JACC: CARDIOVASCULAR INTERVENTIONS VOL. 8, NO. 9, 2015

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcin.2015.04.021

The Effect of Post-Exercise Ankle-Brachial Index on Lower Extremity Revascularization

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ABSTRACT

OBJECTIVES The purpose of this study was to investigate the effect of post-exercise ankle-brachial index (ABI) on the incidence of lower extremity (LE) revascularization, cardiovascular outcomes, and all-cause mortality in patients with normal and abnormal resting ABI.

BACKGROUND The clinical and prognostic value of post-exercise ABI in the setting of normal or abnormal resting ABI remains uncertain.

METHODS A total of 2,791 consecutive patients with ABI testing between September 2005 and January 2010 were classified into group 1: normal resting (NR)/normal post-exercise (NE); group 2: NR/abnormal post-exercise (AE); group 3: abnormal resting (AR)/NE; and group 4: AR/AE. Abnormal post-exercise ABI was defined as a drop of >20% from resting ABI as per the American College of Cardiology/American Heart Association guidelines. The primary endpoint was incidence of LE revascularization. Secondary endpoints were major adverse cardiovascular events (MACE) and all-cause mortality. Associations between post-exercise ABI and outcomes were adjusted using multivariable Cox proportional hazard and propensity analyses.

RESULTS Compared with group 1 (NR/NE), group 2 (NR/AE) had increased LE revascularization (propensity-matched adjusted hazard ratio [HR]: 6.63, 95% confidence interval [CI]: 3.13 to 14.04; $p < 0.001$) but no differences in MACE or all-cause mortality. When resting ABI was abnormal, group 4 (AR/AE) compared with group 3 (AR/NE), abnormal post-exercise ABI was still associated with increased LE revascularization (adjusted HR: 1.59, 95% CI: 1.11 to 2.28; $p = 0.01$), which persisted after propensity matching (adjusted HR: 2.32, 95% CI: 1.52 to 3.54; $p < 0.001$). Compared with group 1 (NR/NE) and after propensity matching, group 4 (AR/AE) had a significant increase in MACE (adjusted HR: 1.44, 95% CI: 1.09 to 1.90; $p = 0.009$) and a trend toward increased all-cause mortality (adjusted HR: 1.37, 95% CI: 0.99 to 1.88; $p = 0.052$); however, group 3 (AR/NE) did not.

CONCLUSIONS Post-exercise ABI appears to offer both clinical (lower extremity revascularization) and prognostic information in those with normal and abnormal resting ABI. (J Am Coll Cardiol Intv 2015;8:1238–44)

Resting ankle-brachial index (ABI) is the most commonly used test to diagnose and grade the severity of lower-extremity (LE) atherosclerosis; thus, it is an important clinical tool when considering revascularization in patients with peripheral artery disease (PAD). In addition to reflecting lower-extremity atherosclerosis, abnormal resting ABI is also a marker of systemic atherosclerosis (1,2), and has been shown to independently predict future cardiovascular events and mortality in several studies

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Manuscript received April 13, 2015; accepted April 23, 2015.

(3–5). However, patients with PAD commonly present with exercise-induced symptoms (claudication); therefore, it is unclear whether post-exercise ABI measurement would have an effect on clinical decision making (LE revascularization rate) beyond that of normal or abnormal resting ABI (6). Furthermore, there are limited data on the prognostic implications of post-exercise ABI beyond that of resting ABI (6–9).

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METHODS

STUDY POPULATION. This was a retrospective cohort study of 2,791 patients who underwent both resting and post-exercise ABI testing at a large tertiary care center between September 2005 and January 2010. Consistent with current American College of Cardiology (ACC)/American Heart Association (AHA) guidelines, abnormal resting (AR) ABI was defined as a resting ABI ≤0.90 and abnormal post-exercise (AE) ABI was defined as a >20% decrease from resting ABI (10). On the basis of these definitions, each leg for each patient was classified into 1 of these 4 groups: group 1: normal resting (NR)/normal post-exercise (NE); group 2: NR/AE; group 3: AR/NE; and group 4: AR/AE. Each patient was then assigned to the worst group of the 2 legs. Those with no audible Doppler sounds were classified as group 4. We excluded those with missing ABI measurements, prior lower extremity revascularization or amputation (n = 1), or incompressible vessels in both legs, defined as ABI at resting >1.4 (n = 50).

ABI MEASUREMENT, ENDPOINTS, AND DATA COLLECTION. Resting and post-exercise ABI data were obtained from the institutional Non-Invasive Vascular Laboratory database. All exercise ABI studies were performed in an accredited vascular laboratory (Intersocietal Accreditation Commission) by a registered vascular technologist. Prior to the test, patients were instructed to rest quietly for at least 5 min in the supine position. Subsequently, systolic blood pressure was measured in all 4 extremities using a Doppler device. Resting ABI was calculated by dividing the higher of the 2 ankle systolic blood pressures in each leg (dorsalis pedis or posterior tibial artery) by the higher of the 2 brachial artery systolic blood pressures. Post-exercise ABI was recalculated after remeasuring systolic blood pressures immediately post fixed-workload exercise protocol on a motorized treadmill. The standardized protocol is walking for 5 min at a 12.5% grade at 2.0 miles/h or until symptoms forced the patient to stop. In general, for post-exercise ABI calculation, the arm that has the higher resting brachial pressure along with the higher of the dorsalis pedis or posterior tibial artery ankle pressure are used to record the post-exercise measurement. Our protocol requires obtaining the post-exercise pressure measurements as promptly as possible once exercise has been terminated to reflect the hemodynamic changes produced by exercise most accurately. AE ABI was defined as a >20% decrease from resting ABI according to the ACC/AHA guidelines.

Lower extremity revascularization was selected as the primary endpoint to examine the effect of post-exercise ABI on clinical decision making, whereas major adverse cardiovascular outcomes (MACE) and all-cause mortality were the secondary endpoints. MACE was defined as a composite of all-cause mortality, stroke, myocardial infarction, and major lower extremity amputation. Stroke was defined as documented new or worsening focal neurological symptoms that persisted for >24 h and confirmed by neuroimaging. Both embolic and hemorrhagic strokes were included. Myocardial infarction was defined as documented positive cardiac enzymes plus electrocardiographic changes or symptoms consistent with myocardial ischemia. Baseline characteristics and outcomes were collected for all patients via electronic medical record review and were supplemented by the Social Security Death Index (SSDI) with a censoring date of September 30, 2011.

STATISTICAL ANALYSIS. Categorical variables were presented as number (percentage) and compared using the chi-square test or Fisher exact test when frequency was <10. Continuous variables were presented as mean ± SD and compared using the *t* test (for parametric variables) or Wilcoxon rank sum test (for nonparametric variables). Data with missing values, only 4 variables (Online Table 1), were imputed using the R package "mice 2.22" (11) under fully conditional specification, where 10 datasets were imputed and one complete dataset was selected at random for further analysis.

Survival analysis was performed by Kaplan-Meier curves and the log-rank comparison. Groups were compared using unadjusted and multivariable-adjusted (for all variables in **Table 1**) Cox proportional hazard regression models. In a separate analysis, propensity score matching was performed for all baseline characteristics in **Table 1**, utilizing a greedy matching algorithm in a 1:1 fashion (12). Outcomes were then analyzed between propensity

ABBREVIATIONS AND ACRONYMS

ABI = ankle-brachial index
ACC = American College of Cardiology
AE = abnormal post-exercise
AHA = American Heart Association
AR = abnormal resting
LE = lower extremity
MACE = major adverse cardiovascular events
NE = normal post-exercise
NR = normal resting
PAD = peripheral artery disease