Cardiac Evaluation of the Patient With Stroke

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Coronary artery disease and ischemic cerebrovascular disease are leading causes of morbidity and mortality in the United States. Coronary artery disease often coexists with asymptomatic carotid artery atherosclerosis, transient ischemic attacks, or ischemic stroke. Numerous studies have shown that mortality from all forms of ischemic cerebrovascular disease is primarily due to coronary artery disease. Thus, there is increasing interest in identifying coronary artery disease in patients with cerebrovascular disease, including those without clinical manifestations of heart disease. We review the use of current noninvasive techniques to detect coronary artery disease and present practical approaches to screen for ischemic heart disease. Current diagnostic imaging methods for potential cardioembolic sources of cerebral infarction are also discussed. (Stroke 1990;21:14-23)

Stroke is the third most common cause of death and the primary cause of long-term disability in the United States today. Coronary artery disease is a major manifestation of generalized atherosclerosis. Frequently, the initial presentation of coronary artery disease is sudden and unexpected death. Many patients with clinically apparent or silent myocardial ischemia have coexistent cerebrovascular disease. Conversely, many patients with cerebrovascular disease have varying degrees of coronary artery disease.

There is a strong association between carotid artery disease and coronary artery disease, which is the major cause of death among patients with different manifestations of cerebrovascular atherosclerosis. Aggregate data show a consistently higher percentage of cardiac deaths than stroke deaths following transient ischemic attacks (TIAs). Of 592 patients followed for 13 years after carotid endarterectomy, half ultimately died of cardiac complications, 13% of stroke, and 9% of cancer. In another series, 70% of all late deaths following carotid endarterectomies were cardiac. The cardiac death rate approximates 5%/yr for patients with asymptomatic carotid bruits, TIAs, or stroke. The Canadian Cooperative Study Group found that cardiovascular deaths were twice as common as deaths due to stroke among 585 patients with threatened stroke.

The close association between coronary and cerebrovascular events should not be surprising. Many risk factors identified for stroke are similar to those for coronary artery disease. Modification of risk factors clearly retards progression and probably promotes regression of atherosclerotic lesions in the coronary arteries. Whether this is also true for carotid atherosclerotic plaques is uncertain. Appropriate screening of stroke-prone patients for coronary artery disease may allow early detection of individuals at risk for myocardial infarction or sudden death. Further efforts to recognize and treat coronary artery disease are needed if cardiac mortality is to be reduced in stroke-prone individuals.

We review current noninvasive methods used in the evaluation of ischemic cardiovascular disease and potential embolic sources in the stroke-prone patient and propose practical approaches to the diagnostic workup. It should be understood that these approaches are general guides; what is appropriate in one clinical center or for one particular patient may not be applicable in others.

Asymptomatic Carotid Bruits

Asymptomatic carotid bruits are more prevalent in women and occur in approximately 5% of the population >45 years of age. The risk of stroke in these patients is approximately 2%/yr and the risk of death is approximately 4%/yr, increasing to 5-6%/yr if there is underlying carotid stenosis. Regardless of whether surgery is performed, mortality rates are approximately 4-6%/yr. The mortality rate is most clearly related to coronary artery disease. In addi-
tion, if carotid endarterectomy is performed, periop-
ratative mortality is mainly related to acute myocar-
dial infarction.\(^{14}\)

The best approach to identifying significant coex-
istent coronary artery disease in patients with asym-
pomatic carotid artery disease is still unproven. Even
if coexistent coronary artery disease is identified,
information regarding the best strategy to prevent a
coronary event is also lacking. Cardiac catheteriza-
tion with selective coronary angiography remains the
gold standard in evaluating coronary artery stenosis.
Angiography is an invasive procedure, with morbidity
and mortality of <0.5% in experienced centers.\(^{15}\) It is
the only diagnostic study available that visualizes the
coronary artery lumen throughout the coronary tree.
However, angiography does not provide adequate
information about the vessel wall. The coronary
artery lumen may appear normal, but thickening of
the arterial wall (which is an early indicator of
atherosclerosis) is often missed by this technique.
For this reason, a number of studies have shown
that angiography may actually underestimate the
severity of a coronary artery stenosis.\(^{16,17}\) Furthermore,
there is considerable variability in the inter-
pretation of angiograms. A simple visual estimation
of percent luminal diameter narrowing frequently
does not predict the physiologic significance of a
lesion, particularly for multivessel disease.\(^ {16}\) Despite
these limitations, coronary angiography is a rela-
tively safe procedure and remains the only widely
available test to visualize the coronary artery anat-
yomy, which is necessary for angioplasty or surgical
revascularization.

Many noninvasive tests to detect coronary artery
disease are available. Current techniques include exer-
cise and ambulatory electrocardiography, stress thallium-
201 myocardial scintigraphy, \(^{201}\)Tl
dipyridamole scintig-
raphy, radionuclide ventriculography, and exercise
echoangiography. Evolving methods of potential use in
defining coronary artery disease include positron emis-
tion tomography, ultrafast x-ray computed tomography
(CT), and magnetic resonance imaging (MRI). This
article concentrates on the most widely available tech-
niques. In reviewing the usefulness of these noninvasive
tests, the limitations of coronary angiography as the
gold standard for detecting significant coronary artery
disease should be kept in mind.

Exercise electrocardiography is an easy and safe
approach to diagnose coronary artery disease. Com-
plication rates per 10,000 tests are 3.6 for myocardial
infarctions and 4.8 for significant cardiac arrhyth-
mas, with a total complication rate of 8.9.\(^{18,19}\) Several
studies have shown a sensitivity of approximately
63%, a specificity of 85%, and a positive predictive
value of 90%.\(^ {20}\) However, it is important to under-
stand that these studies were performed in popula-
tions with a high prevalence of disease. According to
Bayes' theorem of conditional probability, the pre-
dictive value varies with the prevalence of disease in
the study population. Therefore, false-negatives are
relatively frequent among negative results in patients
with a high pretest probability of coronary artery
disease, and false-positives are relatively frequent
among positive results in asymptomatic low-risk
patients, especially middle-aged women.\(^ {21}\) Limita-
tions of exercise (or ambulatory) electrocardiography
include abnormalities of the resting electrocardio-
gram (left bundle branch block, right bundle branch
block, left ventricular hypertrophy with strain, and
drug effects) that make ST segment changes difficult
to interpret.

The important prognostic value of exercise elec-
trocardiography has been shown in a number of
studies.\(^ {22,23}\) In a prospective study, Froelicher and
associates\(^ {24}\) screened 1,390 asymptomatic pilots for
latent coronary artery disease by treadmill testing
and followed them for an average of 6.3 years. Using
angina, acute myocardial infarction, or sudden death
as end points, exercise electrocardiography's sensitiv-
ity was 61% and its specificity was 92% for predicting
future coronary events.

Absolute contraindications for exercise electro-
cardiography include acute myocardial infarction, unsta-
ble angina, uncompensated congestive heart failure,
excessive hypertension (>180 mm Hg systolic, >110
mm Hg diastolic is used in our laboratory), acute
myocarditis/pericarditis, severe aortic stenosis, uncon-
trolled cardiac arrhythmia, known severe coronary
artery disease (i.e., left main disease, severe triple-
vessel disease), atrioventricular block greater than
first degree, and acute systemic illness.\(^ {25}\)

Stress thallium-201 myocardial scintigraphy is a
noninvasive test that yields information on regional
myocardial perfusion at rest and during exercise.
This test is frequently used when exercise electrocardi-
ography is negative or when exercise electrocardio-
grams are difficult to interpret due to preexisting
electrocardiographic abnormalities. Sensitivities
of 75–95% and specificities of 89–97% have been
reported for stress thallium-201 myocardial scintigra-
phy following maximal treadmill exercise. The results
vary depending on the population studied and the
criteria used for the presence of disease. Quantitative
thallium-201 scintigraphy has been reported to have
a sensitivity of 92% and a specificity of 90%,\(^ {26}\) but
this technique needs additional validation studies.
Stress thallium-201 myocardial scintigraphy has shown
better specificity than radionuclide ventriculograms
and can also predict future cardiac events and assist
in prognosis. The number of redistribution defects
correlates significantly with patients at high risk of a
coronary event (i.e., those with left main disease or
multivessel disease).\(^ {27}\)

In patients in whom exercise capacity is limited
(e.g., those with poor exercise tolerance, peripheral
vascular disease, obesity, arthritis, or pulmonary
disease), \(^{201}\)Tl
dipyridamole scintigraphy is used.
Dipyridamole is a coronary artery vasodilator that
augments blood flow in normal vessels; blood flow
increase is limited in those vessels that have a
severe stenosis. The diagnostic sensitivity of
\(^{201}\)Tl
dipyridamole scintigraphy approaches that of
dynamic stress imaging and is in the range 80–90%, with a specificity of approximately 80%. This test has been used to screen asymptomatic patients undergoing major vascular surgery. Although hypotension can occur following dipyridamole administration, \[^{[20]}\text{TI}\]dipyridamole scintigraphy is a relatively safe cardiac screening procedure in patients with cerebrovascular atherosclerosis. However, hypotensive side effects occur more frequently with high doses of oral dipyridamole.

Radionuclide ventriculography visualizes the cardiac chambers and allows assessment of global left ventricular function and systolic wall motion for individual regions of the left ventricle. During exercise, radionuclide ventriculography demonstrates stress-induced ischemic wall motion impairment, thus suggesting regional coronary artery disease. Normally, the ventricular ejection fraction increases by at least 5% with exercise. The sensitivity of exercise radionuclide ventriculography is approximately 82%, and its specificity is approximately 84%. Although its specificity is not quite as good as that of stress thallium-201 myocardial scintigraphy, radionuclide ventriculography costs less and is the preferred technique in obese patients due to its better imaging characteristics.

Exercise echocardiography is a relatively new noninvasive imaging method that uses treadmill testing with two-dimensional echocardiography. A two-dimensional echocardiogram is obtained before and immediately after an exercise test. Segmental wall motion abnormalities appearing with exercise are considered indicative of ischemic heart disease. The sensitivity of exercise echocardiography for detecting coronary artery disease in patients with multivessel disease is approximately 88%; this test has the greatest limitation in those patients with single-vessel coronary artery disease. The precise role of exercise echocardiography as a screening method awaits further studies.

Silent myocardial ischemia is defined as objective evidence of myocardial ischemia, without chest pain or other symptoms considered anginal equivalents. Ambulatory electrocardiographic (Holter) monitoring for ST segment changes is a simple test, but its sensitivity for detecting silent myocardial ischemia is not yet fully validated. Silent myocardial ischemia is prevalent in both asymptomatic individuals and those with episodes of anginal chest pain. The value of ST segment depression using Holter monitoring is only of definite significance in people with coronary artery disease. In the Framingham Study, approximately 25% of all myocardial infarctions were totally unrecognized. The role of ambulatory electrocardiographic monitoring in the evaluation of silent myocardial ischemia and the therapeutic implications of positive tests are still being evaluated.

**Transient Ischemic Attacks**

A TIA is an important precursor of cerebral infarction. In some patients, TIAs are followed by cerebral infarction, which may result in death or disability; in others, the attacks may recur or cease spontaneously with no sequelae. If treatment is not instituted, one third of patients with a TIA will have a stroke within 5 years. Of patients who have a cerebral infarction, approximately 50% do so in the first year and approximately 20% within the first month following a TIA.

TIAs, reversible ischemic neurologic deficits (RINDs), or partial and nondisabling strokes are common expressions of a similar underlying pathophysiology. Because ischemic heart disease is the most common cause of death in these patients, threatened stroke should also be considered a harbinger of myocardial infarction. Estimated annual mortality after a TIA is 5%, mostly due to myocardial infarction. This is similar to the cardiac mortality rate of approximately 4%/yr in patients with stable angina pectoris. Morbidity is also related to ischemic heart disease. A 25% incidence of cardiovascular disease was reported among 225 patients with TIAs followed for 5½ years who were treated either medically or surgically. Abnormal exercise electrocardiograms have been observed in as many as 28% of patients with TIA and no known cardiac symptoms. Rokey and colleagues prospectively evaluated 34 patients without apparent clinical heart disease who were admitted to a hospital for TIAs or mild stroke. All patients had rest and exercise radionuclide ventriculography and stress thallium-201 myocardial scintigraphy; 41% had an abnormal radionuclide ventriculogram, indicating the presence of coronary artery disease.

Coronary angiography in 506 patients with asymptomatic carotid bruit and previous TIAs detected severe "operable" coronary artery disease in approximately one third of those patients suspected of having coronary artery disease on clinical criteria. Severe inoperable coronary artery disease was found in 10% of these patients. Hertzer and colleagues recommend coronary angiography for patients undergoing carotid endarterectomy who have clinically symptomatic coronary artery disease. These authors also recommend noninvasive cardiac testing techniques for those patients without clinical heart disease to determine the need for revascularization prior to the surgical procedure. The cost-effectiveness of this approach needs further validation. Additional prospective studies may help to identify subgroups of patients who are at risk for a particular coronary event.

Figures 1 and 2 illustrate our proposed algorithms to evaluate coronary risk in patients with documented asymptomatic carotid stenosis, TIAs, or RINDs.

**Embolic Strokes of Cardiac Origin**

Of the 400,000 new strokes in the United States each year, approximately 85% are due to cerebral infarction, and approximately 15% of these are from cardiogenic embolization. Emboli frequently lodge in the middle cerebral artery territory and often cause a severe neurologic deficit or death. The frequency of
these devastating events would likely be reduced if the offending cardiac lesion were adequately recognized and treated.

The usefulness of echocardiography for patients with focal cerebral ischemia has been debated. A number of studies have shown a low yield from the indiscriminate use of this test in patients with focal cerebral ischemia.43-49 We believe that the use of two-dimensional echocardiography in older patients should be limited to those with clinical indications of heart disease. Two-dimensional echocardiography should be considered in all patients <45 years old with otherwise unexplained focal cerebral ischemia, and contrast echocardiography should be used in selected individuals.50

The major cardiac sources of cardioembolism are listed in Table 1.

Table 1. Cardiac Sources of Cerebral Emboli

<table>
<thead>
<tr>
<th>Ventricular thrombi</th>
<th>Acute myocardial infarction</th>
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<tr>
<td>Ventricular aneurysm</td>
<td>Dilated cardiomyopathy</td>
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<tr>
<td>Atrial fibrillation</td>
<td>Mitral valve prolapse</td>
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<tr>
<td>Sick sinus syndrome</td>
<td>Mitral valve prolapse</td>
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<tr>
<td>Prosthetic heart valves</td>
<td>Mitral anulus calcification</td>
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<tr>
<td>Others</td>
<td>Calcific aortic stenosis</td>
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<tr>
<td></td>
<td>Atrial myxomas</td>
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<td></td>
<td>Paradoxic emboli</td>
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<td></td>
<td>Endocarditis</td>
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<td></td>
<td>Infective</td>
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<td>Marantic</td>
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Left Ventricular Thrombi

Left ventricular mural thrombus is common in patients with acute myocardial infarction, left ventricular aneurysm, and dilated cardiomyopathy. Mural thrombi are found at autopsy in 20–60% of persons who die of acute myocardial infarction, although systemic embolization occurs in only 3–10% of patients with transmural infarctions.52 Most of these embolic events occur within the first 4 weeks after infarction. Left ventricular aneurysms tend to occur after a large transmural infarction, predominantly in the anterior or apical portion of the left ventricle. Left ventricular aneurysm following myocardial infarction occurs in 7–15% of patients. After an anterior left ventricular aneurysm develops, mural thrombus formation may be found by two-dimensional echocardiography in as many as 35–50% of patients.53 Thrombus formation occurs infrequently in an inferior left ventricular aneurysm. Patients with a thrombus within a left ventricular aneurysm have a 5–7% chance of experiencing a systemic embolic event.53 It is therefore important to identify the subset of patients at risk for an embolic event. Thrombus is also a common finding in dilated cardiomyopathy, with up to 60% of cases having a left ventricular thrombus at
Autopsy. Thrombi that occur in patients with dilated cardiomyopathy are usually larger than those in patients with ischemic heart disease with associated wall motion abnormalities. Most patients with dilated cardiomyopathy and left ventricular thrombi have symptoms of congestive heart failure.

The major noninvasive imaging techniques available to detect left ventricular thrombus include two-dimensional echocardiography, indium-111-labeled platelet scintigraphy, ultrafast CT, MRI, and angiography. Two-dimensional echocardiography is currently the procedure of choice to identify thrombi in the left ventricular cavity. However, it should be noted that systemic emboli can occur in patients without evidence of thrombi on two-dimensional echocardiograms. Echocardiography is easily performed at the bedside, with no risk to the patient. The echocardiographic appearance of a thrombus may vary from fine streak-like densities and bands of echoes to large mobile masses. The morphology of a thrombus can often help predict subsequent embolization in postinfarction patients. Thrombi that have a higher risk of embolization protrude into the left ventricular cavity and are mobile. In one series, embolic events occurred in 80% of patients who had thrombi projecting into the left ventricular cavity. In another series, systemic embolization occurred in 60% of patients with mobile clots and in 40% of patients with clots that protruded into the left ventricular cavity. It should be recognized that in some patients (usually obese and/or with chronic obstructive lung disease), echocardiograms of adequate quality cannot be obtained. In these patients, transesophageal echocardiography may be helpful or other methods may be employed.

Indium-111-labeled platelet scintigraphy can be used in conjunction with two-dimensional echocardiography in the evaluation of intracardiac clots. This technique utilizes [111m]oxine-labeled platelets and gamma camera scintigraphy to study the hematologic activity of thrombi. Platelet scintigraphy detects ongoing platelet deposition on the thrombus surface and can thus estimate thrombus activity. The sensitivity of indium-111-labeled platelet scintigraphy is approximately 71–77%, with a specificity of 88–100%. The optimal time for imaging ventricular thrombi is 48–72 hours after platelet labeling. Platelet scintigraphy is most useful in patients with chronic obstructive pulmonary disease or prostatic valves who are difficult to evaluate with two-dimensional echocardiography. The clinical utility of platelet scintigraphy is limited due to the time required to complete the study and its lack of availability in many hospitals. Radiolabeled antibody (to platelet or fibrin) imaging is currently being developed and is much faster and easier to perform.

Until recently, cardiac CT scanning was obviated by the prohibitively long scanning times of 1–2 seconds. Recently, dynamic or ultrafast (cine) CT methods have been developed, with acquisition rates of >15 scans/sec. The quality of the cardiac images obtained with ultrafast CT is usually excellent. Cardiac ultrafast CT has higher specificity for the detection of ventricular thrombi than two-dimensional echocardiography. However, the need for contrast material is a disadvantage, and one cannot perform serial bedside examinations. Finally, the ultrafast CT systems are not widely available at this time.

MRI is a newer, sophisticated imaging technique currently available at an increasing number of medical centers. With its excellent spatial and contrast resolution and its ability to investigate all cardiac chambers, MRI may be very useful when suspicion is high for intracardiac thrombus and the two-dimensional echocardiogram is negative or equivocal.

Atrial Fibrillation

Atrial fibrillation is the most common arrhythmia associated with cerebral embolism. The mean duration of atrial fibrillation prior to cerebral embolism was 3.3 years in the Framingham Study. Because atrial fibrillation is common among the elderly, the question often arises whether concomitant cerebrovascular atherosclerosis is the cause of cerebral infarction.

Most patients with atrial fibrillation have overt cardiovascular disease such as valvular disease, cardiomyopathy, pericarditis, or congestive heart failure. Cardiovascular disease is initially undetected in as many as 25% of patients. However, some form of cardiovascular disease is later detected in more than half of these. The risk of atrial fibrillation is six times greater with congestive heart failure and rheumatic heart disease. Hypertension, diabetes mellitus, and left ventricular hypertrophy detected on electrocardiography are also linked to an increased risk of atrial fibrillation.

It has long been implied that "lone" atrial fibrillation (e.g., without other evidence of heart disease) is a relatively benign disorder. However, one study has reported that strokes were significantly more common among patients with lone atrial fibrillation than among matched controls (28.2% vs. 6.8%). This increased incidence of stroke in patients with lone atrial fibrillation calls into question the usually presumed benign prognosis. Atrial fibrillation is also more prevalent in older age groups; approximately 2–9% of individuals over the age of 60 years have atrial fibrillation.

Atrial fibrillation in combination with rheumatic valvular heart disease is associated with a 17-fold increased risk of stroke, whereas chronic atrial fibrillation without rheumatic valvular heart disease is associated with a fivefold increased risk of stroke. The risk of stroke is the greatest at the onset of atrial fibrillation; 15% of strokes occurred within the first year after the diagnosis of atrial fibrillation, and thereafter the rate was 5%/yr. It is not uncommon for systemic arterial embolization from the heart with rheumatic valvular disease to occur soon after conversion to sinus rhythm.
The cardiac workup for patients with newly diagnosed atrial fibrillation should include twelve-lead electrocardiography, chest roentgenography, and two-dimensional echocardiography. The latter is obtained to determine left atrial size, to assess the presence of left atrial thrombus, to evaluate the cardiac valves, and to estimate left ventricular function. However, left atrial thrombi often lodge in the left atrial body or atrial appendage, which are relatively poorly visualized by two-dimensional echocardiography.\(^\text{68,69}\) Transesophageal echocardiography, ultrafast CT, or MRI of the heart should also be used, if available, when two-dimensional echocardiography is negative and there is high clinical suspicion for an intra-atrial clot. Table 2 illustrates a schematic investigative approach to the patient with atrial fibrillation.

### Sick Sinus Syndrome

Although atrial fibrillation is the most frequently implicated arrhythmia, cerebral embolism may occur with sick sinus syndrome. This entity is usually encountered in the elderly. The risk of embolization is greatest in patients with atrial fibrillation that alternates with a form of atrioventricular block, frequently termed the "tachy-brady" syndrome.\(^\text{70,71}\) If this occurs in association with a cerebral embolic event, a noninvasive cardiac workup should be pursued. Holter monitoring may be used to document this syndrome. If the results of Holter monitoring are negative and the suspicion is high for sick sinus syndrome, invasive electrophysiologic testing to detect disease of the conduction system may be warranted. A similar approach to that outlined for patients with atrial fibrillation may be used for these patients since the underlying pathology is commonly a left atrial thrombus.

### Prosthetic Heart Valves

When a patient with an artificial heart valve presents with a stroke, immediate attention is focused on the heart as the obvious source, although many of these patients are elderly and often have coexistent cerebrovascular atherosclerosis. In this situation, two-dimensional echocardiography combined with Doppler ultrasonography, and/or color blood flow mapping can supply useful information on the presence of clot as well as on the structural features and flow characteristics of the valve. Clot or fibrous tissue appears as an echo-producing mass in the vicinity of the prosthetic heart valve. However, reverberations and other artifacts produced by metallic valves can make a clot or vegetation difficult to distinguish from the prosthetic apparatus. Indium-111-labeled platelet scintigraphy or radiolabeled platelet antibody imaging can be helpful in these patients.

Doppler echocardiography is helpful in diagnosing valvular stenosis or incompetence.\(^\text{72}\) Alam et al\(^\text{73}\) studied 183 clinically normal and 58 severely dysfunctional bioprosthetic valves. The Doppler-derived orifice dimension correlated well with cardiac catheterization values \((r=0.83)\) for stenosis. Pulsed Doppler echocardiography demonstrated regurgitant flow in 92% of regurgitant valves and in 90% of paravalvular leaks, whereas two-dimensional echocardiography demonstrated the diagnostic features of valve dysfunction in only 10% of patients. This study stresses the importance of Doppler ultrasound in conjunction with two-dimensional echocardiography in evaluating prosthetic valve function. Reisner and Meltzer\(^\text{74}\) have published an extensive review of Doppler indices found in normally functioning prosthetic valves.

Valve fluoroscopy is an easily performed technique for imaging the prosthetic valve in motion on high-film speed (60 frames/sec). Metallic valves are best visualized using this technique, although the radiopaque base ring of porcine valves can be seen during cinefluoroscopy.\(^\text{75}\) An abnormal rocking motion of the valve may indicate dehiscence. Valve fluoroscopy may be used in conjunction with two-dimensional echocardiography and Doppler examination.

Cardiac catheterization remains the gold standard with which to assess the function of a prosthetic valve. However, normally functioning prosthetic valves may still develop clots. Even if a thorough workup fails to reveal a source, a clot is often assumed by exclusion.

### Mitral Valve Prolapse

Mitral valve prolapse is detected in approximately 6% of healthy young women evaluated by echocardiography.\(^\text{76}\) Echocardiography is the procedure of choice in evaluating mitral valve prolapse and is helpful in assessing the extent of concomitant mitral regurgitation. The echocardiographic definition of mitral valve prolapse is the protrusion of one or both valve leaflets past the plane of the mitral valve anulus into the left atrium during systole. The mitral valve anulus region is reasonably well visualized by two-dimensional echocardiography, but there is some disagreement concerning when displacement into the left atrium is an abnormality or a variant of normal.\(^\text{77}\)

The mechanism of cerebral embolization in patients with mitral valve prolapse has not been completely

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**Table 2. Approach for Evaluation of Patient With New-Onset Atrial Fibrillation**

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Take history; perform physical examination, chest x-ray, and electrocardiography.</td>
</tr>
<tr>
<td>2.</td>
<td>Rule out secondary causes.</td>
</tr>
<tr>
<td></td>
<td>Acute myocardial infarction</td>
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<tr>
<td></td>
<td>Congestive heart failure</td>
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<td></td>
<td>Hyperthyroidism</td>
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<td></td>
<td>Chronic lung disease</td>
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<td></td>
<td>Pericarditis</td>
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<tr>
<td></td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>Drugs (i.e., alcohol, caffeine, marijuana)</td>
</tr>
<tr>
<td>3.</td>
<td>Suspect left atrial thrombus.</td>
</tr>
</tbody>
</table>
elucidated. Many reports suggest an accumulation of platelets and fibrin debris on the valve with subsequent embolization. Other causes include complicating infective endocarditis and associated atrial fibrillation, especially in the presence of significant mitral regurgitation.

The extent to which mitral valve prolapse is associated with cerebral infarction is difficult to determine. At the present time, mitral valve prolapse should be considered as a potential cause of stroke, especially in younger patients with typical auscultatory findings and an otherwise negative evaluation.

**Mitral Anulus Calcification**

Mitral anulus calcification is a common echocardiographic finding among the elderly, is more common in women than in men, and is often associated with mitral regurgitation. This is probably due to interference by calcium deposition with normal contraction and function of the mitral anulus. Mitral anulus calcification has been reported to be more common in patients with embolic stroke than in age-matched controls. Although a direct cause-and-effect relation is difficult to establish, mitral anulus calcification is a presumptive diagnosis if a thorough search for other causes of stroke is unrevealing. Two-dimensional echocardiography remains the procedure of choice to evaluate mitral anulus calcification, although a chest film or fluoroscopy may direct suspicion to the disorder.

**Calcific Aortic Stenosis**

Rarely is isolated calcific aortic stenosis a source of cerebral or retinal embolism. Calcium deposition in the aortic valve may be visible by fluoroscopy or chest roentgenogram. The electrocardiogram may show left bundle branch block or advanced atrioventricular block with extensive aortic calcification. Although two-dimensional echocardiography is a sensitive procedure to evaluate aortic calcification, assessment of the size of the aortic valve orifice based on imaging may be misleading. Doppler studies are thus coupled with two-dimensional echocardiography, allowing assessment of the transvalvular gradient and effective orifice area.

**Cardiac Myxomas**

Cerebral emboli remain frequent presentations and complications of atrial myxomas. Myxomas are the most common type of primary cardiac tumor. Most myxomas occur in the atria, with >50% occurring in the left atrium. The usual site of attachment is in the area of the fossa ovalis, although tumors have been found on the posterior wall of the atrium.

Two-dimensional echocardiography is the procedure of choice for the diagnosis and preoperative evaluation of cardiac myxomas. The major limitation of two-dimensional echocardiography is the body habitus of the patient. Obesity and severe pulmonary disease make visualization of the cardiac chambers difficult with transthoracic sonography, although transesophageal echocardiography may avoid these problems. Echocardiography can usually show the size of the tumor, its point of attachment, and its mobility.

The spatial resolution of radionuclide imaging is not adequate to resolve most myxomas. If available, ultrafast CT is very useful in diagnosing cardiac tumors. This technique can determine the degree of myocardial invasion and the involvement of pericardial and extracardiac structures that may not be visualized by echocardiography. In some centers cine CT is often used in conjunction with two-dimensional echocardiography. MRI has also shown promise for evaluating cardiac tumors.

**Paradoxical Emboli**

Most cerebral emboli arise from the carotid bifurcation or left-sided cardiac structures. However, if an arterial or left-sided cardiac source cannot be found, the possibility of a paradoxical cerebral embolus through either a patent foramen ovale or an atrial septal defect should be considered. Atrial septal defect is one of the most common congenital heart abnormalities detected in adulthood. Its initial presentation may be a cerebrovascular embolic event. In most patients with a patent foramen ovale, left atrial pressure remains higher than the right atrial pressure. However, when an acute increase in right-sided pressure occurs, such as with a Valsalva maneuver, a transient right-to-left shunt may occur, providing an avenue for paradoxical cerebral emboli. Using contrast echocardiography, Lechat et al demonstrated a patent foramen ovale in 40% of patients with no other source for an embolic stroke, whereas only 10% of controls had a patent foramen ovale.

Atrial septal aneurysms have been associated with a high prevalence of cerebrovascular and peripheral embolic events; 10% of 36 consecutively identified patients with atrial septal aneurysms had cerebral embolism. Although attached thrombi have been suggested as a cause of these events, a high proportion of patients with atrial septal aneurysms have intra-atrial shunting, suggesting paradoxical emboli as a probable causative factor.

**Endocarditis**

At least 3% of cerebral emboli arise from infected cardiac valves, and emboli may be the presenting sign of endocarditis. It is well known that embolic phenomena may occur weeks to months after the vegetation has been sterilized. Endothelialization of vegetations may take as long as 6 months. Most cases of infective endocarditis occur on abnormal native or prosthetic heart valves. However, there is an increasing number of instances of acute infective endocarditis involving otherwise normal valves. This is associated with the increased use of intravenous illicit drugs.

Nonbacterial thrombotic endocarditis or "marantic" endocarditis consists of sterile valvular thrombi that have the potential to dislodge and embolize.
These vegetations tend to occur in chronically ill patients, especially those with malignant disease. Systemic emboli occur in nearly half of patients with nonbacterial thrombotic endocarditis, and neurologic events are the most common manifestation.90,91

Cerebral infarction in systemic lupus erythematosus (Libman-Sacks endocarditis), thrombotic arterial occlusion related to lupus anticoagulant or anticardiolipin antibodies, and rarely from true immune complex-mediated cerebral vasculitis. The most characteristic cardiac lesion of systemic lupus erythematosus is the Libman-Sacks verrucous valvular lesion that causes endocarditis. These lesions may be discrete or in clumps and are composed of degenerating valve tissue and are usually found on the underside of the base of the mitral valve; aortic valve involvement is rare but well described.92

Two-dimensional echocardiography remains the procedure of choice in diagnosing valvular vegetations. The overall sensitivity of detecting a vegetation using this technique is approximately 60–70%.93–95 Large, bulky, and mobile vegetations (i.e., fungal endocarditis) are easier to visualize by echocardiography and are associated with a higher incidence of embolic events and congestive heart failure.96,97 Nevertheless, if the clinical suspicion is high, a negative procedure of choice in diagnosing valvular vegetations.

Conclusion

There is considerable evidence to support a strong association between cardiac abnormalities and cerebrovascular disease. In patients with asymptomatic carotid stenosis, TIAs, and ischemic stroke, the leading cause of death is myocardial infarction. Clinical evidence of ischemic cerebrovascular disease is a strong marker for underlying coronary artery disease. Therefore, attention should be directed toward evaluation of ischemic heart disease in these patients.

Ideally, the most appropriate cardiac screening test for this population should be the safest, the most reproducible, and the easiest to perform. Also, in this era of cost containment, efforts should be directed toward effective and affordable screening tests. Although one specific cardiac test may not be ideal, efforts to stratify patients may identify those at highest risk of future cardiac events.

References

25. Sirna et al Cardiac Disease and Stroke 21


44. Come PC, Riley MF, Birks NK: Roles of echocardiography and arrhythmia monitoring in the evaluation of patients with suspected systemic embolism. Ann Neurol 1983;13:527–531


64. Herzog CA, Blass D, Kane M, Asinger R: Two dimensional echocardiographic imaging of left atrial appendage thrombi. J Am Coll Cardiol 1984;3:1340–1344


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