Noninvasive characterization of carotid plaque strain

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ABSTRACT

Objective: Current risk stratification of internal carotid artery plaques based on diameter-reducing percentage stenosis may be unreliable because ischemic stroke results from plaque disruption with atheroembolization. Biomechanical forces acting on the plaque may render it vulnerable to rupture. The feasibility of ultrasound-based quantification of plaque displacement and strain induced by hemodynamic forces and their relationship to high-risk plaques have not been determined. We studied the feasibility and reliability of carotid plaque strain measurement from clinical B-mode ultrasound images and the relationship of strain to high-risk plaque morphology.

Methods: We analyzed carotid ultrasound B-mode cine loops obtained in patients with asymptomatic ≥50% stenosis during routine clinical scanning. Optical flow methods were used to quantify plaque motion and shear strain during the cardiac cycle. The magnitude (maximum absolute shear strain rate [MASSR]) and variability (entropy of shear strain rate [ESSR] and variance of shear strain rate [VSSR]) of strain were combined into a composite shear strain index (SSI), which was assessed for interscan repeatability and correlated with plaque echolucency.

Results: Nineteen patients (mean age, 70 years) constituting 36 plaques underwent imaging; 37% of patients ($n = 7$) showed high strain (SSI ≥0.5; MASSR, 2.2; ESSR, 39.7; VSSR, 0.03) in their plaques; the remaining clustered into a low-strain group (SSI <0.5; MASSR, 0.58; ESSR, 21.2; VSSR, 0.002). The area of echolucent morphology was greater in high-strain plaques vs low-strain plaques (28% vs 17%; $P = .018$). Strain measurements showed low variability on Bland-Altman plots with cluster assignment agreement of 76% on repeated scanning. Two patients developed a stroke during 2 years of follow-up; both demonstrated high SSI (≥0.5) at baseline.

Conclusions: Carotid plaque strain is reliably computed from routine B-mode imaging using clinical ultrasound machines. High plaque strain correlates with known high-risk echolucent morphology. Strain measurement can complement identification of patients at high risk for plaque disruption and stroke. (J Vasc Surg 2017;■:1-11.)

The primary contributor in the pathogenesis of stroke from carotid atherosclerotic stenosis is plaque disruption rather than hemodynamic compromise from luminal narrowing.[1] The mechanisms for plaque disruption have yet to be determined. Whereas the degree of diameter-reducing stenosis in the internal carotid artery is the standard approach for risk stratification, two randomized trials have failed to show a relationship between percentage stenosis in asymptomatic patients and subsequent stroke.[2,3] A small proportion of asymptomatic patients, however, do harbor plaques that progress to disruption. Selective revascularization of patients with such vulnerable plaques would prevent strokes if they could be identified with clinically available technology. Conversely, unnecessary procedures would be avoided in patients with low-risk plaques.

American Heart Association type VI plaques with enlarging lipid-rich necrotic cores, intraplaque hemorrhage, and fibrous cap thinning may lead to disruption and atheroembolization.[4-6] Although approximately 50% of asymptomatic patients with a stenosis harbor plaques with vulnerable morphology, only about 2% of asymptomatic patients develop a stroke at 1 year.[2,3,7] Therefore, morphology alone has limited ability to predict stroke. Plaques undergoing increased deformation or strain during the cardiac cycle are thought to be more susceptible to rupture.[8] Strain depends not only on biomechanical forces but also on plaque material properties, such that "softer" plaques may deform more to similar forces. Therefore, disruption could be influenced by biomechanical forces acting on plaques with high-risk morphology, and measurement of strain considers both these factors.[9] Validation of this hypothesis requires the development of plaque strain measures that can be employed in large longitudinal studies.

Carotid plaque strain measurements can be obtained using radiofrequency (RF) ultrasound and speckle

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tracking, although clinical translation is limited by a lack of access to RF data in commercial ultrasound machines.[10-12] B-mode ultrasound imaging is a practical solution for real-time longitudinal evaluation of plaque deformation and strain, but it has not been tested for feasibility or reliability. Moreover, hypoechoic plaques are a morphologic marker for high risk of stroke; however, there is limited information on the relationship between B-mode strain measurements and ultrasound-derived plaque severity indices, such as percentage stenosis, peak systolic velocity (PSV), and echogenicity.[13,14]

In this study, we tested the feasibility of measuring carotid plaque strain from B-mode ultrasound imaging in a clinical vascular laboratory during a routine clinical examination, assessed whether strain measurements allow reliable separation into low-strain and high-strain plaques, correlated strain with known plaque severity indices, and quantified the reliability of our strain indices.

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective single-center cohort study
- **Take Home Message:** Carotid plaque ;strain was measured in 19 patients using standard B-mode ultrasound imaging, and carotid plaques with higher strain correlated with high-risk morphologic features.
- **Recommendation:** This study suggests that plaque strain can be reliably measured by standard B-mode ultrasound and may be useful in identifying patients at high risk for future plaque disruption, atheroembolization, and stroke.

METHODS

Patients. After approval from the University of Maryland Institutional Review Board and signed informed consent, we enrolled 19 asymptomatic adults with ≥50% carotid stenosis without a prior stroke or transient ischemic attack. Demographics and risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking, and coronary artery disease) were recorded. Patients underwent ultrasound imaging at baseline, were managed with optimal medical treatment, and were followed up with annual clinical examinations for 2 years.[15]

B-mode ultrasound imaging. A clinical ultrasound machine (SonixTouch; Ultrasonix, Richmond, BC, Canada) was used with a standard L9-4/38 linear probe. Doppler velocities with consensus velocity criteria were used to estimate the degree of stenosis.[16] B-mode imaging was used to locate the carotid plaque and to acquire cine loops during three to five cardiac cycles with breath-holding, in an operator-selected optimal longitudinal orientation demonstrating the plaque at its thickest. The frame rates and depth settings were selected by the three participating sonographers as appropriate and varied across patients (10 to 30 frames per second and 3.5 to 4.5 cm, respectively). For each patient, two scans were obtained by the same sonographer with a 1-hour interval and used to assess reproducibility and intraobserver variability. The initial sequence was not used as a guide to coregister the second scan. Sonographers were not aware that the images would be used to compute plaque strain or intraobserver reproducibility. Because images were acquired as part of routine scanning and not specifically tailored for optimal strain imaging, these data provide an opportunity to gauge the robustness of strain measurement in a clinical environment. The B-mode images were normalized using the procedure outlined by Nicolaides et al.[17]

Strain field estimation. We employed dense optical flow-based speckle tracking for estimation of plaque displacement fields with high spatial resolution.[18] This allowed evaluation of heterogeneity in plaque motion. We measured the axial, lateral, and shear strain fields because plaque movement can occur in all planes. Strain was analyzed at peak systole to identify effects of the largest hemodynamic forces on the plaque (Fig 1) with respect to baseline displacement at end-diastole, which was insignificant.[19] The peak systolic frame in each study was identified on M-mode images derived from the cine loops using postprocessing. Plaque regions in the far and near walls of each image frame were manually outlined.[20] For each patient, a number of distinct plaque regions could be identified on an image sequence. Two plaque regions were considered distinct if they were located on the near and far arterial walls or the plaques were on the same arterial wall but separated by at least 5 mm. Plaques appearing discontinuous because of shadowing were considered a single region, and pixels in the shadow area were excluded for strain analysis. Fig 2, *A* depicts two outlined plaque regions (*blue and red lines*) located in the near and far walls, respectively. Fig 2, *B* shows a plaque region in the far wall of another patient with significant shadowing. The shear strain fields for each plaque region were analyzed separately.

Computation of shear strain rate and associated parameters. The shear strain field for each B-mode cine-loop sequence was normalized by its frame rate to obtain the shear strain rate field. We computed three parameters to assess the global behavior of the plaque. These included (1) maximum absolute shear strain rate (MASSR), a measure of the magnitude of strain regardless of direction[12]; and two measures that we introduced for the spread or variability in magnitude or direction of the strain fields within the plaque: (2) variance of shear strain rate (VSSR), which specifies the dispersion of strain,