Echocardiographic Evaluation of Young Adults With Nonhemorrhagic Cerebral Infarction

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SUMMARY We reviewed echocardiographic findings in patients aged 15 to 45 years with acute nonhemorrhagic cerebral infarction (NHCI). Among 132 patients with NHCI, 96 (72.7%) had M-mode and two-dimensional echocardiography, including contrast echocardiography with intravenous saline injection when clinically indicated. Echocardiograms were abnormal in 33 patients. Of these, 7 had other conditions that could cause NHCI. Echocardiography corroborated the clinical diagnosis of a cardiogenic source for cerebral infarction in 17 others. The other 9 had no other clues for cardiovascular disease. Potential etiologies of NHCI diagnosed by echocardiography in these 9 cases included: paradoxical embolism, 5 patients; right atrial myxoma, 1; rheumatic mitral valve vegetation, 1; myxomatous mitral valve (marantic endocarditis at postmortem), 1; and left atrial enlargement associated with decreased left ventricular function, 1. Routine echocardiography frequently conveys useful information in patients under age 45 with NHCI. In young patients with cerebral embolism of unknown etiology if routine M-mode and two-dimensional echocardiographic studies are normal, contrast echocardiographic studies should be performed to rule out intracardiac shunts and the possibility of paradoxical cerebral embolism.

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A NUMBER OF STUDIES have shown a low yield from the indiscriminate use of echocardiography in patients with cerebral infarction or transient ischemic attacks (TIA's). However, echocardiography can be invaluable in selected patients, primarily those with some other clue pointing to a cardiac etiology. It may also be useful in younger patients with an otherwise unexplained cerebral infarction. Although the literature contains several studies evaluating the use of echocardiography in cerebral ischemia, none deals specifically with large numbers of young stroke patients or with the use of contrast echocardiography. In an attempt to provide more information we reviewed echocardiographic findings in hospitalized patients aged 15 to 45 years with acute nonhemorrhagic cerebral infarction (NHCI) evaluated by the Stroke Service at the University of Iowa from July 1, 1977 through October 1, 1985.

Patients and Methods

Among 132 hospitalized young patients with NHCI, 96 (72.7%) had M-mode and two-dimensional echocardiography, including contrast echocardiography with intravenous saline injections when clinically indicated. Cerebral infarction was categorized into subtypes of large artery thrombotic occlusion, small artery (lacunar) occlusion or embolic occlusion based upon the clinical and laboratory criteria set forth in the Harvard Cooperative Stroke Registry. All patients were reviewed by two experienced observers (MRJ & REK) and diagnosis arrived at by consensus. Echocardiograms were considered positive if microbubbles appeared in either the left atrium (LA) or left ventricle (LV) no later than 2–3 cardiac cycles after initial appearance in the right atrium (RA). Myxomatous degeneration of the mitral valve was considered present when the echo showed thickened valve leaflet(s) with excessive mobility. Mitral valve prolapse was considered present when one or both mitral leaflets protruded past the plane of the mitral annulus, into the left atrium, in systole. These conditions may coexist. Echocardiograms were reviewed by two experienced observers (MRJ & REK) and diagnosis arrived at by consensus.

Results

There were 54 men and 42 women. The patients ranged from 15 to 45 years of age (mean, 33.3 years).
TABLE 1 Echocardiographic Findings in Patients with Noncardiac Etiology for NHCI

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Stroke DX</th>
<th>Past HX of CVD</th>
<th>HX of A. Fib.</th>
<th>EKG</th>
<th>LA Size</th>
<th>LV Size</th>
<th>VHD</th>
<th>LVEF</th>
<th>Anemia</th>
<th>Clot</th>
<th>Other</th>
<th>Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Large vessel atherothrombosis</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
<td>(1.9–4.0)</td>
<td></td>
<td>MVP</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>Large vessel atherothrombosis</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>MVP</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>Large vessel atherothrombosis</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>MVP</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>Lacunar stroke</td>
<td>Yes</td>
<td>No</td>
<td>IWI</td>
<td></td>
<td></td>
<td></td>
<td>TSO</td>
<td>AVC</td>
<td>NI</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>Embolism from post. comm. art. aneurysm</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>MVP</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>Embolism uncertain source</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>↓</td>
<td>No</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>Sneddon’s syndrome</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>MVP</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>MAC</td>
</tr>
</tbody>
</table>

Abbreviations: CVD, cardiovascular disease; A. Fib., atrial fibrillation; LA Size, left atrial size; LV Size, left ventricular size; VHD, valvular heart disease; LVEF, left ventricular function; MAC, mitral annular calcification; IWI, inferior wall myocardial infarction; TSO, technically suboptimal; MVP, mitral valve prolapse; AVC, aortic valve calcification; Post. Cer. Art, posterior cerebral artery.

Echocardiograms were normal in 60 patients (62.5%), abnormal in 33 (34.3%), and technically suboptimal in three patients (3.1%). Of the 33 patients with an abnormal echocardiogram, seven had other conditions that we determined were the likely cause of NHCI. Three had large artery thrombotic occlusion, two had embolic infarcts, one had small artery (lacunar) occlusion, and another had Sneddon’s syndrome (table 1). The individual with a large fusiform aneurysm of the right posterior communicating artery and mitral valve prolapse on echocardiography had a right proximal posterior cerebral artery occlusion. The infarction was attributed to embolism from his aneurysm. Echocardiography corroborated the clinical suspicion of cardiac source for cerebral infarction in 17 others. Rheumatic valvular heart disease and congestive cardiomyopathy were the most frequent etiologies. We attributed the infarction to mitral valve prolapse in only two patients (table 2). The two patients with infective endocarditis did not have mitral valve prolapse. Case 11 (table 2), a 39-year-old woman with a history of murmur of mitral regurgitation felt to be secondary to rheumatic heart disease. She had a subacute bacte-rial endocarditis due to a non-hemolytic, non-group D streptococcus complicated by a right fronto-parietal infarct. Echocardiography done 6 months earlier was unremarkable. The second patient, (Case 12, table 2) had a bicuspid aortic valve. He had aortic and mitral valve replacements for acute valvular insufficiency secondary to infective endocarditis. He had a left temporal-parietal infarct. Pathological studies of the heart valves demonstrated a bicuspid aortic valve with perforation, vegetations and necrosis. There was necrosis, fibrovascular proliferation, perforations and valvulitis of the mitral valve. The other 9 patients (27.2%), without clinical or electrocardiographic clues for cardiovascular disease, were found to have unsuspected potential cardiac sources on echocardiography. The patient with marantic endocarditis (Case 3, table 3), was a 44-year-old man with osteoporosis. At autopsy he had a bronchogenic carcinoma, large cell type, with hilar node involvement. There were infarctions in the cerebrum, myocardium, kidneys, lungs and spleen. The mitral valve was somewhat thickened along lines of closure with smooth nodules, but was free of vegetations. The aortic valve had 3 cusps. Each cusp had a vegetation with irregular surface. The largest was on the right cusp which was approximately 1 cm × 1 cm × 1 cm. The tricuspid and pulmonary valves were free of lesions. Five of the 9 patients had right-to-left shunting detected by contrast echocardiography. None had arterial, pulmonary or left cardiac sources. Some developed the stroke in association with the Valsalva maneuver. We attributed these infarctions to paradoxical embolism (table 3).

Discussion

The incidence of cardiogenic cerebral embolism is difficult to ascertain but most studies suggest that 20% to 34% of all cerebral infarctions have a cardiac origin. Physicians dealing with cerebrovascular disease are aware that cerebral embolism, "source undetermined," continues to account for a considerable number of strokes. These figures suggest that further effort is required to determine these "sources." The discovery and refinement of new methods to image the heart has improved and accounts for increasing awareness of the heart as a source of cerebral infarction. With the use of contrast echocardiography, pulsed Doppler echocardiography, cardiac CT and cardiac nuclear magnetic resonance, the number of cases of cerebral embolism, source undetermined, will be reduced. Echocardiography is currently the major ancillary investigation aimed at visualizing intracardiac pathology that may be complicated by cerebral embolism. However, its sensitivity is not optimal, especially for left atrial thrombi. Thrombi in the left atrial appendage are even more difficult to identify. A negative echocardiographic result does not rule out an intracardiac source of emboli. Aggregate data from several reports show that echocardiography is not warranted in most patients with cerebral infarction. Abnormal contrast echocardiographic studies have
TABLE 2  Echocardiographic Findings in Clinically Suspected Cases of Cardiogenic Cerebral Embolism

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Cardiac DX</th>
<th>Past HX of CVD</th>
<th>EKG</th>
<th>LA Size</th>
<th>LV Size</th>
<th>VHD</th>
<th>LVP</th>
<th>Anemia</th>
<th>Clot</th>
<th>Other</th>
<th>Shunt</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Normals</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>RVHD</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>5.0</td>
<td>4.0</td>
<td>NI</td>
<td>MS</td>
<td>No</td>
<td>No</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>RVHD</td>
<td>Yes</td>
<td>No</td>
<td>LAE</td>
<td>4.8</td>
<td>5.0</td>
<td>MS</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>LA Rh MS</td>
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<tr>
<td>3</td>
<td>RVHD</td>
<td>Yes</td>
<td>No</td>
<td>RBBB</td>
<td>4.5</td>
<td>3.8</td>
<td>MS</td>
<td>NI</td>
<td>No</td>
<td>No</td>
<td>RVH MS</td>
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<tr>
<td>4</td>
<td>RVHD</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>4.8</td>
<td>5.3</td>
<td>MS</td>
<td>NI</td>
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<td>Rh MS</td>
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<td>5</td>
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<td>Yes</td>
<td>No</td>
<td>P Mitral</td>
<td>4.8</td>
<td>4.4</td>
<td>MS</td>
<td>NI</td>
<td>No</td>
<td>No</td>
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<tr>
<td>6</td>
<td>Idiopathic dilated cardiomyopathy</td>
<td>Yes</td>
<td>No</td>
<td>LBBB + 1st deg AVB</td>
<td>5.0</td>
<td>TSO</td>
<td>No</td>
<td>—</td>
<td>No</td>
<td>LVE congestive cardiomyopathy</td>
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<td>7</td>
<td>Viral myocarditis</td>
<td>No</td>
<td>No</td>
<td>Nodal Tach</td>
<td>4.2</td>
<td>—</td>
<td>No</td>
<td>—</td>
<td>No</td>
<td>Yes</td>
<td>Congestive cardiomyopathy</td>
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<tr>
<td>8</td>
<td>Cardiomyopathy</td>
<td>Yes</td>
<td>No</td>
<td>LAE RVH L ant fasc block</td>
<td>4.4</td>
<td>2.8</td>
<td>No</td>
<td>—</td>
<td>No</td>
<td>No</td>
<td>Asymmetric septal hypertrophy</td>
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<tr>
<td>9</td>
<td>Peripartum cardiomyopathy</td>
<td>No</td>
<td>No</td>
<td>LAE RVH RAE</td>
<td>4.2</td>
<td>5.2</td>
<td>No</td>
<td>—</td>
<td>No</td>
<td>Yes</td>
<td>Dilated cardiomyopathy</td>
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<tr>
<td>10</td>
<td>Paradoxical embolism</td>
<td>Yes</td>
<td>No</td>
<td>RBBB RVH RAE</td>
<td>2.8</td>
<td>4.1</td>
<td>No</td>
<td>Abn septal motion</td>
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<td>No</td>
<td>Enlarged RV; abn septal motion</td>
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<td>11</td>
<td>Infective endocarditis</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>3.7</td>
<td>NI</td>
<td>Thick ant mitral leaflet</td>
<td>Abn ant mitral leaflet; AI</td>
<td>NI</td>
<td>No</td>
<td>No</td>
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<tr>
<td>12</td>
<td>Infective endocarditis</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>2.7</td>
<td>4.7</td>
<td>Abn ant mitral leaflet; AI</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Mitral v.; ruptured chordae tendinae</td>
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<tr>
<td>13</td>
<td>Prosthetic valve</td>
<td>Yes</td>
<td>No</td>
<td>1st degree AV block</td>
<td>5.2</td>
<td>6.7</td>
<td>AVR with NI function</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Enlarged RV; abn septal motion</td>
</tr>
<tr>
<td>14</td>
<td>Prosthetic valve</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>3.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>No</td>
<td>No</td>
<td>Malfunctioning prosthesis</td>
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<td>15</td>
<td>Mitral valve prolapse</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>TSO</td>
<td>TSO</td>
<td>MVP</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Mitral valve prolapse</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>3.8</td>
<td>5.0</td>
<td>MVP myx deg</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Air embolism atrial septal defect</td>
<td>Yes</td>
<td>No</td>
<td>V tach V Fib</td>
<td>TSO</td>
<td>TSO</td>
<td>No</td>
<td>TSO</td>
<td>No</td>
<td>No</td>
<td>RVE, septal wall hypertrophy</td>
</tr>
</tbody>
</table>

Abbreviations: A. Fib, atrial fibrillation; LA Size, left atrial size; LV size, left ventricular size; VHD, valvular heart disease; LVF, left ventricular function; RHVD, rheumatic valvular heart disease; AI, aortic insufficiency; AVR, aortic valve replacement; MVP, mitral valve prolapse; Myx deg, myxomatous degeneration; MS, mitral stenosis; Rh MS, rheumatic mitral stenosis; RVH, right ventricular hypertrophy; PFO, patent foramen ovale; LAE, left atrial enlargement; LVE left ventricular enlargement; RVE, right ventricular enlargement; RBBB, left bundle branch block; V/Fib, Ventricular fibrillation; TSO, technically suboptimal.

been found in 5% of normal volunteers, and in 18% when performed during the Valsalva maneuver. These positive studies, indicative of interatrial right-left shunt have been ascribed to a patent foramen ovale. In 1,100 autopsy cases Thompson and Evans have demonstrated a "pencil patent" foramen ovale in 6% of cases and a "probe patent" foramen ovale in 29% of cases. Cardiologists have emphasized that a patent foramen ovale or an atrial septal defect are by far the most common cardiac defects associated with paradoxical embolism. Numerous studies have addressed the issue of the difficulties in the clinical diagnosis of paradoxical embolism during life. Jones et al examined five patients with cerebral emboli of paradoxical origin. They found a probe patent foramen ovale in three, an atrial septal defect in one, and a suspected patent foramen ovale in the other. Venous thrombosis or pulmonary embolism antedated the ce-
Echocardiography in Cerebral Infarction/Biller et al

TABLE 3 Echocardiographic Findings in Clinically Unsuspected Cardiogenic Cerebral Embolism

<table>
<thead>
<tr>
<th>Case No.</th>
<th>LA Size</th>
<th>LV Size</th>
<th>Aneurysm</th>
<th>Clot</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.9-4.0)</td>
<td>(3.5-5.7)</td>
<td>VHD</td>
<td>LVF</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CVD, cardiovascular disease; A. Fib., atrial fibrillation; LA Size, left atrial size; LV Size, left ventricular size; VHD, valvular heart disease; LVF, left ventricular function; MVP, mitral valve prolapse; Myx. deg, myxomatous degeneration; TSO, technically suboptimal; RBBB, right bundle branch block; RVH, right ventricular hypertrophy; RAE, right atrial enlargement; *patent foramen ovale found at surgery; †pathological diagnosis; ‡probe patent foramen ovale on cardiac catheterization.

rebbral symptoms in only one instance. Cheng has emphasized the value of contrast echocardiography with the Valsalva maneuver and advised requesting a contrast study whenever paradoxical embolism is suspected. Other researchers have recently reported a high incidence of right-left shunt detected by contrast echocardiography in patients with cerebral embolism.

By applying this principle we were able to diagnose paradoxical cerebral embolism in 5 patients without known previous cardiovascular history. Cardiac catheterization documented a probe patent foramen ovale in two of these patients. The other three patients did not undergo cardiac catheterization, although the onset of stroke was clearly associated with Valsalva’s maneuver. Thus, we believe that patients with cerebral embolism, without demonstrable source by cerebral angiography, routine echocardiography, or chest roentgenography, should undergo contrast echocardiography, probably including contrast studies with the Valsalva maneuver if baseline contrast studies are negative.

Acknowledgment

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