Correlation of Carotid Plaque Neovascularization Detected by Using Contrast-enhanced US with Clinical Symptoms[1]

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Purpose: To determine the correlation between the degree of plaque enhancement with contrast agent microbubbles and clinical symptoms in patients with carotid atherosclerotic plaque.

Materials and Methods: The study was approved by the hospital ethical committee, and informed consent was obtained from all patients. One hundred four patients (83 men: mean age, 64 years ± 9 [standard deviation]; 21 women: mean age, 61 years ± 10) with carotid plaques were studied with standard and contrast material–enhanced ultrasonography (US). Contrast enhancement in the plaque was evaluated with visual interpretation and quantitative analysis.

Results: Among the 104 patients, 35 (34%) had transient ischemic attack and/or cerebrovascular ischemic stroke. Plaque enhancement was found in 28 (80%) of 35 symptomatic patients and in 21 (30%) of 69 asymptomatic patients ($P <$ .001). Enhanced intensity in the plaque (13.9 dB ± 6.4) and the ratio of enhanced intensity in the plaque to that in the lumen of the carotid artery (0.54 ± 0.23) in symptomatic patients were significantly greater than those in asymptomatic patients (8.8 dB ± 5.2 [$P <$ .001] and 0.33 ± 0.19 [$P <$ .001], respectively). Sensitivity and specificity were 74% and 62%, respectively, for enhanced intensity in the plaque (cutoff value, 10.0 dB) and 74% and 75%, respectively, for ratio of enhanced intensity in the plaque to that in the lumen of the carotid artery (cutoff value, 0.46).

Conclusion: Symptomatic patients had more intense contrast agent enhancement in the plaque than asymptomatic patients, suggesting that contrast-enhanced carotid US may be used for plaque risk stratification.

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Stroke is a serious public health problem and is a leading cause of morbidity and mortality worldwide. Researchers have classified at-risk patients as "vulnerable patients," representing those with a higher likelihood of developing symptomatic, complicated atherosclerotic disease (1–3). Vulnerable patients have vulnerable plaques, which are most likely to rupture and, thus, precipitate acute thrombotic events (4). Plaque neovascularization has been well established and confirmed in histologic studies as a consistent feature of vulnerable plaque in patients with cerebrovascular disease (5–7). Advances in contrast material–enhanced ultrasonography (US) may allow for detection of neovascularization within atherosclerotic plaque (8–11). This technique takes advantage of the high spatial and temporal resolution of vascular US and of the properties of contrast agent microbubbles, which behave as pure intravascular tracers (12). It has been demonstrated that enhancement of carotid plaque with use of US contrast material correlates with histologic density of neovessels within the carotid plaque (11). Although several histologic studies showed that more extensive plaque neovascularization is associated with clinically symptomatic disease (3,5,7), the association between the carotid plaque enhancement with contrast agent microbubbles and clinical symptoms is not fully understood. Therefore, our study was undertaken to correlate the degree of plaque enhancement obtained by using contrast agent microbubbles with clinical symptoms in patients with carotid atherosclerotic plaque.

Materials and Methods

Study Patients

The protocol was approved by the hospital ethical committee, and informed consent was obtained from all patients before their examination.

Between July 2007 and May 2008, we enrolled 104 patients (mean age, 63 years ± 9 [standard deviation]) in the study. There were 83 men (mean age, 64 years ± 9; range, 42–82 years) and 21 women (mean age, 61 years ± 10; range, 47–75 years). The patients were selected from those referred for carotid US on the basis of clinical indications, including symptoms of cerebrovascular disease and screening for carotid atherosclerosis because of cardiovascular risk factors (obesity, hypertension, hyperlipidemia, diabetes mellitus, and active cigarette smoking). Patients with a body mass index greater than 25 kg/m^2 were considered overweight. Inclusion criteria were at least one carotid atherosclerotic plaque thicker than 2.0 mm. Patients with myocardial infarction or angina pectoris with signs of myocardial ischemia were excluded from the study. The patients were classified as symptomatic or asymptomatic. The symptomatic group was defined as patients with transient ischemic attack and/or cerebrovascular ischemic stroke, and the asymptomatic group was defined as those without a history of cerebrovascular events.

Of the 104 patients, 35 (34%) were symptomatic and 69 (66%) were asymptomatic. In the symptomatic group, nine patients had a transient ischemic attack 3–8 days (mean, 5 days ± 2) before carotid US, 20 patients had a cerebrovascular ischemic stroke 1–85 days (mean, 17 days ± 22) before carotid US, and six patients had a cerebrovascular ischemic stroke 6–36 months (mean, 19 months ± 12) before carotid US and a transient ischemic attack 1–7 days (mean, 3 days ± 2) before carotid US. The clinical characteristics of the two groups are summarized in Table 1. There was no difference between the groups with regard to age or the percentage of male patients. Diabetes mellitus, being overweight, hypertension, and smoking were more common in the symptomatic group, but these differences did not reach statistical significance.

Standard and Contrast-enhanced Carotid US

Carotid US was performed with an ultrasound machine (Logiq 9; GE Healthcare, Milwaukee, Wis) by using a 9-L probe with transmission frequency of 6–8 MHz for both standard and contrast-enhanced studies by one of the researchers (Y.B.D., with 24 years of experience with US), who was blinded to participant history. With the patient lying in the supine position, the extracranial carotid arteries were visualized in the longitudinal and the transverse planes. The entire length of common carotid arteries and carotid bifurcations, including the internal carotid artery as far up as we could observe, was examined for the presence of atherosclerotic plaques. If a plaque was identified, the view showing the thickest cross-section of the plaque was used to measure the maximal carotid plaque thickness with electronic calipers. Intima-media thickness was defined as the distance from the leading edge of the lumen-intima interface to that of the media-adventitia interface. Maximal plaque thickness was measured as maximal intima-media thickness, which was defined as the greatest axial thickness in the carotid artery. In patients with more than one separate plaque, only the thickest one was observed and recorded

Advance in Knowledge

- The degree of contrast enhancement in plaque and the ratio of the enhanced intensity in the plaque to that in the lumen of the carotid artery correlate with cerebrovascular symptoms.

Implication for Patient Care

- Contrast-enhanced carotid US may be a new tool for plaque risk stratification and for monitoring the effects of antiatherosclerotic therapies.

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for analysis during standard and contrast-enhanced US. In one patient with similar plaque thickness for one soft plaque and one mixed plaque, only the soft plaque was observed and analyzed. The examination was digitally stored for later review.

The patients then underwent contrast-enhanced US, with special attention to the previously identified plaques. The preset real-time, contrast-enhanced imaging modality with coded pulse inversion technique was switched on, and image settings were adjusted to maximize visualization of the contrast signal. To reduce microbubble destruction, we preset the mechanical index to 0.13 and the frame rate to 12 per second. Image depth was adjusted to 3–5 cm according to the size of the carotid artery, and the focus position was set at the level of the carotid artery. Time gain compensation was adjusted to achieve a homogeneous signal intensity of the carotid artery while reducing noise from the wall of the carotid artery and the plaque. All these settings were kept constant throughout each examination.

SonoVue (Bracco, Geneva, Switzerland), which consists of phospholipid-stabilized microbubbles of sulfur hexafluoride at $1–5 \times 10^8$/mL and mean diameter of 2.5 μm (13), was used as the contrast agent. The microbubbles contain inert and nontoxic gas, behave as strict intravascular tracers, and are rapidly removed from the circulation through the pulmonary route (14). The contrast agent solution was prepared by adding 5 mL of saline solution to a septum-sealed glass vial containing 25 mg of lyophilisate power in sulfur hexafluoride atmosphere and gently shaking the vial until complete dissolution of lyophilisate in the suspension. The contrast agent was administered intravenously as a 1.5-mL bolus through the antecubital vein within 2–3 seconds, followed by a saline bolus of 2–3 mL. The appearance of the contrast effect was observed inside the lumen of the carotid artery within 15–30 seconds after the injection. A real-time contrast-enhanced carotid cine-loop following injection of contrast material, including images obtained at least 3 seconds before and 5 minutes after the appearance of the contrast effect in the lumen of the carotid artery, was acquired and digitally stored for later analysis. The participants were observed for any complications for 30 minutes before leaving.

Data Analysis

Standard and contrast-enhanced images were reviewed and analyzed by two investigators (L.X., with 5 years of experience with US, and Y.B.D.), who were blinded to participant history. The standard carotid US images were considered to be of good quality if the surface and the internal structure of the plaque could be visualized and classification of the plaque echogenicity was possible. The contrast-enhanced carotid US images were considered to be of good quality if the lumen of the carotid artery was enhanced and outlined and the plaque was delineated.

Plaques were characterized by their appearance on standard US images and were classified according to widely used criteria (15) as follows: *(a)* soft plaques, whose echogenicity was less than that of the surrounding adventitia for more than 80% of the plaque area, without acoustic shadowing; *(b)* hard plaques, whose echogenicity was greater than or equal to that of the surrounding adventitia for more than 80% of the plaque area, without acoustic shadowing; *(c)* calcified plaques, which contained more than 90% of circumferential calcification, showing as bright echoes within the plaque along with acoustic shadowing; or *(d)* mixed plaques, which contained less than 90% of circumferential calcification or had associating echodense and anechoic regions occupying less than 80% of the plaque area. Plaque ulceration was defined as a recess on the surface of the plaque that was at least 2 mm deep and 2 mm long and had a well-defined back at its base (16).

On contrast-enhanced images, all the soft and hard plaques appear dark and hypoechoic, and the calcified plaques have relatively lower echogenicity than on standard images; however, they are still echogenic before injection of contrast material because of suppression of the tissue signal (Figure). The enhancement of the plaque after injection of contrast material was quantitatively analyzed offline by use of a time–signal intensity curve analysis software package (GE Healthcare) that can display the signal intensity (ie, ultrasound energy reflected from the tissue and contrast agent)–versus-time curve in the region of interest during the process of enhancement. A region of interest with the size and shape fitted to the plaque was drawn manually and positioned at the plaque (Figure). Another region of interest, with a circular shape and a diameter of 3 mm, was produced automatically by the software and positioned at the lumen of the carotid artery near the plaque. Quantitative analysis was performed by one investigator (Y.B.D.) in all plaques to maintain consistency in drawing the region of interest. Special care was taken to keep the region of interest in the plaque to be drawn along the lumen-intima interface and the media-adventitia interface.

The carotid plaque and lumen signal intensity–versus-time curves during the process of enhancement were automatically produced and fitted to an exponential function: $Y(t) = At \cdot e^{-kt} + B$, where

Table 1

Characteristics of Study Patients

Characteristic	Symptomatic Group ($n = 35$)	Asymptomatic Group ($n = 69$)	*P* Value
Age (y)*	61 ± 10	64 ± 9	.06
Men	29 (83)	54 (78)	.80
Diabetes mellitus	14 (40)	21 (30)	.38
Overweight	16 (46)	24 (35)	.29
Hypertension	27 (77)	50 (72)	.65
Smoking	15 (43)	23 (33)	.39

Note.—Unless otherwise indicated, data are numbers of patients, with percentages in parentheses.

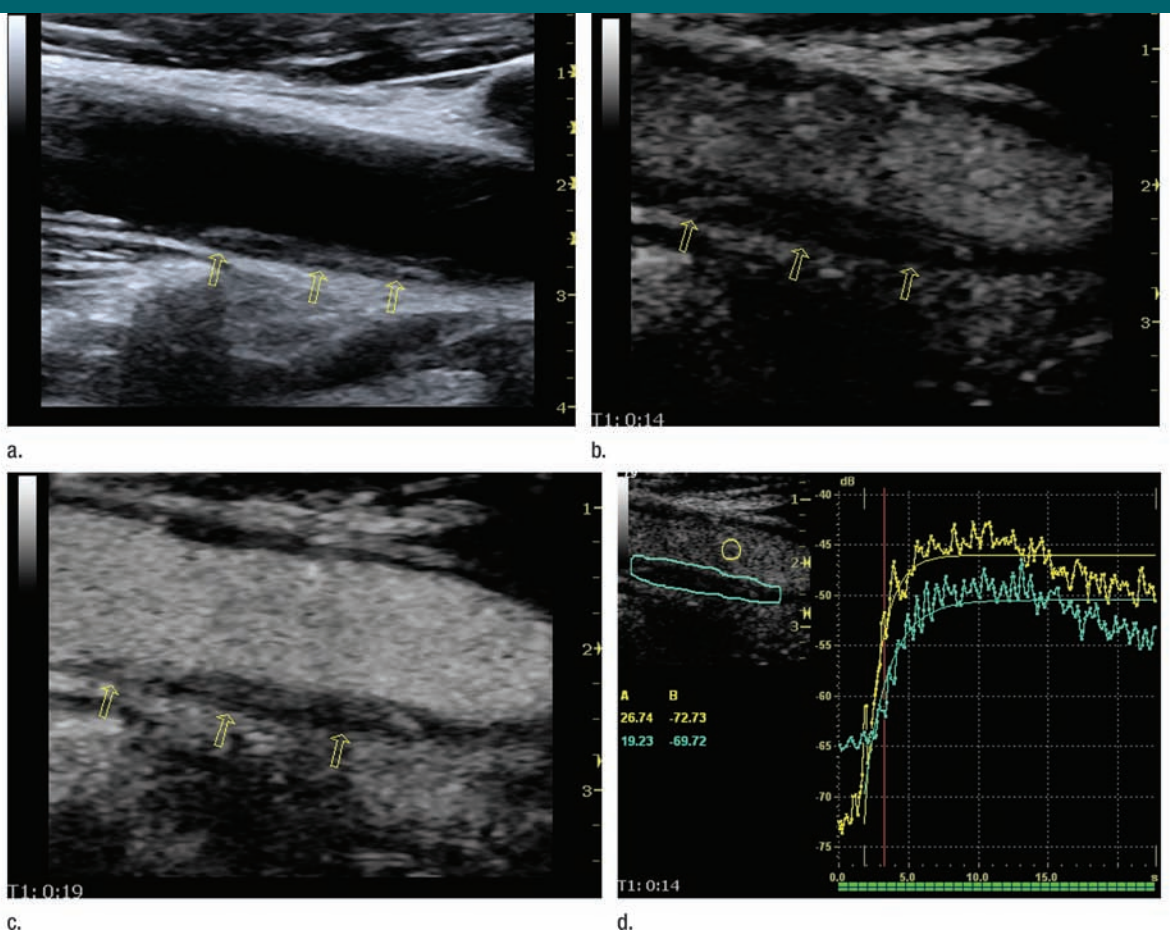
* Data are means ± standard deviations.

Y is signal intensity at time *t*, *k* is a factor proportional to the transit time of the contrast agent, *A* is the derived peak signal intensity, and *B* is the intercept signal intensity at the origin of the curve (baseline intensity) (17). Baseline intensity before injection of contrast agent and peak intensity after injection of the contrast agent in the regions of interest were obtained from the signal intensity–versus-time curve. The enhanced intensity was calculated by subtracting the baseline intensity from the peak intensity. The degree of enhancement of the plaque after injection of contrast material was investigated by looking at the enhanced intensity in the plaque and the ratio of the enhanced intensity in the plaque to that in the lumen of the carotid artery.

For each plaque, contrast enhancement was categorized as follows according to the visual interpretation by two independent investigators (L.X. and Y.B.D.) who were blinded to participant history: Grade 1 indicated no enhancement within the plaque or enhancement confined to the adventitial side of the plaque and/or the shoulder, and grade 2 indicated enhancement reaching plaque core or extensive contrast enhancement throughout the plaque. In case of disagreement between investigators, a consensus was reached. To identify the patients with highly vascularized plaques among plaques with different echogenicity, the percentages of contrast enhancement in the subgroup of patients with different types of plaques were compared in symptomatic and asymptomatic groups. The percentages of contrast enhancement in symptomatic and asymptomatic groups were also compared.

Statistical Analysis

Data analysis was performed with software (SPSS, version 15.0; SPSS, Chicago, Ill). An unpaired *t* test was used to



Standard and contrast-enhanced carotid US images in 78-year-old man who experienced serial transient ischemic attacks 2 days before examination. **(a)** Longitudinal view obtained without contrast agent shows large soft plaque in the carotid artery near the carotid bulb (arrows). **(b)** Longitudinal view obtained 14 seconds after injection of contrast agent. No enhancement was observed in the plaque (arrows). **(c)** Longitudinal view obtained 19 seconds after injection of contrast agent. Plaque (arrows) was extensively enhanced 19 seconds after injection of contrast agent. **(d)** Time–signal intensity curves in the lumen of the carotid artery (yellow area and curve) and plaque (blue area and curve). *T1* = time from the injection of contrast agent, *A* = enhanced intensity after injection of contrast agent, *B* = baseline intensity before injection of contrast agent.

compare parameters between groups with and without cerebrovascular symptoms. Parameters among different types of plaques were compared by using analysis of variance. Significant differences between groups were assessed by using the Scheffé F test for multiple comparisons. Differences in proportions were tested with χ^2 analysis. The sensitivity and specificity of each parameter for predicting the cerebrovascular symptoms were derived by using receiver operating characteristic curve analysis. We selected the cutoff values to obtain nearly the same sensitivity and specificity in our study. The relationship between plaque thickness and enhanced intensity and the ratio of the plaque were assessed by using simple linear regression analysis. A P value less than .05 was considered to represent a statistically significant difference.

Table 2

Carotid Plaque Features in Patients with and without Symptoms

Variable	Symptomatic Group ($n = 35$)	Asymptomatic Group ($n = 69$)	P Value
Plaque thickness (mm)*	2.86 ± 0.96	3.00 ± 0.88	.45
Plaque ulceration	8 (23)	11 (16)	.43
Plaque echogenicity			
Soft	26 (74)	26 (38)	.001
Hard	2 (6)	6 (9)	.71
Calcified	2 (6)	9 (13)	.33
Mixed	5 (14)	28 (40)	.007
Contrast enhancement	28 (80)	21 (30)	<.001
Enhanced intensity in plaque (dB)*	13.9 ± 6.4	8.8 ± 5.2	<.001
Ratio*†	0.54 ± 0.23	0.33 ± 0.19	<.001

Note.— Unless otherwise indicated, data are numbers of patients, with percentages in parentheses.

* Data are means ± standard deviations.

† Ratio of enhanced intensity in the plaque to that in the carotid artery lumen.

Results

Correlation between Plaque Echogenicity and Symptoms

Standard carotid US depicted 133 plaques in 104 patients (Figure, part a). Multiple plaques were found in 27 patients. Among 133 plaques, 35 plaques were located in the proximal internal carotid artery, 71 were in the carotid bulb, and 27 were in the midsegment of the common carotid artery. The plaque thickness ranged from 2.10 to 6.10 mm (mean, 2.96 mm ± 0.91). Plaque thickness did not significantly differ between symptomatic and asymptomatic patients ($P = .45$) (Table 2). The percentage of soft plaque in the symptomatic patients was significantly greater than that in the asymptomatic patients ($P = .001$) (Table 2). The percentage of plaque ulceration in the symptomatic group was not significantly different from that in the asymptomatic group ($P = .43$) (Table 2).

Correlation between Contrast Enhancement of Plaque and Symptoms

Contrast-enhanced carotid US was well tolerated in all patients, and good-quality images were available for all the plaques identified with standard US (Figure, part c). When the contrast-enhanced carotid US images were assessed with visual interpretation, a higher prevalence of plaque enhancement after injection of contrast material was found in symptomatic patients than in asymptomatic patients ($P < .001$, Table 2). When contrast enhancement of the plaque assessed with visual interpretation was used to predict symptoms, its sensitivity and specificity were 80% (28 of 35) and 70% (48 of 69), respectively. Quantitative analysis showed that the enhanced intensity in the plaque (13.9 dB ± 6.4) and the ratio of enhanced intensity in the plaque to that in the lumen of the carotid artery (0.54 ± 0.23) in the symptomatic patients were significantly greater than those in asymptomatic patients (8.8 db ± 5.2, $P < .001$ and 0.33 ± 0.19, $P < .001$, respectively; Table 2). In the subgroup of patients with soft plaques, contrast enhancement was observed in 24 of 26 (92%) symptomatic patients and 10 of 26 (38%) asymptomatic patients ($P < .001$). In the subgroups of patients with hard, calcified, and mixed plaques, no significant differences were found in the percentage of contrast enhancement between symptomatic and asymptomatic patients (one of two [50%] vs zero of six [0%], $P = .25$ for hard plaques; zero of two [0%] versus zero of nine [0%] for calcified plaques; three of five [60%] versus 11 of 28 [39%], $P = .63$ for mixed plaques). Contrast enhancement was found in seven of 19 (37%) patients with plaque ulceration and 42 of 85 (49%) patients without ulceration ($P = .45$).

Correlation between Plaque Echogenicity and Contrast Enhancement

Soft plaques had a significantly higher proportion of contrast enhancement compared with the other types of plaques ($P < .001$). The enhanced intensity in the plaque and the ratio in the soft plaques were significantly higher than those in the other three types of plaques (all P values $< .05$) (Table 3). No significant correlation was found between plaque thickness and enhanced intensity in the plaque ($P = .26$) and the ratio of the enhanced intensity ($P = .13$).

Receiver Operating Characteristic Curve Analysis

Sensitivity and specificity were 74% and 62%, respectively, for enhanced intensity in the plaque (cutoff value, 10.0 dB; area under the receiver operating characteristic curve, 0.74) and 74% and 75%, respectively, for ratio of enhanced intensity in the plaque to that in the lumen of the carotid artery (cutoff value, 0.46; area under the curve, 0.76).

Discussion

Our study showed a higher prevalence of plaque enhancement with visual in-

terpretation in symptomatic than in asymptomatic patients. We found good correlation between the degree of contrast enhancement measured with quantitative analysis and patient symptoms and a relatively high sensitivity and specificity for enhanced intensity in the plaque and the ratio of enhanced intensity in the plaque to that in the lumen of the carotid artery for predicting symptoms. These findings have important clinical implications in that contrast-enhanced carotid US may be used for plaque risk stratification and for the assessment of progression and regression of atherosclerosis.

Investigations (5–7) have targeted neovascularization as an important factor contributing to vulnerability of atherosclerotic plaque. The ability to detect neovascularization in plaque by using a noninvasive method is therefore of major clinical interest. Contrast-enhanced US is a promising noninvasive tool for visualization of plaque neovascularization (9). This method has been used in carotid imaging to enhance blood flow signal from the main arterial lumen and improve vessel wall delineation for the measurement of intima-media thickness (18) and degree of stenosis (19). Rajaram et al (8) described contrast enhancement in carotid plaque as an unexpected finding during conventional studies and ascribed this phenomenon to plaque neovascularization. Contrast-enhanced US has already been used to identify tissue perfusion in the myocardium (20) and other organs and to study tumor angiogenesis (21), supporting the concept that microbubbles observed within the carotid plaque represent neovascularization. Feinstein et al (9) and Vicenzini et al (22) described contrast agent microbubbles within carotid plaques as a marker of vascularization. Shah et al (10) reported a good correlation between contrast-enhanced US of plaque neovascularization in the carotid artery and histologic score on surgical specimens. Very recently, a study by Coli et al (11) demonstrated that the degree of contrast enhancement evaluated with semiquantitative visual analysis was well correlated with histologic neovessel density of the plaque. In our study, contrast enhancement was shown with visual interpretation in 49 of 104 plaques after injection of contrast material. Our study and previous ones demonstrated that carotid contrast-enhanced US allows assessment of plaque neovascularization. The assessment of contrast enhancement by using visual interpretation has the limitation of subjectivity. Therefore, we also used a quantitative method to analyze the degree of contrast enhancement by calculating the enhanced intensity in the plaque and the ratio of enhanced intensity in the plaque to that in the lumen of the carotid artery. To our knowledge, this information has not been reported in prior studies. Because enhanced intensity obtained by using the present quantitative analysis method has been demonstrated to correlate strongly with microvessel density in the ischemic myocardium (20) and hepatocellular carcinoma (23), our study implies that the quantitative analysis of contrast enhancement of the carotid plaque might help quantify the degree of plaque neovascularization. The relatively high sensitivities and specificities obtained in our study when the parameters of quantitative analysis of contrast-enhanced images were used to predict the patient symptoms may be partly explained as follows: Plaque neovascularization has been well established and confirmed in histologic studies as a consistent feature of vulnerable plaque in patients with cerebrovascular disease (5–7), and enhanced intensity obtained by using the present quantitative analysis method has been shown to correlate strongly with microvessel density in the ischemic myocardium (20) and with hepatocellular carcinoma (23).

Plaque neovascularization was found to be more extensive in symptomatic and pathologically vulnerable carotid plaques (3,5,7). In a series of carotid endarterectomy samples, McCarthy et al (5) found significantly more neovessels in plaques in symptomatic patients than in asymptomatic patients. In a postmortem study, Fleiner et al (3) found that patients with symptomatic atherosclerotic plaque had a denser network of vasa vasorum than patients with asymptomatic disease. In our study, we observed good correlation between the degree of contrast enhancement in the carotid plaque assessed with both visual interpretation and quantitative analysis and patient symptoms. To our knowledge, this is the first published, extensive article directly comparing contrast-enhanced US and patient symptoms in carotid atherosclerotic plaques.

We found that soft plaques have greater contrast enhancement than other types of plaques. This observation is in agreement with previous findings of Coli et al (11). Previous study showed good relation of contrast enhancement with histologic neovessel density of the plaque; however, this relation may be masked in plaques other than soft plaque, particularly calcified plaque because of acoustic shadowing. It is possi-

Table 3

Plaque Echogenicity and Contrast Enhancement

Variable	Soft Plaque ($n = 52$)	Hard Plaque ($n = 8$)	Calcified Plaque ($n = 11$)	Mixed Plaque ($n = 33$)	*P* Value
No. of patients with contrast enhancement*	34 (65)	1 (13)	0 (0)	14 (42)	<.001
Enhanced intensity in plaque (dB)	13.1 ± 5.6†	7.0 ± 5.2	5.0 ± 3.6	9.1 ± 5.8	<.001
Ratio‡	0.51 ± 0.20§	0.26 ± 0.21	0.17 ± 0.11	0.34 ± 0.22	<.001

Note.—Unless otherwise indicated, data are means ± standard deviations.

*Data are numbers of patients, with percentages in parentheses.

† $P < .05$ versus other three groups.

‡ Ratio of enhanced intensity in the plaque to that in the carotid artery lumen.

§ $P < .01$ versus other three groups.

ble that the calcified plaque showed no enhancement because of acoustic shadowing, even though it had a high neovessel density. Although more echolucent plaques are considered to have more vulnerable pathologic features and to bear a higher risk of cerebrovascular events (24), recent study indicates that echolucency by itself does not correlate with histologic density of the vasa vasorum (11) and was not associated with the risk of major adverse cardiovascular events in the near future (25). In a subgroup of patients with soft carotid plaque, we found that symptomatic patients had a higher percentage of contrast enhancement at visual interpretation and more intense enhancement assessed with quantitative analysis. This finding is in agreement with the concept that contrast-enhanced US may help identify among soft carotid plaques a subgroup of highly vascularized and vulnerable plaques (11).

Our study had several limitations. Only the thickest plaque was observed and analyzed in patients with more than one separate plaque on standard and contrast-enhanced carotid US images. The thickest plaque might not be the one with the most contrast enhancement. Given the low number of female patients in our study, we did not analyze the association between sex and contrast enhancement, but this should be an area of further research. At the time of this study, we could not define all the factors, such as hemodynamic status of the participant, that influence the signal intensity level beyond neovessel density. It is impossible to completely blind the researchers performing the standard and contrast-enhanced carotid US imaging because patients with prior stroke might appear clinically different from those without prior stroke. In addition, we did not correlate the findings obtained with contrast-enhanced US with velocity measurements in the carotid artery, so the incremental benefit of contrast enhancement of plaque was not assessed. Although our study showed good correlation between the degree of contrast enhancement and patient symptoms, further studies are needed to confirm our findings in larger patient populations. Clinical follow-up studies in patients after contrast-enhanced carotid US are also required to evaluate the potential effect of contrast-enhanced US of plaque in determining the risk of cerebrovascular events.

In conclusion, contrast-enhanced carotid US allows assessment of neovascularization within plaque. Symptomatic patients had more intense contrast enhancement in plaque than asymptomatic patients, suggesting that contrast-enhanced carotid US may be used as a method for plaque risk stratification.

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