### Detection of Subclinical Atherosclerosis in Subclavian Arteries of Subjects with Vascular Risk Factors and Normal Carotid Ultrasound

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> Background and Purpose: Most risk scores that use imaging methods to determine the presence of subclinical atherosclerosis assess the carotid and coronary arteries. The value of assessing subclavian arteries to improve the predictive capacity of traditional imaging studies is not known. Materials and Methods: We studied subjects without cardiac, cerebral, or peripheral vascular symptoms and normal carotid ultrasound. They had at least 1 traditional vascular risk factor. We assessed prevalence of atherosclerotic plaques in the right subclavian artery. Results: We studied 625 subjects aged 54 ± 12. Most participants had 1 vascular risk factor. Using the Framingham Heart Study score, 62% were categorized as low risk, 29% intermediate risk, and 9% high risk. A total of 169 subjects (27%) had atheromatous plaques in the right subclavian artery. The prevalence of this finding was greater in women than in men (64% versus 36%, P < .00001) and was greater in subjects older than 54 years than in younger individuals (72% versus 28%, P < .00001). Plaques in the subclavian artery were present in 27% of subjects with high risk, 34% with intermediate risk, and 24% with low risk. Conclusions: Plaques in subclavian arteries are often detected in asymptomatic subjects with vascular risk factors and normal carotid arteries even with low vascular risk scores. Study of the subclavian arteries appears as a simple strategy for the detection of subclinical atherosclerosis. Its role for improving cardiovascular risk scales and predicting coronary and cerebrovascular events needs to be further explored. Key Words: Atherosclerosis-risk assessment—ultrasonography—Framingham Heart Study—subclavian artery. © 2018 National Stroke Association. Published by Elsevier Inc. All rights reserved.

#### Introduction

Atherosclerotic vascular disease is the leading cause of death in most countries.<sup>1</sup> Vascular events are usually

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preceded by a subclinical phase and the detection of disease often occurs at advanced stages or after clinical manifestations.<sup>2</sup> Most of these deaths are due to cardiac and brain vascular diseases.<sup>2</sup> Presence of atherosclerosis in asymptomatic subjects is a strong predictor of clinical events and may precede symptoms by many years.<sup>3-5</sup> Several methods have been developed for the early detection of atherosclerotic disease, and they have been incorporated to some risk prediction scores or serve as complementary tools in others.<sup>5</sup> The Framingham Heart Study (FHS) score, European Score, carotid intimamedia thickness (IMT), measurement of C-reactive protein, lipoprotein-A levels, and determination of the calcium score in the coronary arteries (CAC) all attempt to identify subjects at risk of future clinical events.<sup>6</sup> However, most of

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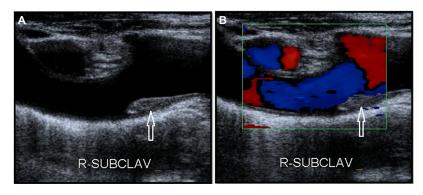
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**Figure 1.** Visualization of right subclavian artery in *B*-mode ultrasound (A) and with color Doppler (B) showing an atherosclerotic plaque (arrow). Abbreviation: R-SUBCLAV, right subclavian. (Color version of figure is available online.)

these risk assessments have well-recognized limitations.<sup>7</sup> Atherosclerosis may be present in a substantial number of subjects assessed as low risk by the FHS score.<sup>7</sup>

New assessments including inflammatory markers and ultrasonography may identify asymptomatic subjects with elevated vascular risk and help guide more intensive management to reduce events at an early stage. The ultrasound assessment of carotid IMT carries one of the highest degrees of evidence among the abovementioned new markers. The American Heart Association guidelines recommend (level of evidence IIa) carotid IMT measurement in asymptomatic subjects with an intermediate vascular risk.<sup>8</sup>

Most risk scores that use imaging methods to determine the presence of subclinical atherosclerosis assess the carotid or coronary arteries. However, many events still occur in subjects with low risk scores and absence of atherosclerosis in those territories.<sup>7,9</sup> The prevalence and significance of the detection of atherosclerosis in other vascular beds have not been fully elucidated. The presence of atherosclerotic disease in the lower limbs was a robust predictor of clinical events in the Progression of Early Subclinical Atherosclerosis (PESA) cohort.<sup>7</sup> However, the evaluation of atherosclerosis of the lower limbs requires an additional diagnostic procedure, and it is not routinely obtained in asymptomatic subjects.

The subclavian arteries are anatomically close to the carotid arteries, and the right subclavian artery can be easily insonated at the time of a routine carotid ultrasound (Fig. 1).

There are scant data in the literature about the prevalence of atherosclerotic disease in the subclavian arteries in subjects without carotid plaques.

We aimed to assess the prevalence of atherosclerotic disease in the subclavian arteries in subjects with vascular risk factors and normal carotid ultrasound.

#### Methods

The study was approved by the institutional ethics committee and subjects gave consent for participation.

We prospectively evaluated a group of patients with vascular risk factors referred for carotid ultrasound as part of their evaluation of vascular risk. We identified subjects with normal carotid ultrasound and without history of cardiac, cerebral, or peripheral vascular symptoms. All subjects had at least 1 vascular risk factor, including hypertension, diabetes mellitus, smoking, or dyslipidemia. Arterial hypertension was defined as systolic blood pressure above140 mm Hg, diastolic pressure above 90 mm Hg, or use of antihypertensive drugs.8 Diabetes mellitus was considered when fasting plasma glucose was above 126 mg/dL or the individual was receiving treatment with insulin or oral hypoglycemic medication.8 Smokers were defined by current smoking status or lifetime consumption of more than 100 cigarettes.8 Dyslipidemia was diagnosed when total cholesterol was above 240 mg/ dL, low-density lipoprotein cholesterol was above 160 mg/ dL, or the subject was receiving lipid-lowering drugs.<sup>10</sup> Vascular risk was calculated using the 10-year risk of coronary heart disease from the FHS, and subjects were stratified as low (<10%), moderate (10%-20%), or high (>20%) risk.11

All the subjects were studied using a standardized protocol for the examination of carotid, vertebral, subclavian, and ophthalmic arteries investigating the presence of atherosclerotic disease.<sup>12</sup> The studies were performed by the same experienced operator (SE) who had no knowledge of any clinical data. We used a Doppler Color Toshiba Xario SSA-660A echography device (Toshiba Medical Systems Corp, Ottawa, Japan) with special software for measurement of the intima-media complex, Dynamic Flow and Power Doppler. A vascular ultrasound protocol was used in every subject.<sup>6,13</sup> Cervical vessels assessment included cross-sectional sweep of the common carotid artery, the carotid bulb, the internal carotid artery, the vertebral artery, and the subclavian artery. Due to the frequent technical difficulties involving the correct identification of the left subclavian arteries, only the findings of the right subclavian arteries are reported for this investigation. A plaque was defined as a focal protrusion into the arterial lumen of thickness that is greater than .5 mm or greater than 50% of the surrounding IMT or a diffuse thickness greater than 1.5 mm measured between the media-adventitia and intima-lumen interfaces.<sup>12,14</sup>

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