Incidence of Transcranial Doppler–Detected Cerebral Microemboli in Patients Referred for Echocardiography

David C. Tong, MD; Ann Bolger, MD; Gregory W. Albers, MD

Background and Purpose  Transcranial Doppler can detect cerebral microemboli. These emboli may be a risk factor for embolic stroke. We studied the prevalence of microemboli in patients referred for echocardiography.

Methods  Forty-two patients were evaluated. Patients were studied with continuous monitoring over one middle cerebral artery for 30 minutes, and the number of microemboli was recorded. Patients were divided into three groups, those with prosthetic heart valves (group A, n=15), atrial fibrillation (group B, n=14), and no major cardiac risk factor (group C, n=14).

Results  Seventeen percent (7 of 42) of all patients had microemboli. In group A, 5 of 15 (33%) had microemboli. In group B, 2 of 13 (15%) patients had microemboli. Twenty-five percent (7 of 28) of patients in groups A and B combined (A+B) had microemboli. No patients (0 of 14) in group C had microemboli. Groups A and A+B had significantly more emboli than group C (P<.05). Prosthetic heart valve patients with emboli more commonly had a history of prior stroke than valve patients without emboli (3 of 5 versus 2 of 10). The number of emboli seen per 30-minute monitoring session was greater in patients with a prior history of stroke than in patients without (10 microemboli versus 3).

Conclusions  Microemboli can be found in a significant percentage of selected patients referred for echocardiography. The prevalence of microembolism is greater in patients with a high risk of embolization (eg, prosthetic valves) and less in patients with a lower risk of embolization (eg, atrial fibrillation). These microemboli may be associated with an increased prevalence of previous stroke in patients with prosthetic valves. (Stroke. 1994;25:2138-2141.)

Key Words  • Doppler • echocardiography • embolism

Transcranial Doppler (TCD) ultrasonography has recently been found to be capable of detecting cerebral microemboli. These emboli have been identified in patients with prosthetic cardiac valves,1-2 recent stroke,3 and atrial fibrillation,4 as well as during carotid5 and cardiac surgery.6 In experimental models, similar embolic signals have been reproduced with various embolic materials including fat, air, and platelet aggregates.7,8 The significance of these TCD-detected embolic signals has not been defined, but it is possible that they could be markers for increased stroke risk. Embolism from cardiac sources may account for 15% to 30% of strokes9; artery-to-artery embolism may be involved in an additional 30%.10 An indicator of future cerebral embolism would therefore be of great value in the prevention and treatment of stroke.

The purpose of this study was to investigate the prevalence of TCD-detected microemboli in patients considered to be at increased risk for embolic stroke. Another objective was to assess the rate of embolism in specific subgroups. We also attempted to determine whether the presence of emboli predicted a history of prior stroke. Such information is essential in defining the usefulness of TCD in the management of patients at high risk for embolic stroke.

Methods  This protocol was approved by the institutional human subjects committee. From August 1993 to February 1994, patients referred to the Palo Alto Veterans Administration Medical Center Echocardiography Laboratory were screened. Selected consecutive patients with known or potential cardioembolic risk factors were eligible. This included patients with atrial fibrillation (AF), prosthetic cardiac valves, and cardiac thrombus. Patients with stroke who were referred to "rule out a cardiac source of embolization" were also eligible. From these patients a consecutive selected population was chosen for evaluation on the basis of cardiac and neurological history as well as echocardiographic findings.

After informed consent was obtained, data concerning the patients' past medical and neurological histories were recorded. Information regarding antiplatelet and anticoagulant treatment was also gathered, if available. All patients underwent trans-thoracic or transesophageal echocardiography. The results of other diagnostic tests including computed tomography (CT), magnetic resonance imaging (MRI), cerebral angiography, and carotid ultrasound were recorded when available.

Patients were divided into three groups. Group A (n=15) consisted of all patients with cardiac valve replacement. These patients are considered to be at "high risk" for cerebral embolism on the basis of previous epidemiological studies of stroke and valve replacement.11 Group B (n=13) consisted of patients with AF. These patients are known to have an increased stroke risk. However, their risk is generally lower than in prosthetic valve patients, and therefore they were considered to be at "moderate risk."11,12 A final group of patients, group C (n=14), with conditions such as patent foramen ovale and mitral valve prolapse, was felt to be at relatively "low risk" for stroke compared with patients in the other two categories. Patients referred because of a prior
recent history of stroke were also included in this group. Three patients with chronic left ventricular thrombus were assigned to group C because patients with persistent thrombus (>6 months in duration) are believed to have a low risk of embolism, particularly when receiving long-term anticoagulation.11 One patient had both AF and an aortic valve replacement and was assigned to group A. Another patient with mitral valve prolapse and AF was assigned to group B.

Transcranial Doppler examination was performed using a Medasonics CDS color transcranial Doppler system with a 2-MHz probe (Medasonics). TCD embolus monitoring was performed for a total of 30 minutes on each subject through the transtemporal window. The middle cerebral artery (MCA)/anterior cerebral artery (ACA) bifurcation was monitored at a depth ranging from 55 to 65 mm in most patients. If this area could not be located, then the MCA alone was monitored. If the patient had had a prior stroke or transient ischemic attack (TIA) in the anterior circulation, then monitoring was performed in the ipsilateral vascular territory. An elastic headband was used to hold the monitoring probe in position. Hand monitoring was performed if headband monitoring was unsuccessful. Interpretable ultrasound signals were obtained in 100% of patients monitored, and all but one patient could be monitored using the headband.

Emboli were counted using the criteria published by Spencer.13 These criteria require that embolic signals have a duration of less than 0.1 second, be greater than 3 dB above the background, have variable frequency and duration through the cardiac cycle, and produce a distinctive chirp, whistle, or click sound. Potentially embolic signals were excluded if they coincided with patient movement or had atypical embolus characteristics. Embolic signals were detected in real time by the TCD operator and recorded on computer disk and/or audiotape for off-line analysis.

Data were compiled and analyzed on a microcomputer. Analysis of the data was performed using off-line statistical analyses was P<.05.

### Results

Forty-two patients were enrolled in the study (Table 1). All were men. The average age was 65.2 years. There was no significant age difference among groups. There were no statistically significant differences among groups except for a higher prevalence of diabetes in the emboli-positive subgroup (P<.05). The specific types of patients included in each subgroup are summarized in Table 2.

Microemboli (Figure) were detected in 7 of 42 patients (17%) AF patients had emboli. None of the patients in group C (0 of 14) had emboli, including 3 patients with chronic left ventricular thrombi. The number of patients with emboli detected was significantly greater in group A than group C (P<.05). If the two high-risk subgroups were combined, the prevalence of emboli was 25% (7 of 28).

### Table 1. Clinical Characteristics of Emboli-Positive and Emboli-Negative Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=42)</th>
<th>Emboli-Positive (n=7)</th>
<th>Emboli-Negative (n=35)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>42 (100)</td>
<td>7 (100)</td>
<td>35 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10 (24)</td>
<td>5 (71)</td>
<td>5 (14)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 (67)</td>
<td>5 (71)</td>
<td>23 (66)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>12 (26)</td>
<td>2 (29)</td>
<td>8 (23)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>29 (69)</td>
<td>3 (43)</td>
<td>26 (74)</td>
<td>NS</td>
</tr>
<tr>
<td>Ethanol consumption</td>
<td>20 (48)</td>
<td>2 (28)</td>
<td>18 (51)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values in parentheses are percent.

*Emboli-positive versus emboli-negative groups.
The number of microemboli varied from 1 to 17 per 30 minutes (Table 4). The lowest rate was in a patient with AF (1 per 30 minutes). The highest rate was seen in a patient with a mechanical valve replacement (17 per 30 minutes). The average number of emboli per monitoring session was 1.8 per 30 minutes (range, 2 to 8) in the porcine valve replacement group and 8 per 30 minutes (range, 2 to 17) in the mechanical valve group. The embolization rate was higher in the patients with prior stroke compared with those without prior stroke. In the 3 patients with emboli and stroke, the average number of emboli was 10 per 30 minutes. In the patients with emboli and no prior stroke, the rate was 3 per 30 minutes (Table 4). This did not reach statistical significance.

Discussion

We found that TCD-detected microemboli are not uncommon in groups at high risk for embolic stroke. Although our population had a predominance of aortic and/or porcine valves, and the majority were taking therapeutic anticoagulation or antiplatelet therapy, emboli were still detected in 17% of patients in this selected population. There was also a trend toward finding a history of previous TIA or stroke in prosthetic valve patients with microemboli, as well as a higher embolism rate more commonly in patients with a history of prior cerebrovascular symptoms.

The highest prevalence of microembolization was in patients with prosthetic cardiac valves (5 of 15 or 33%). Previous reports have documented microembolism prevalence rates of 0% to 50% in patients with bioprosthetic valves and of 54% to 89% in patients with mechanical valves. Our data are consistent with these reports (2 of 5 or 40% of mechanical valves with emboli, 3 of 10 or 30% of bioprosthetic valves). As noted above, our lower prevalence was probably influenced by the large number of aortic (13 of 15) and porcine (10 of 15) valves in our sample. Both these valve types are associated with a lower risk of cerebral embolization.

Patients with AF had fewer microemboli. Prior studies have reported prevalence rates ranging from 30% to 88% in AF patients with recent stroke. Tegeler et al found 11% (1 of 9) of patients with AF and no acute stroke had microemboli. Our AF subgroup had a similar prevalence of microembolism of 15% (2 of 13). The number of emboli seen during a monitoring session was low (1 embolus per 30 minutes). This is comparable to or perhaps somewhat lower than rates reported by others for patients with bioprosthetic valves (average, 2 emboli per hour; range, 0 to 7). There was no detectable relationship between the presence of microemboli and a history of prior stroke in this group, although the small sample size could have obscured such a finding.

One explanation of the lower rate of embolization in AF patients could be that virtually all the patients were receiving antithrombotic therapy (12 of 13). In treated patients the rate of symptomatic cerebral embolism may be 2% per year or less. In addition, 2 patients had a history of paroxysmal AF and were not in AF at the time of examination. The mechanism of embolism might also
be different in AF patients compared with mechanical valve patients. In addition, the lower rate of TCD-detected microembolization in AF patients suggests that monitoring times may need to be increased in this group.

Microemboli were not seen in patients in group C. This is consistent with the assumption that these patients are less likely to have cerebral embolization and that strokes in these patients are probably due to other mechanisms.

There is a possibility that some of the microemboli could have originated from carotid lesions, since only 3 of 7 emboli-positive patients had carotid ultrasound examinations. However, in 2 of the patients who did not have carotid ultrasound evaluations, microemboli were detected bilaterally. Of the 2 remaining patients, 1 was young and had a bioprosthetic aortic valve replacement. The other had AF and severe congestive heart failure. Therefore, we believe that carotid lesions are unlikely to account for the microemboli detected in this study.

The relationship between microemboli and stroke risk is uncertain. Several reports have associated microembolism with recent stroke,4,18 acute myocardial infarction (MI),19 and cardiogenic4,18 or carotid20-21 risk factors. In one study of acute MI patients, 16 of 76 (21%) had microemboli.19 However, the emboli were not predictive of future cerebrovascular events, possibly because all patients were placed on anticoagulation therapy. In another study, patients with microemboli associated with AF or other cardiac sources of emboli were found to have a higher incidence of recurrent neurological events.18 Unfortunately, only 42% of patients were available for follow-up. More recently, in a study of 179 prosthetic valve patients, no relationship between the presence of emboli and prior neurological events was found.1

Our preliminary data suggest that microemboli can be found more frequently in prosthetic valve patients with a prior history of stroke. Of patients with microemboli, 60% had a history of prior stroke versus only 20% of patients without microemboli. The number of emboli seen per insonation period was also greater in valve patients with a history of prior stroke than in patients without a prior history of stroke. While not statistically significant, these trends suggest that microemboli may be predictive for a history of prior stroke. Whether these microemboli are an independent risk factor or a risk related to the presence of a prosthetic valve alone is unclear.

In addition, this study suggests that the yield from unselected TCD embolus-detection sessions will be low. Patients with known but low-risk cardiac lesions did not have microemboli. However, the effect of longer monitoring sessions needs to be investigated.

In conclusion, we believe that TCD is a promising modality for evaluating embolic stroke. We detected emboli in a substantial number of patients, even though the majority were receiving treatment and did not have the highest-risk cardiac lesions for microemboli. Our data suggest an association between the presence of microemboli and known cardiogenic risk factors. There may also be a relationship between microemboli and a history of prior stroke. The rate of embolization could also be an important determinant of stroke risk. Larger prospective studies will be needed to determine whether these microemboli are an independent risk factor for recurrent stroke. Additional investigations into the nature of microemboli and their response to treatment will also be needed. Such investigations will help to further delineate the role of TCD in stroke prevention and treatment.

Acknowledgments

We wish to thank Dr. Midori Yenari for her helpful editorial commentary regarding this study. We wish to thank Paige Bracci for her assistance with the statistical methods.

References

Incidence of transcranial Doppler-detected cerebral microemboli in patients referred for echocardiography.
D C Tong, A Bolger and G W Albers

Stroke. 1994;25:2138-2141
doi: 10.1161/01.STR.25.11.2138

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/25/11/2138

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/