0.03 to 0.05) | 0.55 |
| ***Ethnicity*** | | 0.05 |
| **Non-Hispanic White** | Reference | |
| **Hispanic** | -0.05 (-0.1 to -0.003) | |
| **African American** | -0.02 (-0.06 to 0.02) | |
| **Asian** | 0.03 (-0.02 to 0.07) | |
| ***Smoking history*** | | 0.04 |
| **Never smoker** | Reference | |
| **Former smoker** | -0.03 (-0.06 to 0.002) | |
| **Current smoker** | -0.08 (-0.2 to -0.004) | |
| ***COPD*** | | |
| **No** | Reference | |
| **Yes** | -0.10 (-0.2 to -0.01) | 0.03 |
| ***CHF*** | | |
| **No** | Reference | |
| **Yes** | 0.10 (0.007 to 0.2) | 0.04 |

**Table V**

**Adjusted odds ratios for the categorical change (as a percent) in the ABI with exercise**

| | **Categorical Post-exercise ABI Decrease*** | | | |
|---|---|---|---|---|
| | **Group 2, 10-20%** | | **Group 3, >20%** | |
| | **OR (95% CI)** | **P-value** | **OR (95% CI)** | **P-value** |
| ***Age, years*** | 1.1 (1.01 to 1.1) | 0.01 | 1.03 (0.99 to 1.1) | 0.15 |
| ***Gender*** | | | | |
| **Female** | 1 (reference) | | 1 (reference) | |
| **Male** | 0.6 (0.2 to 1.4) | 0.22 | 1.1 (0.5 to 2.7) | 0.82 |
| ***Ethnicity*** | | | | |
| **Non-Hispanic White** | 1 (reference) | | 1 (reference) | |
| **Hispanic** | 2 (0.8 to 5.1) | 0.17 | 2.2 (0.8 to 6.5) | 0.13 |
| **African American** | 1.5 (0.7 to 3.5) | 0.32 | 1.9 (0.7 to 4.6) | 0.19 |
| **Asian** | 1.2 (0.5 to 3.1) | 0.73 | 0.4 (0.08 to 1.9) | 0.23 |
| ***Smoking history*** | | | | |
| **Never smoker** | 1 (reference) | | 1 (reference) | |
| **Former smoker** | 2.1 (1.1 to 4.1) | 0.02 | 1.1 (0.7 to 3.1) | 0.35 |
| **Current smoker** | 7.3 (1.2 to 43.8) | 0.03 | 12.8 (1.3 to 48.3) | 0.02 |
| ***COPD*** | | | | |
| **No** | 1 (reference) | | 1 (reference) | |
| **Yes** | 2.1 (0.2 to 25.1) | 0.55 | 10.4 (1.04 to 103.8) | 0.05 |

*<10% is the reference group