Carotid Angioplasty
Detection of Embolic Signals During and After the Procedure
Hugh S. Markus, MRCP; Andrew Clifton, FRCR; Tim Buckenham, FRACR; Martin M. Brown, MD

Background and Purpose
Carotid angioplasty may offer an effective treatment for carotid stenosis, but there has been concern about the incidence and clinical consequences of distal embolization. Transcranial Doppler monitoring in carotid endarterectomy has demonstrated embolic signals during this procedure. We used this technique in patients undergoing carotid angioplasty.

Methods
Transcranial Doppler ultrasound was used to monitor for embolic signals in the ipsilateral middle cerebral artery before and during 10 technically successful carotid angioplasties and at various standardized times in the following month.

Results
In the month before angioplasty asymptomatic embolic signals were detected in 3 of 10 patients. During angioplasty multiple embolic signals were detected immediately after balloon inflation in 9 of 10 subjects. A minor ipsilateral cerebral ischemic event occurred in 1 of these 9, but the other 8 were asymptomatic. Embolic signals were common immediately after the procedure and intra-arterial femoral catheter removal (8 of 10 subjects) but thereafter became less frequent and were present in 1 of 5 at 4 hours, 2 of 10 at 48 hours, 1 of 6 at 7 days, and 1 of 10 at 1 month.

Conclusions
Embolization at the time of carotid angioplasty is very common but usually asymptomatic; monitoring by means of Doppler ultrasound will allow the effectiveness of measures to reduce this embolization to be studied. Late embolization occurs in a minority of patients and may account for the small but significant risk of delayed stroke. Doppler monitoring may allow identification of patients at risk and assessment of the effectiveness of prophylactic therapy.

Key Words • angioplasty • carotid artery diseases • cerebral embolism and thrombosis • hemodynamics • ultrasonics

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arotid endarterectomy reduces stroke risk in patients with severe symptomatic carotid stenosis, but recent trials have reported a perioperative risk of stroke or death of 7.5%1 and 5%.2 Carotid percutaneous transluminal angioplasty (PTA) has a number of potential advantages including a shorter admission, avoidance of an anesthetic and surgical incision, and an ability to dilate surgically inaccessible lesions such as high internal carotid artery stenoses.3 An understandable concern about distal embolization has led to a reluctance to use carotid PTA; this is in marked contrast to coronary and peripheral artery PTA, which have been widely adopted. In these situations the risk of embolization, estimated by the rate of myocardial infarction and clinical distal arterial emboli, ranges from 4% to 5%.4,5 However, the true incidence of asymptomatic embolization may be much higher, and emboli of a size that are asymptomatic in the coronary and peripheral arterial circulation may cause neurological deficits in the cerebral circulation. No prospective studies have yet published data on the risks of clinical embolization with carotid PTA, but an overview of a number of retrospective studies suggested a stroke rate of less than 5%.

Circulating atheroma, platelet, and thrombus emboli can be detected by means of Doppler ultrasound when they appear as short-duration high-intensity signals in the Doppler spectrum.6 Similar embolic signals have been noted during ultrasound recordings from cerebral arteries in patients with potential embolic sources.7,8 They have been recorded from the ipsilateral middle cerebral artery during carotid endarterectomy9 and related to the development of postoperative magnetic resonance imaging lesions.11 We performed a prospective study in patients undergoing carotid PTA using transcranial Doppler ultrasonography (TCD) of the middle cerebral artery to monitor for embolic signals.

Subjects and Methods
Fifteen consecutive subjects undergoing PTA for symptomatic carotid stenosis were studied. Patients were part of a randomized trial comparing carotid PTA with carotid endarterectomy for which ethical permission had been obtained. In 2 patients adequate Doppler signals could not be obtained from the middle cerebral artery. In 3 the guide wire could not be passed through the carotid stenosis. In 10 subjects technically successful carotid PTA was performed, and the data from these 10 patients are presented. Mean (SD) age was 62.2 (7.7) years (range, 53 to 76 years); 8 subjects were male. The vessel undergoing angioplasty was the left internal carotid artery in 7, the right internal carotid artery in 2, and the left common carotid artery in 1. In 1 case the stenosis was in the distal internal carotid artery. The degree of carotid stenosis determined angiographically1 was 50% to 59% in 1, 60% to 69% in 3, 70% to 79% in 1, 80% to 89% in 3, and 90% to 99% in 2 subjects. Patients had presented with amaurosis fugax or retinal infarct (5), nondisabling stroke (2), transient ischemic attack (2), and amaurosis fugax and transient ischemic attack (1).
computed tomography showed ipsilateral cerebral infarcts in 3 patients and was normal in the other 7.

Carotid PTA was performed via the femoral artery route. A 6F sheath was placed in the femoral artery, through which a 5F Medi-Tech cerebral catheter was passed into the common carotid artery, and angiography was performed to confirm the degree of stenosis. An exchange wire was passed across the stenosis, and a balloon catheter was passed over this. An Optiplast Vasacath was used with a diameter of the inflated balloon of 5, 6, or 7 mm and a balloon length of 2 cm. Inflations were performed for 5 to 10 seconds, except for one 30-second inflation in 1 patient; the number of inflations was 1 in 1 subject, 2 in 2 subjects, 3 in 5 subjects, 4 in 1 subject, and 5 in 1 subject. Immediately after angioplasty selective arterial angiography of the angioplastied artery was performed.

The same TCD machine with a 2-MHz probe (TC2000 S, Eden Medizinische Elektronik GmbH) was used for all studies. The middle cerebral artery ipsilateral to the treated carotid artery was insonated via the transtemporal route at a depth of 46 to 54 mm with a sample volume of 10 mm. The probe was fixed in position by means of a head strap. The signal was recorded onto digital audiotape. Recordings before and after PTA, each of 20 minutes’ duration, were analyzed at a later date by an observer blinded to the diagnosis; recordings from normal volunteers were interspersed. Perioperative recordings were analyzed in a similar way but unblinded because it was clearly apparent that they were operative recordings from the flow velocity changes and the embolic signals during PTA. Embolic signals were identified according to their previously documented characteristics,6-10 short-duration, unidirectional high-intensity signals visible in the Doppler spectrum accompanied by a characteristic “clicking” or “chirping” sound. Random fluctuations in the background Doppler signal or Doppler “speckle” are associated with intensity increases of up to 3 dB,12 and therefore an intensity cutoff of 4 dB was used as an additional criterion. Using this method we have found a very high interobserver correlation in the reporting of embolic signals.

The recorded Doppler signal was played back into the TCD machine for subsequent off-line analysis with specially designed software (EME Ltd) that allowed each time frame of the Fourier transform to be analyzed.12 The relative intensity increase (in decibels) of each embolic signal was calculated using the following equation: relative intensity increase=10 log (maximum relative power amplitude of embolic signal/background relative power amplitude measured at the same velocity from the same point in the next cardiac cycle). The duration of high-intensity signal (in milliseconds) was calculated from the number of time frames over which the relative intensity increase of the embolic signal was greater than 4 dB. Each time frame represents a 5-millisecond time interval.

Comparisons between intensity and duration at different time points were made by means of ANOVA and then Scheffes’s test for comparisons between individual groups.

Results

In the month before carotid PTA, embolic signals were recorded in 3 of 10 subjects during the 20-minute recording period in the middle cerebral artery ipsilateral to the carotid stenosis. In these subjects 4, 3, and 3 embolic signals were detected.

Frequent embolic signals were detected during angiographic contrast injection. Multiple embolic signals were detected immediately after balloon deflation in 9 of 10 patients and usually persisted for two to five cardiac cycles (Figure). Embolic signals were seen with all deflations in these patients except in 1 patient in whom they were detected during three of four deflations. The signals became less Numerous with successive deflations. There was no change in velocity during passage of the embolic signals. In contrast, neurological symptoms occurred in only 1 of 10 patients. This patient suffered an expressive dysphasia and a right-sided weakness with onset at the time of balloon deflation; he was 1 of the 9 with embolic signals detected after balloon deflation. The neurological signs rapidly resolved, and by 1 week the only residual deficit was a subjective numbness over the ulnar border of the right hand. Computed tomographic brain scan was normal. His preoperative stenosis was 90%, his mean middle cerebral blood flow velocity and pulsatility index were normal (47 cm/s and 0.88, respectively), and there was no reduction in flow velocity at the time of angioplasty.

Embolic signals were very common immediately after completion of the procedure and femoral catheter removal (8 of 10 subjects) and 2 hours after angioplasty (5 of 6 subjects) but became progressively less common after this, being present in 1 of 5 subjects at 4 hours, 2 of 10 at 48 hours, and 1 of 6 at 7 days (Table 1). One month after PTA all subjects remained asymptomatic, and embolic signals were only detected in 1 of 10 (subject 9); this subject has remained asymptomatic, and monitoring at 6 months revealed no embolic signals. The mean (SD) number of embolic signals per 20 minutes at each time point was as follows: immediately after PTA, 6.0 (10.0); 2 hours, 3.4 (3.5); 4 hours, 0.4 (0.9); 48 hours, 0.9 (1.9); 7 days, 0.5 (1.2); and 1 month, 0.2 (0.4). Embolic signals tended to be more intense and of longer duration immediately after PTA (Table 2), but differences between different times were not significant. All embolic signals in the month after PTA were asymptomatic, and none were accompanied by any alteration in middle cerebral artery blood flow velocity or waveform. We assessed carotid stenosis by carotid duplex at 1 month using published Doppler criteria,15 stenosis was less than 50% in 8 subjects and 51% to 75% in 2 (patients 9 and 10).

Discussion

Numerous embolic signals were detected in almost all patients during and after carotid PTA. The evidence that these signals represent the passage of emboli is strong. Similar signals can be produced by experimental emboli in both flow14 and animal15 models. Similar
signals have been detected in patients with cerebral embolic sources, including cardiac valvular disease and carotid stenosis, but are rare in normal subjects. Their incidence parallels clinical stroke risk being greater with metallic than with bioprosthetic cardiac valves and with symptomatic than with asymptomatic carotid stenosis.

During routine angiography multiple asymptomatic embolic signals can be detected by TCD, and experimental studies suggest that these represent air emboli. Although air bubbles result in more intense signals than solid embolic materials such as atheroma and thrombus, with current Doppler equipment it is not possible to definitively differentiate air bubbles from solid embolic material. Therefore, it is uncertain whether individual embolic signals detected during passage of the balloon catheter through the stenosis represent solid emboli or residual air emboli from previous contrast injections.

The multiple emboli released at the time of balloon deflation are likely to represent solid emboli for a number of reasons. Signals of a similar extent were not seen during passage of the balloon catheter through the stenosis, no angiographic contrast injections had been given for a few minutes before balloon inflation, and the signals were less intense than those usually recorded with air emboli. Emboli release during angioplasty has been demonstrated experimentally in a model that used canine vessels acutely occluded by thrombus. In patients with carotid artery stenosis treated with carotid PTA by use of a distal occlusive balloon, the debris released after deflation of the proximal angioplasty balloon was extracted, and cholesterol crystals were found in two thirds of the cases. Our TCD results are consistent with the frequent immediate embolization seen in these models. Despite this frequent embolization, an overall stroke rate of less than 5% has been reported in an overview of studies of carotid PTA, suggesting that most emboli are asymptomatic. Consistent with this, despite the frequency of embolic signals after balloon deflation in our study, only 1 of 10 patients had a clinically evident neurological event; the detection of embolic signals after balloon deflation and the absence of any reduction in middle cerebral flow velocity at the time of onset suggest an embolic pathogenesis. Therefore, the very large majority of emboli were asymptomatic. Analysis of the duration and intensity increase of the embolic signals suggests that they result from emboli smaller than those studied in animal models, which range from greater than 200 to 400 μm; their small size may contribute to their usually asymptomatic nature. TCD monitoring will allow evaluation of the effectiveness of methods to reduce distal embolization at the time of balloon deflation, such as a distal occlusive balloon, and the comparison of embolization during PTA with that during other equivalent procedures, such as atherectomy or rotational thrombectomy.

Late ischemic events have also been reported after carotid PTA; in one study of 35 carotid dilations in 32

### Table 1. Number of Embolic Signals Detected in Individual Subjects Before and After Carotid Percutaneous Transluminal Angioplasty and Number of Balloon Deflations During Which Embolic Signals Were Detected

<table>
<thead>
<tr>
<th>Pt</th>
<th>No. of Balloon Inflations</th>
<th>No. of Deflations With ES</th>
<th>Before PTA Immed</th>
<th>2 h</th>
<th>4 h</th>
<th>48 h</th>
<th>7 d</th>
<th>1 mo</th>
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<tr>
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<td>4</td>
<td>3</td>
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<td>4</td>
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<td>0</td>
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<tr>
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<td>3</td>
<td>3</td>
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<td>0</td>
<td>1</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>3</td>
<td>3</td>
<td>1</td>
<td>10</td>
<td>...</td>
<td>0</td>
<td>...</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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<tr>
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<td>2</td>
<td>0</td>
<td>1</td>
<td>...</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>6</td>
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<td>5</td>
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<td>0</td>
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<td>3</td>
<td>3</td>
<td>3</td>
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<td>0</td>
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<tr>
<td>8</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
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<td>3</td>
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<td>1</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>10</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>33</td>
<td>9</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

Pt indicates patient; ES, embolic signals; PTA, percutaneous transluminal angioplasty; and Immed, immediately.

### Table 2. Relative Intensity Increase and Duration (>4 dB) of Embolic Signals at Various Times After Carotid Percutaneous Transluminal Angioplasty

<table>
<thead>
<tr>
<th>No.</th>
<th>Relative Intensity Increase, dB</th>
<th>Duration, ms</th>
<th>Before PTA</th>
<th>2 h</th>
<th>4 h</th>
<th>48 h</th>
<th>7 d</th>
<th>1 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>5.3 (1.2)</td>
<td>13.8 (8.8)</td>
<td>17.8 (14.3)</td>
<td>12.9 (11.4)</td>
<td>10.0 (14.1)</td>
<td>18.3 (10.32)</td>
<td>25.0 (18.0)</td>
<td>8.0 (6.7)</td>
</tr>
<tr>
<td>Time after PTA</td>
<td>Immediately</td>
<td>2 h</td>
<td>4 h</td>
<td>48 h</td>
<td>7 d</td>
<td>1 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>6.3 (1.5)</td>
<td>17.8 (14.3)</td>
<td>12.9 (11.4)</td>
<td>10.0 (14.1)</td>
<td>18.3 (10.32)</td>
<td>25.0 (18.0)</td>
<td>8.0 (6.7)</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>5.4 (1.1)</td>
<td>12.9 (11.4)</td>
<td>10.0 (14.1)</td>
<td>18.3 (10.32)</td>
<td>25.0 (18.0)</td>
<td>8.0 (6.7)</td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>4.1 (0.4)</td>
<td>10.0 (14.1)</td>
<td>18.3 (10.32)</td>
<td>25.0 (18.0)</td>
<td>8.0 (6.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>5.8 (1.1)</td>
<td>18.3 (10.32)</td>
<td>25.0 (18.0)</td>
<td>8.0 (6.7)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7 d</td>
<td>3.2 (2.0)</td>
<td>25.0 (18.0)</td>
<td>8.0 (6.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 m</td>
<td>5.2 (1.3)</td>
<td>8.0 (6.7)</td>
<td>8.0 (6.7)</td>
<td></td>
<td></td>
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</table>

PTA indicates percutaneous transluminal angioplasty. Values are mean (SD). There was a trend toward lower intensity increase with increasing time after PTA (ANOVA, P = .03), but individual comparisons (Scheffe's multiple comparison test) between relative intensity increases at different time periods were not significant. There were no significant differences between embolic signal duration at different times.
patients there were no neurological adverse events during the procedure, but in 3 patients contralateral sensorimotor deficits developed at 18, 24, and 36 hours after the procedure. After PTA with plaque rupture a complex series of events takes place, including endothelial denudation, cracking and disruption of the atherosclerotic plaque, and stretching of the media and adventitia. In animal models the denuded luminal surface returns to near normal thrombogenicity usually within approximately 24 hours, although this may take longer. Platelet aggregates and thrombus may form on the luminal surface, and their embolization may account for the risk of delayed stroke after carotid PTA. Although embolic signals were not detected after 24 hours in most patients, consistent with the animal experiments, they were still present in 2 of 10 subjects at 48 hours despite the prophylactic use of intravenous heparin and aspirin in our patients. TCD may allow both identification of patients in whom late embolization is occurring and assessment of the effectiveness of prophylactic pharmacological treatments.

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References

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