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Acoustic shadowing impairs accurate characterization of stenosis in carotid ultrasound examinations

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Objective: Duplex ultrasonography (DUS) has been the mainstay for diagnosing carotid artery stenosis and is often the sole diagnostic modality used prior to intervention. Highly calcified plaque, however, results in an acoustic shadow (AcS) that obscures the vessel lumen and inhibits the sonographer's ability to obtain Doppler velocity measurements. It is unknown whether DUS can accurately determine the degree of carotid stenosis in these settings.

Methods: From July 2012 to December 2013, all patients with AcS on DUS measuring ≥5 mm in the longitudinal axis were cross-referenced with multidetector computed tomographic angiography (MD-CTA) images of the neck to define the study population. After standardizing the MD-CTA windows, percent stenosis was determined by cross-sectional area reduction using two separate previously described methods based on North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) criteria. DUS waveform parameters in the internal carotid artery near the AcS were then compared with these MD-CTA measurements to determine the accuracy of DUS in characterizing the severity of carotid stenosis.

Results: During this period, 8517 DUS studies were performed at the Massachusetts General Hospital, 550 of which had AcS, for an incidence of 6.45%. There were 92 lesions with a concomitant MD-CTA; however, seven were excluded because of poor study quality, because ≥6 months had elapsed between DUS and MD-CTA, or because the patient had undergone carotid reconstruction between studies. Of the 85 remaining lesions, DUS characterized 17 as severe (peak systolic velocity [PSV] >250 cm/s), 31 as moderate (PSV = 151-250 cm/s), and 37 as mild (PSV ≤150 cm/s) stenoses using PSV criteria. PSV weakly correlated with CTA-NASCET ($r = 0.361$; $P = .004$) and CTA-ECST ($r = 0.306$; $P = .004$) percent stenosis. Using PSV >250 cm/s as the predictor of >70% stenosis, and a ≥70% cutoff by both CTA-ECST and CTA-NASCET methods as the reference measure, DUS sensitivity ranged from 22.7% to 32.5%, specificity from 89.4% to 91.1%, positive predictive value from 88.2% to 76.4%, and negative predictive value from 25% to 60.2%. A subgroup analysis of lesions identified as non-severe by DUS revealed that waveforms with lower deceleration were associated with severe stenosis on CTA.

Conclusions: In the presence of AcS, DUS alone is inadequate to accurately determine the degree of carotid stenosis with sensitivity, specificity, and negative predictive values far below that needed for clinical decision-making. MD-CTA may be necessary for improved characterization of plaque in these AcS lesions. Further studies are needed to determine DUS parameters that may identify patients who should undergo further evaluation with MD-CTA to characterize the true severity of the stenosis. (J Vasc Surg 2015;62:1236-44.)

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Current practice guidelines rely on the reliable and readily obtained assessment of internal carotid stenosis severity by measuring peak systolic velocity (PSV) using duplex ultrasound (DUS).[1] Furthermore, there is a substantial literature base indicating that such degree of stenosis is a reliable surrogate to identify patients at risk of stroke.[2,3] Clinicians accordingly rely on DUS for the assessment of carotid stenosis, and often this is the only diagnostic modality used prior to surgical intervention.[4]

The historical "gold standard" for carotid evaluation has been digital subtraction angiography (DSA); however, the invasive nature of this technique can be associated with a variety of complications, including a significant risk of stroke approaching 4%.[5,6] Subsequently, noninvasive techniques such as DUS have become the mainstay of carotid evaluation. The degree of DUS diameter reduction stenosis is typically determined by PSV and end-diastolic velocities (EDVs) in the internal carotid arteries (ICAs), and the ratio of the

PSV in the ICA and common carotid artery.[7] Numerous studies have demonstrated excellent sensitivity and specificity of DUS in detecting the degree of stenosis as defined by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) as well as the Carotid Endarterectomy for Asymptomatic Carotid Atherosclerosis Study (ACAS).[8-10] In fact, it has become accepted that, with few exceptions, DUS can be utilized as the sole methodology to determine the degree of carotid stenosis and whether surgical carotid revascularization is indicated.[6,11,12]

Concern has been raised, however, about the accuracy of DUS in the presence of heavily calcified arteries.[13,14] Calcified plaque is a common characteristic seen in carotid atherosclerotic disease and is associated with age, hypertension, diabetes, smoking, and chronic renal disease.[15-17] Furthermore, as the mean population age increases, calcified plaque is likely to become more prevalent. The exact etiology of artery calcification is unknown; however, studies have suggested that inflammation, oxidation of lipids in the arterial wall, and osteoblastic differentiation of vascular cells contribute to this phenomenon.[18] While some studies have demonstrated that calcified plaque is an independent predictor of cerebrovascular events,[15] many suggest a protective effect, with calcification resulting in decreased inflammation and greater plaque stability.[19-21]

On DUS, calcified plaque appears as an area of high echogenicity,[22,23] as the majority of ultrasonic waves are reflected back to the transducer. Subsequently, waves are unable to penetrate the area beyond the calcified plaque, and if different angulations of the probe cannot interrogate the arterial lumen, this results in an acoustic shadow (AcS; Fig 1).[24,25] As no Doppler spectral waveform or velocity measurements can be obtained within the AcS, the true degree of stenosis in this region remains uncertain. This is particularly problematic should the region of maximal carotid stenosis occur within this area, as DUS may underestimate the true degree of diameter reduction stenosis in this setting. As this has not been previously investigated, the goal in this study was to assess the accuracy and diagnostic performance of DUS in the presence of AcS.

METHODS

AcS was defined as a ≥5 mm segment of calcium in the vessel wall, prohibiting any interrogation by carotid DUS. From July 2012 to December 2013, all patients who underwent carotid DUS at the Massachusetts General Hospital accredited vascular diagnostic laboratory and met these criteria were retrospectively cross-referenced with those patients who underwent concomitant multidetector computed tomographic angiography (MD-CTA) of the neck. This cohort defined the study population. Percent stenosis diameter reduction by DUS was defined according to criteria previously validated in the noninvasive vascular laboratory. PSV ≤150 cm/s was defined as mild stenosis, 151-250 cm/s as moderate stenosis, and >250 cm/s as severe stenosis.[26]

Additionally, in an effort to identify indirect downstream Doppler spectral waveform predictors of stenosis

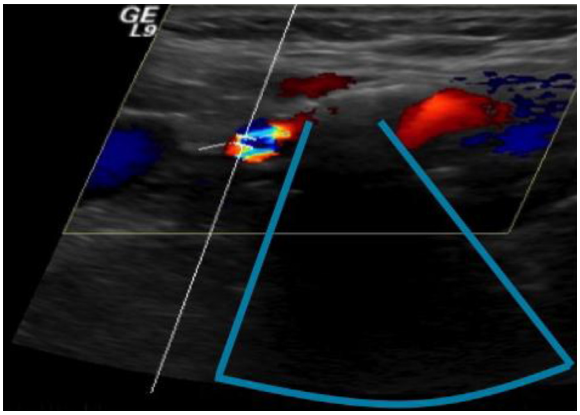

Fig 1. A typical acoustic shadow (AcS), which prevents interrogation of an area of the vessel lumen, is outlined (*blue*).

when the proximal segment of disease was shielded from interrogation by AcS, each DUS ICA waveform was analyzed with ADINative image analysis software (2007, 2008, Museum of Science, Boston, Mass) distal to the AcS. Waveform parameters calculated included acceleration-time,[14] acceleration slope, resistive index, deceleration, deceleration slope, and the ratio of the acceleration slope to the deceleration slope. Acceleration time was calculated as the time in milliseconds from the initial waveform upstroke to the time of PSV as previously described. (Fig 2, *a*).[14] Acceleration slope was calculated as the change in velocity from the beginning of the upstroke to the PSV divided by the acceleration time. Deceleration was calculated as the change in velocity from the time of PSV to 200 milliseconds beyond the peak (Fig 2, *b*). Deceleration slope was calculated as deceleration divided by 200 milliseconds. The slope ratio was calculated as the acceleration slope divided by the deceleration slope. Resistive index was calculated as (PSV − EDV)/EDV. These waveform parameters were correlated to MD-CTA reference standards to determine their ability to predict the extent of the severity of the stenosis in the AcS.

MD-CTA carotid lumen cross-sectional areas were determined using IMPAX version 6.5 software tools (AGFA Health Care, Mortsel, Belgium) by two reviewers (J.M., G.M.L.) blinded to DUS results. All MD-CTA windows were standardized to a width (W) of 700 and a level (L) of 300 to optimize the distinction between calcified plaque and intra-luminal contrast, as well as to minimize pixel averaging (Fig 3).

Review of the literature revealed two methods for determining percent stenosis based on CTA lumen cross-sectional area reduction.[27-31] One method, based on the NASCET method of comparing residual lumen diameter with the diameter of the non-diseased ICA distal to the lesion where the walls of the ICA are longitudinally parallel, compares the residual lumen cross-sectional area at the point of maximal stenosis to the cross-sectional area of the first "normal-appearing" region of the ICA