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High-risk plaque in the superficial femoral artery of people with peripheral artery disease: Prevalence and associated clinical characteristics

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ABSTRACT

Objective: We used magnetic resonance imaging (MRI) to study the prevalence and associated clinical characteristics of high-risk plaque (defined as presence of lipid-rich necrotic core [LRNC] and intraplaque hemorrhage) in the superficial femoral arteries (SFA) among people with peripheral artery disease (PAD).
Background: The prevalence and clinical characteristics associated with high-risk plaque in the SFA are unknown.
Methods: Three-hundred-three participants with PAD underwent MRI of the proximal SFA using a 1.5 T S platform. Twelve contiguous 2.5 mm cross-sectional images were obtained.
Results: LRNC was present in 68 (22.4%) participants. Only one had intra-plaque hemorrhage. After adjusting for age and sex, smoking prevalence was higher among adults with LRNC than among those without LRNC (35.9% vs. 21.4%, $p = 0.02$). Among participants with vs. without LRNC there were no differences in mean percent lumen area (31% vs. 33%, $p = 0.42$), normalized mean wall area (0.71 vs. 0.70, $p = 0.67$) or maximum wall area (0.96 vs. 0.92, $p = 0.54$) in the SFA. Among participants with LRNC, cross-sectional images containing LRNC had a smaller percent lumen area (33% ± 1% vs. 39% ± 1%, $p < 0.001$), greater normalized mean wall thickness (0.25 ± 0.01 vs. 0.22 ± 0.01, $p < 0.001$), and greater normalized maximum wall thickness (0.41 ± 0.01 vs. 0.31 ± 0.01, $p < 0.001$), compared to cross-sectional images without LRNC.
Conclusions: Fewer than 25% of adults with PAD had high-risk plaque in the proximal SFA using MRI. Smoking was the only clinical characteristic associated with presence of LRNC. Further study is needed to determine the prognostic significance of LRNC in the SFA.
Clinical trial registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00520312.

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1. Introduction

Data from autopsies and direct atherosclerotic plaque visualization demonstrate that presence of high risk plaque, defined as the presence of lipid rich necrotic core (LRNC) with a thin fibrous cap or intra-plaque hemorrhage in the carotid and coronary arteries is associated with an increased rate of local plaque rupture resulting in stroke or myocardial infarction, respectively [1–10]. However, given regional variations in factors such as patterns of inflammation, artery size and sheer stress the plaque composition and its clinical correlates may differ across vascular beds [11–13].

High resolution magnetic resonance imaging (MRI) identifies characteristics of high-risk plaque in the carotid arteries non-invasively [14,15]. Studies of individuals with established atherosclerosis in the carotid arteries document a LRNC prevalence of at least 70% in the carotid arteries, with even higher rates among individuals who also experienced symptoms of stroke or transient ischemic attack [16,17]. Prevalence rates of intra-plaque hemorrhage in the carotid arteries range from approximately 10%–64% [7,16].

Prior studies regarding MRI of atherosclerotic plaque in the femoral arteries have focused on plaque burden and lumen area, and have shown associations of MRI measures with the ankle-brachial index (ABI), functional performance and lower extremity symptoms [18,19]. However, to our knowledge, a more detailed assessment of plaque composition to describe the prevalence and associated clinical characteristics of MRI-measured LRNC and intra-plaque hemorrhage in the femoral arteries has not been reported previously. We used MRI of plaque in the superficial femoral artery (SFA) to determine the prevalence of LRNC and intra-plaque hemorrhage among adults with peripheral arterial disease (PAD). We identified clinical characteristics associated with LRNC and intra-plaque hemorrhage in the SFA, and determined the association of LRNC with arterial wall dimensions. Finally, because of the association with plaque eccentricity and future events in the carotid and coronary arteries, we evaluated whether presence of LRNC was associated with eccentric vs concentric plaque [20,21,32]. We hypothesized that the presence of LRNC would be associated with more severe local atherosclerosis.

2. Methods

2.1. Subjects

Participants with PAD were part of the WALCS (Walking and Leg Circulation Study) III cohort, a prospective observational study designed to examine the association of MRI-measured atherosclerotic plaque with functional impairment and decline in men and women with PAD. PAD was defined as an ankle-brachial index (ABI) <1.00. Enrollment occurred between October 26, 2007 and December 22, 2009. During the recruitment period, all patients who were diagnosed with PAD in the non-invasive vascular laboratories and/or all PAD patients seen in defined vascular surgery, cardiology, and/or general medical practices at four Chicago-area hospitals were approached for participation according to our IRB approved methods (see Fig. 1). To maximize enrollment, we also invited patients in a general internal medicine practice who were age 70 or older and did not have a history of PAD to be screened for PAD with the ABI to determine eligibility. Those with an ABI <1.00 who met inclusion criteria were invited to participate. The Institutional Review Board at all participating sites approved the protocol. Participants gave written informed consent. MRI was performed between January 2008 and April 2010.

Of 473 individuals with PAD in the WALCS III cohort, 16 participants were excluded because of poor image quality on proton-density or time-of-flight MRI images. Of the remaining 457 participants, 303 underwent additional MRI data collection (T1- and T2-weighted imaging) to obtain data for plaque composition. Between 1/1/08 and 5/31/08 time constraints on the MR machine did not allow us to collect plaque characterization images on all participants and therefore data collection for plaque characterization was only performed on a randomly selected 50% subset of participants. Between 6/1/08 and 4/3/2010, all participants underwent additional image collection for plaque characterization. The full imaging protocol is described below.

2.2. Inclusion and exclusion criteria

The inclusion criterion for WALCS III was an ABI <1.00. We chose an ABI cutoff of 1.00 because previous studies show that individuals with an ABI 0.90–1.00 have higher rates of mobility loss, exertional leg pain, cardiovascular events, and total mortality compared to individuals with an ABI 1.10-1.40 [22–24].

WALCS III exclusion criteria have been described previously and are summarized here. Potential participants with dementia and those with a Mini-Mental Status Examination score <23 were excluded because it was unclear whether they could answer questions accurately [25]. Nursing home residents, wheelchair-bound patients, and patients with foot or leg amputations were excluded because of their impaired functioning. Non-English-speaking patients were excluded because investigators were not fluent in non-English languages. Patients with major surgery during the past three months or contraindications to MRI testing were excluded. We also excluded potential participants who required oxygen therapy, those who stopped a 6-min walk test due to shortness of breath, and those with severe knee osteoarthritis, defined as pain in or around the knee joint combined with a radiograph-measured osteoarthritis K/L score of four [26]. In addition, PAD participants with a completely occluded SFA were excluded from analyses.

2.3. Ankle brachial index measurement

ABI methods in the WALCS III cohort have been reported [19]. After participants rested supine for 5 min, a hand-held Doppler probe (Nicolet Vascular Pocket Dop II, Golden, CO) was used to measure systolic pressures in this order: right brachial, dorsalis pedis, and posterior tibial arteries and left dorsalis pedis, posterior tibial, and brachial arteries. Pressures were then repeated in reverse order. The ABI was calculated in each leg by dividing average pressures in that leg by the average of the four brachial pressures [27]. Average brachial pressures in the arm with the highest pressure were used when one brachial pressure was higher than the opposite brachial pressure in both measurement sets, and the two brachial pressures differed by 10 or more mm Hg in at least one measurement set, since in such cases subclavian stenosis was possible. The lowest leg ABI was used for analyses.

2.4. Magnetic resonance imaging

We imaged the SFA of the leg with the lowest ABI. MRI data were obtained with a 1.5 T (Espree, Siemens Medical Solutions, Malvern, PA) platform using a four-element phased-array surface coil (Nova Medical, Wilmington, MA). We imaged the proximal region of the SFA because its superficial location was more amenable to high quality images than the distal SFA. The bifurcation of the common femoral artery was the reference point. MRI images were collected with a standard, turbo spin echo (TSE) acquisition proton density weighted (TR/TE = 2160 ms/8 ms, bandwidth 230 Hz/pixel, turbo factor 15). The field of view was 120 × 120 mm^2 and images were