The Patient With Transient Ischemic Attacks — Is This the Time for a New Therapeutic Approach?

HAROLD P. ADAMS, JR., M.D.,* NEAL F. KASSELL, M.D.,† HAIA MAZUZ, B.A., B.S.

SUMMARY Current and future improvements in treatment to prevent cerebral infarction among patients with transient ischemic attacks may reduce neurological morbidity but may not lead to a proportional improvement in life expectancy. Because the long-term primary cause of death in these patients is myocardial infarction, it is most likely that the most important way to prolong survival may be the vigorous investigation of their cardiac status and the treatment of their coronary artery disease, even if asymptomatic.

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caused by cardiac disease, should we not investigate. If a major proportion of deaths after TIA are
and treat the heart as aggressively as we try to protect
sequent medical or operative treatment directed only at
carotid endarterectomy and thus survival is not prolonged by
complications of generalized atherosclerosis. It is also
with TIA that the event is a serious warning of all the
process of atherosclerosis is not changed by carotid
same to that of patients with angiographically
disease in patients with TIA. 36 We cannot de-
operation.33
it expresses itself as a sudden
coronary artery disease. 36 Some or all of these procedures could
and severity of coronary atherosclerosis. The amount
of the left ventricular myocardium in jeopardy as well
might be weighed in the decision
tors than among those with solely cardiac symptoms.
Morris et al24 found more severe coronary artery
among patients with TIA and cardiac symptoms who had coronary bypass than among
patients who had only cardiac symptoms. These fac-
tors support the high probability of serious cardiac
among operated patients is approximately 5%. 20 Lye
Heart disease is also the primary late cause of mortality
after superficial temporal artery-middle cerebral artery
anastomosis.30 The annual mortality from heart disease
among operated patients is approximately 5%. 20 Lye
patients with TIA is not established. The goal is to recognize
and treat the coronary artery disease before an acute
myocardial infarction or sudden death occurs. While
unstable angina pectoris or a recent myocardial infarc-
tion are obvious warnings of subsequent, potentially
fatal cardiac events, their absence in a patient with TIA
does not eliminate the risk of myocardial infarction or
sudden cardiac death.1,13 Coronary artery disease is often asymptomatic until it expresses itself as a sudden
cardiac death.34 In the experience of the Framingham
Study, one half of all persons who suffered sudden
cardiac death had no prior clinical heart disease.35
While classic angina pectoris is very suggestive of
 coronary artery disease, less than 30% of patients with severe coronary atherosclerosis have classical anginal
pain.38 No physical abnormalities identify the patient
with severe coronary artery disease.38 We cannot de-
pend upon clinical symptomatology to select which
patients with TIA should undergo cardiac evaluation.
We must depend on diagnostic studies to detect the
presence of severe heart disease in patients with TIA.
The diagnostic studies used to detect coronary artery
disease in patients with chest pain could be applied to
patients with atherosclerotic cerebrovascular disease.
The evaluation of a patient with suspected coronary
artery disease is directed toward defining the extent
and severity of coronary atherosclerosis. The amount
of the left ventricular myocardium in jeopardy as well
as the function of the left ventricle are appraised.33
Non-invasive cardiac tests identify the patients most at
risk but demonstration of the extent of coronary artery
atherosclerosis still requires arteriography. Chest
roentgenograms and resting electrocardiograms are the
initial diagnostic studies in patients with suspected
coronary artery disease and already are standard parts
of the diagnostic evaluation of the patient with TIA.
Exercise electrocardiograms, resting and exercise rad-
ionuclide studies of the heart, left ventricular angio-
grams and coronary arteriography are now parts of the
evaluation of selected patients with suspected coronary
artery disease.35 Some or all of these procedures could

<table>
<thead>
<tr>
<th>Series</th>
<th>Patients</th>
<th>Mean follow-up (years)</th>
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<th>n Cardiac deaths (%)</th>
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<td>314</td>
<td>7.8</td>
<td>8 (15)</td>
<td>28 (51)</td>
<td>19 (34)</td>
</tr>
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*Number of cerebrovascular deaths; all types including hemorrhage.
†% of all deaths.
‡Other deaths includes patients dying of malignancy, trauma, or other illnesses or patients in whom the cause of death
was not established.

Possible Cardiac Evaluation
The extent of cardiac evaluation required in a patient
with TIA is not established. The goal is to recognize
and treat the coronary artery disease before an acute
myocardial infarction or sudden death occurs. While
unstable angina pectoris or a recent myocardial infar-
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Exercise electrocardiography is the most common non-invasive diagnostic study used in the evaluation of patients with possible coronary artery disease. Testing is performed in the presence of a physician and assesses both symptoms and electrocardiographic and blood pressure responses during exercise. It has a remarkable safety record. Complications are 3.6 myocardial infarctions, 4.8 serious cardiac arrhythmias and 0.5 deaths per 10,000 tests. The study is terminated if the patient develops severe anginal pain, if the patient’s blood pressure drops despite an increased work load, if neurological signs or pallor develop, if serious arrhythmias occur or if there is a 0.2 mV depression or elevation of the ST segment on the electrocardiogram. It is not diagnostic if the patient is taking digitalis or antianginal drugs. An abnormal resting electrocardiogram, in particular if changes are consistent with hypertensive heart disease are present, will invalidate an exercise study.

The sensitivity of exercise electrocardiography in the detection of coronary artery disease may approach 70%. Its specificity is approximately 90%. The patient’s clinical presentation influences the sensitivity and specificity of exercise electrocardiography. A positive exercise test is highly predictive of coronary artery disease in a patient with classic angina, but a negative study has a low correlation with the absence of significant disease. Stress testing has been recommended to detect latent coronary artery disease in patients who do not have cardiac symptoms but who may be at high risk. However, the value of exercise electrocardiography in asymptomatic patients has been questioned because false positive results do occur. Radionuclide angiography enhances the accuracy of diagnosis when done in association with standard treadmill exercise testing. Thallium-201 perfusion scintigrams using either exercise or dipyridamole to induce coronary artery vasodilation may detect areas of myocardium at risk. Thallium-201 accumulates in myocardial cells at a rate proportional to coronary flow. Perfusion images of the left ventricular myocardium are obtained. Areas of borderline perfusion will be detected by impaired uptake of the radioisotope during exercise. Defects in the septal region correlate with disease of the left anterior descending coronary artery. Posterolateral wall defects accompany stenosis of the left circumflex artery. Inferior wall perfusion defects are associated with stenosis of the posterior descending coronary artery. Thallium-201 scintigrams have a sensitivity in detecting coronary artery disease of approximately 80% and a specificity that approaches 90%.

Exercise radionuclide ventriculography can detect regional or generalized impaired cardiac performance. Technetium-99 labeled red blood cells are injected immediately before scanning. Exercise will demonstrate abnormalities in ventricular function not apparent at rest. The study is abnormal if the left ventricular ejection fraction fails to increase by more than 5–10% or if regional wall abnormalities develop. The study has a sensitivity and specificity that exceeds 90% for detection of coronary artery disease. False negative studies are more likely to occur in patients with single vessel disease than among patients with diffuse disease. The presence of antianginal drugs such as calcium-channel blockers, propranolol or nitrates invalidates the radionuclide studies. Complications of Thallium-201 perfusion scans and exercise radionuclide ventriculography are very low. The precautions for exercise electrocardiography can be applied to exercise radioisotope studies. If the patient cannot exercise because of neurological or other deficits, Thallium-201 scans using dipyridamole induced vasodilation can be obtained. The amount of radiation exposure in these two studies is much less than arteriography.

Coronary arteriography is the most definite diagnostic procedure for detection of coronary artery disease. It will demonstrate the site and severity of coronary artery stenosis in all coronary vessels. In a review of the more than 14,000 coronary arteriograms performed in the state of Washington, there were 26 deaths (0.19%), 18 myocardial infarctions (0.13%) and nine strokes (0.06%). A similarly low rate of neurological complications of coronary arteriography was reported by Dawson and Fischer.

The cardiac evaluation of the patient with TIA should be determined on a case-by-case basis. In an attempt to reduce unnecessary studies and expenses, it may be reasonable to dispense with the non-invasive procedures and proceed directly to coronary arteriography to determine the extent of coronary artery disease in those patients with TIA who have a history of classic angina pectoris or who have had a well-documented myocardial infarction. In those patients without cardiac symptoms, an exercise electrocardiogram could be a screening procedure. If the patient with TIA has an abnormal exercise electrocardiogram, coronary arteriography could then be recommended. While its sensitivity in the detection of coronary artery disease is less than the radionuclide techniques, the widespread availability and lower costs of the exercise electrocardiogram makes it the most reasonable initial non-invasive cardiac study in patients with TIA.

The fact that radionuclide cardiac studies are available in only a small number of hospitals is a drawback. In addition, the cost of these studies (approximately $500.00 per procedure) is a formidable obstacle to their widespread utilization in a patient with TIA. Coronary arteriography would be reserved for those patients with at least suggestive evidence of coronary artery disease as detected by the non-invasive methods. The risks of the non-invasive cardiac studies are sufficiently low in patients with known severe coronary artery diseases, that they can safely be applied in patients who are without cardiac symptoms.

The high yield of the cardiological evaluation in patients with cerebrovascular disease has been recently demonstrated by Rolak et al. They performed Thallium-201 scans and exercise radionuclide ventriculo-
Possible Cardiac Treatment in the Patient with TIA

The ideal management of associated heart disease in a patient with TIA has not been established. Patients without cardiac symptoms and negative non-invasive cardiac studies could receive only treatment directed at cardiac disease risk factors, such as hypertension and hypercholesterolemia. Follow-up visits could include a review of cardiac symptoms and sporadically repeated non-invasive cardiac studies.

Cardiac revascularization in patients with cerebrovascular disease has been advocated. Coronary artery bypass should be considered for those patients who have severe or unstable angina refractory to medical therapy. Those patients with three vessel coronary artery disease or stenosis of the left main coronary artery who do not have symptoms may warrant surgery. The timing of coronary and cerebrovascular operations in patients with symptoms in both the cerebral and coronary circulations has not been resolved. In patients with symptomatic coronary and carotid artery stenoses, a simultaneous coronary bypass operation and carotid endarterectomy may be the most prudent, although unproven, course. The risk of the cardiac operation needs to be considered. The operative mortality of coronary artery bypass is approximately 1% and the incidence of complicating stroke is 1–3%. Although one report did not find a higher incidence of cerebrovascular risk factors among patients with stroke after bypass, it is possible that the stroke complication rate might be higher among patients with TIA.

Before recommending cardiac surgery to patients who are asymptomatic, the influence of coronary artery bypass on survival must be positive. Two long-term studies show a favorable trend of increased survival among surgically treated patients when compared to medically-managed patients. Surgery prolongs survival among patients with stenosis of the left main coronary artery, those with severe three-vessel disease or those persons with angina and ST depression on resting electrocardiogram. The four-year survival after surgery among operated patients aged 45–65 is 93% and among older patients is 84%. The quality of life is improved, myocardial ischemia is decreased and survival is prolonged after coronary artery bypass surgery in selected subsets of patients. Whether coronary artery bypass surgery on asymptomatic, severe coronary atherosclerosis could improve survival among patients with TIA is not known. The available evidence suggests that the risks of surgery are sufficiently low and the risks of subsequent cardiac death sufficiently high, that coronary artery bypass surgery would be reasonable in carefully selected patients with TIA.

Percutaneous transluminal coronary angioplasty is an alternative to surgery in many patients with coronary artery disease. Patients with single-vessel disease appear to be the most suitable for this procedure. As many as 15% of patients who might otherwise have surgery may be successfully treated by transluminal angioplasty.

Medical alternatives include beta-adrenergic blocking drugs, long-acting nitrates, calcium channel blockers, anti-platelet aggregating drugs and control of risk factors. While the medical therapies offer relief of symptoms with coronary artery disease, data showing improved survival are not presently available. The value of medical treatment of the heart in patients with TIA has not been studied.

The challenge for the physician who cares for the stroke-prone patient is not only to avoid the complications of cerebrovascular atherosclerosis but also to recognize and treat if possible the co-developing coronary artery disease. We need to know the degree of coronary atherosclerosis and its prognosis. We need to know the influence of surgical or medical cardiologic therapy on survival of patients with TIA. Now is the time for a careful study of heart disease in patients with TIA.

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