Accurate Noninvasive Method to Diagnose Minor Atherosclerotic Lesions in Carotid Artery Bulb

Tiny van Merode, MD, Jan Lodder, MD, Frans A.M. Smeets, Arnold P.G. Hoeks, PhD, and Robert S. Reneman, MD, PhD

In a prospective study using a multigate pulsed Doppler system, minor (<30% diameter reduction) carotid artery lesions were diagnosed by detecting not only abnormalities in the blood flow pattern, but also local changes in artery wall distensibility. For the diagnosis of more severe lesions, additional information was obtained from disturbances in the Doppler audio spectrum. Biplane arteriography was used as a reference. The observed agreement, sensitivity, and specificity were 86.6%, 90.3%, and 88.6%, respectively, for all lesions and 85.7%, 82.1%, and 88.6%, respectively, when only minor lesions were considered. $\kappa$ (a chance-corrected measure of agreement) was 81.7%. If only blood flow abnormalities were used to detect minor lesions, 43.5% would be missed. Our results indicate that minor carotid artery lesions can be diagnosed noninvasively more accurately when both local blood flow irregularities and local changes in vessel wall distensibility are taken into account. (Stroke 1989;20:1336–1340)

Pulsed Doppler techniques are commonly used for noninvasive diagnosis of atherosclerotic lesions in the cervical carotid arteries in patients suffering from cerebral ischemic attacks. A high overall diagnostic accuracy may be obtained when these techniques are combined with B-mode imaging devices\textsuperscript{1–3} or when multigate pulsed Doppler systems are employed.\textsuperscript{4} However, accurate noninvasive diagnosis of minor atherosclerotic lesions (diameter reduction of <30%) is still problematic. The detection of these minor lesions could have clinical importance because such lesions, especially when combined with ulceration, may cause thromboembolization that leads to symptomatic carotid artery disease.\textsuperscript{5,6} Accurate noninvasive diagnosis of minor lesions is also important to obtain better insights into the natural history of the disease and for follow-up of medical treatment or dietary interventions.

With pulsed Doppler systems, minor atherosclerotic lesions are generally diagnosed by detecting the blood flow disturbances created by these lesions. A complicating factor in this approach is that atherosclerotic lesions are often located in the carotid artery bulb, where the blood flow pattern is complex.\textsuperscript{7,8} Multigate pulsed Doppler systems can detect abnormal blood flow patterns in the carotid artery bulb, thereby improving diagnostic accuracy for moderate lesions (<50% diameter reduction).\textsuperscript{4} However, these systems do not distinguish blood flow disturbances induced by minor lesions from the complex blood flow patterns in normal carotid bifurcations. Multigate pulsed Doppler systems also allow on-line recording of changes in artery diameter during the cardiac cycle,\textsuperscript{9} giving insight into local artery wall properties along the carotid artery bifurcation.\textsuperscript{8,10} Since local changes in artery wall distensibility may be anticipated in atherosclerosis, information about these changes might eventually improve the accuracy of diagnosing minor atherosclerotic lesions.

In our prospective study, we used a multigate pulsed Doppler system to assess minor atherosclerotic lesions on the basis of abnormalities in the blood flow pattern and local changes in artery wall distensibility, and we obtained additional information for the diagnosis of more severe lesions from changes in the Doppler audio spectrum. We validated our approach by comparing these results with those obtained at arteriography.

**Subjects and Methods**

We prospectively studied 114 carotid arteries in 57 patients from the neurology department of the...
TABLE 1. Classification of Carotid Artery Bifurcation Lesions on Basis of Local Blood Flow Pattern and DR on Multigate Pulsed Doppler Investigation

<table>
<thead>
<tr>
<th>Diameter reduction</th>
<th>Spectral analysis Doppler signal shows no or minor spectral broadening (A or B classification according to Strandness)$^{13}$</th>
<th>DR $\leq 0.40$</th>
<th>No blood flow abnormalities in carotid artery bulb</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% (normal artery)</td>
<td>Spectral analysis Doppler signal shows no or minor spectral broadening (A or B classification according to Strandness)$^{13}$</td>
<td>DR $&gt; 0.40$ or DR $\geq 0.40$ with blood flow irregularities in carotid artery bifurcation (profile skewed toward side opposite flow divider and/or back flow at nonspecific site, for instance on side of flow divider)</td>
<td></td>
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<tr>
<td>1–29%</td>
<td>Spectral analysis Doppler signal shows moderate spectral broadening (C classification according to Strandness)$^{13}$</td>
<td>DR $&lt; 0.40$ or DR $&gt; 0.40$ with blood flow irregularities in carotid artery bifurcation (profile skewed toward side opposite flow divider and/or back flow at nonspecific site, for instance on side of flow divider)</td>
<td></td>
</tr>
<tr>
<td>30–49%</td>
<td>Spectral analysis Doppler signal shows severe spectral broadening (D classification according to Strandness)$^{13}$</td>
<td>No peak systolic artery diameter increase in carotid artery bulb can be recorded</td>
<td></td>
</tr>
<tr>
<td>50–99%</td>
<td>Spectral analysis Doppler signal shows severe spectral broadening (D classification according to Strandness)$^{13}$</td>
<td>No peak systolic artery diameter increase in carotid artery bulb can be recorded</td>
<td></td>
</tr>
<tr>
<td>100% (occlusion)</td>
<td>Spectral analysis Doppler signal shows severe spectral broadening (D classification according to Strandness)$^{13}$</td>
<td>DR $\leq 0.40$</td>
<td>No signal in carotid artery bulb and internal carotid artery</td>
</tr>
</tbody>
</table>

DR, distensibility ratio, peak systolic artery diameter increase in carotid artery bulb relative to that in common carotid artery.

University Hospital Maastricht. All patients were submitted to biplane arteriography of the carotid circulation because of focal neurologic symptoms. Arteriography was performed by injection of contrast material through the femoral artery (Seldinger technique). The arteriograms were made bidirectional (anteroposterior and lateral views) by selective injection of contrast material into the common carotid artery (CCA) in most patients; in only a few patients was the contrast material injected into the aortic arch. We used only good-quality arteriograms, which were read by one investigator without knowledge of the outcome of the noninvasive examination. The diameter reduction was calculated from the smallest residual lumen diameter on either projection and from the estimated normal diameter at the site of the lesion on this projection. At the site of the lesion, the normal diameter was estimated by the diameters proximal and distal to the lesion. The lesions were classified as absent (normal artery diameter, 0% diameter reduction), minor stenosis (1–29% diameter reduction), moderate stenosis (30–49% diameter reduction), severe stenosis (50–99% diameter reduction), or total occlusion (100% diameter reduction). Only 97 arteries were analyzed because 12 patients underwent unilateral carotid endarterectomy before the ultrasound examination could be performed and because five arteries could not be investigated for technical reasons.

The principles and features of the high-resolution multigate pulsed Doppler system have been described in detail.$^{8,9,11,12}$ For adequate interpretation of the data and accurate measurements, it is necessary to know the site of velocity assessment in relation to the position of the flow divider and the angle of interrogation. Hence, we connected the multigate pulsed Doppler system to an ATL Mark V B-mode imager with a short-focus scanhead (Bothell, Washington). In this configuration, the multigate device, which functionally replaces the single-gate Doppler device of the ATL system, has the following characteristics: pulse-repetition frequency 16 kHz, emission frequency 5.2 MHz, emission duration 1.2 μsec (in current mode of opera-
FIGURE 2. Instantaneous mean velocity waveforms and axial velocity profiles as recorded in abnormal carotid artery bifurcation. Note back flow in carotid bulb on side of flow divider (broad arrows), c.c.a., common carotid artery; i.c.a., internal carotid artery; e.c.a., external carotid artery; ant., anterior; post., posterior.

The investigations were performed with the patient in the supine position with the head tilted somewhat to the contralateral side. The velocity profiles at discrete time intervals during the cardiac cycle, the instantaneous velocity tracings along the ultrasound beam, and the relative artery diameter changes during the cardiac cycle (Δd/d×100%) were recorded on-line in the CCA 3 cm proximal to the flow divider, in the carotid artery bulb at the level of the tip of the flow divider (B₀) and 1 cm more distally (B₁), and in the internal carotid artery 3-4 cm distal to the tip of the flow divider. For recording of the velocity information, the vessels were interrogated in the plane of the carotid artery bifurcation at angles of 60° and 90° to the vessel axis to obtain information about the axial and radial blood flow patterns, respectively. The relative artery diameter changes during the cardiac cycle were recorded at these sites as well, using a 60° angle of interrogation. This direction was used because the assessment of vessel wall displacement is based upon the detection of low-frequency Doppler signals originating from the sample volumes coinciding with the anterior and posterior walls. To ensure that the initial relative change at the beginning of the cardiac cycle was constant, this initial relative change was reset to 0 by a trigger derived from the R-wave of a standard lead of the electrocardiogram. This trigger was also used to mark the start of the cardiac cycle when velocities were recorded. The relative artery diameter changes are independent of the angle of interrogation and can be determined with an absolute accuracy of 0.5%, which compares favorably with the relative peak excursions observed. This means that for a relative excursion of, for example, 7%, a relative change in artery diameter of 6.5-7.5% can be measured. The Doppler spectra were recorded midstream and analyzed with a Nicolet spectrum analyzer (UA500A, Northvale, New Jersey; 100 frequency bins, each 100 Hz), providing amplitude as a function of frequency. The spectra were classified according to the criteria of spectral broadening as developed for pulsed Doppler systems.

Distensibility ratio (DR) was calculated as the peak systolic artery diameter increase at the level of
the flow divider in the carotid artery bulb relative to that in the CCA. From a previous study in our laboratory on the distensibility of the carotid artery bifurcation, we concluded that DR varied from 0.91 to 1.47 in young (20–30 years) subjects and from 0.41 to 0.93 in older (50–60 years) subjects; DR of ≥0.40 was therefore considered to be normal, regardless of the age of the patient.

Blood flow abnormalities in the carotid artery bifurcation were recorded and evaluated with particular attention to the direction of the skewness of the blood velocity profile in the carotid artery bulb and the site of back flow, if any, in the carotid artery bifurcation. A velocity profile skewed toward the side opposite the flow divider and/or back flow at a nonspecific site in the bulb (e.g., on the side of the flow divider) were classified as blood flow abnormalities. Our investigator performed and classified these Doppler studies without knowing the results of arteriography. The lesions were classified on the basis of the blood flow pattern and DR in a way similar to that described for arteriography. The criteria used for classification of the lesions are described in Table 1. Normal and abnormal blood flow patterns in the carotid artery bifurcation are illustrated in Figures 1 and 2. Figures 3 and 4 show normal and abnormal DRs.

To describe diagnostic reliability, we used $\kappa$, a chance-corrected measure of agreement, in addition to observed agreement (diagnostic accuracy), sensitivity, specificity, and positive and negative predictive values. $\kappa$ takes into account the marginal distribution of the data and may therefore be considered a better parameter to describe diagnostic accuracy since it measures pairwise agreement as determined both by diagnostic accuracy and by marginal distribution. Small changes in a three-way table following reallocation of falsely classified items may not influence diagnostic accuracy, but they are always reflected by changes in the marginal distribution and thus are expressed through $\kappa$.

**Results**

The results are given in Table 2. For all lesions, diagnostic accuracy was 86.6%, with a sensitivity of 90.3% and a specificity of 88.6%; the positive and negative predictive values were 93.3% and 83.8%, respectively, and $\kappa$ was 0.87. When only minor lesions were considered, diagnostic accuracy was 85.7%, with a sensitivity of 82.1% and a specificity of 88.6%.

**Discussion**

Our findings show that minor carotid artery lesions can be accurately diagnosed when local changes in artery wall distensibility are considered in addition to local disturbances in the blood flow pattern.

In the past, it has been especially difficult to diagnose minor lesions in the carotid artery bulb accurately, taking into account only disturbances in the local blood flow pattern, since complicated blood flow patterns and recirculation zones are.

### Table 2. Results of Multigate Pulsed Doppler Investigation Compared With Biplane Arteriography (Seldinger Technique)

<table>
<thead>
<tr>
<th>Angiography (% diameter reduction)</th>
<th>Doppler (% diameter reduction)</th>
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<tbody>
<tr>
<td>Normal 1–29%</td>
<td>Normal 1–29%</td>
</tr>
<tr>
<td>Normal 31</td>
<td>4</td>
</tr>
<tr>
<td>1–29%</td>
<td>5</td>
</tr>
<tr>
<td>30–49%</td>
<td>1</td>
</tr>
<tr>
<td>50–99%</td>
<td>0</td>
</tr>
<tr>
<td>100%</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
</tr>
<tr>
<td>Observed agreement ($P_o$): $\frac{31+23+9+16+5}{97} = 0.866$</td>
<td></td>
</tr>
<tr>
<td>$P_e$: $\frac{35}{97} \times \frac{37}{97} + \frac{28}{97} \times \frac{29}{97} + \frac{13}{97} \times \frac{9}{97} + \frac{16}{97} \times \frac{17}{97} + \frac{5}{97} \times \frac{5}{97} = 0.268$</td>
<td></td>
</tr>
<tr>
<td>Chance-corrected agreement ($\kappa$): $\frac{P_o - P_e}{1 - P_e} = 0.817$</td>
<td></td>
</tr>
<tr>
<td>$1 - 0.268$</td>
<td>0.817</td>
</tr>
</tbody>
</table>

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observed in the carotid artery bulb under normal circumstances. These complicated blood flow patterns result in changes in the Doppler spectrum that are difficult to distinguish from those induced by minor carotid artery lesions.

It is interesting to note that both blood flow abnormalities and vessel wall distensibility must be determined for accurate, noninvasive diagnosis of minor atherosclerotic lesions. When only decreased artery wall distensibility was used to detect the 23 minor lesions, seven (30.4%) were missed; when only blood flow abnormalities were considered to indicate such lesions, 10 (43.5%) were not diagnosed. Thus, only six minor lesions showed both blood flow abnormalities and diminished artery wall distensibility in the carotid artery bulb. These observations indicate that minor atherosclerotic lesions may be associated with locally diminished distensibility of the artery wall, intraluminal processes, or both.

Our results may be improved by employing a high-resolution B-mode imager, which provides more detailed pathoanatomic information. In this way, the configuration and texture of an atherosclerotic plaque can be related effectively to local irregularities in the blood flow pattern and in vessel wall distensibility, as assessed with the multigate pulsed Doppler system.

We conclude that the detection of minor carotid artery disease with a multigate pulsed Doppler device is accurate when local changes in vessel wall distensibility are considered in addition to local blood flow disturbances. This approach could therefore be relevant to the management of patients with cerebral ischemic attacks since normal findings might prevent unnecessary arteriography.

References


Key Words • carotid artery diseases • ultrasonic diagnosis
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