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 devices¹-³ or when multigate pulsed Doppler systems are employed.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.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.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).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,⁹ giving insight into local artery wall properties along the carotid artery bifurcation.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)\textsuperscript{13}</th>
<th>DR&lt;0.40 or DR≥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)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% (normal artery)</td>
<td>No blood flow abnormalities in carotid artery bulb</td>
<td>DR&gt;0.40 or DR&gt;0.40 with blood flow irregularities in carotid artery bifurcation (profile skewed toward side opposite flow divider)</td>
</tr>
<tr>
<td>1–29%</td>
<td></td>
<td>DR&lt;0.40 or DR&gt;0.40 with blood flow \textsuperscript{13}</td>
</tr>
<tr>
<td>30–49%</td>
<td>Spectral analysis Doppler signal shows moderate spectral broadening (C classification according to Strandness)\textsuperscript{13}</td>
<td>Blood flow abnormalities in carotid artery bifurcation</td>
</tr>
<tr>
<td>50–99%</td>
<td>Spectral analysis Doppler signal shows severe spectral broadening (D classification according to Strandness)\textsuperscript{13}</td>
<td>Jet-shaped profile No peak systolic artery diameter increase in carotid artery bulb can be recorded</td>
</tr>
<tr>
<td>100% (occlusion)</td>
<td>No signal in carotid artery bulb and internal carotid artery</td>
<td>DR, distensibility ratio, peak systolic artery diameter increase in carotid artery bulb relative to that in common carotid artery.</td>
</tr>
</tbody>
</table>

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.\textsuperscript{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+₁), 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...
van Merode et al. Diagnosis of Minor Carotid Lesions

FIGURE 4. Relative changes in artery diameter during cardiac cycle as recorded in common carotid artery (c.c.a.) and carotid artery bulb of abnormal carotid bifurcation. From this information distensibility ratio (DR) was calculated. DR<0.40. ant., anterior; post., posterior.

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 81.7. 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>
<thead>
<tr>
<th>Angiography (% diameter reduction)</th>
<th>Doppler (% diameter reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>1–29%</td>
<td>1–29%</td>
</tr>
<tr>
<td>30–49%</td>
<td>30–49%</td>
</tr>
<tr>
<td>50–99%</td>
<td>50–99%</td>
</tr>
<tr>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>Total</td>
</tr>
<tr>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>97</td>
<td>97</td>
</tr>
</tbody>
</table>

Observed agreement (\( P_o \)):

\[ P_o = \frac{31 + 23 + 9 + 16 + 5}{97} = 0.866 \]

\( P_o = \frac{31 \times 23 + 29 \times 16 + 13 \times 9 + 16 \times 5 + 5 \times 9}{97} = 0.268 \)

Chance-corrected agreement (\( \kappa \)):

\[ \kappa = \frac{0.866 - 0.268}{1 - 0.268} = 0.817 \]
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 diag-
nosed. Thus, only six minor lesions showed both
blood flow abnormalities and diminished artery wall
distensibility in the carotid artery bulb. These obser-
vations indicate that minor atherosclerotic lesions
may be associated with locally diminished distensi-
bility 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 irregular-
ities 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 there-
fore be relevant to the management of patients with
cerebral ischemic attacks since normal findings might
prevent unnecessary arteriography.

References

1. Langlois Y, Roederer GO, Chan A, Phillips DJ, Beach KW,
Martin D, Chikos PM, Strandness DE: Evaluating carotid
artery disease. The concordance between pulsed Doppler/
spectrum analysis and angiography. Ultrasound Med Biol
1983;9:51–63
2. Roederer GO, Langlois YE, Jager KA, Primozi EJ, Beach
KW, Phillips DJ, Strandness DE: The natural history of
carotid arterial disease in asymptomatic patients with cervi-
3. Knox RA, Greene FM, Beach K, Phillips DJ, Chikos PM, Strandness
13:589–594
4. Van Merode T, Hick PJJ, Hoeks APG, Reneman RS: The
diagnosis of minor to moderate atherosclerotic lesions in
the carotid artery bifurcation by means of spectral broadening
combined with the direct detection of flow disturbances
using a multi-gate pulsed Doppler system. Ultrasound Med
7. Ku DN, Giddens DP: Pulsatile flow in a model carotid
8. Reneman RS, van Merode T, Hick PJJ, Hoeks APG: Flow
velocity patterns in and distensibility of the carotid artery
9. Hoeks APG, Ruisen CJ, Hick PJJ, Reneman RS: Transcu-
taneous detection of relative changes in artery diameter.
10. Reneman RS, van Merode T, Hick PJJ, Muytjens AM,
Hoeks APG: Age related changes in carotid artery wall
11. Hoeks APG, Renemen RS, Peronneau PA: A multi-gate
pulsed Doppler system with serial data processing. IEEE
12. Reneman RS, van Merode T, Hick PJJ, Hoeks APG: Car-
diovascular applications of multi-gate pulsed Doppler sys-
13. Breslau PJ: Ultrasonic duplex scanning in the evaluation of
carotid artery disease (thesis). University of Limburg, Maas-
tricht, The Netherlands, 1982
Psych M 1960;20:37–46
15. Schouten HJA: Measuring pairwise agreement among many
16. Bharadwaj BK, Mabon RF, Giddens DP: Steady flow in
a model of the human carotid bifurcation. J Biomech 1982;
15:349–378
17. Ku DN, Giddens DP, Zarins CK, Glogov S: Pulsatile flow
and atherosclerosis in the human carotid bifurcation. Arter-
iosclerosis 1985;5:293–302

KEY WORDS • carotid artery diseases • ultrasonic diagnosis
Accurate noninvasive method to diagnose minor atherosclerotic lesions in carotid artery bulb.

T van Merode, J Lodder, F A Smeets, A P Hoeks and R S Reneman

Stroke. 1989;20:1336-1340
doi: 10.1161/01.STR.20.10.1336

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1989 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/20/10/1336

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/