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Carotid Plaque Characterization Using Digital Image Processing and Its Potential in Future Studies of Carotid Endarterectomy and Angioplasty

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Purpose: To corroborate the validity of a computerized methodology for evaluating carotid lesions at risk for stroke based on plaque echogenicity.

Methods: The records of 96 carotid endarterectomy patients (59 men; median age 69.5 years, range 52 to 83) with stenoses > 50% were studied retrospectively. Forty-one patients (43%) had been symptomatic preoperatively. All patients had undergone computed tomography (CT) to detect infarction in the carotid territory and a duplex scan to measure carotid stenosis. Plaque echogenicity was analyzed by computer, expressing the echodensity in terms of the gray scale median (GSM). The incidence of CT-documented cerebral infarction was analyzed in relation to symptomatology, percent stenosis, and echodensity.

Results: Symptoms correlated well with CT evidence of brain infarction: 32% of symptomatic patients had a positive CT scan versus 16% for asymptomatic plaques ($p = 0.076$). The mean GSM value was 56 ± 14 for plaques associated with negative CT scans and 38 ± 13 for plaques from patients with positive scans ($p < 0.0001$). However, there was no difference in the GSM value between plaques with > or < 70% stenosis. Furthermore, the incidence of CT infarction was 40% in the cerebral territory of carotid plaques with a GSM value < 50 and only 9% in those with a GSM > 50 ($p < 0.001$).

Conclusions: Computerized analysis of plaque echogenicity appears to provide clinically useful data that correlates with the incidence of cerebral infarction and symptoms. This method of analyzing plaque echolucency could be used as a screening tool for carotid stent studies to identify high-risk lesions better suited to conventional surgical treatment.

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Key words: carotid stenosis, carotid occlusive disease, duplex scan, transluminal angioplasty, stent

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Since transluminal angioplasty of the carotid artery was first reported by Kerber et al.[1] in 1980, both devices and techniques have been modified to meet the challenges of this precarious vascular territory. As a consequence, the clinical outcome after carotid transluminal angioplasty has improved, with morbidity and mortality rates in the latest series comparable to those of traditional endarterectomy.[2–4] The more recent application of stents in the carotid arteries is likewise showing promise,[5–7] but cerebral embolization is still a potential—and devastating—complication of endovascular carotid therapy.[8]

Several investigators have focused on the problem of embolism to reduce the risk of carotid angioplasty. Distal and proximal occlusion balloons have been used to protect the brain and allow flow reversal, with aspiration and flushing to remove particulate material.[4,9] Distal filters able to catch fragments and remove them from the bloodstream are also being studied (personal communications). The technique of "primary" stenting has demonstrated efficacy in preventing arterial dissection, recoil, and plaque fragmentation, likely lowering the risk of embolization.[10–12]

While these intraprocedural attempts to prevent cerebral sequelae are laudable, a more useful, safer, and probably less expensive approach would be to *preoperatively* identify plaques that are at high risk for embolization during angioplasty. The reliability of duplex ultrasonography to identify plaque structure and composition has been widely studied in the past few years[13–19] with variable results.[19,20] However, the advent of high-resolution B-mode scanners has improved histologic and clinical correlation for plaque characterization,[15–18,20] increasing the likelihood that duplex scanning can serve as a noninvasive screening tool to more accurately classify potential carotid stent candidates according to lesion severity *and* morphology. The ability of modern duplex to accurately measure carotid luminal stenosis using velocity criteria has been well documented.[21–23] Moreover, investigators have suggested that plaque echogenicity may be a useful indicator of embolic potential in the carotid arteries.[14–18,24,25] If so, then one or more categories of carotid plaque may be identified as predisposed to shed embolic material when manipulated by an intraluminal device. At the same time, more stable lesions may be deemed better suited to angioplasty. Hence, there may be so-called "safe" and "dangerous" carotid plaques that can be identified prior to an endovascular intervention.

Based on these assumptions, our two research teams separately evolved a similar computerized method for analyzing the echographic carotid plaque image.[26,27] This methodology has been used to correlate the echogenicity of the plaque with cerebral infarctions documented by computed tomography (CT).[27,28] To confirm the method's reliability in a different clinical setting and with an eye toward possible application of this technique as a screening tool, we at the Bassini Teaching Hospital retrospectively studied a group of carotid endarterectomy patients to correlate brain infarction data with plaque echogenicity.

METHODS

Ninety-six consecutive patients (59 men; median age 69.5 years, range 52 to 83) who underwent carotid endarterectomy for atherosclerotic occlusive disease were studied retrospectively. The indications for surgery were based on lesion severity, symptomatology, plaque morphology, or the need to prevent cerebral ischemia during subsequent major vascular procedures. Fifty-five (57%) patients were asymptomatic or had nonhemispheric symptomatology. Of the 41 (43%) symptomatic patients, 24 had experienced one or more transient ischemic attacks, 7 had amaurosis fugax, and 10 had a history of stroke.

All patients had preoperative cerebral CT and a color flow duplex examination using an Acuson 128 EchoColor Scanner (Acuson Co., Mountain View, CA, USA) with a 7.5-MHz probe. The carotid bifurcation was extensively interrogated, as was the internal carotid artery. Plaque morphology, percent stenosis, blood flow velocity, and the Doppler spectral analysis of the plaque were recorded.

The level of maximal stenosis was determined using the peak flow velocity measurement, and a longitudinal image of the vessel was captured on Polaroid photographic paper at that level. For this study, the best image was digitized using an Epson 8000 scanner. Each plaque was outlined by the computer mouse (Fig. 1) and then analyzed using a software program (Adobe Photoshop 2.5.1, Adobe Systems Inc., Mountain View, CA, USA); the gray scale content (assuming 0 for the bloodstream

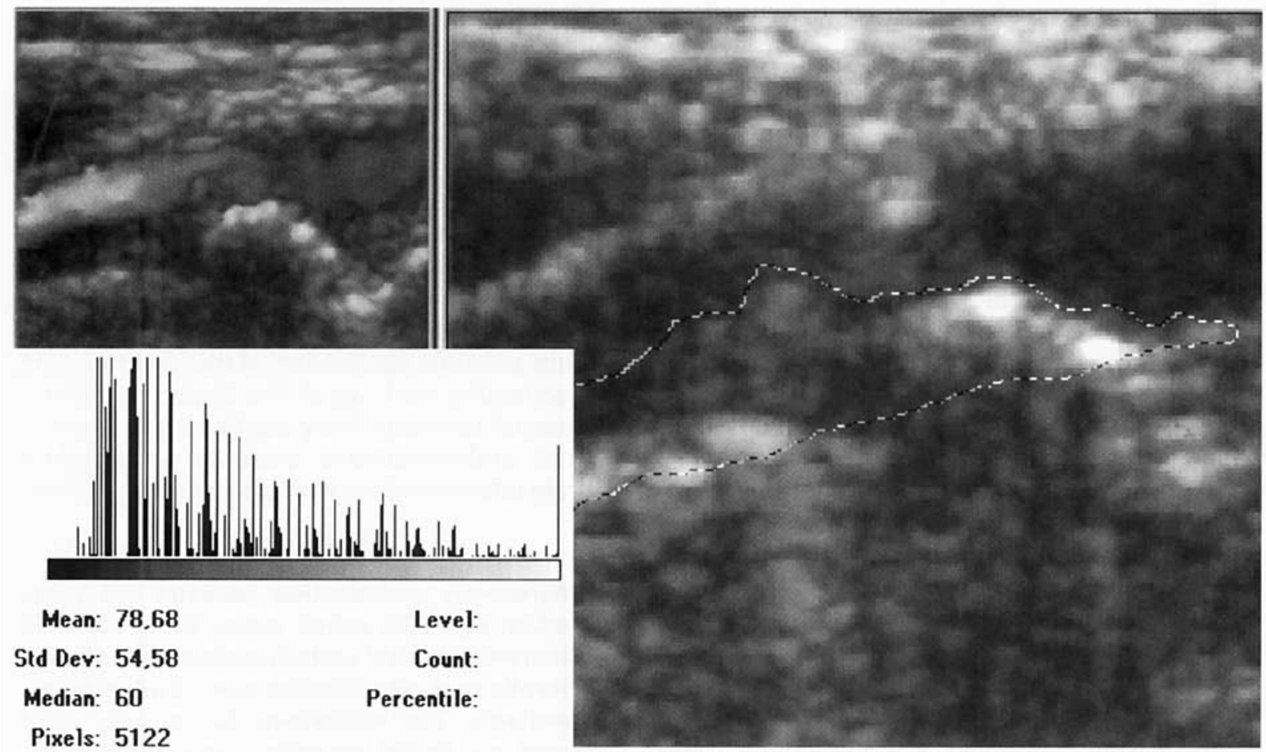

Figure 1 ◆ After standardization of the echographic image, the plaque is outlined and analyzed by the computer, obtaining the GSM.

and 256 for the intimal lining) was determined and expressed as the mean, median, standard deviation, and total pixel count. The gray scale median (GSM) was used as a measure of the overall plaque echogenicity. Finally, plaque characteristics (percent stenosis and echogenicity), symptomatology, and CT findings of the same cerebral hemisphere were correlated.

Statistical Analyses

The patients were grouped according to symptomatology, percent stenosis, GSM value, and positive or negative CT scan for analysis. The chi-square test for proportions was used for group comparisons of categorical variables. Relative risk was measured using the Cox regression analysis. The Student's *t*-test was used for group comparisons of continuous data.

RESULTS

Selecting from a consecutive group of patients provided a heterogeneous array of carotid artery lesions for analysis. Symptomatic and asymptomatic patient groups were subdivided according to the presence of ischemic lesions in the hemisphere ipsilateral to the carotid plaque (positive or negative CT scans). The relationship between echolucency (represented by GSM) and the percent stenosis for these subgroups is shown in Figure 2.

The CT scan was positive in 32% (13/41) of symptomatic and 16% (9/55) of asymptomatic plaques (Table 1), producing a close correlation between the presence of symptoms and CT evidence of brain infarction ($p = 0.076$, $\chi^2 = 3.13$ with a relative risk of 1.94 [95% confidence interval (CI) 0.92 to 4.09]). However, there was only a weak association ($\chi^2 = 0.40$, $p = 0.52$) between CT-documented infarction and percent stenosis: 25% for stenoses > 70% versus 20% for < 70% stenoses. Surprisingly, the correlation was much more evident between echolucency and CT-documented infarction: 40% for GSM < 50 versus 9% for GSM > 50 ($\chi^2 = 13.03$, $p < 0.001$, with a relative risk of 4.37 [95% CI 1.76 to 10.90]).

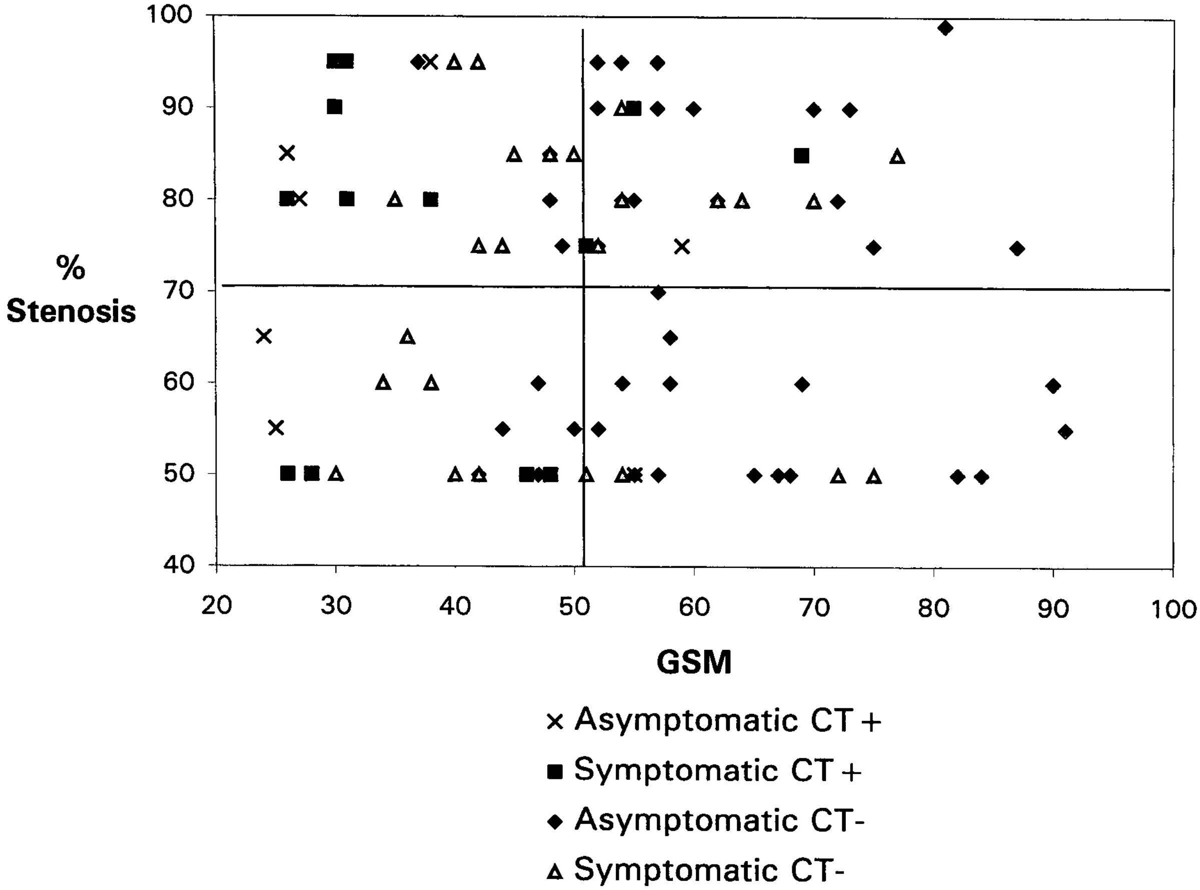

Figure 2 ◆ Relationship between percent stenosis, GSM, and presence of CT-documented brain infarction in symptomatic and asymptomatic patients.

TABLE 1
Comparison of Symptomatology, Percent Stenosis and GSM to CT Findings

	CT+	CT−	Totals
Symptomatic	13 (32%)*	28 (78%)	41
Asymptomatic	9 (16%)	46 (84%)	55
> 70% Stenosis	13 (25%)	38 (75%)	51
< 70% Stenosis	9 (20%)	36 (80%)	45
GSM < 50	17 (40%)†	25 (60%)	42
GSM > 50	5 (9%)	49 (91%)	54

* Significant correlation ($p = 0.076$) for symptomatology and positive CT scan; † = highly significant correlation ($p < 0.001$) for GSM < 50 and a positive CT scan.

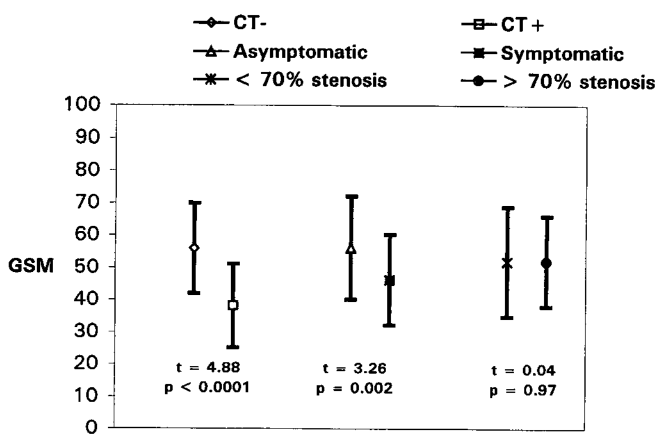

Figure 3 ◆ GSM values in relation to the presence or absence of CT-documented brain infarction, presence or absence of symptoms, and degree of stenosis.

The echolucency of plaques was also analyzed against the percent stenosis (> or < 70%), the presence or absence of symptoms, and a positive or negative CT scan (Fig. 3). While there was no association between GSM values and stenosis, there was a significant difference in echolucency for plaques causing symptoms ($t = 3.26$, $p = 0.002$) and an even greater significance to the difference in GSM values for patients with positive (38 ± 13) versus negative (56 ± 14) CT scans ($t = 4.88$, $p < 0.0001$).

DISCUSSION

Surgical intervention for carotid occlusive disease, whether by a classical or intraluminal procedure, can precipitate the very event it is supposed to forestall. While perioperative stroke from carotid endarterectomy can be embolic or ischemic in origin, the stroke risk attending endovascular instrumentation is related primarily to embolization.[5–7,11] Moreover, unlike the traditional surgical operation in which the risk of postoperative embolization is removed along with the plaque, carotid angioplasty leaves the plaque in place, where it can give rise to brain embolization at any time in the future. Although "primary" stenting and covered prostheses have been advocated as solutions to angioplasty's embolization problem,[10–12,20] it would seem advantageous to draw on our knowledge of the carotid plaque and preoperatively identify lesions likely to precipitate an embolic event.

The morphology of the carotid atherosclerotic plaque has been studied extensively as it relates to symptomatology[16–18,24,29,30] and embolic potential.[17,18,25–28] Mature atherosclerotic plaques whose fibrous caps have become unstable are prone to rupture, exposing the soft, necrotic, cholesterol-laden cores to the bloodstream.[20,29,30] These late-stage plaques are found in the majority of symptomatic patients and in asymptomatic patients with high-grade stenosis.[20,29,30] They are characterized by calcification, intraplaque hemorrhage, ulceration, and luminal thrombosis, features that have been associated with spontaneous embolization in high-grade internal carotid stenoses.[17,18,20,30,31]

Although unstable carotid plaques predominate in patients with cerebral ischemia, their morphological characteristics have not been as uniformly associated with stroke or microembolization during interventions. In a clinical study of 231 elective carotid stent procedures, the presence of long or multiple stenoses was the only morphological variable found to be an independent predictor of procedural stroke.[12] Ohki et al.,[32] in an ex vivo human carotid artery stent model, observed that neither plaque ulceration nor calcification influenced the number of embolic particles detected during balloon angioplasty and stenting. Only high-grade stenosis was statistically associated with particulate volume, a recognized correlate to subsequent neurological events during surgery.[33,34] Interestingly, Ohki et al.[32] found that plaques with low reflectivity (echolucency) to ultrasound interrogation generated significantly more particles compared with echogenic plaques.

In this study, we have corroborated our earlier work[18,27,28] that showed a close correlation between plaque echolucency, quantified by the GSM, and CT evidence of cerebral infarction. Moreover, the computer analysis of plaque echogenicity appears more accurate than the degree of stenosis in identifying plaques associated with an increased incidence of brain infarction.

Given that CT-documented infarctions reflect cerebral embolic events and are associated with unstable carotid plaques, we believe computer quantification of plaque echolucency is a simple and clinically valid means of stratifying carotid stent candidates according to lesion type. This test for plaque characterization is currently being used in a prospective multicenter trial (ACSRS, Asymptomatic Carotid Stenosis and Risk of Stroke).[35] We anticipate that this trial will further corroborate the utility and validity of computerized echographic carotid plaque analysis.

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