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Women With Peripheral Arterial Disease Experience Faster Functional Decline Than Men With Peripheral Arterial Disease

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Objectives We hypothesized that women with lower extremity peripheral arterial disease (PAD) would have greater mobility loss and faster functional decline than men with PAD.

Background Whether rates of mobility loss or functional decline differ between men and women with PAD is currently unknown.

Methods Three hundred eighty men and women with PAD completed the 6-min walk, were assessed for mobility disability, and underwent measures of 4-m walking velocity at baseline and annually for up to 4 years. Computed tomography-assessed calf muscle characteristics were measured biannually. Outcomes included becoming unable to walk for 6 min continuously among participants who walked continuously for 6 min at baseline. Mobility loss was defined as becoming unable to walk for a quarter mile or to walk up and down 1 flight of stairs without assistance among those without baseline mobility disability. Results were adjusted for age, race, body mass index, physical activity, the ankle brachial index, comorbidities, and other confounders.

Results At 4 years of follow-up, women were more likely to become unable to walk for 6 min continuously (hazard ratio: 2.30, 95% confidence interval: 1.30 to 4.06, $p = 0.004$), more likely to develop mobility disability (hazard ratio: 1.79, 95% confidence interval: 1.30 to 3.03, $p = 0.030$), and had faster declines in walking velocity ($p = 0.022$) and the distance achieved in the 6-min walk ($p = 0.041$) compared with men. Sex differences in functional decline were attenuated after additional adjustment for baseline sex differences in calf muscle area.

Conclusions Women with PAD have faster functional decline and greater mobility loss than men with PAD. These sex differences may be attributable to smaller baseline calf muscle area among women with PAD. (J Am Coll Cardiol 2011;57:707–14) © 2011 by the American College of Cardiology Foundation

Lower extremity peripheral arterial disease (PAD) affects 8 million men and women in the U.S. (1). Among older individuals, the prevalence of PAD is similar to or even slightly higher in women as compared with men (1–3). A previous cross-sectional study demonstrated that women with PAD have greater functional impairment and poorer lower extremity strength than men with PAD (4). However, little is known about sex differences in rates of functional decline or changes in calf muscle characteristics over time between men and women with PAD.

In this observational, longitudinal study, we compared rates of mobility loss, decline in 6-min walk performance, and decline in walking velocity between men and women with PAD at 4 years of follow-up. We also compared baseline measures of calf muscle characteristics and leg strength and changes in these muscle outcomes between men and women with PAD at 4 years of follow-up. We hypothesized that women with PAD would have greater mobility loss, faster functional decline, and more adverse changes in calf muscle characteristics over time compared with men with PAD. We further hypothesized that greater mobility loss and faster functional decline among women with PAD as compared with

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Abbreviations and Acronyms

ABI = ankle brachial index
BMI = body mass index
CT = computed tomography
PAD = peripheral arterial disease

men with PAD is explained by more adverse muscle characteristics among women with PAD as compared with men with PAD.

Methods

Study overview. The Institutional Review Boards of Northwestern University and Catholic Health Partners Hospital approved the protocol. Participants gave written informed consent. Participants were in the WALCS (Walking and Leg Circulation Study) II cohort, a prospective, observational study designed to identify mechanisms of functional decline in PAD (5,6). Participants underwent baseline measures and returned annually for follow-up for up to 4 follow-up visits. Data collection took place between November 6, 2002, and October 16, 2009. Every effort was made to maximize follow-up by scheduling follow-up visits before or after their due date, if a participant was otherwise unable to return for follow-up testing.

Participant identification. PAD participants were 59 years of age and older and were identified from among consecutive patients diagnosed with PAD in Chicago-area noninvasive vascular laboratories (5,6). A small number of PAD participants were identified from among consecutive patients in a large general internal medicine practice at Northwestern with a low ankle brachial index (ABI) at their study visit. PAD was defined as ABI <0.90 (2,5,6). Absence of PAD was defined as ABI 0.90 or more and 1.30 or less (5,6).

Participation rates and exclusion criteria for the WALCS II cohort have been described and are summarized briefly here (6). Patients with dementia were excluded because of their inability to answer questions accurately. Nursing home residents, wheelchair-bound patients, and patients with foot or leg amputations were excluded because they had severely impaired functioning at baseline. Non–English-speaking patients were excluded because investigators were not fluent in non-English languages. Patients with recent major surgery were excluded.

ABI measurement. A hand-held Doppler probe (Nicolet Vascular Pocket Dop II, Nicolet Biomedical, Inc., Golden, Colorado) was used to obtain systolic pressures in the right and left brachial, dorsalis pedis, and posterior tibial arteries (5–7). Each pressure was measured twice. The ABI was calculated by dividing the mean of the dorsalis pedis and posterior tibial pressures in each leg by the mean of the 4 brachial pressures (7). Zero values for the dorsalis pedis and posterior tibial pulses were set to missing for the ABI calculation. Average brachial pressures in the arm with highest pressure were used when 1 brachial pressure was higher than the opposite brachial pressure in both measurement sets and the 2 brachial pressures differed by 10 mm Hg or more in at least 1 measurement set, because in such cases, subclavian stenosis is possible (8). The lowest leg ABI was used in analyses.

Functional outcomes. Functional outcomes were assessed annually and consisted of mobility loss, becoming unable to walk for 6 min continuously without stopping, decline in 6-min walk performance of 20% or more, and average annual declines in 6-min walk performance, usual paced 4-m walking velocity, and fastest paced 4-m walking velocity (5,9).

6-min walk. Following a standardized protocol (9), participants walk up and down a 100-foot hallway for 6 min after instructions to cover as much distance as possible. The test administrator recorded whether the participant stopped during the 6-min walk. Participants who stopped at baseline were excluded from analyses of becoming unable to complete the 6-min walk without stopping.

4-m walking velocity. Walking velocity was measured with a 4-m walk performed at usual and fastest pace, based on a previous study (9,10). Each walk was performed twice. The faster walk in each pair was used in analyses (9,10).

Mobility measures. At baseline and at each follow-up visit, participants were asked to indicate whether they could walk a quarter mile and whether they could climb up and down 1 flight of stairs: 1) on their own; 2) with assistance; or 3) not at all (5,10). Mobility loss was defined as becoming unable to walk up and down one flight of stairs or to walk a quarter mile without assistance among those without mobility limitations at baseline (5,10). Those unable to return for follow-up were interviewed by telephone for the mobility outcome measure.

Calf muscle characteristics. Calf muscle measurements were assessed with computed tomography (CT) at baseline and at the 2- and 4-year follow-up visits using a CT scanner (LightSpeed, General Electric Medical Systems, Waukesha, Wisconsin) (5,6). Cross-sectional images of the calves measuring 2.5 mm were obtained at 66.7% of the distance from the distal to the proximal tibia (6,7). Cross-sectional images were analyzed using BonAlyse (BonAlyse Oy, Jyvaskyla, Finland), a software for processing CT images that identifies muscle tissue, fat, and bone (11). The muscle outline was traced manually, excluding subcutaneous fat and bone. When quantifying muscle area, the BonAlyse software quantifies voxels within a range corresponding to muscle density (9 to 271 mg/cm^3) and excludes voxels corresponding to fat density (−270 to 8 mg/cm^3). Intramuscular fat is quantified by summing voxels corresponding to fat within muscle tissue. Cadaver studies demonstrate that these methods provide an estimate of muscle cross-sectional area that is highly correlated with direct anatomic measures (12). Because larger individuals require greater muscle mass to support their frame, muscle area was adjusted for the square of individual tibia length (5). Muscle density measures the quantity of muscle per volume within the voxel range corresponding to muscle (9 to 271 mg/cm^3) and is a measure of muscle quality.