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Coronary Risk Evaluation in Patients With Transient Ischemic Attack and Ischemic Stroke

A Scientific Statement for Healthcare Professionals From the Stroke Council and the Council on Clinical Cardiology of the American Heart Association/American Stroke Association

Robert J. Adams, MD; Marc I. Chimowitz, MD; Joseph S. Alpert, MD; Issam A. Awad, MD; Manuel D. Cerqueria, MD; Pierre Fayad, MD; Kathryn A. Taubert, PhD

Stroke and myocardial infarction (MI) share common risk factors and pathological mechanisms, and coronary artery disease (CHD) is an important cause of death in patients with cerebrovascular disease. This Scientific Statement addresses issues in management of the relatively healthy patient with brain ischemia (a transient ischemic attack [TIA] or an ischemic stroke) who does not have recognized CHD but often has risk factors in addition to having had a TIA or stroke that indicate an increased likelihood of disability or death from cardiac disease in the future. This Statement should not be confused with the official American College of Cardiology (ACC)/American Heart Association (AHA) practice guidelines. The reader is referred to the ACC/AHA guidelines for management of recognized and symptomatic CHD¹ and the American College of Chest Physicians (ACCP)² and American Stroke Association (ASA)³⁻⁵ guidelines for evaluation of cardiac causes of TIA and stroke, which are important related but separate issues.

Prevalence of Asymptomatic CHD in Patients With TIA or Stroke

Several small studies have shown that patients with TIA and stroke have a high prevalence of asymptomatic CHD.⁶⁻⁸ Rokey et al⁶ performed exercise thallium (Tl) 201 scintigraphy and exercise radionuclide ventriculography on 50 consecutive patients with TIA or stroke. Sixteen patients had symptoms suggestive of cardiac ischemia; the other 34 patients were asymptomatic. The results of myocardial perfusion imaging were abnormal in 15 of 16 symptomatic patients (94%) and 14 of 34 asymptomatic patients (41%). Twenty-two patients who had abnormal myocardial perfusion imaging results underwent coronary angiography, which

showed severe CHD ($\geq 70\%$ stenosis of the lumen of ≥ 1 coronary artery) in 18 patients (10 of 13 symptomatic patients and 8 of 9 asymptomatic patients). Twelve of the 18 patients with severe CHD had multivessel disease.

In a study by Di Pasquale et al,⁷ 83 consecutive patients with TIA or minor stroke and no symptoms of ischemic heart disease underwent exercise electrocardiography. Patients with positive results on exercise ECG subsequently underwent exercise Tl-201 myocardial scintigraphy. Asymptomatic CHD was detected in 28% of patients studied with these noninvasive techniques. Coronary angiography was performed in 2 patients, one with 3-vessel CHD and the other with 2-vessel CHD. In a later report by Di Pasquale et al⁸ of 190 consecutive patients with cerebral ischemia but without symptoms or ECG signs of ischemic heart disease, a positive exercise test was found in 26%. Follow-up exercise thallium myocardial scintigraphy was abnormal in 33 of 36 patients, of whom 26 had reversible and 7 had fixed perfusion deficits. Love et al⁹ performed Tl-201 myocardial scintigraphy in 27 patients with asymptomatic carotid disease, TIA, or small stroke and no symptoms of CHD. Nine patients (33%) had perfusion defects (reversible in 7 patients, fixed in 1 patient, and both in 1 patient). Gates et al¹⁰ found a 20% prevalence of unsuspected cardiac disease among 132 stroke patients without a history of cardiac disease. Although these studies are small, they indicate that abnormal results of provocative tests for myocardial ischemia are not uncommon in patients with TIA and stroke. These small studies suggest that 20% to 40% of stroke patients may have abnormal tests for silent cardiac ischemia.

Cardiac Comorbidity in Cerebrovascular Patients

To what extent are stroke patients at increased risk for cardiac-related death? Data on short- (<90 days),

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TABLE 1. Recent Acute Ischemic Stroke Treatment Trials Reporting Cardiac Mortality Rate

Name of Author or Study	No. of Patients	Cardiac Mortality Rate, %	Follow-Up
Bath et al ¹³	1771	0.5 (fatal MI only)	0.5 to 6 mo
ECASS 1 ¹²	620	2	3 mo
Lubeluzole (Europe) ¹⁴	1786	3.9	3 mo
Lubeluzole (US) ¹⁵	721	5.4	3 mo
TAIST ¹⁶	1486	3.3	3 mo
STAT ¹⁷	500	6.2	3 mo
TOPAS ¹⁸	404	2	3 mo
Enlimomab ¹⁹	625	1.9 (cardiac arrest)	5 d
Aptiganel ²⁰	628	2.8 (cardiac arrest)	3 mo
IST ¹¹	19 435	0.75	0.5 mo

intermediate- (30 days to 2 years), and long-term risk were examined from recent studies conducted primarily in US and European populations. Estimates of short-term risk can be obtained from acute ischemic stroke treatment trials in which cardiac outcomes were separated from stroke events (Table 1). Although treatment trials tend to recruit healthier patients and may underestimate rates of disease or death from cardiac causes generally, they are the best source of data for the present review for the following reasons:

- (1) Although the patients may have a history of CHD or prior MI, those with severe cardiac comorbidity are often excluded from these trials.
- (2) Patients are recruited within hours after stroke onset and typically are monitored closely for 30 to 90 days, giving a complete picture of short-term outcome and comorbidities.
- (3) Patients with brain hemorrhage and often those with cardioembolic stroke who have known cardiac disease are, for the most part, excluded from studies, which make these data more applicable to the patients targeted in the present Statement.

Some of the recent treatment trials (Table 1) distinguish cardiac-related deaths from those due to stroke or other causes, although MI is not always distinguished from other cardiac causes of morbidity and mortality such as congestive heart failure (CHF). The International Stroke Trial (IST)¹¹ randomly assigned ≈20 000 patients to short-term treatment, including aspirin, heparin, and placebo. For all treatment groups from the IST combined, 14-day deaths from CHD were reported in 1.5% of the study group. The European Cooperative Acute Stroke Study (ECASS I)¹² reported 13 nonneurological vascular deaths (2%) in 620 treated patients.

The meta-analysis of trials of low-molecular-weight heparins and heparinoids in acute ischemic stroke, which included the Trial of Org10172 in Acute Stroke Treatment (TOAST), reported a 0.5% rate of fatal MI among 1771 trial patients.¹³ Of 1786 patients in the European lubeluzole study, 48 (2.7%) died of cardiovascular-related causes; 10 of these deaths were due to MI (0.5%).¹⁴ In the US lubeluzole study, among 721 patients monitored for up to 90 days, there were 39 cardiac-related deaths (5.4%), but only 4 of these deaths were due to MI (0.5%).¹⁵ In the Tinzaparin in Acute Ischemic Stroke (TAIST) study,¹⁶ 49 fatal cardiac events (including sudden death) were reported among 1486 patients (3%), but deaths from MI were not reported separately. Of 31 cardiac-related deaths (6%), 4 fatal MIs (0.1%) were recorded from among 500 patients in the Stroke Treatment With Ancrod (STAT) trial.¹⁷ Eight cardiac deaths (2%) occurred in the Thrombolysis or Peripheral Arterial Surgery (TOPAS) trial, which recruited 404 patients.¹⁸ Cardiac arrest was reported in 1% of the 625 patients in the Enlimomab trial.¹⁹ About 3% of the 628 patients in the Aptiganel study had cardiac arrest, but mortality rate was not reported.²⁰

The data from these studies were obtained from almost 30 000 patients primarily from the United States and Europe who were typically followed up for 90 days. According to these studies, ≈2% to 5% of patients with acute ischemic stroke have fatal cardiac-related events in the short term after stroke. The prevalence of cardiac disease at entry is typically in the range of 20% to 30%. Although no study reported cardiac events in relation to entry history of cardiac disease, it is probable that a substantial fraction—perhaps most—of the cardiac events observed in these studies were in patients who had established cardiac disease, making the early estimate of death from cardiac disease in stroke patients without a history of CHD (ie, the target population for the present Statement) possibly less than what was observed in these studies.

Estimates of intermediate-term (30-day to 2-year) risk can be obtained from the results of large secondary stroke prevention studies: European Stroke Prevention Study (ESPS), Ticlopidine and Aspirin in Stroke Study (TASS), ESPS 2, and Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) (Table 2). The information gained from these studies is relevant because patients are typically enrolled in a study 30 to 90 days after stroke, and most patients were treated with aspirin or other agents that lower risk of MI as well as stroke. This makes data from these studies applicable to current practice, in which stroke patients (should) leave the hospital with secondary prevention treatment. Patients with early mortality were excluded from these

TABLE 2. Data From Stroke Secondary Prevention Studies

Study	No. of Patients	Cardiac Event Rate, %	Follow-Up, y
ESPS ²¹	2500	4.1 (fatal MI, sudden death, other cardiovascular death)	2
TASS ²²	3069	5.4 (fatal MI, sudden death, other cardiovascular deaths)	2 to 6
ESPS 2 ²³	6602	2.5 (fatal and nonfatal MI)	2
CAPRIE ²⁴ (stroke subgroup)	6431	1.5 (fatal and nonfatal MI)	1.9

TABLE 3. Late Mortality From Stroke Versus Other Vascular Causes

Study	No. of Patients	Follow-Up, y	Stroke Mortality Rate, %	Other Vascular Mortality Rate, %	Years Included in Study
Danish WHO/Monica ⁹⁰	4162	5	22	45	1982–1991
Perth Community Stroke Study ²⁶	362	5	27	31	1989–1990
Oxfordshire ⁹⁰	675	6.5	36	34	1981–1986
Rochester, Minn ³¹	1111	See text	27	24	1975–1993
NOMASS ²⁵	1180	5	15	29	1990–1997

studies. In ESPS,²¹ 2% of patients died from cardiac causes. In TASS,²² over a mean of 3 years, cardiovascular causes accounted for 5% of deaths. In ESPS 2,²³ over 24 months, 2.5% of patients experienced an MI. In the CAPRIE subgroup²⁴ enrolled because of recent stroke, over an average of 1.9 years, MI (fatal or nonfatal) was the first event in 1.5% of patients. In addition, antiplatelet trials typically exclude patients with cardioembolic stroke, a group at higher coronary risk. It should be noted that ≈30% of those enrolled in these 3 studies had an established cardiac disease history at entry. It is reasonable to assume that many—perhaps most—of the cardiac-related events recorded in these studies were seen in these patients. Thus, the risk of cardiac-related events after stroke in the intermediate term in patients being treated with antiplatelet agents who do not have an established history of cardiovascular disease is probably low, possibly in the range of 2% to 3% per year. Treatment trials underestimate risk because healthier patients tend to be enrolled, but the present Statement is aimed at management of healthier stroke patients, and thus these data are pertinent.

Epidemiological studies provide another view of this issue. Recent data (1990 to 1997) from the Northern Manhattan Stroke Study (NOMASS) of a mixed racial/ethnic population in northern Manhattan indicate that although stroke-related death accounted for 55% of the 30-day mortality rate, 19% of deaths were due to cardiac causes.²⁵ In a study from Perth, Australia, however, <7% of the early deaths were related to cardiac disease.²⁶

A recent study used administrative databases of secondary atherosclerotic ischemic events in 1518 Medicare patients with ischemic stroke (mean age, 79 years) and 1631 ischemic stroke patients with commercial insurance (mean age, 62 years). The average observation period was 1.2 to 1.3 years after the index event. The occurrence of MI was distinguished from recurrent stroke. In the commercial database, the rates of all secondary events were 4.2% (6 months), 6.5% (1 year), 9.8% (2 years), and 11.8% (3 years); 20% of these events were MIs (compared with 79% for recurrent stroke). The rates for MI can thus be computed as: 0.84% (6 months), 1.3% (1 year), 1.96% (2 years), and 2.36% (3 years). As expected, the rates in the Medicare sample were higher overall, but only 21% were MIs. The comparable MI rates were: 0.90% (6 months), 1.62% (1 year), 2.96% (2 years), and 3.8% (3 years). These samples afford data from less selected samples than clinical trials and serve to bracket the higher end of MI risk, compared with clinical trials, in ischemic stroke patients.²⁷

Two conclusions may be drawn:

- (1) Short-term risk without a history of CHD is low; there is no compelling reason to test for silent myocardial ischemia during short-term hospitalization. Doing so could lengthen hospital stay.
- (2) Risk in the subsequent few years is still relatively low, and evaluation of all ischemic stroke patients is probably not justified.

The long-term risk of CHD in stroke patients, however, is not benign, and risk of death, in part due to cardiac disease, is at least 2-fold that of age-matched controls in most studies. In a retrospective study of 1044 patients from the Mayo Clinic with cerebral infarction, the long-term (10-year) risk of MI or sudden death was compared with that of age- and sex-matched patients without stroke from 1960 to 1979. The risk of these outcomes was increased at 5 years, but a divergence in risk curves was noted after 6 months. The 6-month probability of these outcomes was 0.8%; at 5 years, it was 10.6%, or about twice the expected rate.²⁸ In the Framingham study, the 10-year survival rate was only 35% for 394 patients with TIA or stroke and CHD and CHF, the strongest predictors of mortality.²⁹ In an older study, the 5-year risk for MI and sudden death in TIA patients was 21% and MI was more likely to be fatal than recurrent stroke.³⁰ In a study from Rochester, Minn, that spanned 15 years from 1975 to 1989 and examined survival after first cerebral infarction, the survival rate was significantly lower ($P<0.001$) than expected compared with age- and sex-specific mortality rates of the Minnesota population during the time period of the study. Cardiac and probable cardiac (eg, sudden death) causes were almost as important as stroke in terms of morbidity.³¹ The Cardiovascular Health Study (1989 to 1997), a US study of 5888 elderly patients, recently reported the cause of death in 1310 patients. Among the study participants, there were 455 incident strokes; of those, stroke was the cause of death ≈3 times as often as CHD. CHD, however, still accounted for 11.4 deaths per 1000 patient-years, compared with 36.1 deaths from stroke-related causes.³² The report did not exclude patients who died in the period immediately after stroke—deaths largely related to the incident stroke.

Several population studies have been reported that excluded early deaths (<30 days after stroke) and separated long-term mortality related to stroke from mortality due to cardiac or other vascular causes (Table 3). The long-term study by Petty et al³¹ reported the outcomes of patients with

cerebral infarctions that occurred in the period from 1975 to 1989, with follow-up to 1993. Unlike the other studies in Table 3, early deaths were not excluded, and therefore, on long-term follow-up, the proportion of deaths due to heart disease (MI, CHF, or sudden unexplained death) relative to stroke is probably underestimated. In these studies, 24% to 45% of the late mortality was related to vascular disease other than stroke, and in some studies this risk exceeded that due to recurrent stroke. Other vascular and cardiac diseases are important causes of long-term mortality in stroke patients.

Except for NOMASS²⁵ and the Mayo Clinic study,³¹ these reports included stroke due to hemorrhage, which may carry a long-term risk of CHD different from that of ischemic stroke. All of the cited studies included patients with strokes due to cardiac emboli; by definition, these patients have heart disease and a higher risk of death compared with most other ischemic stroke subtypes.^{33,34} For this reason, these figures probably overestimate the long-term relative contribution of cardiac risk for the population targeted in the present Statement.

Ischemic Stroke Subtype and Cardiac Risk

Atherosclerosis is invariably the cause of CHD. It is likely that subtypes of ischemic stroke related to underlying atherosclerosis (eg, carotid/vertebral/intracranial stenosis) are associated with a higher risk of CHD than are nonatherosclerotic subtypes of stroke. Chimowitz et al³⁵ compared the frequency of abnormal cardiac stress test results in 30 patients with atherosclerosis of a major cerebral artery (ie, cervical carotid artery or a major intracranial artery) against 39 patients with other causes of cerebral ischemia (penetrating artery disease, cardioembolism, cryptogenic stroke). All 69 patients in the study presented with TIAs or ischemic stroke and no overt CHD. The presence of risk factors was similar in the 2 groups, except that patients with cervical carotid or intracranial atherosclerosis had a significantly higher frequency of peripheral vascular disease ($P=0.04$), whereas patients with other causes of cerebral ischemia had a significantly higher frequency of hypertension ($P=0.03$). The rate of abnormal stress test results was 50% (15 of 30 patients) for those with atherosclerotic stenosis of a cervical carotid or major intracranial artery stenosis compared with 23% (9 of 39 patients) for those with other causes of stroke ($P=0.04$). In patients with other causes of stroke, the most common diagnoses were penetrating artery disease (3 of 15 had a positive stress test result) and stroke of undetermined cause (4 of 20 had a positive stress test result). Nonvalvular atrial fibrillation was the cause of stroke in the other 4 patients, 2 of whom had a positive stress test result. Logistic regression analysis showed that smoking and carotid or intracranial atherosclerosis were the only independent risk factors for abnormal stress test results in this study.

Other studies suggest that cardiac risk may be lower in patients with small-vessel stroke. In a population-based study of outcomes after ischemic stroke, Petty et al³³ reported a 1.4% probability of death at 1 year after lacunar stroke compared with a probability of 8.1% after atherosclerotic stroke and a probability of 30% after cardioembolic stroke, although the specific contribution of cardiac death was not

separated from other causes. In the Oxfordshire Community Stroke Study, 2 of 133 lacunar stroke patients died of cardiac causes within 30 days after stroke, compared with 6 of 209 patients with partial or total anterior circulation infarcts.³⁶ Salgado et al³⁷ reported a high 5-year survival rate (86%) for patients with lacunar infarcts, with 4 MIs and 3 other vascular deaths among 145 patients followed up for an average of 39 months. The Cardiovascular Health Study³² report on incident stroke also showed that patients who were classified as having small-vessel strokes had lower mortality rates than those classified as having other ischemic or hemorrhagic stroke subtypes. NOMASS reported the lowest mortality rate from small-vessel disease among stroke subtypes.²⁵ Similar findings were recently reported from the German Stroke Data Bank, a hospital-based registry of 5017 acute ischemic strokes. The death rate within 90 days of stroke was highest in patients with cardioembolic stroke (22.6%) and lowest in those with microangiopathy (3.3%), although cardiac causes of death were not distinguished.³⁸ Similar findings were reported from a population study in Bavaria that examined outcomes in 583 patients with ischemic stroke between 1994 and 1998. Among 185 deaths over 2 years of follow-up, the highest survival rate (85%) was seen in patients with small-artery occlusion; the lowest survival rate (55%) was seen in patients with cardioembolic stroke.³⁴ Ischemic stroke subtype is a strong predictor of long-term survival, and although data on causes of death are not always reported, it can be assumed that a significant contribution to risk of death on extended follow-up is cardiac related, and by inference, that patients with small-vessel disease appear to be at lower risk.

Determining the most probable ischemic stroke subtype thus may provide useful prognostic information that may be helpful when deciding whether to study a stroke patient for the presence of unrecognized CHD. A variety of schemes for classifying ischemic stroke subtypes have been proposed. Many ongoing studies are using the scheme³⁹ used in TOAST, which classifies ischemic stroke into the following 5 categories:

- (1) *Large-Artery Atherosclerosis.* Large-artery strokes generally occur in patients with a cortical infarct in the distribution of a large cerebral artery demonstrated to have luminal occlusion, or narrowing of $\geq 50\%$, of atherosclerotic origin. This category of stroke is often preceded by a TIA in the same arterial distribution. The mechanism of these infarcts is presumed to be either artery-to-artery embolism or hemodynamic insufficiency.
- (2) *Cardioembolism.* Cortical or large subcortical infarctions with a recognized high-risk cardiac source are presumed to be caused by cardioembolism. The arterial occlusion in these infarcts is caused by an embolus originating from the heart and, in some classification schemes, the aorta as well. The presence of a moderate-risk source alone qualifies for a "possible cardioembolism." The presence of atherosclerotic narrowing in the parent large artery should be excluded to arrive at this diagnosis.
- (3) *Small-Artery or Lacunar Stroke.* This type of stroke is usually diagnosed when a patient has symptoms consistent with a lacunar syndrome, such as pure motor hemiparesis and a small (<1.5 cm) lesion found on neuroimaging. The cause is an occlusive arteriopathy involving

the small vessels deep in the brain or brain stem. These strokes are generally associated with diabetes or hypertension and are not usually caused by atherosclerosis. Potential sources of cardioembolism and ipsilateral large-artery stenosis are not infrequent concomitants and should be excluded in patients with apparent lacunar stroke.

- (4) *Uncommon Causes of Stroke.* Other causes of stroke are uncommon and are identified by diagnostic testing. These include nonatherosclerotic vasculopathies, hypercoagulable states, or hematologic disorders. There is no restriction on size or location of the infarct on brain imaging.
- (5) *Undetermined Causes of Stroke.* In more than one third of all strokes, the cause cannot be determined with confidence. This broad category includes patients in whom ≥ 2 potential mechanisms for the stroke are identified. Patients with an incomplete or completely negative evaluation are also included in this category.

Two additional clinical syndromes may bring the patient to medical attention and raise issues pertinent to the present guideline: TIA and retinal ischemia. TIAs are episodes of focal neurological deficits that resolve completely within 24 hours (although usually within a few minutes or hours) and are best explained by an ischemic etiology.

Retinal or hemispheric TIA is not classified in most schemes but requires that the patient be evaluated to determine the cause. Diagnostic testing can identify patients whose symptoms may be due to large-artery disease or emboli from the heart or great vessels.

Inferring the ischemic stroke subtype requires a sufficient amount of clinical and test information. In some cases this is relatively simple, such as in an ischemic cortical stroke distal to a high-grade carotid artery stenosis. Cases of "persistent uncertainty" are not unusual, and frequently more than one mechanism of stroke is possible. The reader is referred to the ACCP and AHA/ASA publications on the management of TIA, treatment of ischemic stroke, and secondary prevention of stroke for recommendations about diagnostic testing to determine the cause of stroke.²⁻⁵

Asymptomatic CHD in Patients With Atherosclerotic Carotid Stenosis

A case can be made for looking for CHD if the workup for stroke or TIA shows significant carotid stenosis. Several studies have shown that patients with carotid stenosis have a high frequency of asymptomatic CHD. Urbinati et al⁴⁰ performed TI-201 myocardial perfusion imaging in 106 patients without cardiac symptoms before carotid endarterectomy (CE) and found that 27 patients (25%) had abnormal results. Sconocchini et al⁴¹ found that 21 of 85 patients (25%) with carotid stenosis $\geq 50\%$ and no history of CHD had abnormal results on exercise ECG.

In a study in which adenosine or exercise TI-201 myocardial imaging was used in patients without cardiac symptoms, Chimowitz et al³⁵ showed that 13 of 22 patients (60%) with isolated cervical carotid stenosis or coexistent carotid and intracranial stenoses had abnormal results in myocardial imaging studies. Coronary angiography was performed in 7 patients with cervical carotid or intracranial artery stenosis in this study; the results showed severe ($\geq 70\%$ stenosis)

1-vessel CHD in 2 patients, severe 2-vessel CHD in 2 patients, and severe 3-vessel CHD in 3 patients. Two of the 7 patients also had left main CHD (50% to 60% stenosis in 1 patient and 40% to 50% stenosis in the other).

Okin et al⁴² performed carotid ultrasound and exercise ECG in 204 asymptomatic subjects free of clinical evidence of cardiovascular disease. Exercise-induced myocardial ischemia was detected in 35 patients; 6 of 12 (50%) had carotid atherosclerosis, and 29 of 192 (17%) had no carotid disease ($P=0.007$). Multivariate analysis showed that carotid artery cross-sectional area ($P=0.0007$) and systolic hypertension ($P=0.005$) were the only variables independently associated with exercise-induced myocardial ischemia. The occurrence of silent myocardial ischemic episodes has also been evaluated with 24-hour ambulatory ECG in 161 patients with carotid occlusive disease with and without a history of CHD. Silent ischemic episodes were detected in 38 of 93 patients (41%) with CHD and in 18 of 68 patients (26%) without a history of CHD.⁴³

Only one study has systematically used coronary angiography to define the frequency of asymptomatic CHD in a population with carotid disease. Hertzler et al⁴⁴ performed coronary angiography on 200 patients without symptoms of CHD, most of whom presented with carotid bruits. Eighty patients (40%) had severe CHD, defined as $>70\%$ stenosis of ≥ 1 coronary artery; 93 patients (46%) had mild or moderate CHD. Only 27 patients (14%) had normal coronary arteries. The numbers of patients with 1-vessel, multivessel, and left main CHD were not stated; 22% were considered to have severe but compensated CHD; 16% had severe, surgically correctable CHD; and 2% had inoperable CHD.

Data from the Framingham study⁴⁵ indicate a higher risk of MI and vascular death in patients with carotid bruit compared with those without carotid bruit.⁴⁶ In the Toronto prospective study of carotid bruit⁴⁴ and stenosis,⁴⁷ both bruit and degree of stenosis indicated higher cardiovascular risk.

Overall, these studies suggest that 25% to 60% of patients with carotid disease and no symptoms of CHD have abnormal provocative test results for myocardial ischemia or angiographic evidence of severe CHD. Because provocative tests for myocardial ischemia do not identify patients with atherosclerotic coronary plaques that do not limit flow, the true frequency of asymptomatic CHD (ie, flow-limiting and non-flow-limiting plaques combined) in patients with carotid stenosis may be substantially higher. Patients with non-flow-limiting coronary plaques are at risk for acute MI or sudden death from rupture of an atherosclerotic plaque; however, there are no reliable noninvasive techniques to identify this important subgroup of patients with asymptomatic CHD.

In summary, the evidence suggests that ischemic stroke subtype provides important information on concomitant cardiac risk, especially in 3 situations: (1) significant symptomatic or asymptomatic carotid stenosis (higher risk), (2) small-vessel cause of stroke (lower risk), and (3) cardiac embolism as the suspected cause of stroke (very high risk). Because carotid artery evaluation is recommended for most TIA and stroke patients, this information should be available in the great majority of patients whose management is the subject of the present Scientific Statement. It is less clear when the

Age (Low-risk level)*	30-34 (2%)	35-39 (3%)	40-44 (3%)	45-49 (4%)	50-54 (5%)	55-59 (7%)	60-64 (8%)	65-69 (10%)	70-74 (13%)	Absolute Risk	Absolute Risk†
Points ‡										Total CHD‡	Hard CHD‡
0	1.0									2%	2%
1	1.5	1.0	1.0							3%	2%
2	2.0	1.3	1.3	1.0						4%	3%
3	2.5	1.7	1.7	1.3	1.0					5%	4%
4	3.5	2.3	2.3	1.8	1.4	1.0				7%	5%
5	4.0	2.6	2.6	2.0	1.6	1.1	1.0			8%	6%
6	5.0	3.3	3.3	2.5	2.0	1.4	1.3	1.0		10%	7%
7	6.5	4.3	4.3	3.3	2.6	1.9	1.6	1.3	1.0	13%	9%
8	8.0	5.3	5.3	4.0	3.2	2.3	2.0	1.6	1.2	16%	13%
9	10.0	6.7	6.7	5.0	4.0	2.9	2.5	2.0	1.5	20%	16%
10	12.5	8.3	8.3	6.3	5.0	3.6	3.1	2.5	1.9	25%	20%
11	15.5	10.3	10.3	7.8	6.1	4.4	3.9	3.1	2.3	31%	25%
12	18.5	12.3	12.3	9.3	7.4	5.2	4.6	3.7	2.8	37%	30%
13	22.5	15.0	15.0	11.3	9.0	6.4	5.6	4.5	3.5	45%	35%
>14	26.5	>17.7	>17.7	>13.3	>10.6	>7.6	>6.6	>5.3	>4.1	>53%	>45%

* Low absolute risk level = 10-year risk for total CHD end points for a person the same age, blood pressure < 120/<80 mmHg, total cholesterol 160-199 mg/dL, HDL-C ≥45 mg/dL, nonsmoker, no diabetes. Percentages show 10-year absolute risk for total CHD end points.

† Points = number of points estimated from Table 4

‡ 10-year absolute risk for total CHD end points estimated from Framingham data corresponding to Framingham points (Table 4)

§ 10-year absolute risk for hard CHD end points approximated from Framingham data corresponding to Framingham points (Table 4)

Color Key for Relative Risk

Green	Violet	Yellow	Red
Below Average risk	Average risk	Moderately above average risk	High risk

cause of stroke comfortably can be ascribed to small-vessel etiology. As many as 25% of patients in NOMASS who presented with clinical syndromes suggesting small-vessel disease had other significant markers of risk, such as carotid disease or possible cardiac source of embolus.⁴⁸ Therefore, evaluation of patients with apparent small-vessel disease should be at least extensive enough to identify concomitant carotid artery disease and major cardiac sources of embolism.

The Writing Committee recognized that randomized controlled data are needed to make any recommendations secure. In the absence of large-scale, systematic application of subtyping to guide CHD testing, however, the following is offered as a reasonable approach:

- (1) Consider CHD testing when the workup reveals carotid or other large-vessel atherosclerosis.
- (2) Defer testing in patients with small-vessel disease without other indicators of cardiac risk.
- (3) For other stroke subtypes, use the patient’s risk profile to guide testing decisions (see below).

Estimating Cardiac Risk on the Basis of Patient Risk Factors

In addition to information from the diagnostic workup of the patient with TIA or stroke, risk of CHD can be estimated by using schemes that take into account readily available information from the patient’s history and risk profile. A scoring system based on data from the Framingham Study has been developed and is described in detail in an AHA Scientific Statement (Figures 1 and 2).⁴⁹ The patient’s score is based on age, sex, total blood cholesterol level, high-density lipoprotein cholesterol level, systolic blood pressure measurement,

Figure 1. Relative and absolute risk estimates for CHD in men as determined for Framingham scoring.⁴⁹ The number of Framingham points is derived as shown in Table 4. Relative risk estimates for each age range are compared with baseline risk conferred by age alone (in the absence of other major risk factors). Relative risk is graded and color-coded: Green indicates below-average risk; violet, average risk; yellow, moderately above-average risk; and red, high risk. Distinctions in relative risk are arbitrary. Average risk refers to that observed in the Framingham population. Absolute risk estimates are given in the 2 right-hand columns. Absolute risk is expressed as the percent likelihood of developing CHD per decade. Total CHD risk equates to all forms of clinical CHD, whereas hard CHD includes clinical evidence of MI and coronary death. Hard CHD estimates are approximated from the published Framingham data. *Low absolute risk level equals 10-year risk for total CHD end points for a person of the same age, a nonsmoker without diabetes and with blood pressure <120/80 mm Hg, total cholesterol of 160 to 199 mg/dL, high-density lipoprotein cholesterol ≥45 mg/dL. †Number of points estimated from Table 4. ‡Ten-year absolute risk for total CHD end points estimated from Framingham data corresponding to Framingham points (Table 4). §Ten-year absolute risk for hard CHD end points approximated from Framingham data corresponding to Framingham points (Table 4). Reproduced with permission from: Grundy SM, Pasternak R, Greenland P, et al. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*. 1999;100:1481–1492.⁴⁹

the presence or absence of diabetes, and whether the patient smokes cigarettes. The scores are transposed to a table that identifies patients as being at low, average, moderate, or high risk on the basis of their age and sex.

Although this system is based on data from the Framingham Heart Study, which primarily evaluated white patients of European descent, these guidelines are believed to be useful for other populations as well. This caveat was provided: “Although potential differences among various populations must be kept in mind when applying the Framingham scores, quantitative differences in risk predictions are likely to be small among most populations.”⁵⁰ In a recent report of a validation study of these predictors, the sex-specific coronary heart disease functions derived from Framingham data were applied to 6 prospectively studied, ethnically diverse cohorts (n=23 424), which included blacks, Native Americans, Japanese-American men, and Hispanic men. The Framingham functions performed reasonably well for white and black men and women but overestimated the risk of 5-year CHD events among Japanese-American and Hispanic men and Native American women. Recalibration factors that improved prediction for these latter groups were reported.⁵¹ Although a prospective application of this scoring system in stroke patients has not been reported and is needed, this scoring system could be used in ethnically diverse populations and is recommended for estimating CHD risk when assessing patient groups discussed in the present Statement. Patients with scores that indicate high risk should be counseled and considered for further testing and CHD risk factor control. See Table 4 for the risk assessment scheme.

Age (Low-risk level)*	40-44 (2%)	45-49 (3%)	50-54 (5%)	55-59 (7%)	60-64 (8%)	65-69 (8%)	70-74 (8%)	Absolute Risk	Absolute Risk
Points †								Total CHD‡	Hard CHD¶
0	1.0							2%	1%
1	1.0							2%	1%
2	1.5	1.0						3%	2%
3	1.5	1.0						3%	2%
4	2.0	1.3						4%	2%
5	2.0	1.3						4%	2%
6	2.5	1.7	1.0					5%	2%
7	3.0	2.0	1.2					6%	3%
8	3.5	2.3	1.4	1.0				7%	3%
9	4.0	2.7	1.6	1.1	1.0	1.0	1.0	8%	3%
10	5.0	3.3	2.0	1.4	1.3	1.3	1.3	10%	4%
11	5.5	3.7	2.2	1.6	1.4	1.4	1.4	11%	7%
12	6.5	4.3	2.6	1.9	1.6	1.6	1.6	13%	8%
13	7.5	5.0	3.0	2.1	1.9	1.9	1.9	15%	11%
14	9.0	6.0	3.6	2.6	2.3	2.3	2.3	18%	13%
15	10.0	6.7	4.0	2.9	2.5	2.5	2.5	20%	15%
16	12.0	8.0	4.8	3.4	3.0	3.0	3.0	24%	18%
≥ 17	>13.5	>9.0	>5.4	>3.9	5.4	5.4	5.4	>27%	>20%

* Low absolute risk level = 10-year risk for total CHD end points for a person the same age, blood pressure < 120/<80 mmHg, total cholesterol 160-199 mg/dL, HDL-C ≥55 mg/dL, nonsmoker, no diabetes. Percentages show 10-year absolute risk for total CHD end points.

† Points = number of points estimated from Table 4

‡ 10-year absolute risk for total CHD end points estimated from Framingham data corresponding to Framingham points (Table 4)

¶ 10-year absolute risk for hard CHD end points approximated from Framingham data corresponding to Framingham points (Table 4)

Key for Relative Risk

Green	Violet	Yellow	Red
Below average risk	Average risk	Moderately above average risk	High risk

Testing for Unrecognized CHD

The ACC/AHA practice guidelines for the management of chronic stable angina give specific recommendations for noninvasive testing for diagnosis of CHD in asymptomatic patients.¹ Although not specific to poststroke patients, the recommendations and levels of evidence can be useful in selecting tests for the stroke patient.

Several testing options are available for stroke patients who are being evaluated for unrecognized CHD. The most commonly used provocative tests for myocardial ischemia are exercise ECG, nuclear myocardial perfusion imaging, and stress echocardiography. The advantage of exercise stress ECG is that it provides an estimate of the patient's functional capacity, but it is unreliable in patients with an abnormal resting ECG, eg, left bundle-branch block or left ventricular hypertrophy. Echocardiography of the patient at rest is the preferred approach for evaluation of the cardiac chambers and heart valves.

In patients with significant functional impairment, however, dynamic exercise may not be possible, and pharmacological stress protocols with either nuclear myocardial perfusion imaging or echocardiography should be considered. For nuclear imaging, vasodilators such as adenosine or dipyridamole are frequently used agents for pharmacological stress. These drugs induce hyperemia in normal but not abnormal zones of the peripheral and coronary arterial circulation and

Figure 2. Relative and absolute risk estimates for CHD in women as determined for Framingham scoring.⁴⁹ The number of Framingham points is derived as shown in Table 4. Relative risk estimates for each age range are compared with baseline risk conferred by age alone (in the absence of other major risk factors). Relative risk is graded and color-coded: green indicates below-average risk; violet, average risk; yellow, moderately above-average risk; and red, high risk. Distinctions in relative risk are arbitrary. Average risk refers to that observed in the Framingham population. Absolute risk estimates are given in the 2 right-hand columns. Absolute risk is expressed as the percentage likelihood of developing CHD per decade. Total CHD risk equates to all forms of clinical CHD, whereas hard CHD includes clinical evidence of MI and coronary death. Hard CHD estimates are approximated from the published Framingham data. *Low absolute risk level equals 10-year risk for total CHD end points for a person of the same age, a nonsmoker without diabetes and with blood pressure <120/80 mm Hg, total cholesterol of 160 to 199 mg/dL, high-density lipoprotein cholesterol ≥45 mg/dL. †Number of points estimated from Table 4. ‡Ten-year absolute risk for total CHD end points estimated from Framingham data corresponding to Framingham points (Table 4). ¶Ten-year absolute risk for hard CHD end points approximated from Framingham data corresponding to Framingham points (Table 4). Reproduced with permission from: Grundy SM, Pasternak R, Greenland P, et al. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*. 1999;100:1481-1492.⁴⁹

are associated with a drop in systemic systolic and diastolic blood pressure of ≈10 mm Hg. Caution must be used in patients with hypotension at baseline, as there may be further decreases in blood pressure.

For stress echocardiography, dobutamine is the preferred pharmacological stress agent. Dobutamine is infused at increasing doses, starting at 5 or 10 μg/kg per minute and continuing to 50 μg/kg per minute. The lower doses may cause a drop in systemic blood pressure, and at higher doses, there may be hypertension. For this reason, patients need to be monitored closely, and inappropriate decreases or increases in blood pressure must be detected and treated. Guidelines on the use of these tests⁵² as well as on the use of coronary angiography have been published.⁵³ The current ACC/AHA practice guideline on exercise testing identifies exercise testing as a Class IIb recommendation for asymptomatic individuals with multiple risk factors as a guide to risk-reduction therapy, as well as for men >45 years of age and postmenopausal women >55 who are at high risk for CHD because of other diseases.⁵⁴ Although stroke was not specifically identified, the data cited above suggest that some types of stroke impart an intermediate or high pretest probability of coronary heart disease and may warrant testing. Although not specifically addressed in the literature, diagnostic tests for CHD, eg, electrocardiographic or nuclear exercise tests or dobutamine stress echocardiography, seem safe in

TABLE 4. Global Risk Assessment Scoring*

Risk Factor	Risk Points	
	Men	Women
Age, y		
<34	-1	-9
35-39	0	-4
40-44	1	0
45-49	2	3
50-54	3	6
55-59	4	7
60-64	5	8
65-69	6	8
70-74	7	8
Total cholesterol, mg/dL		
<160	-3	-2
169-199	0	0
200-239	1	1
240-279	2	2
280	3	3
HDL cholesterol, mg/dL		
<35	2	5
35-44	1	2
45-49	0	1
50-59	0	0
60	-2	-3
Systolic blood pressure, mm Hg		
<120	0	-3
120-129	0	0
130-139	1	1
140-159	2	2
>160	3	3
Diabetes		
No	0	0
Yes	2	4
Smoker		
No	0	0
Yes	2	2
Adding up the points:		
Age		
Cholesterol		
HDL cholesterol		
Blood pressure		
Diabetes		
Smoker		
Total Points		

*Add up total points and use Figures 1 and 2 to calculate relative and absolute risk estimates for coronary heart disease.

patients with cerebrovascular disease. Many of the studies reported below included patients with cerebrovascular disease. No disease-specific complications have been observed in these individuals.

There are limited data on the safety of stress testing after stroke. Macko et al⁵⁵ used a low-velocity graded treadmill in 31 hemiparetic patients who had stroke ≥ 3 months before testing. Seven of these patients had prior CHD history. Most patients (30 of 31) tolerated testing, achieving $84 \pm 10\%$ of maximal age-predicted heart rate. None had angina, but 13% had the testing terminated for cardiopulmonary signs/symptoms (dyspnea, 1; ST-segment depression, 2; ST depression with dyspnea, 1). The most common reason for termination was volitional fatigue (75%). In this series, 7 of 24 (29%) patients without clear CHD history had abnormal testing, confirmed with TI-201 testing in 5 of 6 who were further tested.

In the absence of more systematic data on stress testing, cardiac complications during stroke rehabilitation provide an estimate of potential risks of testing. In a review of 1029 patients treated in an academic rehabilitation facility after stroke, Roth et al⁵⁶ reported the frequency of medical complications that developed or were exacerbated during acute inpatient rehabilitation. No MIs were reported in this series, but 2.9% had angina; 3.2%, atrial arrhythmias; 2%, hypotension; 2%, CHF; and 0.5%, acute respiratory failure.⁵⁶

These data suggest that overall, exertion after stroke (at least that involved in rehabilitation) and exertion entailed in stress testing are associated with a low risk of serious cardiovascular complications. The enhanced monitoring involved in stress testing and the selection of patients without established CHD history provide a further measure of safety for the application of stress testing in the context of the present Scientific Statement.

Treatment of Asymptomatic CHD

The optimal management of patients with hemodynamically significant coronary arterial obstruction and asymptomatic or silent myocardial ischemia is unresolved.⁵⁷ Patients with silent ischemia and noninvasive manifestations of that ischemia, eg, very abnormal ECG exercise test results, have the same poor prognosis as persons with symptomatic ischemia and similar evidence of myocardial ischemia on noninvasive testing.⁵⁸⁻⁶⁰ Patients with silent ischemia can have severe coronary artery obstruction, and their prognosis is worse than that of an age- and sex-matched population without silent ischemia.⁶⁰⁻⁶⁷

Although definitive data are lacking, current information suggests that medical treatment or revascularization (coronary bypass surgery, angioplasty) anti-ischemic therapy favorably alters prognosis in patients with silent ischemia. Given the fact that the prognosis for these patients is worse than that for comparable healthy persons, it is reasonable to consider some form of therapy beyond risk factor reduction, pending further definitive research. However, it is important to state that definitive data are lacking for therapeutic outcomes in patients with concomitant coronary and cerebrovascular arterial disease. Thus, the following discussion and recommendations are based on opinion and not on hard clinical trial outcomes.

Two older small trials evaluated the outcome of therapy in patients with silent ischemia: the Asymptomatic Cardiac Ischemia Pilot Study (ACIP)⁶⁸ and the Atenolol Silent Ische-

mia Trial (ASIST).⁶⁹ Only the ASIST study used a placebo group. The ASIST trial involved 306 ambulatory patients with minimal or no angina pectoris, an abnormal exercise test result, and silent ischemia seen on ambulatory ECG monitoring. The patients were randomly assigned in double-blind fashion to receive 100 mg of atenolol per day or matching placebo. After 4 weeks of treatment, there was a significant decrease in the number of episodes of silent ischemia observed during ambulatory ECG monitoring. Event-free survival was also improved in the patients who received atenolol. The investigators concluded that antiischemic therapy with atenolol reduced both daily episodes of silent ischemia and adverse outcomes in this patient population. This study supports the widely held supposition that antiischemic therapy reduces adverse events in patients with CHD. Again, it is important to note that the number of patients in this trial with cerebrovascular disease is unknown, and hence, actual outcomes for this latter group of patients as compared with individuals with CHD alone are unknown.

The ACIP trial involved 558 patients with angiographically documented CHD and silent ischemia during ambulatory ECG monitoring.^{70–73} These patients were randomly assigned to 1 of 3 treatment strategies: (1) combination medical therapy consisting of either atenolol/nifedipine or diltiazem/isosorbide dinitrate; (2) coronary angioplasty; or (3) coronary bypass surgery. Patients were followed up for 1 year with ambulatory ECG monitoring and exercise testing. Revascularization therapy suppressed myocardial ischemia more effectively than medical therapy.

Coronary bypass surgery was also more effective than angioplasty in eradicating myocardial ischemia. The frequency of MI, unstable angina, stroke, and CHF did not differ among the 3 therapeutic options used. However, the total number of adverse events was lower in patients who underwent coronary bypass surgery than in those treated with angioplasty.⁷³ These studies indicate improved outcome if asymptomatic CHD is addressed. Definitive evidence and data on the cost-effectiveness of such an approach are not currently available from this older trial. Once more, it is important to reiterate that the number of patients with concomitant CHD and cerebrovascular disease in this trial is unknown, as are the outcomes for this subgroup of patients.

The ACC/AHA practice guidelines for coronary artery bypass graft (CABG) surgery in asymptomatic patients designate CABG as a Class I recommendation for (1) significant left main CHD, (2) left main equivalent (significant stenosis of proximal left anterior descending artery and proximal left circumflex artery), and (3) 3-vessel disease. CABG is a Class IIa recommendation for patients with proximal left anterior descending artery stenosis with 1- or 2-vessel disease.⁷⁴ Although these guidelines were not specifically developed with stroke patients in mind, they constitute a reasonable approach to take if significant evidence of CHD with severe, induced myocardial ischemia emerges from noninvasive diagnostic testing in the absence of other specific guidance. Stroke patients often share risk factors for CHD that adversely affect untreated prognosis but are also likely to have factors that increase the risk of complications with surgery, and this must be considered in individual treatment decisions.

Clearly, more randomized, controlled studies are needed in this area.

In the Setting of CE

The association of CHD and cerebrovascular occlusive disease is particularly relevant in patients undergoing CE because it may have an impact on surgical risk or potentially alter patient selection for CE. It may also dictate specific strategies of perioperative management of CE, including prophylactic, concurrent, or staged treatment of CHD.

No prospective studies have compared mortality and morbidity of CE among randomized strata of associated medical risks, including CHD. Retrospective analyses of large CE series, including recent randomized trials, have consistently demonstrated a statistically significant association between preoperative history of CHD and surgical risk, including operative mortality and early and late postoperative cardiac morbidity.^{75–79} In a study of 22 165 cases randomly selected from Medicare beneficiaries undergoing CE between 1988 and 1990 and followed up through 1992, there was a significant correlation between preoperative history of acute myocardial ischemia and CHF and perioperative death and stroke, as well as longer-term postoperative survival.⁸⁰

Several studies have assessed the prevalence of asymptomatic or clinically silent CHD by using consistent protocols of preoperative screening and have correlated silent CHD with postoperative mortality and cardiac morbidity after CE. In one study of 402 patients who underwent 447 CEs, there were no fatalities and only one instance of postoperative reversible cardiac ischemia (0.5%) among 198 patients without preoperative evidence of CHD; there were 2 deaths (1%) and 11 cases of postoperative ischemia (5.4%) among 204 patients with preoperative CHD detected by clinical or stress test screening ($P<0.05$).⁸¹ The mortality rate was 6.6%, all from cardiac causes, among 60 patients who underwent combined CE and coronary revascularization procedures for severe symptomatic concurrent carotid and coronary artery disease.

In another study, 172 consecutive CE procedures for symptomatic cerebrovascular disease conducted at a single institution were subjected to a consistent protocol of preoperative cardiac evaluation, including stress testing. There was a statistically significant stratification of postoperative risk for cardiac events among cases without CHD, those with silent CHD documented by preoperative stress test screening, and those with clinically overt CHD.⁸² A similar significant correlation of surgical cardiac morbidity and mortality was demonstrated in a retrospective study of 562 CEs, in which cardiac risk was stratified according to Goldman class I to IV and clinically silent CHD.⁸³ In the Veterans Affairs trial of CE for asymptomatic disease, a subgroup of patients without overt history of CHD but with other associated atherosclerotic vascular risk factors had a high perioperative risk of cardiac events similar to that of patients with symptomatic CHD.⁷⁵

No study with adequate statistical power has shown absence of association with CHD, including clinically silent disease, with morbidity after CE. Paradoxically, a recent analysis of surgical complications in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) re-

TABLE 5. Adapted From AHA/ACC Secondary Prevention for Patients With Coronary and Other Vascular Disease: 2001 Update

Goals	Intervention Recommendations									
<p>Smoking</p> <p>Goal: complete cessation</p>	<ul style="list-style-type: none"> ● Assess tobacco use. ● Strongly encourage patient and family to stop smoking and to avoid secondhand smoke. Provide counseling, pharmacological therapy (including nicotine replacement and bupropion), and formal smoking cessation programs as appropriate. 									
<p>Blood pressure control†</p> <p>Goal:</p> <p><140/90 mm Hg or <130/80 mm Hg if diabetes or chronic kidney disease</p>	<ul style="list-style-type: none"> ● Initiate lifestyle modification (weight control, physical activity, alcohol moderation, moderate sodium restriction, and emphasis on fruits, vegetables, and low-fat dairy products) in all patients with blood pressure \geq120 mm Hg systolic or 80 mm Hg diastolic. ● Add blood pressure medication, individualized to other patient requirements and characteristics (eg, age, race, need for drugs with specific benefits) if blood pressure is not <140 mm Hg systolic or 90 mm Hg diastolic or if blood pressure is not <130 mm Hg systolic or <80 mm Hg diastolic for individuals with diabetes or chronic kidney disease. 									
<p>Lipid management</p> <p>Primary goal: LDL 100 mg/dL</p>	<ul style="list-style-type: none"> ● Start dietary therapy in all patients (<7% saturated fat and <200 mg/d cholesterol), and promote physical activity and weight management. Encourage increased consumption of omega-3 fatty acids. ● Assess fasting lipid profile in all patients and within 24 h of hospitalization for those with an acute event. If patients are hospitalized, consider adding drug therapy on discharge. Add drug therapy according to the following guide: <table border="1" style="width: 100%; margin-top: 10px;"> <thead> <tr> <th colspan="3" style="text-align: center;">LDL at Baseline or on Treatment, mg/dL</th> </tr> <tr> <th style="text-align: center;">100</th> <th style="text-align: center;">100 to 129</th> <th style="text-align: center;">\geq130</th> </tr> </thead> <tbody> <tr> <td style="vertical-align: top;">Further LDL-lowering therapy not required. Consider fibrate or niacin (if low HDL or high TG).</td> <td style="vertical-align: top;">Therapeutic options: Intensify LDL-lowering therapy (statin or resin*). Fibrate or niacin (if low HDL or high TG). Consider combined drug therapy (statin, fibrate, or niacin) (if low HDL or high TG).</td> <td style="vertical-align: top;">Intensify LDL-lowering therapy (statin or resin*). Add or increase drug therapy with lifestyle therapies.</td> </tr> </tbody> </table>	LDL at Baseline or on Treatment, mg/dL			100	100 to 129	\geq 130	Further LDL-lowering therapy not required. Consider fibrate or niacin (if low HDL or high TG).	Therapeutic options: Intensify LDL-lowering therapy (statin or resin*). Fibrate or niacin (if low HDL or high TG). Consider combined drug therapy (statin, fibrate, or niacin) (if low HDL or high TG).	Intensify LDL-lowering therapy (statin or resin*). Add or increase drug therapy with lifestyle therapies.
LDL at Baseline or on Treatment, mg/dL										
100	100 to 129	\geq 130								
Further LDL-lowering therapy not required. Consider fibrate or niacin (if low HDL or high TG).	Therapeutic options: Intensify LDL-lowering therapy (statin or resin*). Fibrate or niacin (if low HDL or high TG). Consider combined drug therapy (statin, fibrate, or niacin) (if low HDL or high TG).	Intensify LDL-lowering therapy (statin or resin*). Add or increase drug therapy with lifestyle therapies.								
<p>Lipid management</p> <p>Secondary goal: If TG \geq200 mg/dL, then non-HDL† should be <130 mg/dL</p>	<ul style="list-style-type: none"> ● If TG \geq150 mg/dL or HDL <40 mg/dL: Emphasize weight management and physical activity. Advise smoking cessation. ● If TG 200 to 499 mg/dL: Consider fibrate or niacin after LDL-lowering therapy.* ● If TG \geq500 mg/dL: Consider fibrate or niacin before LDL-lowering therapy.* ● Consider omega-3 fatty acids as adjunct for high TG. 									
<p>Physical activity</p> <p>Minimum goal</p> <p>30 minutes 3 to 4 days per week</p> <p>Optimal daily</p>	<ul style="list-style-type: none"> ● Assess risk, preferably with exercise test, to guide prescription. ● Encourage minimum of 30 to 60 minutes of activity, preferably daily, or at least 3 or 4 times weekly (walking, jogging, cycling, or other aerobic activity) supplemented by an increase in daily lifestyle activities (eg, walking breaks at work, gardening, household work). Advise medically supervised programs for moderate- to high-risk patients. 									
<p>Weight management</p> <p>Goal: BMI 18.5–24.9 kg/m²</p>	<ul style="list-style-type: none"> ● Calculate BMI and measure waist circumference as part of evaluation. Monitor response of BMI and waist circumference to therapy. ● Start weight management and physical activity as appropriate. Desirable BMI range is 18.5 to 24.9 kg/m². ● When BMI \geq25 kg/m², goal for waist circumference is \leq40 inches in men and \leq35 inches in women. 									
<p>Diabetes management</p> <p>Goal: HbA_{1c} <7%</p>	<ul style="list-style-type: none"> ● Appropriate hypoglycemic therapy to achieve near-normal fasting plasma glucose, as indicated by HbA_{1c}. ● Treatment of other risks (eg, physical activity, weight management, blood pressure, and cholesterol management). 									
<p>Antiplatelet agents/anticoagulants</p>	<ul style="list-style-type: none"> ● Start and continue indefinitely aspirin 75 to 325 mg/d if not contraindicated. ● Consider clopidogrel 75 mg/d or warfarin if aspirin contraindicated. Manage warfarin to international normalized ratio =2.0 to 3.0 in post-MI patients when clinically indicated or for those not able to take aspirin or clopidogrel. 									
<p>ACE inhibitors</p>	<ul style="list-style-type: none"> ● Treat all patients indefinitely after MI; start early in stable high-risk patients (anterior MI, previous MI, Killip class II [S₃ gallop, rales, radiographic CHF]). ● Consider chronic therapy for all other patients with coronary or other vascular disease unless contraindicated. 									
<p>β-Blockers</p>	<ul style="list-style-type: none"> ● Start in all post-MI and acute ischemic syndrome patients. Continue indefinitely. Observe usual contraindications. ● Use as needed to manage angina, rhythm, or blood pressure in all other patients. 									

TG indicates triglycerides; BMI, body mass index; and HbA_{1c}, major fraction of adult hemoglobin.
 *The use of renin is relatively contraindicated when TG >200 mg/dL.
 †Non-HDL cholesterol=total cholesterol minus HDL cholesterol.
 ‡Blood pressure section consistent with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).⁹⁴

vealed a lower rate of perioperative events in patients with a history of treated CHD,⁸⁴ indicating potential protection from perioperative events in patients with diagnosed and treated CHD compared with patients who were not treated for CHD who may have harbored silent myocardial ischemia.

There is no consensus with regard to the most optimal or necessary preoperative assessment of cardiac and medical risks before CE. Associated medical risks including CHD may affect indications for CE, especially in asymptomatic patients and those with less severe carotid stenosis for whom surgery may be less beneficial. In patients with symptomatic carotid artery stenosis, more advanced medical risk factors were associated with higher surgical risk and with greater absolute and relative reduction in stroke and death after CE.⁸⁴

There is no specific evidence to support altering perioperative management protocols in the setting of silent or clinically overt CHD. Most authors have advocated judicious anesthetic and medical measures in the perioperative period in patients with known, treated, or asymptomatic CHD. Others have advocated aggressive treatment of CHD before, with, or closely staged after CE. No level I or level II evidence supports a particular strategy of management of concurrent CHD and CE, and an earlier AHA guideline on CE⁸⁵ did not identify a best treatment strategy on the basis of current evidence.

Risk Factor Reduction

Regardless of the choice for medical or surgical management, stroke patients, especially those with atherosclerotic risk factors and subclinical CHD detected by testing, should undergo comprehensive and aggressive risk factor reduction. The 2001 AHA/ACC guidelines for preventing heart attack and death in patients with coronary and other vascular disease provide risk factor goals and intervention recommendations for these patients.⁸⁶ The summary table (Table 5) from the guidelines is included for reference. Patients with stroke not related to atherosclerosis should receive primary prevention risk reduction counseling.⁸⁷

Summary Recommendations

More research is needed to determine the optimal approach to recognition and treatment of asymptomatic coronary disease in patients with cerebral ischemia, preferably on the basis of ischemic stroke subtype. For more information, the reader is also referred to other reviews on this subject.^{88–91} However, the existing information is sufficient to allow the following recommendations, pending more definitive data.

- (1) All patients with ischemic stroke or TIA should undergo a comprehensive assessment of cardiovascular risk, preferably scored on the basis of existing recommendations (such as those in Table 5) to identify those with the highest likelihood of morbidity and mortality from unrecognized CHD. In all cases, risk factor reduction is recommended independent of the decision to perform noninvasive cardiac testing.⁸⁶
- (2) Because unrecognized CHD is prevalent in patients with carotid artery disease, selected patients with high cardiovascular risk profiles and symptoms of brain ischemia in

the presence of significant carotid disease should be considered for noninvasive testing for CHD.

- (3) Regardless of stroke subtype, patients with high CHD risk factor scores based on Framingham algorithms (10-year CHD risk $\geq 20\%$) should also be considered for such evaluation.⁴⁹
- (4) Those with fewer CHD risk factors who do not have significant carotid artery disease or who present with stroke subtypes not clearly related to atherosclerosis are at lower risk for CHD, and routine testing is not recommended on the basis of the current state of knowledge.
- (5) Testing for CHD can be accomplished by using one of several methods described in the ACC/AHA Practice Guidelines.^{1,54} Pharmacological stress testing may be needed in cases of significant physical impairment. Because the short-term risk for cardiac morbidity/mortality is relatively low, in most cases, cardiac evaluation generally should not be done in the acute stroke setting unless there is concern that the patient may not be available at a later time for this evaluation.
- (6) What constitutes significant coronary disease as well as medical versus surgical treatment must be individualized pending further studies. Both evaluation and subsequent treatment should be guided by current guidelines.^{1,49,53,54,74,86,87,92}
- (7) Routine testing for CHD before CE is not recommended but may be prudent for subgroups at high risk on the basis of the patient's atherosclerotic risk profile.
- (8) Diagnostic testing to determine stroke mechanisms of the patient with symptoms of brain ischemia is recommended because these evaluations, especially determination of the presence and severity of carotid artery disease, provide useful information for quantifying the patient's risk for unrecognized cardiac disease, as well as selection of the best secondary stroke prevention strategies.⁹³
- (9) Systematic research on CHD testing in specific subtypes of stroke should be undertaken to determine optimal methods for patient selection, testing, and treatment, as well as the economic impact of strategies that seek to minimize cardiac comorbidity in the patient with ischemic stroke.

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