Original Contributions

Echocardiographic Evaluation of Young Adults With Nonhemorrhagic Cerebral Infarction

JOSE BILLER, M.D.,* MARYL R. JOHNSON, M.D.,† HAROLD P. ADAMS, JR., M.D.,* RICHARD E. KERBER, M.D.,* GILBERT J. TOFFOL, D.O.,* AND MICHAEL J. BUTLER, M.D.*

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 seen by the investigators and data were entered into our Stroke Registry. The presumed etiology for cerebral infarction, history, physical examination and electrocardiogram were analyzed in all patients. M-mode and two dimensional echocardiographic examinations were performed with the patients in the left lateral decubitus position. Parasternal long and short axis as well as apical two and four chamber views were recorded. Contrast echocardiograms were performed using the apical four chamber view and a rapid hand injection of 10 ml of agitated sterile normal saline solution through a peripheral intravenous cannula. At least four saline injections were performed and recorded in each patient. All injections were made during normal quiet respiration; Valsalva maneuver was not performed. Contrast 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).
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 cardio-genic source for cerebral infarction in 17 others. 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 (1.9-5.7)</th>
<th>LV Size (3.5-5.7)</th>
<th>VHD</th>
<th>LVE</th>
<th>Aneurysm</th>
<th>Clot</th>
<th>Other</th>
<th>Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RVHD</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>5.0</td>
<td>NI</td>
<td>MS</td>
<td>No</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>4.5</td>
<td>5.0</td>
<td>MS</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<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>No</td>
<td>No</td>
<td>No</td>
<td>LA Rh MS</td>
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<tr>
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<td>RVHD</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>4.8</td>
<td>5.3</td>
<td>MS</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Rh MS</td>
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<tr>
<td>5</td>
<td>RVHD</td>
<td>Yes</td>
<td>No</td>
<td>P Mitrale</td>
<td>4.8</td>
<td>4.4</td>
<td>MS</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
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<tr>
<td>6</td>
<td>Idiopathic</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>No</td>
<td>LVE congestive cardiomyopathy</td>
</tr>
<tr>
<td>7</td>
<td>Viral myocardiopathy</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>
</tr>
<tr>
<td>8</td>
<td>Cardiomyopathy, Friedreich's ataxia</td>
<td>Yes</td>
<td>Yes</td>
<td>No</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 L. ant fasc block</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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<td>10</td>
<td>Paradoxic embolism</td>
<td>Yes</td>
<td>No</td>
<td>PFO</td>
<td>RBBB RVH RAE</td>
<td>2.8</td>
<td>4.1</td>
<td>No</td>
<td>Abn septal motion</td>
<td>No</td>
<td>No</td>
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<tr>
<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>NI</td>
<td>No</td>
<td>No</td>
<td>Mitral veg vs. myx valve</td>
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<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>NI</td>
<td>No</td>
<td>No</td>
<td>Mitral veg; ruptured chordae tendineae</td>
</tr>
<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>NI</td>
<td>No</td>
<td>No</td>
<td>Enlarged RV; abn septal motion</td>
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<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>NI</td>
<td>No</td>
<td>No</td>
<td></td>
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<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>NI</td>
<td>No</td>
<td>No</td>
<td></td>
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<tr>
<td>17</td>
<td>Air embolism atal 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; RVHD, 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; RBBB, right bundle branch block; Nodal Tach, nodal tachycardia; AVB, atrioventricular block; V. Tach, ventricular tachycardia; 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>Cardiac DX</th>
<th>LA Size</th>
<th>LV Size</th>
<th>VHD</th>
<th>LVF</th>
<th>Aneurysm</th>
<th>Clot</th>
<th>Other</th>
<th>Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Right* atrial myxoma</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>2.1</td>
<td>4.1</td>
<td>?MVP</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Rheumatic mitral valve with vegetation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3.8</td>
<td>4.8</td>
<td>No</td>
<td>NI</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Myxomatous mitral valve (marantic endocarditis*)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>4.0</td>
<td>5.5</td>
<td>Myx. deg mitral valve</td>
<td>NI</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Left atrial enlargement and decreased LV function</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>4.4</td>
<td>TSO</td>
<td>No</td>
<td>↓</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Paradoxical embolism</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3.0</td>
<td>4.8</td>
<td>No</td>
<td>NI</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Paradoxical embolism</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>4.0</td>
<td>6.1</td>
<td>No</td>
<td>NI</td>
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<td>7</td>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>2.9</td>
<td>4.6</td>
<td>?MVP</td>
<td>NI</td>
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<td>8</td>
<td>Paradoxical‡ embolism</td>
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<td>No</td>
<td>No</td>
<td>3.7</td>
<td>5.0</td>
<td>No</td>
<td>NI</td>
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<td>9</td>
<td>Paradoxical‡ embolism</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3.7</td>
<td>5.0</td>
<td>No</td>
<td>NI</td>
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</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.

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