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EDITORIAL COMMENT

3-Dimensional Ultrasound in Carotid Stenosis Quantitation and Beyond*

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In 2013, the prevalence of stroke was 25.7 million worldwide (1). Each year, ≈795 000 people have a new or recurrent stroke in the United States; ischemic strokes account for 87%, and of these, carotid artery (CA) stenosis accounts for ≈20% (2). Surgical correction of asymptomatic 70% CA stenosis or symptomatic >50% CA stenosis is associated with a reduction in stroke risk (3,4). The advent of carotid duplex ultrasound (CDU) in the 1980s led to its widespread use. CDU is used as the stand-alone diagnostic test of choice for quantifying carotid stenosis in as many as 80% of patients before carotid endarterectomy (CE) in the United States (5). Magnetic resonance angiography (MRA) (6) and computed tomography angiography (CTA) (7,8) are other imaging tests used in the presence of a nondiagnostic CDU or intermediate-grade stenosis noted on CDU or when intracranial disease is suspected (9,10). These tests are costly and nonportable, however, and they do not demonstrate important hemodynamic variables. They also involve exposure to radiation for CTA and exposure to potential contrast nephrotoxicity.

The 2-dimensional (2D) imaging used in CDU shows vessels in a single plane, and it is not capable of measuring the percentage of luminal narrowing as measured by invasive angiography (3). Hence CDU criteria for CA stenosis assessment are currently determined on the basis of the Doppler systolic and diastolic velocities and flow pattern, resulting from flow obstruction produced by the plaque. This methodological assessment suffers from the pitfalls of Doppler, including the insonation angle of the ultrasound (US) beam with blood flow (11), stenosis characteristics, and cardiac output. CDU is cost effective and safe, and it allows early and rapid assessment to prevent recurrent stroke, which has a risk as high as 10% to 20% within the first 14 days (12). However, the low specificity (68%) of CDU for stenosis between 50% and 69%, partly attributable to the Doppler velocity overlap, leads to a need for MRA or CTA to prevent unnecessary procedures (13). Most patients with ≥60% stenosis do well with medical management alone. There is therefore a clinical need for improving the US diagnosis of stenosis quantitation (14). Three-dimensional (3D) US provides full-volume data inclusive of vessel wall, lumen, and plaque and has the capability for direct stenosis quantitation similar to that of angiography.

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In this issue of *iJACC,* Macharzina et al. (15) report a study in which they performed live 4-dimensionally guided (4D-guided) 3D color Doppler measurement of carotid lumen and vessel wall diameter to calculate the percentage of vascular stenosis and compared it with carotid angiography as the gold standard as well as with the conventional CDU. During live 4D imaging, these investigators placed 3 orthogonal planes perpendicular to each other at the center of the vessel lumen to obtain the enface cross section of the vessel with the best plaque visualization. A single-beat 3D color Doppler full-volume loop was then acquired and processed online or off-line to measure the smallest lumen diameter as defined by the color Doppler image relative to the normal vessel diameter. As determined by 3D US, 15% of patients had 0% to 49% stenosis, 34% had 50% to 69% stenosis, and 50% had 70% to 99% stenosis.

The study was designed to show noninferiority of the 3D method compared with the conventional methods (Doppler and carotid angiography), and this was demonstrated for all grades of stenosis severity. For binary clinically relevant cutoffs, Macharzina et al. (15) found that 3D color imaging showed a sensitivity of 97% and a specificity of 92% to detect stenosis ≥50%, a significant improvement on the

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established CDU modality. The sensitivity and specificity for >70% CA stenosis were 8% to 10% lower and were comparable to those of CDU. The use of 3D US resulted in correct assignment of 12% of the 70% stenoses and 8% of the 50% stenoses that were erroneously classified by DUS. In 2013, 88,000 CEs and 15,700 carotid stenting (CS) procedures were performed in the United States (2). Refinement of binary diagnostic criteria for 50% and 70% stenoses therefore translates into significant clinical benefit if acquisition of 3D technology and the learning time were not barriers.

The study also highlights the limitations of the 3D method, which was feasible in 86% of the study subjects. The frame rate for 3D color full-volume, single-beat acquisition was 15.0 to 25.0 Hz and 5.5 Hz for real-time 4D images. Macharzina et al. (15) used color Doppler to delineate the lumen from plaque, thus indicating that the resolution of the 3D image was not enough by itself for accurate diameter or area measurement of the residual lumen. The decrease in sensitivity and specificity for 70% stenosis compared with 50% stenosis suggests that the presence of significant plaque calcification and the attendant calcific shadowing limit evaluation by 3D US. Digital beam forming technology available in cardiac 3D transducers is not available in linear vascular transducers. Improvement of field of view (37.4 mm in the current study) and volume angle (29° in the current study), as well as real-time 3D and color Doppler 3D frame rate, will enhance image resolution and improve stenosis classification further. Despite these limitations, the image acquisition and post-processing times were clinically acceptable, and the reader variability on angiographic measurements was comparable to the variability between 3D US and angiographic measurements. Findings imply that 3D US has a promising clinical role in the diagnosis of carotid stenosis.

Could we use the findings from this study in our clinical practice? The time required for 3D data collection and analysis reported in the study makes a valid case for the use of 3D quantitation as a complementary method for assessment of stenosis severity. Automated processing of 3D datasets to calculate stenosis severity will provide rapid evaluation and has been used earlier for plaque volume quantitation (16). When CE or CS appears indicated by CDU, imaging with 3D imaging may be used to confirm the diagnosis without the need for MRA or CTA. In a subset of patients with borderline Doppler criteria cutoffs for 50% to 70% stenosis, 3D measurement may improve specificity. For plaques with significant calcification (as occurs with increasing stenosis severity), CDU Doppler velocity criteria may assist in more accurate stenosis identification, thus limiting MRA or CTA use if the diagnosis is still uncertain.

An important issue not addressed in the current study is the evaluation of plaque morphology. MR imaging allows detection of vulnerable plaques (17). 3D imaging has been shown to detect vulnerable plaques by plaque texture analysis (17,18) and of plaque ulcer volume using reconstruction from 2D datasets (19,20). Reliable detection of ulceration has been shown with 3D US (21) and predicts an increased risk of cardiovascular events (19). Another quantitative measure not performed in the current study is 3D measurement of plaque volume relative to vessel volume (similar to quantitation of coronary artery stenosis on intravascular US). This has been demonstrated to be reproducible by 3D single sweep US (22) and may allow accurate stenosis quantitation.

Use of a combined 2D and 3D approach to evaluate % vessel stenosis and plaque phenotype may change the treatment paradigm so that CE or CS is offered to patients with plaques with vulnerable surface characteristics despite causing less severe stenosis, whereas an asymptomatic patient with a significant stenosis resulting from a nonvulnerable plaque is treated medically.

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