Cerebral Microembolism in Acute Myocardial Infarction

Zurab G. Nadareishvili, MD, PhD; Zahid Choudary, MD; Campbell Joyner, MD; Dianne Brodie, RVT; John W. Norris, MD

Background and Purpose—This study was undertaken to determine the frequency of cerebral microemboli (high-intensity transient signals; HITS) detected by transcranial Doppler (TCD) in patients with acute myocardial infarction (AMI) and to relate them to the various putative risk factors and clinical embolic events.

Methods—We investigated 112 consecutive patients within 72 hours of admission to an acute coronary care unit using TCD to monitor for cerebral microemboli. Twelve patients were excluded because of failure of ultrasound insonation. All patients had 2-dimensional echocardiograms within the study period.

Results—HITS were detected in 17% of patients, with significantly higher frequency in patients with reduced (<65%) left ventricular (LV) ejection fraction (P=0.019), akinetic LV segments (P=0.002), and LV thrombus (P=0.015). A marginally significant (P=0.059) increase of HITS was found in patients with anterior AMI. Stroke was significantly more frequent in patients with cerebral microemboli (P=0.01).

Conclusions—HITS were detected in 17% of patients in spite of adequate antithrombotic therapy and were increased in patients with reduced LV function, akinetic myocardial segments, and LV thrombus. They were present in all 3 patients with stroke and may represent a predictor of clinical embolic events. (Stroke. 1999;30:2679-2682.)

Key Words: embolism ■ myocardial infarction ■ ultrasonography, Doppler, transcranial

Of the 50 000 patients in Canada who experience a stroke each year,1 almost 35 000 have ischemic stroke, and cardioembolism accounts for 25% to 38%.2,3 Most of these are due to atrial fibrillation (AF), and only 2% to 3% of strokes result from acute myocardial infarction (AMI).4 The annual incidence of ischemic stroke after AMI varies from 1.5% in the general population5 to 7% in individuals with diabetes mellitus.6 The reported incidence of stroke during hospitalization for AMI is 0.9% to 2.4%. Thirty-three percent of these cases occur within 24 hours and =70% within the first week.7,8 There are various causes for systemic embolism, including mural thrombus usually associated with anterior wall infarction, cardiac arrhythmias (especially AF), and impaired left ventricular ejection fraction (LVEF).9,10

Many asymptomatic patients with potential sources of cardiac embolism have signs of cerebral embolism on brain-imaging studies.11 The ability to detect circulating asymptomatic emboli might have predictive value for future embolic events.

Transcranial Doppler (TCD) sonography can detect circulating cerebral microemboli (high-intensity transient signals; HITS), and these have been observed in a variety of potential embolic sources, including symptomatic and asymptomatic carotid stenosis,12,13 prosthetic heart valves,14,15 AF,16,17 cardiac aneurysm, and severe ventricular dysfunction.18 However, there have been no studies in patients with AMI.

We decided to perform an initial study to determine the incidence of HITS and relate various putative risk factors (such as left ventricular [LV] dysfunction) to the presence of microemboli.

Subjects and Methods

We prospectively studied consecutive patients admitted to the coronary care unit of Sunnybrook and Women’s College Health Sciences Center with AMI between January 1997 and April 1999, excluding those with AF. Carotid stenosis >50%, or prosthetic heart valves and patients with no significant transmural myocardial damage (non-Q-wave AMI). AMI was diagnosed according to the established clinical and electrocardiographic criteria.6 Sources of aortic emboli were excluded either by angiography performed for other reasons (preoperative and interventional procedures) or at operation by direct palpation of aorta.19

Demographics, history of ischemic heart disease, stroke, or transient ischemic attack (TIA), and other clinical details were recorded for all patients. In addition, standardized neurological examination was performed before the TCD monitoring. All reports of cerebral, neurovascular, and cardiac imaging were recorded.

Two-Dimensional Echocardiography

Two-dimensional echocardiographic studies were performed in all patients with 2.5-MHz phased-array transducer (Hewlett Packard...
Sonos 2000 or Sonos 5500). LVEF was assessed with a visual quantitative grading system. Patients were divided into groups according to LVEF function: those with normal LVEF (>65%) and those with decreased LVEF (≤65%). The presence of LV wall-motion abnormalities (hypokinetic/akinetio segment) was also recorded for each subject. LV thrombus was diagnosed when an echogenic mass adjacent to but distinguishable from LV endocardium was detected in an area of wall-motion abnormality.20 The echocardiograms were interpreted by experienced cardiologists blinded to the results of the TCD recordings.

### TCD Monitoring

TCD was performed with a Pioneer TC 2020 (Nicolet-EME Ltd) with a 2-MHz transducer in the first 72 hours after the patient’s admission to the coronary care unit. A sample volume of 10 mm was used for all patients. After identification of the middle cerebral arteries (MCAs) via the transtemporal windows, the probes were fixed on the temporal skull by use of a standard headset, and recordings were performed for 30 minutes. Depth of insonation of the MCA was 56 to 60 mm. The TCD device was equipped with a software program that permitted the online detection of HITS, which were all saved on hard disk. During monitoring, the investigator was present to watch for patient movement and to detect the HITS acoustically online. All HITS were analyzed offline by 3 experienced observers blinded to the clinical presentation of the patient. In cases of disagreement between the observers, the HITS were not accepted as microemboli and were considered an artifact. HITS were identified as a predominantly unidirectional short-duration intensity increase, accompanied by a characteristic clicking or chirping sound.21

### Statistical Analysis

Statistical analyses were performed with the Excel software package. Continuous data are summarized as mean ± SD. We used 2-sided Student’s t test for comparison of means (±SD). Proportional differences between the groups were evaluated with Fisher’s exact χ² test.

### Results

#### Subject Characteristics

We evaluated 112 patients; because of failure to find acoustic windows (12 cases), TCD recordings were performed only in 100 patients. There were 68 men and 32 women (mean age 66.0 ± 11.1 years). Women were significantly (P < 0.05) older than men (66.0 ± 11.2 versus 73.1 ± 11.0 years). Fifty-three patients had anterior and 47 had inferior AMIs. Thirty patients had normal LVEF on their echocardiograms. In the remaining 70 with decreased LVEF (<65%), 25 had LVEF 20% to 35%, 16 had LVEF 35% to 50%, and 29 had LVEF 50% to 65%.

Carotid duplex sonography was performed in all patients with and 25 patients without cerebral microemboli. Only 4 patients had LV thrombus. Normal LV wall motion was documented in 29 patients, whereas 71 patients had significant LV wall-motion abnormalities, including akinetic segments.

Forty-five patients had thrombolytic treatment, 94 had been given intravenous heparin, and 93 received aspirin. There was a large overlap between these groups, and 99% of patients were treated either with heparin or aspirin. There was no significant difference in the presence of anterior lesions, LV thrombus, decreased LVEF, or LV akinetic segments between patients treated with or without thrombolysis.

<table>
<thead>
<tr>
<th>Cerebral Microemboli in AMI</th>
<th>n</th>
<th>HITS, % (n)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>68</td>
<td>22.1 (15)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td>6.2 (2)</td>
<td>0.084</td>
</tr>
<tr>
<td>Anterior, MI</td>
<td>53</td>
<td>24.5 (13)</td>
<td></td>
</tr>
<tr>
<td>Inferior, MI</td>
<td>47</td>
<td>8.5 (4)</td>
<td>0.059</td>
</tr>
<tr>
<td>LV thrombus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>75.0 (3)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>96</td>
<td>14.6 (14)</td>
<td>0.015</td>
</tr>
<tr>
<td>LVEF (&gt;65%)</td>
<td>30</td>
<td>3.3 (1)</td>
<td></td>
</tr>
<tr>
<td>LVEF (&lt;65%)</td>
<td>70</td>
<td>22.8 (16)</td>
<td>0.019</td>
</tr>
<tr>
<td>Normal LV wall motion</td>
<td>29</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>LV akinetic segment</td>
<td>71</td>
<td>23.9 (17)</td>
<td>0.002</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>45</td>
<td>22.2 (10)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>55</td>
<td>12.7 (7)</td>
<td>0.285</td>
</tr>
<tr>
<td>Heparin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>94</td>
<td>17.0 (16)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>6</td>
<td>16.6 (1)</td>
<td>1.000</td>
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<tr>
<td>Aspirin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>93</td>
<td>16.1 (15)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>28.5 (2)</td>
<td>0.339</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>17.0 (17)</td>
<td></td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; LV left ventricle; LVEF left ventricular ejection fraction; HITS % means percentage of patients with microembolic signals.

### Microemboli Detection

HITS were detected in 17 patients, with a mean rate of 0.5 ± 1.6 per 30 minutes. Twelve patients had 1 HITS, 3 had 2 HITS, 1 had 3 HITS, and 1 had 14 HITS. HITS were detected significantly more frequently in patients with reduced LVEF (22.8% versus 3.3%; P = 0.019) and LV thrombus (75.0% versus 14.6%; P = 0.019). No patients with normal LV motion had HITS, but they were seen in 23.9% of the 67 patients with akinetic LV segments (P = 0.002). HITS were documented in 24.5% of patients with anterior and 8.5% of those with inferior infarctions. This finding is marginally significant (P = 0.059; Table).

There was a trend toward an increase in the frequency of HITS in patients treated with thrombolysis (22.2% versus 12.7%; P = 0.285) and in patients who had not received aspirin (16.1% versus 28.5%; P = 0.339), but heparin treatment made no difference (P = 1.000; Table).

During the follow-up period (median 8 days), 3 patients experienced stroke. Two had ischemic stroke and 1 a hemorrhagic transformation of cerebral infarction after thrombolysis. All 3 patients had anterior myocardial infarctions with a decreased LVEF (20% to 35%) and severe LV motion abnormalities, but none of them had LV thrombus. HITS were documented in all of these patients. Twenty percent (3/17) of HITS-positive patients had strokes, but none occurred in the 83 patients without them (P = 0.01). TCD recording was performed in 2 cases before the stroke. One
patient had 14 HTTs per 30 minutes. Despite treatment with intravenous heparin and aspirin, this 73-year-old woman developed a right-sided dense hemiplegia and aphasia the next day. Carotid ultrasound did not reveal any significant stenosis. TCD monitoring after 2 days continued to reveal 6 HTTs/30 minutes. The second patient had an ischemic stroke within 24 hours of treatment with tissue plasminogen activator, and HTTs were documented before the event. The first CT scan was negative, and the repeated (after 24 hours) CT scan showed minor bleeding within the MCA infarct.

Discussion

Seventeen percent of our patients with AMI had cerebral microembolism in spite of adequate antithrombotic treatment started immediately after admission. HTTs were significantly more frequently detected in patients with decreased LVEF in the presence of akinetic myocardial segments and LV thrombus. A nearly significant increase of HTTs was documented in patients with anterior AMI.

Decreased LVEF was an independent risk factor for stroke in a post hoc analysis of the SAVE study, and every decrease of 5% in LVEF increased the risk of stroke by 18%.6 In another study,18 HTTs were detected in 26% of patients with severe LV dysfunction (LVEF <30%), but these patients also had idiopathic dilated cardiomyopathy.

Anterior AMI is an established risk factor for stroke.5,10 In a study of 77 patients with anterior AMI, 46% had LV thrombi,22 and the frequency increased progressively with the extent of myocardial dyskinesia and LV end-diastolic pressure. Van Danzig et al23 also noted that hypokinetic segments were risk factors for LV thrombi formation.

LV thrombus is a major cause of cerebral embolism in AMI,24 and in the present study, HTTs were more frequently seen in patients with LV thrombi. Only 4 patients in our series had LV thrombus, probably because most patients were given heparin, which prevents thrombus formation.25 The Healing and Early Afterload Reducing Therapy (HEART) study26 also reported a lower incidence of LV thrombus than previously reported and ascribed this to changes to AMI management. In the present study, none of the patients had transesophageal echocardiography, which is a more sensitive method of LV thrombi detection than transthoracic echo. This may be another explanation for the low incidence of LV thrombi in our study population.

Three percent of our patients had a stroke during the first week, similar to rates reported in other studies.7,8,27 All 3 patients with stroke had HTTs. In addition to the established risk factors for stroke in AMI, including anterior lesions, mural thrombus, impaired LV function, and atrial fibrillation, HTTs may be also an independent risk factor for clinical embolic events.

Almost 99% of our study population were treated with anticoagulant or antiplatelet drugs, and although antithrombotic therapy prevents the formation of large emboli,28 our results show that it may not suppress microemboli. Nearly half the patients had thrombolytic therapy, and cerebral microemboli were more frequent in this group. The incidence of LV thrombus is reduced after thrombolytic therapy,29 but the risk of ischemic cerebral infarction is not influenced by thrombolytic therapy.30,31 The increase of cerebral microemboli documented in the present study may represent disintegrating LV thrombus.22

The relevance of cerebral microembolism detection to clinical events is uncertain. At present, there is limited direct evidence that HTTs have predictive value in determining clinical embolic events. However, there is extensive indirect evidence.33 Embolic signals were more common in symptomatic than in asymptomatic patients with carotid stenosis,34 in those with prosthetic heart valves,35 and in AF.18 The present study is another example of indirect evidence that HTTs are predictors of stroke in patients with AMI.

References


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