Ultrasonic Duplex Scanning for Disease of the Carotid Artery

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SUMMARY The duplex ultrasonic scanner combines real-time B-mode imaging with a single-gate, variable-range pulsed Doppler. The detection and categorization of the severity of carotid artery atherosclerosis is achieved by performing spectral analysis of the pulsed Doppler velocity signal obtained from vessels of interest. Using this technique, 750 patients with suspected extracranial carotid artery disease were evaluated between January 1978 and January 1980. One hundred thirty-five of these 750 patients (18%) underwent cerebral arteriography performed with planar views of the carotid bifurcation. The degree of stenosis was measured independently in these patients and was available for comparison with the results of duplex scanning and spectral analysis.

Duplex scanning correctly detected the presence of disease in 252 of 259 carotid arteries studied (97%). The extent of involvement varied from plaques that produced less than 10% diameter reduction to those that resulted in a total occlusion. The technique was less accurate with lesions that produced less than 10% diameter reduction.

VARIOUS noninvasive tests have been developed to assess carotid bifurcation atherosclerosis. The most frequently used include periorbital Doppler and plethysmographic methods, which are theoretically capable of detecting lesions that produce a reduction in pressure and flow. However, these methods cannot distinguish between high-grade stenosis and occlusion of the internal carotid artery. Transient ischemic attacks and strokes can be produced by lesions of the carotid bifurcation that range from minimal to total occlusion. Therefore, noninvasive tests must be able to identify both normal vessels and those with varying degrees of involvement.

We developed an ultrasonic duplex scanner that not only images the bifurcation, but also attempts to identify flow changes secondary to the presence of disease. In this report, we compare the results of duplex scanning and planar arteriography in 135 patients (270 sides).

Materials and Methods

The peripheral vascular scanner III (ultrasonic duplex scanner) has three 5-MHz ultrasonic transducers mounted on a rotating drum encased in a water-filled Silastic boot used to generate a real-time B-mode image. Within the Silastic boot, a single-gate, variable-range, 5-MHz pulsed Doppler with a directional phase quadrature output is mounted in the plane of the B-mode image. The beam axis of the pulsed Doppler is represented on the image by an enhanced white line; the point from which flow is sampled is represented by a white dot (fig. 1).

The examination is carried out with the patient supine and the head resting on a padded donut-type support. The study is started low in the neck by visualizing the common carotid artery along its longitudinal axis. The transducer is then moved toward the base of the skull to identify the carotid bulb, which is relatively easy because the artery widens at this point. The internal and external carotid arteries at their origin are then visualized, and their positions and courses are carefully noted. The pulsed Doppler sample volume at each point is positioned either in the center of the artery or at the point that provides the greatest audible velocity change.

The B-mode images are inspected for acoustic shadowing and bright echoes from plaques and regions of calcification. During the examination, the audible characteristics of the velocity signals are noted. These characteristics are useful not only in identifying the vessel of interest, but also in detecting velocity changes associated with flow disturbances. Both the B-mode image and directional Doppler signal are recorded on videotape for review and processing of the velocity signal. A digital fast Fourier transform (FFT) spectrum analyzer was used to further process the Doppler signal. The FFT analyzer provides 400 spectra/sec, with a total frequency display of 10 kHz and a frequency resolution of 100 kHz. Hard copy is produced on light-sensitive paper to display the amplitude (levels of grey) (fig. 2), frequencies and directional characteristics of the audible Doppler signal from which both qualitative and quantitative measurement may be performed. On the hard copy, 7 kHz are reserved for forward and 3 kHz for the reverse velocity components of the signal.

The spectral changes evaluated included the peak frequency, the degree of spectral broadening during systole and the nature (forward, zero or reverse flow) of the diastolic component of the signal. Five angiographic categories were defined according to characteristic spectral changes of the pulsed Doppler signal.

(1) Normal — peak frequency less than 3.5 kHz
with no spectral broadening; (2) less than 10% diameter reduction — peak frequency less than 3.5 kHz with spectral broadening during the deceleration phase of systole; (3) 10-49% diameter reduction — peak frequency less than 3.5 kHz with an accentuation of the spectral broadening throughout the systolic period; (4) 50-99% diameter reduction — peak frequency greater than 4 kHz with spectral broadening throughout the whole of the pulse cycle; and (5) total occlusion — no Doppler signal from the imaged vessel and specifically for internal carotid occlusion, low peak systolic frequency and flow reversal or flow to zero during diastole in the signal obtained from the common carotid artery (fig. 2).

The amount of spectral broadening is determined by visual inspection of the FFT output. The criteria for using the above classification were derived by our initial experiences in comparing the spectral changes with known degrees of stenosis determined angiographically. After determining that velocity and spectral changes did appear to correlate, this classification scheme was prospectively evaluated in the manner described in this report.

Between January 1978 and December 1979, 750 patients were referred for evaluation of suspected extracranial cerebrovascular disease. All patients underwent ultrasonic duplex scanning and spectral analysis. Of the 750 patients, 135 (18%) underwent biplane carotid arteriography. The arteriograms were independently reported by two radiologists unaware of the results of the noninvasive study. The degree of stenosis of the internal carotid artery was measured from the arteriogram using calipers to assess the percentage reduction in diameter (to the nearest 5%). The vessels were then placed into one of the five categories previously mentioned. If multiple areas of the internal carotid artery were involved, the greatest diameter reduction was used.

**Results**

The results are summarized in tables 1 and 2. In the 135 patients in whom arteriography was performed, 270 carotid bifurcations were available for comparison. Duplex scanning correctly identified that disease was present in 252 of 259 vessels (sensitivity 97%). Only four of the 11 vessels considered normal arteriographically were correctly identified by duplex scanning and spectral analysis (specificity 37%). The ability to correctly predict the degree of stenosis from the spectral changes was variable. Only four of the 11 normal arteries were correctly identified, and nine of 20 arteries considered arteriographically to be the site of disease producing less than 10% diameter reduction were correctly identified by ultrasonic duplex scanning. Of the 90 arteries with 10-49% diameter reduction, 51 (58%) were correctly identified; of the 103 arteries with 50-99% diameter reduction, 84 (81.5%) were correctly identified. Thirty-two of the 46 completely occluded vessels (70%) were correctly identified.

**Discussion**

Noninvasive tests that could accurately predict the presence and extent of atherosclerosis of the carotid bifurcation would be useful clinically and in research. Identification of a normal carotid bifurcation or an internal carotid artery occlusion may preclude the need for cerebral arteriography. The significance of the ex-
tent of disease in the genesis of cerebral ischemia is also clinically important.

Duplex scanning does not appear to identify normal carotid arteries with acceptable accuracy, although the numbers available for analysis are small and the arteries misclassified were assigned to categories that defined relatively minor disease (Table 1). Because relatively few patients with normal carotid arteries underwent arteriography and because of the scatter associated with the results, we examined this subset of patients more closely.

The arteriograms were interpreted independently by two radiologists, using the categories defined above. Interobserver agreement that a carotid bifurcation was normal was only 56.8%. When the films were reviewed on two separate occasions, the intraobserver agreement that the carotid bifurcation was normal was 74.8%. This poses the question of the best method of identifying normal carotid arteries when arteriography is the standard with which other testing methods are compared.

There are several ways to define the extent of stenosis from the arteriograms. In this study, we used the unsubtracted arteriogram because the presence of calcification in the outer layers of the vessel wall in the region of the stenosis greatly facilitates the estimation of vessel diameter. We expressed the degree of stenosis as the percentage reduction of the normal wall diameter at the level of the bulb. Other authors have measured the minimal transverse diameter and compared it with the diameter of the internal carotid artery beyond the diseased region. The latter technique may well miss or underestimate lesions of the carotid bulb that can be seen on B-mode real-time imaging or be represented as velocity disturbances detectable by spectral analysis of the audible Doppler velocity signal. It would be inappropriate to disregard these changes because of a measurement technique, because they do represent disease that may be responsible for symptoms.

Using the methods we have outlined, Chikos et al. determined that inter- and intraobserver variability gradually decreases as the severity of the stenosis increases. Thus, for complete occlusion of the internal carotid artery the interobserver agreement approaches 100%, and for lesions greater than 50% diameter reduction, the agreement remains acceptable. For lesions of less than 10% diameter reduction and lesions from 10–49% diameter reduction, inter- and intraobserver variability is significant. The difficulties of interpreting the carotid arteriograms present a significant problem in evaluating the accuracy of non-invasive methods.

Relatively few normal carotid arteries were available for evaluation. With few exceptions, the decision to perform angiography was not the responsibility of the personnel performing the noninvasive study. The results of ultrasonic duplex scanning were reported to the referring physician without any recommendation as to the subsequent management of the patient. At regular intervals, referring physicians and hospitals were asked if arteriography had been subsequently performed. Arteriography was performed in only 18% of the 750 patients in this phase of the study. We do not know why the referring physicians requested contrast arteriography after duplex scanning. The impact of ultrasonic duplex scanning studies on the subsequent course and management of the patient is being investigated. The results will have significant implications for the potential role of such noninvasive studies in the future. However, arteriographic confirmation in patients whose vessels are considered normal by duplex scanning remains a significant problem.

Of the 11 arteries considered normal by arteriography, four were classified normal by duplex scanning, three were reported as having minimal wall irregularities and four were considered to have 10–49% reduction in diameter. However, of these 11 carotid arteries, disease was present on the contralateral side in each patient. Given the generalized nature of the atherosclerotic process, it is likely that some disease could have been present in the arteries considered normal.

Of the 20 arteries classified as having less than 10% diameter stenosis arteriographically (Table 1), only three had normal spectra by our criteria. Although the difficulties in accurately detecting minor lesions by arteriography or by ultrasonic duplex scanning are

<table>
<thead>
<tr>
<th>Diameter stenosis by angiography</th>
<th>Normal</th>
<th>10%</th>
<th>10-49%</th>
<th>50-99%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>11</td>
<td>4%</td>
</tr>
<tr>
<td>10%</td>
<td>3</td>
<td>9</td>
<td>8</td>
<td>20</td>
<td>7.5%</td>
</tr>
<tr>
<td>10-49%</td>
<td>12</td>
<td>52</td>
<td>20</td>
<td>2</td>
<td>33.3%</td>
</tr>
<tr>
<td>50-99%</td>
<td>10</td>
<td>84</td>
<td>6</td>
<td>103</td>
<td>38.2%</td>
</tr>
<tr>
<td>100%</td>
<td>2</td>
<td>12</td>
<td>32</td>
<td>46</td>
<td>17%</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>27</td>
<td>76</td>
<td>116</td>
<td>40</td>
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</tbody>
</table>

**Table 1. Accuracy of Duplex Scanning for 270 Internal Carotid Arteries**

Diameter reduction by duplex spectral analysis

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>252/259 (97%)</td>
<td>4/11 (36.5%)</td>
</tr>
<tr>
<td>False positive</td>
<td>False negative</td>
</tr>
<tr>
<td>7/11 (63.5%)</td>
<td>7/259 (2.7%)</td>
</tr>
</tbody>
</table>
similar to those in detecting normal vessels, the implications of these findings for patient management should be considered. Thus, 15% of patients with minor lesions might not have undergone arteriography if the decision to obtain had been based solely on the spectral analysis of the Doppler signal. Among the arteries with 10-49% stenosis by arteriography, only 4.5% (four of 90) were classified as normal. This finding shows that ultrasonic duplex scanning differentiates well between normal vessels and those with relatively minor disease. Obviously, if these patients were symptomatic, arteriography would be performed regardless of the duplex scan results. If, however, the patients were asymptomatic, and one considered only high-grade stenoses clinically significant,20 duplex scanning would not contribute to unnecessary arteriographic investigation. Because noninvasive tests should be able to detect all degrees of disease, however, this low rate of false-negative results remains unacceptable.

In addition, 20 arteries considered on the basis of arteriography to be the site of 10-49% stenosis were classified as having 50-99% stenosis by duplex scanning. If flow-reducing lesions in the asymptomatic patient are considered an indication for arteriography, 22% (20 of 90) of the patients in this group would have undergone arteriography unnecessarily. The reasons for this misclassification are not clear, but may reflect some of the problems associated with arteriographic classification discussed earlier.

The best agreement was obtained for the evaluation of 50-99% stenoses (table 2). Three of these patients were misclassified as having minimal wall irregularity and six of 103 (6%) were misclassified as having occluded arteries. These misclassifications occurred because with high-grade stenoses, the signal obtained from the common carotid artery resembles that found with total occlusion of the internal carotid artery. Even with direct methods of testing, the flow disturbances that differentiate complete occlusion from high-grade stenosis in some patients may be subtle and require meticulous attention to detail during the examination.

The problem of inaccurate classification of total occlusions is in some regards of greater concern. In the variability study of Chikos et al.,17 the interobserver agreement for totally occluded internal carotid arteries was 97%. Obviously, angiographic misinterpretation in total occlusions could not be used as a potential source of misclassification. Closer examination of our interpretation of the spectral analysis findings readily identified the source of the problems. The commonest error was insufficient attention to the velocity patterns obtained from the common carotid artery on the side of the occlusion. In this regard, flow to zero, with or without flow reversal during diastole, is an important finding and should be noted during the study. Further, when occlusion is suspected, it is mandatory that the examiner attempt to positively identify both branches of the carotid artery. Identification of only a single artery high in the neck region should alert the examiner to pay meticulous attention to the quality of the signal in the vessel being imaged. In patients in whom the internal carotid is occluded, the external carotid artery serves as a major source of collateral blood supply to the ipsilateral hemisphere and its flow and velocity increase markedly. In addition, because the artery is now supplying a relatively low-resistance vascular bed within the skull, the velocity patterns may assume some characteristics normally seen with the internal carotid artery, particularly an absence of flow reversal. Thus, the combination of high velocity and absence of flow reversal may cause the examiner to diagnose a high-grade stenosis of an internal carotid artery when, in fact, a normal external carotid artery is being examined. In 12 vessels, the spectra from the Doppler signal were compatible with a 50-99% stenosis. Awareness of these problems increased our accuracy in predicting total occlusion of the internal carotid artery in subsequent studies.

Although the present study was primarily designed to evaluate the sensitivity and specificity of the ultrasonic duplex scanning method, it has raised additional questions. The arteriogram may not be ideal, given the problems mentioned. Thus, the problem of establishing a suitable means for comparing noninvasive tests that can identify relatively minimal disease is unsolved.

Clinically, particularly in symptomatic patients, the variability of these results is not really relevant, because the physician is primarily interested in identifying the site of involvement and its potential for producing symptoms. However, in symptomatic patients, noninvasive testing plays a minor role. Only in attempting to determine the natural history of disease at the carotid bifurcation does identification of normal vessels and disease of varying degrees become important. The patient with an asymptomatic bruit remains a difficult management problem. Noninvasive tests that can identify all degrees of disease are valuable for documenting the status of the carotid bifurcation and also provide the means by which useful studies can be performed to determine the natural history of a bruit produced by stenosis of the internal carotid artery.

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Fluorescence Microlymphography

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SUMMARY Microneedles, 0.2 mm o.d., were connected to a microsyringe and mounted on a micro-manipulator. Under microscopic control, 0.01 ml of a 25% solution of FITC-labeled dextran-40 or dextran-150 were injected into the subepidermis at the big toe near the nailfold or in the medial ankle region. Fluorescence intravital microscopy revealed a network of lymphatic microvessels. The comparison with recent anatomic studies reveals that the reticular network visualized by FITC-dextran corresponds to the network in the stratum papillare. In 20 healthy subjects lymphatic capillaries were detected in a restricted area on the lateral aspect of the big toe. In 10 patients with primary lymphedema, the dye expanded to almost the entire dorsal skin surface of the big toe. In two cases, enlarged and tortuous microvessels of pathologic shape were observed.

Fluorescence microlymphography is a simple and nearly atraumatic approach for depicting the intravital anatomy of human skin lymphatic capillaries.

The Anatomy of human skin capillaries has been studied by noninvasive intravital microscopy. The excellent light absorption properties of red blood cells and the presence of plasma gaps between them allow one to measure the flow speed if videomicroscopy systems are used.

Unlike blood capillaries, lymphatic microvessels are not visible with conventional intravital microscopy. After local injections of dyes or contrast media, however, lymphatics may be visualized. Different techniques were applied in experimental animals, where it became possible to evaluate prelymphatic pathways.

In man, the interdigital injection of patent blue delineates the lymphatic vessels of the foot to be cannulated for lymphography with contrast media. Macroscopic images of larger trunks have been obtained in various clinical conditions. However, patent blue and other nonfluorescent dyes are not suited to depict lymphatic capillaries because they provide insufficient contrast (personal observation).

In the present report we introduce a method of studying lymphatic microvessels in human skin previously not accessible to visualization in vivo. The fluorescence video microscopy system used was developed to measure transcapillary diffusion and inter-

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