section one

SCREENING

1. Screening for Asymptomatic Coronary Artery Disease

RECOMMENDATION

There is insufficient evidence to recommend for or against screening middle-aged and older men and women for asymptomatic coronary artery disease, using resting electrocardiography (ECG), ambulatory ECG, or exercise ECG. Recommendations against routine screening can be made on other grounds for individuals who are not at high risk of developing clinical heart disease (see *Clinical Intervention*). Routine screening is not recommended as part of the periodic health visit or pre-participation sports examination for children, adolescents, or young adults. Clinicians should emphasize proven measures for the primary prevention of coronary disease (see *Clinical Intervention*).

Burden of Suffering

Ischemic heart disease is the leading cause of death in the U.S., accounting for approximately 490,000 deaths in 1993.[1] The American Heart Association estimates that approximately 1.5 million Americans will suffer a myocardial infarction (MI) in 1995, and one third will not survive the event.[2] Atherosclerotic coronary artery disease (CAD) is the underlying cause of most ischemic cardiac events and can result in myocardial infarction, congestive heart failure, cardiac arrhythmias, and sudden cardiac death. Clinically significant CAD is uncommon in men under 40 and premenopausal women, but risk increases with advancing age and in the presence of risk factors such as smoking, hypertension, diabetes, high cholesterol, and family history of heart disease. Although mortality from heart disease has declined steadily over the past three decades in the U.S.,[2] the total burden of coronary disease is predicted to increase substantially over the next 30 years due to the increasing size of the elderly population.[3] The cost of medical care and lost economic productivity due to heart disease in the U.S. has been projected to exceed $60 billion in 1995.[2]

Angina is the most common presenting symptom of myocardial ischemia and underlying CAD, but in many persons the first evidence of CAD may be myocardial infarction or sudden death.[4] It has been estimated that 1–2 million middle-aged men have asymptomatic but physiologically significant coronary disease, also referred to as silent myocardial ischemia.[4,5]

Accuracy of Screening Tests

There are two screening strategies to reduce morbidity and mortality from CAD. The first involves screening for modifiable cardiac risk factors, such as hypertension, elevated serum cholesterol, cigarette smoking, physical inactivity, and diet (see Chapters 2, 3, and 54–56). The second strategy is early detection of asymptomatic CAD. The principal tests for detecting asymptomatic CAD include resting and exercise ECGs, which can provide evidence of previous silent myocardial infarctions and silent or inducible myocardial ischemia. Thallium-201 scintigraphy, exercise echocardiography, and ambulatory ECG (Holter monitoring) are less commonly used for screening purposes. The efficacy of each of these tests may be evaluated by (a) its ability to detect atherosclerotic plaque, and (b) its ability to predict the occurrence of a serious clinical event in the future (acute MI, sudden cardiac death).

Several resting ECG findings (ST depression, T-wave inversion, Q waves, and left axis deviation) increase the likelihood of coronary atherosclerosis and of future coronary events. However, these findings are uncommon in asymptomatic persons, occurring in only 1–4% of middle-aged men without clinical evidence of CAD,[6,7] and they are not specific for CAD. One third to one half of patients with angiographically normal coronary arteries have Q waves, T-wave inversion, or ST-T changes on their resting ECG.[8–10] Conversely, a normal ECG does not rule out CAD. In the Coronary Artery Surgery Study, 29% of patients with symptomatic, angiographically proven CAD demonstrated a normal resting ECG.[11] Asymptomatic persons with baseline ECG abnormalities (Q waves, ST-segment depression, T-wave inversion, left ventricular hypertrophy, and ventricular premature beats) have a higher risk of future coronary events.[6,12–19] However, prospective studies lasting between 5 and 30 years have found that symptomatic CAD develops in only 3–15% of persons with these ECG findings.[6,13,18,20] Furthermore, most coronary events occur in persons without resting ECG abnormalities.[6,7,18,21,22] Thus, routine ECG testing in asymptomatic persons, in whom the pretest probability of having CAD is relatively low, is not an efficient process for detecting CAD or for predicting future coronary events.

The exercise ECG is more accurate than the resting ECG for detecting clinically important CAD. Most patients with asymptomatic CAD do not have a positive exercise ECG, however.[23–26] ECG changes often do not become apparent until an atherosclerotic plaque has progressed to the point that it significantly impedes coronary blood flow.[24,27] In addition, most asymptomatic persons with an abnormal exercise ECG result (usually defined by a specific magnitude of ST-segment depression) do not have underlying CAD.[27,28] A 1989 meta-analysis found considerable variability in the accuracy of exercise-induced ST depression for predicting CAD (sensitivity 23–100%, specificity 17–100%).[29] Although several investigators reported that adjusting the ST segment for heart rate (ST/HR slope or ST/HR index) improves the ability to predict significant CAD[30–32] and future coronary events,[25] other studies have not shown an advantage.[33–37]

The exercise ECG is also more accurate than the resting ECG in predicting future coronary events. While asymptomatic persons with a positive exercise ECG are more likely to experience an event than those with negative tests,[25,38–43] longitudinal studies following such patients from 4 to 13 years have shown that only 1–11% will suffer an acute MI or sudden death.[25,42,44,45] As with resting ECG, the majority of events will occur in those with a negative exercise test result.[24,26,44–47] The pathophysiology of acute coronary syndromes may explain the insensitivity of exercise ECG for subsequent coronary events. Unstable angina, MI, and sudden death often result from an acute, occluding thrombus precipitated by the rupture of a mild, non-flow-limiting plaque.[48–50] Among healthy men who subsequently developed symptomatic CAD after a negative screening test, 73% experienced a MI or sudden death as their initial manifestation.[24,45] In contrast, the majority of asymptomatic persons with a positive exercise ECG develop angina as their initial event.[5,24,45,51] Thus, while exercise ECG may predict the presence of more severe coronary stenosis and risk of angina in asymptomatic persons, it does not accurately predict risk of acute coronary events.

The addition of thallium-201 scintigraphy to conventional exercise testing improves its accuracy in detecting CAD, making it a useful diagnostic test in persons with symptoms of CAD.[52,53] However, the probability of CAD after a positive scan is low in asymptomatic persons, and most coronary events occur in those with a negative test result.[23,44] Because of these limitations and its expense, thallium-201 scintigraphy is not a practical screening test for asymptomatic persons.[23,44,52,54] The ambulatory ECG can detect episodes of ST-segment depression which may indicate silent ischemia in asymptomatic persons with CAD. These episodes, however, also occur commonly in healthy volunteers[55–57] and are not reliable predictors of future coronary events, even in asymptomatic or mildly symptomatic patients with documented CAD.[58,59] There have been no studies of exercise echocardiography in screening asymptomatic populations for CAD.

False-positive screening test results are undesirable for several reasons. Persons with abnormal results frequently undergo invasive diagnostic procedures such as coronary angiography. Abnormal test results may produce considerable anxiety. An abnormal ECG tracing may disqualify some patients from jobs, insurance eligibility, and other opportunities, although the extent of these problems is not known. Proposed strategies for reducing false-positive results include: performing workups in accordance with a Bayesian model;[60] using discriminant functions to interpret the stress ECG;[41] and targeting testing to high-risk groups.

Effectiveness of Early Detection

Although case-control and cohort studies show that asymptomatic persons with selected ECG findings are at increased risk of MI and cardiac death,[5,7,22,25,38–43] there is little evidence that routine screening is an effective means to reduce the incidence of acute coronary events in asymptomatic persons. Antianginal drugs such as nitroglycerin, β-adrenergic blockers, and calcium channel blockers reduce the frequency and the duration of silent ischemia.[61–63] In a recent study, atenolol reduced the incidence of cardiac events (MI, cardiac arrest, or worsening angina) in patients who had both silent ischemia and CAD documented by angiography or prior MI;[64,65] extrapolating these benefits to completely asymptomatic patients with silent ischemia on routine screening may not be justified, given their much lower risk of acute events.[46]

Both aspirin therapy and drug treatment for high cholesterol reduce the incidence of MI and cardiac mortality in patients with symptomatic coronary disease, but the balance of risks and benefits of these therapies in asymptomatic patients is not resolved (see Chapters 2 and 69). Benefits are more likely to exceed risks in asymptomatic patients with underlying coronary disease, however, due to their higher absolute risk of MI and coronary death. New diagnostic techniques may prove more sensitive than angiography in identifying the mild-to-moderate plaques that are a risk factor for developing an acute occlusive thrombus.[66,67] Their utility will remain in question, however, until appropriate trials demonstrate that early detection and treatment of small coronary plaques is more effective than treatment based on identifiable risk factors (e.g., high blood pressure or high cholesterol) in asymptomatic patients.[48,49]

Among patients with symptomatic coronary disease, coronary artery bypass grafting prolongs life compared with medical therapy in patients with left main coronary or three-vessel disease with poor left ventricular function.[11] The prevalence of high-risk coronary disease among asymptomatic persons, however, is very low; while some patients may suffer a MI or sudden cardiac death as their initial manifestation of CAD, most patients with severe coronary disease initially develop angina.[5,45] As a result, it is not clear that the benefit of identifying a small number of individuals with severe coronary disease before they develop symptoms is sufficient to justify routine screening of large populations of asymptomatic persons. Recent randomized trials have demonstrated that percutaneous transluminal coronary angioplasty (PTCA) reduces the frequency of angina in patients with symptomatic CAD, but it does not reduce the incidence of MI or cardiac death.[68,69] The value of coronary angioplasty for asymptomatic coronary stenoses is not known.

A screening ECG has been recommended to provide a "baseline" to help interpret changes in subsequent ECGs.[70] Even when important differences are noted between the baseline ECG and a subsequent tracing, these do not necessarily reflect ongoing or recent ischemia. Using the development of a new Q wave on serial ECG as a criterion, the Framingham Study reported an annual incidence of unrecognized MI of 5.4/1,000 men aged 65–74.[71] Less specific changes develop more commonly than Q waves. Baseline ECGs are often not available when needed for comparison, nor do they significantly contribute to decision making for patients being evaluated for chest pain,[72–75] especially in those with no history of cardiovascular disease.[76] One large study found that a baseline ECG was available in 55% of patients evaluated for acute chest pain.[73] The availability of a prior ECG was associated with small but significant reduction in hospitalization rates for those patients who had chest pain not due to acute MI. Only a small subset of the asymptomatic population is likely to benefit from having a baseline ECG, however: those with baseline ECG abnormalities suggestive of ischemia who subsequently develop acute noncardiac chest pain. Savings from preventing a few unnecessary hospitalizations among these patients must be weighed against the high costs of routine ECG screening in the large population of asymptomatic persons.

Another argument for ECG screening is that the early identification of persons at increased risk for CAD on the basis of ECG findings may help to modify other important cardiac risk factors such as cigarette smoking, hypertension, and elevated serum cholesterol.[70] While the efficacy of risk factor modification is well established,[22,77] no studies have evaluated whether identifying high-risk patients with abnormal ECGs improves efforts to modify risk factors or leads to better clinical outcomes.

Periodic ECG screening is often recommended for persons who might endanger public safety were they to experience an acute cardiac event at work (e.g., airline pilots, bus and truck drivers, railroad engineers). Cardiac events in such individuals are more likely to affect the safety of a large number of persons, and clinical intervention, either through medical treatment or work restrictions, might prevent such catastrophes. No studies have addressed the efficacy of ECG screening in these persons, however.

Preliminary exercise ECG testing has also been recommended for sedentary persons planning to begin vigorous exercise programs, based on evidence that strenuous exertion may increase the risk of sudden cardiac death. The usual underlying cause of sudden cardiac death during exercise is hypertrophic cardiomyopathy or congenital coronary anomalies in young persons and CAD in older persons. Cardiac events during exercise in persons without symptomatic heart disease are uncommon, however, and exercise ECG may not accurately predict those who are at risk. Among over 3,600 asymptomatic, hypercholesterolemic middle-aged men who underwent submaximal exercise ECG during the Lipid Research Clinics Coronary Primary Prevention Trial, 62 (2%) subsequently experienced an acute cardiac event during moderate or strenuous physical activity during follow-up (average 7.4 years).[78] Although men with exercise-induced ECG changes were at increased risk, only 11 of 62 events occurred in men with an abnormal baseline exercise test (sensitivity 18%). Moreover, few of the men with abnormal test results experienced an activity-related event during follow-up (positive predictive value 4%). Although the negative predictive value of baseline ECG was high (over 98%), it was no better than multivariate analysis based on clinical risk factors alone. Given the low incidence of activity-related events in middle-aged men, and the uncertain benefit of restricting activity in those with abnormal exercise tests, the potential benefits of pre-exercise testing appear small. In populations at low risk for heart disease, any benefits of detecting the rare individual with asymptomatic CAD may be offset by adverse effects of labeling and exercise restrictions for the larger number of persons with false-positive ECG results.

Recommendations of Other Groups

The routine use of resting electrocardiogram to screen for CAD in asymptomatic adults is not recommended by the American College of Physicians (ACP)[79] or the Canadian Task Force on the Periodic Health Examination.[80] The American Academy of Family Physicians (AAFP) recommends a baseline electrocardiogram for men 40 years and older with two or more cardiac risk factors and sedentary men about to begin a vigorous exercise program; this recommendation is under review.[81] A task force sponsored by the American College of Cardiology and the American Heart Association (ACC/AHA) recommends baseline testing for all persons over 40 years of age and for those about to have exercise stress testing.[82]

The AAFP recommends exercise electrocardiography for those whose jobs are linked to public safety (e.g., pilots, air traffic controllers) or that require high cardiovascular performance (e.g., police officers, firefighters).[81] The American College of Sports Medicine recommends exercise ECG testing for men over age 40, women over age 50, and other asymptomatic persons with multiple cardiac risk factors, prior to beginning a vigorous exercise program.[83] The ACC/AHA recognize that the exercise

ECG is frequently used to screen asymptomatic persons in some high-risk groups but concluded that there is divergence of opinion with respect to its usefulness.[84] The ACP does not recommend exercise testing with ECG or thallium scintigraphy as a routine screening procedure in asymptomatic adults.[79,85]

Discussion

Heart disease is the leading cause of death in the U.S., and interventions that produce even modest reductions in the incidence of acute ischemic events may have substantial public health benefits. Although the resting electrocardiogram can detect evidence of coronary heart disease in asymptomatic persons and identify individuals at increased risk of future coronary events, the ECG has important weaknesses as a screening test. The large majority of asymptomatic persons with abnormal ECG results do not have CAD and are at relatively low risk for developing symptomatic heart disease in the near future. Routine screening may subject many of them to the inconvenience, expense and potential risks of follow-up testing (i.e., cardiac catheterization or radionuclide imaging) to evaluate false-positive screening results. Although exercise testing is more sensitive and specific for high-grade coronary stenoses, the exercise ECG is too time-consuming and expensive for routine use in asymptomatic persons. Finally, neither resting nor exercise ECG reliably detects the mild to moderate atherosclerotic lesions which are often responsible for acute coronary events.

A second important problem with screening for asymptomatic CAD is the lack of evidence that earlier detection leads to better outcomes. The only interventions proven to reduce coronary events in asymptomatic persons are modifications of risk factors such as smoking, high cholesterol, and elevated blood pressure. These interventions, however, should be encouraged for all patients with modifiable risk factors, not only those with screening tests suggestive of CAD. The benefits of more invasive treatments for coronary stenosis (e.g., bypass surgery, angioplasty) are unproven in asymptomatic persons. For certain occupations, such as pilots and heavy equipment operators, where sudden death or incapacitation would endanger the safety of others, considerations other than benefit to the individual patient may favor screening. Although screening cannot reliably identify all persons at risk of an acute event, it may increase the margin of safety for the public.

To minimize the potential adverse effects of false-positive test results, routine screening with ECG should be avoided in populations where the prevalence of CAD is low, including most adults under 40, and middle-aged men and women without coronary risk factors. Even in high-risk individuals, the benefits of screening to identify asymptomatic CAD are unproven. For some persons, however, identifying those at high risk of coronary mortality may help guide treatment decisions (e.g., use of aspirin or cholesterol-lowering drugs).

There are major costs associated with widespread screening with resting ECG in asymptomatic adults, and use of other screening tests (ambulatory ECG, exercise testing, and echocardiography) would be substantially more expensive.[79] The inconvenience, expense, and potential risks of routine screening might be justified if it significantly reduced the incidence of MI and sudden cardiac death, but such evidence is not yet available. Until appropriate studies demonstrate a benefit of screening for CAD, identification and treatment of major cardiac risk factors such as hypertension, elevated serum cholesterol, and cigarette smoking remain the only proven measures for reducing coronary morbidity and mortality in asymptomatic persons.

CLINICAL INTERVENTION

There is insufficient evidence to recommend for or against screening middle-aged and older men and women for asymptomatic coronary artery disease with resting electrocardiography (ECG), ambulatory ECG, or exercise ECG ("C" recommendation). Recommendations against routine screening may be made on other grounds for persons who are not at high risk of developing symptomatic CAD; these grounds include the limited sensitivity and low predictive value of an abnormal resting ECG in asymptomatic persons, and the high costs of screening and follow-up. Screening selected high-risk asymptomatic persons (e.g., those with multiple cardiac risk factors) is indicated only where results will influence treatment decisions (e.g., use of aspirin or lipid-lowering drugs in asymptomatic persons). Screening individuals in certain occupations (pilots, truck drivers, etc.) can be recommended on other grounds, including possible benefits to public safety. The choice of specific screening test for asymptomatic CAD is left to clinical discretion: exercise ECG is more accurate than resting ECG but is considerably more expensive.

Routine ECG screening as part of the periodic health visit or preparticipation sports physical is not recommended for asymptomatic children, adolescents, and young adults ("D" recommendation).

Clinicians should emphasize proven measures for the primary prevention of coronary disease in all patients (see Chapter 3, Screening for Hypertension; Chapter 2, Screening for High Blood Cholesterol; Chapter 54, Counseling to Prevent Tobacco Use; Chapter 55, Counseling to Promote Physical Activity; and Chapter 56, Counseling to Promote a Healthy Diet).

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