Carotid artery stenosis in peripheral vascular disease

Natalia A. Alexandrova, MD, Wendy C. Gibson, BSc, RVT, John W. Norris, MD, FRCP, and Robert Maggisano, MD, FRCS(C), Toronto, Ontario, Canada

Purpose: The goal of the study was to assess the prevalence and severity of symptomatic and asymptomatic carotid artery disease in patients with peripheral vascular disease (PVD).

Methods: Consecutive patients with clinically and Doppler scanning-proven PVD (category 1 or greater) underwent prospective screening for the presence of carotid atherosclerosis with color-coded duplex ultrasonography. Preexisting risk factors were recorded with a standard questionnaire and included sex, age, diabetes mellitus, history of smoking, hypertension, prior stroke/transient ischemic attacks, and coronary artery disease.

Results: Three hundred seventy-three consecutive patients were studied over 2 years. The mean age of the patients was 70 ± 10 years; there were 223 (60%) men and 150 (40%) women; 71% of the patients had a history of smoking, 47% had coronary artery disease, 43% had hypertension, and 21% had diabetes mellitus. Two hundred eleven (57%) patients had 30% or greater carotid artery stenosis detected by carotid artery duplex scanning. Sixty-seven (32%) of these had symptoms of ischemic cerebral events, of whom 22 had potentially operable carotid artery stenoses (70% to 99%), whereas 72 of the 144 symptom-free patients had 60% to 99% stenosis. An additional 34 patients would be eligible candidates for the ongoing carotid endarterectomy trials (North American Symptomatic Carotid Endarterectomy Trial and European Carotid Surgery Trial). Although all the risk factors were associated significantly with PVD and carotid artery disease (p < 0.002), male sex and prior stroke/transient ischemic attack were the strongest predictors.

Conclusions: Routine carotid ultrasound screening of 373 consecutive patients with category I or greater PVD revealed that 22 patients with symptoms and 72 symptom-free patients were potential surgical candidates, representing 25% of the study cohort. An additional 34 patients were potential candidates for enrollment into the North American Symptomatic Carotid Endarterectomy Trial and European Carotid Surgery Trial. (J VASC SURG 1996;23:645-9.)

Carotid atherosclerosis is associated with a risk of stroke that increases with the severity of the stenosis.1-3 Two major ongoing trials of carotid endarterectomy, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial,2,3 have clearly demonstrated the benefit of surgery for patients with symptoms of high-grade carotid artery stenosis. Another major trial of symptom-free patients, the Asymptomatic Carotid Atherosclerosis Study (ACAS)4 recently reported on an analysis of interim data, indicating benefit from carotid endarterectomy in patients with greater than 60% carotid artery stenosis.5

Because peripheral vascular disease (PVD) is associated with a high probability of carotid atherosclerosis, screening for carotid artery disease with duplex ultrasonography has been advocated in patients with PVD to identify patients at risk of stroke.6-7 The concept linking carotid artery stenosis and PVD was studied extensively over the past 20 years.6-12 With noninvasive screening by Doppler ultrasonography, it became evident that carotid artery lesions may be present in up to 33% of patients with peripheral atherosclerosis.9-12 Careful selection of a population for screening and the use of color-coded duplex ultrasonography may yield even higher prevalence of carotid atherosclerosis.6,7
The effectiveness of a screening test is determined by its accuracy and yield, or the amount of previously unrecognized disease that is diagnosed and brought to treatment.\textsuperscript{13} We therefore aimed to assess the incidence and severity of carotid atherosclerosis in patients with PVD with a view to predict operable carotid artery stenosis after the results of the NASCET, European Carotid Surgery Trial, and ACAS trials.

\textbf{PATIENTS AND METHODS}

We prospectively screened consecutive patients admitted with signs and symptoms of PVD referred to our peripheral vascular laboratory for the first time. The diagnosis of PVD was confirmed by use of ankle/brachial indexes and Doppler wave recordings, followed by treadmill exercise if necessary. All testing was performed by experienced vascular technologists. The diagnosis of PVD was based on previously published criteria,\textsuperscript{14} and only patients with category 1 or greater were included in the study. Color-coded duplex scanning of the carotid arteries was performed on a Diasonic Spectra (Diasomics, Milpitas, Calif.) within 2 months of the initial diagnosis of PVD.

Angle-corrected velocity measurements were made to grade the stenosis according to the published criteria.\textsuperscript{15} Our laboratory demonstrated an accuracy of ultrasound testing exceeding 90%.\textsuperscript{16,17} Our local diagnostic criteria were verified in these studies against angiography and the planimetry of the surgical specimens. Furthermore, recent analysis indicates that our laboratory has a 93% sensitivity, 98% specificity, and 96.4\% positive and 95.7\% negative predictive values for screening for operable (\geq60\%) carotid artery stenosis (Alexandrova AV et al., unpublished data, 1995).

In this study, grading of carotid artery stenosis was performed by a vascular surgeon and radiologist independently from each other and "blindly" to the results of the other test. The severity of stenosis recorded was the highest degree of stenosis found; for example, if both a symptomatic 70\% left internal carotid artery stenosis and an asymptomatic 30\% right internal carotid artery stenosis were found in the same patient, the patient was entered into the 70\% to 99\% symptomatic group. The stenosis parameters recorded for patients in the symptomatic and asymptomatic groups were grouped to correspond to the percentage stenoses used in the NASCET and ACAS studies, respectively.

To confirm that grading of carotid artery stenosis by duplex ultrasonography carried out in our vascular laboratory correlated accurately to NASCET/ACAS angiographic criteria, we compared carotid angiography and carotid duplex findings in 156 carotid arteries (78 patients) with angiographic data used as the gold standard. As in NASCET and ACAS, the angiographic linear measurement method was used to correlate peak systolic and end diastolic Doppler flow velocities to the angiographic diameter reduction of the ICA.

A standard questionnaire was used to record demographic data and details of preexisting risk factors (sex, age, diabetes mellitus, history of smoking, hypertension, prior stroke/or transient ischemic attack (TIA), and coronary artery disease). Carotid artery disease was considered symptomatic only if the patient had a prior history of stroke, TIA, or transient monocular blindness ipsilateral to the carotid artery stenosis. Although we did not attempt to validate our questionnaire, potential inaccuracies inherent to its subjective nature would be minimal because the patients' complaints would trigger proper investigations (i.e., neurologic examination and computed tomography) to confirm the diagnosis of stroke or TIA.

We therefore report the incidence of cerebral events on the basis of data obtained with our questionnaire because further investigations were beyond the scope of our study. Multiple logistic regression analysis was used to correlate the risk factors to the presence of PVD and carotid artery stenosis.

\textbf{RESULTS}

Three hundred seventy-three consecutive patients with PVD were studied over 2 years. The mean age of the patients was 70 \pm 10 years, and there were 223 (60\%) men and 150 (40\%) women (p = 0.001). Seventy-one percent of the patients had a history of smoking, 47\% had a history of coronary artery disease, 43\% had hypertension, and 21\% had diabetes. Eighty-seven (23\%) patients reported prior symptoms of cerebral or retinal ischemia, and 286 (77\%) were symptom free.

With 30\% stenosis used as the cut point on carotid artery duplex scanning, 211 (57\%) patients had detectable carotid artery stenosis, of whom 67 had prior neurologic events attributable to the carotid artery lesion, whereas the other 144 patients were symptom free (Fig. 1, Table I). In the symptomatic group, all patients had a history of TIA or minor stroke that occurred before duplex scanning. Of these, 22 had 70\% to 99\% carotid artery stenosis and so were potentially eligible for carotid endarterectomy, whereas 34 had stenosis 30\% to 70\%, making them potential candidates for entry into the current NASCET trial.\textsuperscript{2} In the asymptomatic group,
Table 1. Distribution of severity of carotid artery stenosis in patients with and without symptoms

<table>
<thead>
<tr>
<th>Patients</th>
<th>No.</th>
<th>0%-29%</th>
<th>30%-59%</th>
<th>60%-69%</th>
<th>70%-99%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>With symptoms</td>
<td>87</td>
<td>20 (23%)</td>
<td>28 (32%)</td>
<td>6 (7%)</td>
<td>22 (25%)</td>
<td>11 (13%)</td>
</tr>
<tr>
<td>Without symptoms</td>
<td>286</td>
<td>142 (50%)</td>
<td>62 (22%)</td>
<td>22 (8%)</td>
<td>50 (17%)</td>
<td>10 (3%)</td>
</tr>
</tbody>
</table>

72 patients had carotid artery stenoses 60% to 99%, compatible with carotid artery surgery according to recently published ACAS guidelines. The 94 potential candidates for operation represent 25% of the study cohort.

In the comparison of carotid artery duplex scanning to angiography (Table II) in 35 of 156 (22%) arteries, duplex scanning appeared to overestimate the angiographic stenosis in predicting operable carotid artery disease, and in one patient (0.6%) duplex scanning underestimated the stenosis detected by angiography.

All putative risk factors were associated with the presence of both PVD and carotid artery stenosis (p = 0.002) with multiple logistic regression analysis, but with the stepwise model, only male sex (p = 0.01) and a prior history of stroke or TIA (p = 0.0005) predicted the presence of carotid artery stenosis.

DISCUSSION

Our screening with carotid artery ultrasonography yielded a much higher prevalence (57%) of carotid artery stenosis than studies in the general population. In the Cardiovascular Health Study, only 6% of patients had detectable carotid artery lesions and in the Framingham Study, 8%. In a recent consensus report by an Ad Hoc Committee of the American Heart Association, the costs of large scale screening programs appear to negate any potential benefits of carotid artery surgery in asymptomatic
Table II. Correlation of stenosis detected by angiography versus ultrasonography in 156 carotid arteries

<table>
<thead>
<tr>
<th>Duplex scanning</th>
<th>0%-29%</th>
<th>30%-59%</th>
<th>60%-69%</th>
<th>70%-99%</th>
<th>100%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-29%</td>
<td>38</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>43</td>
</tr>
<tr>
<td>30-59%</td>
<td>19</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>60-79%</td>
<td>11</td>
<td>10</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>80-99%</td>
<td>4</td>
<td>10</td>
<td>10</td>
<td>26</td>
<td>1</td>
<td>51</td>
</tr>
<tr>
<td>100%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

carotid artery stenosis. However, in a population already demonstrated to have at least moderate PVD, the selection bias may work in favor of simple screening by carotid artery duplex scanning, because 25% of the asymptomatic group were potential candidates for operation.

Our data do not take into consideration factors that might preclude carotid endarterectomy, such as fitness for surgery or consent. However, NASCET data indicate that 13% of the patients were ineligible for surgery because of a variety of causes. Applying this statistic to our data would still leave about 22% (63 of the 72) of symptom-free patients eligible for surgery. Furthermore, many patients with PVD have either gangrene or other comorbid factors that may preclude carotid artery surgery. Although this group of patients yields a high incidence of carotid artery stenosis, it is in general one of the oldest patients' populations that may warrant urgent correction of limb ischemia before carotid endarterectomy could be considered.

The results of the duplex scanning versus angiography comparison demonstrated that duplex scanning in many cases (22% in our study) overestimates the angiographic stenosis measured by NASCET criteria, but this discrepancy is well known, and this controversial issue has already been addressed. Our data show that stenosis less than 60% as recorded by duplex scanning is rarely associated with stenosis of greater than 60% as recorded by angiography. Only one of 71 patients with stenosis less than 60% by duplex scanning had a stenosis greater than 60% by angiography. This patient would have been missed and denied potential surgical treatment.

In light of these data, carotid artery duplex screening of consecutive patients with PVD reveals that at least 94 (25%) would be eligible for further study, including angiography and possible carotid endarterectomy, with a more realistic figure of 82 (22%) after exclusions with use of NASCET data. A further 34 (9%) patients would be eligible for enrollment into this NASCET study. Clinical and laboratory screening of their cardiac status would be a desirable step before exposing them to the potential hazards of carotid endarterectomy.

The cost-effectiveness of this strategy remains unknown, but use of a predetermined group with established PVD in the legs targets candidates at potential risk of stroke, regardless of whether they have symptoms. We plan a more detailed prospective study to determine the cost-benefit of this maneuver.

REFERENCES

11. Hennerici M, Aulich A, Sandmann W, Freund HJ. Incidence of


Submitted May 17, 1995; accepted Sept. 13, 1995.