Three-Dimensional Ultrasound Observation of Carotid Artery Plaque Ulceration

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Background and Purpose—Carotid artery plaque ulceration is associated with an increased risk of cerebral embolism. However, because of the rather poor diagnostic quality of conventional 2-D ultrasound and angiography compared with the evaluation of pathological specimens, little information exists on the natural course of carotid plaque ulceration. Recently, the introduction of 3-D ultrasound has made reproducible investigation of plaque morphology possible, providing a reliable plaque surface analysis.

Methods—We performed 3-D ultrasound examinations of 17 carotid artery plaques with an ulcerated surface in a prospective study of 16 patients (10 men, 6 women; mean±SD age 68.9±7.1 years) over a mean observation period of 17.6±6.3 months. Exactly parallel B-mode ultrasound scans (slice distance 0.1 mm) were acquired with a 5-MHz linear array probe clamped in a carriage device and driven by a mechanical step motor. The recorded images were reconstructed into a volumetric data set in a Cartesian coordinate system.

Results—At the end of the observation period, surface configuration had changed in 4 cases (23.5%). Plaque ulceration regressed in 3 cases, whereas ulcer progression occurred in 1 case. The remaining 13 plaques (76.5%) showed an unchanged surface configuration.

Conclusions—Through the use of 3-D ultrasound, it is possible to noninvasively examine the regression and progression of carotid artery plaque ulceration. (Stroke. 2000;31:1651-1655.)

Key Words: atherosclerosis • carotid artery • ulcer • ultrasonography

A recent consensus on the morphology of atherosclerotic lesions of the carotid artery pointed out that ultrasonic characteristics of plaque echogenicity and surfaces may have prognostic implications. In particular, plaque ulceration seems to be associated with an increased risk of cerebral embolism. However, there is still controversy about the ability of conventional 2-D ultrasound and digital subtraction angiography (DSA) to identify ulcerated plaques. The literature shows that their sensitivity in predicting carotid plaque ulceration in comparison to the evaluation of pathological specimens ranges from <30% to >80%. Furthermore, an accurate and reproducible assessment of plaque morphology and surface is limited when only 2-D cut planes are analyzed. Position artifacts can cause a sonolucent space between the plaque and the wall, which may be falsely identified as an ulceration. Restriction of the image angle may make inaccessible the optimal image plane necessary to diagnose a plaque ulceration. These difficulties in reproducibly visualizing carotid artery plaque ulceration account for the scarcity of information on the natural course of carotid plaque ulceration.

The technique of 3-D ultrasound has recently been introduced as a valid and reproducible method for characterization of plaque morphology. Repeatability studies revealed excellent intraobserver and interobserver agreement for plaque segmentation and subsequent volume measurement (variability ranging from 3.5% to 6.5%). Additionally, the accuracy of volume determination has been evaluated in an in vitro model, with bovine fibroadipose tissue inserted in a polyurethane cylindrical tube.

However, segmentation and extraction of the voxels representing the carotid artery plaque from the 3-D data set allows not only plaque volume quantification but also visualization of the luminal plaque surface and depiction of plaque ulceration. The purpose of this exploratory pilot study was to follow plaque ulceration over time with this new 3-D ultrasound technique.

Subjects and Methods

Patients
We performed 3-D ultrasound examinations of 17 carotid artery plaques with an ulcerated surface in a prospective study with 16 patients (10 men and 6 women; mean±SD age 68.9±7.1 years). Vascular risk factors, clinical symptoms, morphological plaque characteristics, and treatment for stroke prevention are listed in the Table. During the observation period, all patients received sufficient treatment of their risk factors and, except for one, stopped smoking.
Plaque echo-structure (texture) and echogenicity were classified according to the criteria of a recent consensus paper \(^1\) concerning plaque morphology, as follows: class I, homogeneous texture, uniformly hypoechoic echogenicity; class II, heterogeneous texture, predominantly hypoechoic echogenicity; class III, heterogeneous texture, predominantly hyperechoic echogenicity; class IV, homogeneous texture, uniformly hyperechoic echogenicity; and class V, unclassified calcified plaques. Because of acoustic shadowing, calcified plaques (class V) were excluded from the study because acoustic shadowing may obscure deeper aspects of the arterial wall and thus make a conclusive plaque surface analysis impossible.

In Echogenicity, graded as classes I–V according to the criteria of the consensus meeting on plaque morphology.\(^1\)

Reproducibility Study

The recorded 3-D data sets of the initial investigation of each patient were reviewed separately by 2 independent observers, each blinded to the results of the other, and repeated by one of them on different days. After plaque segmentation and 3-D reconstruction of the luminal plaque surface, the diameter of the 3-D displayed ulceration was determined.

Data Analysis

All data were expressed as mean±SD. The agreement between 2 readings was evaluated with Bland-Altman analysis for comparison of 2 methods of clinical measurement in the absence of a gold standard.\(^2\) Estimation of the sample size of a case-control study required for predicting cerebral ischemia in the presence of plaque ulceration was performed according to Lemeshow et al.\(^2\)

Results

Reproducibility Study

In all patients, the plaque ulceration could be visualized after 3-D surface reconstruction in good quality by both investigators. The mean diameter of the plaque ulceration was 2.3±1.1 mm when measured by the first investigator and 2.4±1.2 mm according to the second investigator. Bland-Altman analysis revealed limits of interobserver agreement (mean±2 SD) ranging from −0.21 to 0.22 mm (−8.9% to 9.4%) and limits of interobserver agreement ranging from −0.23 to 0.05 mm (−9.7% to 2.3%), which indicated sufficient repeatability (Figure 2).
Clinical Study

The mean observation period was 17.5±6.3 months. During this period, 2 of the 16 patients (12.5%) had a cerebral ischemic event: one patient suffered a stroke that was probably related to intermittent atrial fibrillation, and the other had a TIA due to carotid artery occlusion contralateral to the observed carotid artery plaque.

At the end of the observation period, the surface configuration had changed in 4 of 17 cases (23.5%). Plaque ulceration regressed completely in 2 cases (Figure 3) and partially in 1 case; ulcer progression occurred in 1 case. The remaining 13 plaques (76.5%) showed a stable surface configuration. Of the 4 plaques with a changing surface configuration, echogenicity was predominantly hypoechoic in 3 (75%) and hyperechoic in 1 (25%).

Discussion

The present study has shown an excellent repeatability for 3-D display of plaque ulceration, comparable to that of previous 3-D ultrasound studies. Changes in plaque surface configuration during the observation period occurred in 23.5% of ulcerated atherosclerotic lesions. The majority of those plaques with a changing configuration regressed toward a smoother surface; in 1 case, however, the ulceration was progressive, indicating an unstable plaque configuration. These results are consistent with former studies which had established that atherosclerosis is a dynamic disease with phases of progression and regression. Whereas these studies looked for changes in plaque volume, the present study investigated the natural course of plaque ulceration, which could be of importance for the management of asymptomatic carotid artery disease.

The most important implication emerging from the carotid surgery trials (NASCET, ACAS, ECST, and Veterans Administration trial) is the need for more accurate identification of which asymptomatic patients stand to benefit most from surgery. Plaque surface characteristics and ultrasonic internal structures are considered potential criteria for a stratification of patients into stroke risk categories. Although clinicopathologic studies suggest that intraplaque hemorrhage and intimal ulceration are more frequent in symptomatic lesions, a clear correlation of ultrasonic plaque characteristics with an increased incidence of ipsilateral hemispheric ischemic events is still lacking. In particular, the importance of ulcerated plaques remains controversial. Review of the NASCET angiographic data reveals a clear prognostic significance of ulcerated plaques only when a severe carotid stenosis is present. In contrast, Grotta and coworkers found an association of plaque ulceration with clinical symptoms only in patients with nonstenotic lesions but not in >50% carotid artery stenoses. Studies combining symptomatic and asymptomatic patients, lesions with or without concomitant carotid stenosis, and the absence of a sensitive and reliable technique for the investigation of carotid artery plaque ulceration have contributed to these discrepancies.
The presented 3-D ultrasound technique, by providing a 3-D virtual reality image of the carotid artery plaque and, specifically, its luminal surface, may help to overcome these diagnostic limitations. However, the annual stroke rate in the presence of asymptomatic carotid artery stenoses or even of nonstenotic ulcerated plaques is fairly low. To decide whether 3-D ultrasound will contribute to treatment optimization remains to be established in further studies with a considerably larger number of patients. Assuming an annual stroke rate of 2% in asymptomatic carotid artery disease, as shown in the ACAS trial, the estimated sample size of a case-control study necessary to predict ipsilateral hemispheric ischemia in a 5-year follow-up period would require 1200 to 1400 patients with ulcerated carotid artery plaques and the same number of control subjects (estimation according to Lemeshow et al., with \( \epsilon = 0.2 \) and \( \omega = 2 \) to 3).

As a technique in development, however, 3-D ultrasound still has some limitations. The rigid probe carriage assembly, which allows only a linear movement, implies that the insonation angle cannot be adapted to the course of the vessel. This restriction could be overcome by the development of a freehand scanning system that maintains the flexibility of the 2-D examination with a hand-held transducer. The use of 3-D ultrasound is further limited by artifacts from swallowing and respiration, in addition to cardiac arrhythmia, which compromises the ECG trigger. Moreover, acoustic shadowing caused by calcification—which occurs not infrequently in tight stenoses—makes the identification of plaque ulceration difficult.

In conclusion, 3-D ultrasound allows noninvasive monitoring of the natural course of carotid artery plaque ulceration. Almost 25% of ulcerated plaques presented changes in their surface configuration at the end of the observation period. The low incidence of progressive ulceration is consistent with the low clinical event rate. However, the total number of progressive and regressive plaques in this exploratory study was too small for performance of a statistical analysis to correlate plaque echogenicity and texture, vascular risk factors, and clinical symptoms with the occurrence of changes in plaque surface configuration. This should be the subject of further studies.

References

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