PERSPECTIVE

MICHAEL S. LAUER, MD*
Director, Division of Prevention and Population Science, National Heart, Lung, and Blood Institute, National Institutes of Health; Contributing Editor, *JAMA*

Screening for coronary heart disease: Has the time for universal imaging arrived?

ABSTRACT

The Screening for Heart Attack Prevention and Education (SHAPE) Task Force has recommended a strategy of screening for coronary heart disease in which nearly all middle-aged and older adults would undergo an imaging test. However, this approach is not supported by evidence and is not endorsed by professional societies or the US Preventive Services Task Force. Physicians should follow established guidelines such as those of the third Adult Treatment Panel of the National Cholesterol Education Program.

KEY POINTS

Observational studies can overestimate the benefit of screening tests in reducing disease-specific mortality rates, owing to lead-time bias, length-time bias, and overdiagnosis bias.

The Framingham risk score uses clinical variables to give an estimate of a patient's 10-year risk of coronary events. Imaging tests may have a role in patients at intermediate risk.

Rather than subjecting all adults to a screening test with its expense and potential harms, a better use of resources might be in public health efforts to improve the national diet, promote exercise, and discourage smoking. Resources could also be directed to performance of definitive randomized trials aimed at testing the therapeutic value of screening tests.

*Dr. Lauer receives support from the National Heart, Lung, and Blood Association (R01 HL-66004, R01 HL-072771, and P50 HL-77107, and K12 HD049091). He reports no personal financial relationships with any private commercial pharmaceutical, device, or imaging companies.

A 48-YEAR-OLD MAN is concerned about coronary heart disease because two of his colleagues recently had heart attacks. Yesterday, while driving home from work, he heard an advertisement on the radio for a heart scan, which he understood as being a test that could "save his life."

He remembers that 2 months ago you did an office evaluation, including lipid blood tests, and you told him that his heart risk was low. Still, rattled by the two heart attacks at his office, he worries that your evaluation may not be enough. "Shouldn't I get that heart scan I heard about on the radio, doctor?" he asks, and then adds, "Were all those blood tests you did really needed?"

When you evaluated him, his blood pressure was 125/78 mm Hg, his total cholesterol level was 220 mg/dL, and his high-density lipoprotein cholesterol (HDL-C) level was 40 mg/dL. You noted no history of chest discomfort or shortness of breath, cigarette smoking, diabetes, obesity or other evidence of the metabolic syndrome, or family history of premature coronary disease. You assessed his risk using the Framingham risk score,[1] which indicated that his risk of having a major cardiac event within the next 10 years was 5% (**FIGURE 1**).

Should you order the imaging test as he asks? Should you have done the imaging test first, without assessing his global risk with the Framingham risk score? What is the best evidence-based approach to your patient's concerns?

Our patient's Framingham risk score

Risk score results	
Age	48
Sex	Male
Total cholesterol	220 mg/dL
HDL cholesterol	40 mg/dL
Smoker	No
Systolic blood pressure	125 mm Hg
On medication for high blood pressure	No
Risk score*	5%

*The risk score shown was derived on the basis of an equation. Other National Cholesterol Education Program materials, such as the third Adult Treatment Panel (ATP III) print products, use a point-based system to calculate a risk score that approximates the equation-based one.
To interpret the risk score and for specific information about coronary heart disease risk assessment as part of detection evaluation, and for treatment of high blood cholesterol, see ATP III Executive Summary and ATP III At-a-Glance.

FIGURE 1. The Framingham risk score is the patient's risk of having a coronary event in the next 10 years. This tool can be accessed at http://hp2010.nhlbihin.net/atpiii/calculator.asp?user type=prof.

A PROPOSAL FOR MORE AGGRESSIVE SCREENING

The issue of when and how to evaluate patients for their risk of cardiovascular disease came to the forefront in July 2006 with the publication of the paper, "From vulnerable plaque to vulnerable patient—part III; executive summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force report."[2] This paper, from a group of prominent authors, recommended aggressive screening with imaging, notably calcium scanning or ultrasound measurement of the carotid arteries.

However, I believe that such an approach, which de-emphasizes the use of traditional cardiovascular risk-assessment techniques, is premature and is not supported by the evidence.

WHAT IS SCREENING, AND WHEN IS IT APPROPRIATE?

Screening is a process by which patients without symptoms undergo testing to determine whether they have a disease. Examples of accepted screening tests are mammography,[3] cervical cytology,[4] and sphygmomanometry.[5] Screening is appropriate for common serious diseases that have a prolonged, asymptomatic phase.[6] By detecting the disease early, physicians and patients can initiate effective treatments that can prevent symptoms, premature life-threatening events, or both.

Screening is appropriate only if early detection and early therapy yield better outcomes than late detection and late therapy.[6] For example, some breast cancers develop so slowly that, if detected at an early stage by mammography, they can be completely eradicated; this would be more difficult should one wait for symptoms. Investigators have shown that screening reduces the rate of deaths due to breast cancer.[3]

Another example of appropriate screening is ultrasound imaging of the abdominal aorta, at least in older men who smoke, in whom routine screening has been shown to detect aneurysms accurately and prevent aneurysm-related deaths.[7]

Current screening strategies for adults at risk of coronary heart disease events who have no symptoms of it are based on scoring algorithms that use only classic risk factors, such as age, sex, diabetes, hypertension, smoking, and cholesterol levels.[8,9] Assessing these risk factors is reasonable, since randomized trials have shown, for example, that treatment of asymptomatic hypertension[5] and hypercholesterolemia[1] prevents clinical events.

Some investigators believe that the estimates of risk can be sharpened by adding information from screening tests such as coronary calcium scoring, to better identify people at high risk who have advanced atherosclerosis (**FIGURE 2**) so that drugs such as aspirin or statins can be added to lifestyle interventions to prevent premature death or myocardial infarction.[10]

But is screening for coronary heart disease effective?

HOW DO WE KNOW SCREENING SAVES LIVES?

Determining whether a screening test is effective is difficult. It is not enough to show that the test predicts future events: we need to

prove that a screening strategy, as opposed to a symptom-based approach, reduces the rate of major clinical events.[11]

Observational studies are fraught with problems

Some investigators perform large observational studies, comparing outcomes of people who do or do not undergo screening. If the people who undergo a screening test have a lower death rate, it is tempting to conclude that the screening is effective. However, this observational approach is fraught with problems, including lead-time bias, length-time bias, and overdiagnosis bias.[12,13] Clinicians need to understand these biases and explain them to their patients.

Lead-time bias occurs when physicians diagnose a disease earlier than they would have if they had waited for symptoms to arise, but the natural history is the same.[12] Imagine a patient with a disease that ultimately will kill him in 2010. With screening we can diagnose the disease this year (2007), but without screening we would have to wait until symptoms occur (say, in 2009). However, if the current treatments are not very effective, it would make no difference whether we diagnose the disease in 2007 or 2009, as the patient is fated to die in 2010. Screening might *appear* to help, because he lived 3 years after diagnosis rather than 1 year. Yet, in reality, the screening test did nothing except detect the disease earlier.

Length-time bias is more difficult to understand.[12] Imagine two patients who both decide to see their doctor for a screening test next July. The first patient has a rapidly growing tumor, which he does not yet know about. By April, unfortunately, the tumor causes symptoms, and therefore he cancels his July screening test. The second patient has a slow-growing tumor, and therefore he shows up for his July screening test. Since only the patient with the slowly growing tumor underwent screening, the screening strategy appears to improve his outcome, when in fact it is actually the tempo of the disease that determines who gets screened.

Overdiagnosis bias is perhaps the most serious screening bias.[12] In this case, a physician diagnoses a disease that, while real, is unlikely to ever be clinically important. For example, among older men, prostate cancers are common but some never cause clinical symptoms or death. One is simply diagnosing a disease that, had it not been discovered, never would have troubled the patient.

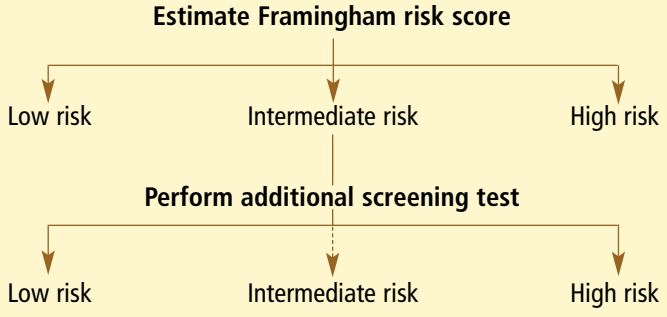


FIGURE 2. Schematic illustrating how a screening test such as calcium scoring can be used to identify people at high risk. Among those determined to be at intermediate risk by a global scoring system like the Framingham risk score, the screening test refines risk prediction; some are now determined to be at low risk, some are at high risk (and therefore candidates for aggressive treatments), and some (dotted arrow) are still classified as at intermediate risk.

Only randomized trials can show if screening improves outcomes

The only way to know definitively whether a screening test improves outcome is by performing a randomized trial. This has been done for a number of diseases, including breast cancer[3] and abdominal aortic aneurysm.[7] For example, the recently published Multicentre Aneurysm Screening Study[14] found that a strategy of inviting older men for an abdominal aortic ultrasound scan safely reduced the rate of death from aortic aneurysms.

Randomized trials of screening are difficult to perform because, to succeed, they require large sample sizes and long periods of follow-up. However, only the randomized trial design makes it possible to eliminate the effects of lead-time bias, length-time bias, and overdiagnosis bias.

Sometimes screening uncovers disease that would never have troubled the patient

ARE THERE DOWNSIDES TO SCREENING?

One might think that screening is so logically beneficial that it cannot cause any harm. It

makes perfect sense to diagnose a disease early before it causes symptoms or death. How could there possible be any downside to screening?

In fact, screening can cause serious harm, and the harm is not merely theoretical.[13]

Consider neuroblastoma, a serious brain cancer of children.[15,16] Recently, a number of public health groups decided to institute mass screening for neuroblastoma by testing urine samples for metabolites produced by these tumors. What happened? Many more children with neuroblastoma were diagnosed and underwent surgery.

So far so good. However, when the investigators calculated the death rate from neuroblastoma, it turned out that screening had little impact. In retrospect, a number of children were diagnosed with neuroblastomas that never would have been clinically important. They were subjected to the anxiety of being diagnosed with what they thought was a serious disease and to the risks and inconveniences of surgery. The screening regimen caused harm, not benefit.[15,16]

HOW DO WE KNOW WHICH SCREENING TESTS ARE APPROPRIATE?

Screening can cause harm, which is not merely theoretical

Screening is appropriate only if high-quality evidence exists that the strategy prevents clinical events. Does mammography prevent breast cancer deaths? Yes.[3] Does abdominal ultrasonography prevent deaths from abdominal aortic aneurysm without causing harm otherwise? For at least some groups of patients, the answer appears to be yes.[7]

While in theory this may be a useful framework, the busy clinical practitioner still wants to know where to find useful advice about screening.

In my opinion, one of the best sources of information on the value of screening comes from the US Preventive Services Task Force (USPSTF).[6,17] This is a group of highly respected experts from the private sector assembled by the US Agency for Health Care Research and Quality (AHRQ). The existence of the USPSTF is mandated by public law section 915, which requires that the "AHRQ convene the USPSTF to conduct scientific evidence reviews of a broader array of clinical preventative services, develop recommendations for the health care community, and provide administrative, research, technical, and dissemination support."[18] When assembling recommendations, the USPSTF performs a series of carefully orchestrated systematic evidence reviews and syntheses, using established criteria for assessing quality of evidence and extensive peer review.[18]

Reliable information also comes from nonprofit specialty societies such as the American Heart Association, American College of Cardiology, and American Cancer Society. These organizations have established procedures for acquiring evidence and assessing its quality. Documents written by these organizations undergo extensive peer review. In fact, recently these organizations have gone so far as to publish the names of the peer reviewers along with those of the authors of the recommendations, thereby making it clear that the reviewers also share responsibility.[19]

WHAT SCREENING IS RECOMMENDED FOR CORONARY HEART DISEASE?

Coronary heart disease seems like an obvious candidate for screening.[20,21] The disease is serious and continues to be the number-one killer in developed societies. Nearly half of patients initially present with a major event, ie, myocardial infarction or sudden death, and coronary atherosclerosis can exist for a long time before it causes symptoms.[22] Lay people are well aware of the phrase "ticking time bomb," describing a person with a heavy disease burden just waiting for the "big day" to happen.

A number of tests have been shown to detect asymptomatic coronary heart disease or to predict coronary events or premature death.[8] The simple exercise treadmill test can identify people at high risk.[23] More recently, interest has focused on powerful imaging techniques such as electron-beam computed tomography for calcium scoring and carotid intimal medial thickness measurements. A number of high-quality studies have demonstrated that these tests predict risk.[8,24]

Given that coronary heart disease is common and serious and has a prolonged asymptomatic phase, and given that we have tests that predict risk, wouldn't it make perfect

sense to recommend routine screening for coronary disease?

Yet, when one consults peer-reviewed guidelines, one finds that this is not the case. The USPSTF, for example, specifically recommends against screening adults who are at low risk for coronary heart disease events and found "insufficient evidence to recommend for or against screening" in adults who are at increased risk.[21] Similarly, recent recommendations from the American Heart Association and American College of Cardiology [25,26] recommend that screening tests be considered only for people who are at intermediate risk of disease, not for people thought to be at low risk or at high risk.

One current recommended approach to coronary heart disease screening starts with a clinical evaluation.[8] This can be formally quantified by global risk scores, such as those of the Framingham Heart Study or the European Score Group. The Framingham risk score can be easily calculated: the only variables needed are the patient's age, sex, smoking status, total cholesterol level, HDL-C level, systolic blood pressure, and whether he or she is taking medications for hypertension (FIGURE 1). Another version of the Framingham score also includes diabetes, since this is a strong risk factor for coronary events. One then uses this information to determine whether further testing is necessary.

Among patients at intermediate risk, a number of tests could be considered,[8] such as the exercise test, carotid imaging, the ankle-brachial index, and electron-beam computed tomography of the heart.

However, no randomized trials of coronary heart disease screening have been performed. We simply do not know whether screening prevents premature death or major cardiac events. Therefore, published recommendations are cautious in their approach. For example, whereas the USPSTF is clear that screening should not be done in patients at low risk for disease, all that they say for patients at high risk, is that there is "insufficient evidence to recommend for or against routine screening."[21] A reasonable, conservative practitioner, therefore, might conclude that it would be best not to obtain screening tests so as to avoid potential harm induced by screening.

WHAT DO THE SHAPE GUIDELINES RECOMMEND?

On July 17, 2006, the *American Journal of Cardiology* published the SHAPE Task Force report,[2] which recommended a radically different approach to screening for coronary heart disease (FIGURE 3).

The proposed SHAPE algorithm calls for some form of imaging test for atherosclerosis in nearly all men between the ages of 45 and 75 years and women between the ages of 55 and 75 years. The only people who would not undergo testing would be those at "very low risk," ie, whose total cholesterol level is lower than 200 mg/dL and whose blood pressure is lower than 120/80 mm Hg and who do not have diabetes, do not smoke, have no family history of coronary heart disease, and have no elements of the metabolic syndrome.[2] Only after the atherosclerosis test result is back would risk factors be considered regarding further tests and regarding an optimal low-density lipoprotein cholesterol (LDL-C) goal.

Whereas the current recommended approach is to perform imaging only in patients deemed to be at intermediate risk, the new SHAPE guidelines would lead to the performance of imaging tests in nearly all middle-aged and older adults.[2] SHAPE therefore represents a major paradigm shift in determining cholesterol treatment goals. Whereas current Adult Treatment Panel (ATP III) recommendations focus on global risk assessment based on risk factors,[1,27] SHAPE focuses on atherosclerosis imaging, with risk factors playing a supplementary role (TABLE 1).

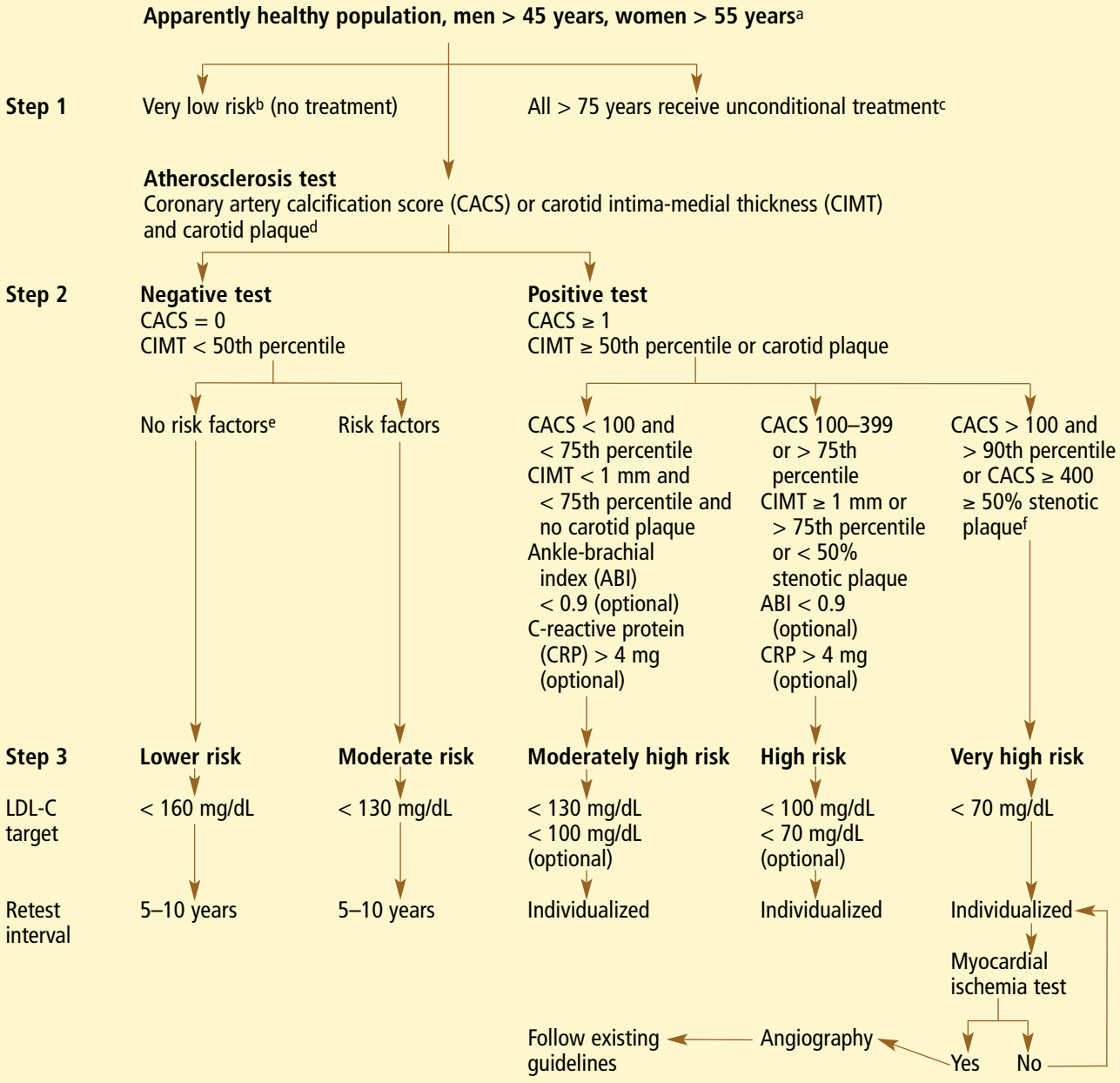
Coronary heart disease seems like an obvious candidate for screening, but this may not be the case

Criticisms of the SHAPE guidelines

Almost immediately after publication, the SHAPE guidelines came under sharp criticism.[28] It was pointed out, for example, that the document had not been endorsed by any official society and had not undergone an extensive and transparent peer review.[28]

Furthermore, the supplement in which the article was published was paid for by Pfizer,[28] the manufacturer of atorvastatin (Lipitor). Presumably, patients identified as having atherosclerosis would be good candidates for atorvastatin therapy; were the SHAPE guidelines to be widely adopted, sales

The SHAPE Task Force guideline



[a]No history of angina, heart attack, stroke, or peripheral arterial disease
[b]Must not have any of the following: total cholesterol level > 200 mg/dL (5.18 mmol/L), blood pressure > 120/80 mm Hg, diabetes mellitus, smoking, family history of coronary heart disease, or the metabolic syndrome
[c]Population age > 75 years is considered at high risk and must receive therapy without testing for atherosclerosis
[d]Pending the development of standard practice guidelines
[e]No high cholesterol, high blood pressure, diabetes, smoking, family history of coronary heart disease, or the metabolic syndrome
[f]For stroke prevention, follow existing guidelines

FIGURE 3. The Screening for Heart Attack Prevention and Education (SHAPE) guideline. Nearly all adults (men ages 45–75, women ages 55–75) undergo atherosclerosis screening with calcium scanning or carotid intima-media thickness imaging. Only after these test results are known are coronary risk factors considered to determine a goal LDL cholesterol level. Patients deemed at very high risk are referred for myocardial ischemia testing followed by coronary angiography.

FROM NAGHAVI M, FALK E, HECHT HS, ET AL. FROM VULNERABLE PLAQUE TO VULNERABLE PATIENT—PART III: EXECUTIVE SUMMARY OF THE SCREENING FOR HEART ATTACK PREVENTION AND EDUCATION (SHAPE) TASK FORCE REPORT. AM J CARDIOL 2006; 98:2H–15H, WITH PERMISSION

TABLE 1

Differences between the ATP-III and SHAPE guidelines regarding determination of LDL-cholesterol goals

	ATP-III GUIDELINES[a]	SHAPE GUIDELINES[b]
Eligible population	Adults age 20 years and older	Apparently healthy men 45–75 years, women 55–75 years
Initial evaluation	Fasting lipid profile	Atherosclerosis imaging[c]
Secondary evaluation	Coronary risk equivalents[d] Global risk score (Framingham risk score)	If imaging is negative, risk factors If imaging is positive, LDL-cholesterol goal and myocardial ischemia testing based on imaging specifics
Atherosclerosis imaging	Not applicable[e]	For all subjects except those at very low risk

[a]The third report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults[1,27]
[b]The Screening for Heart Attack Prevention and Education Task Force report[2]
[c]Except for people at "very low risk," meaning total cholesterol less than 200 mg/dL, blood pressure lower than 120/80 mm Hg, no diabetes, no smoking, no family history of coronary heart disease, and no elements of the metabolic syndrome
[d]Clinical coronary heart disease, symptomatic carotid artery disease, peripheral arterial disease, abdominal aortic aneurysm. These markers identify people at high risk with LDL-cholesterol goals < 100 mg/dL or, for people at very high risk, < 70 mg/dL.[2]
[e]According to some, imaging may be of value in people at intermediate risk.[8]

of atorvastatin and other statins might dramatically increase.

Moreover, a number of SHAPE authors had major personal conflicts of interest. Not only were some of them financially connected to companies that make statins, but others directly received financial benefit from imaging centers that they owned.[28]

And these screening tests are being marketed directly to consumers, a practice that poses several ethical problems, not the least of which is that some doctors stand to benefit financially from performing these imaging procedures[29] and from follow-up testing or procedures that result from abnormal findings. The authors' failure to disclose potential conflicts of interest is in contrast with the current practice of cardiovascular professional societies, which, in their practice guideline statements, add detailed tables of the authors' and reviewers' disclosures.[10]

WHAT'S WRONG WITH THE SHAPE GUIDELINES?

In my opinion, the major problems with the SHAPE guidelines are that they are not evidence-based and that they have not undergone extensive, objective, and transparent peer review.

The major problem with the SHAPE guidelines is they are not evidence-based

Although we have a plethora of tests for diagnosing asymptomatic coronary disease and predicting coronary events, the unfortunate reality is that no randomized trials to demonstrate their clinical efficacy have been performed.[19,21] If we really want to know whether atherosclerosis imaging prevents heart attacks, we need to follow the lead of investigators in the fields of cancer[3] and aortic aneurysm,[7] who have performed large-scale, randomized trials. There is reason to think that atherosclerosis screening may not be valuable. We already aggressively treat hypertension, hypercholesterolemia, and diabetes. Randomized trials have demonstrated that aggressive treatment of these conditions can prevent premature coronary events.[1,5] When it comes to the disease of atherosclerosis per se, as opposed to just the risk factors for atherosclerosis, we should require no lower standard.

The potential harms of coronary disease screening have, in my view, not been adequately considered. Although statins are prob-

ably safe, their long-term use has not been well studied, particularly in people at lower risk.

Furthermore, some patients with asymptomatic disease may be referred for invasive procedures, including stenting or even coronary bypass grafting, whether these procedures are recommended by guidelines or not. There is no evidence from randomized trials to demonstrate that coronary revascularization in asymptomatic patients improves long-term survival rates or prevents premature myocardial infarctions. A recent trial showed no benefit of performing coronary revascularization in patients at high risk but without symptoms before they underwent vascular surgery.[30]

Another concern is that the SHAPE guidelines draw attention away from potentially more effective ways of reducing the coronary heart disease burden in our society. SHAPE relies almost entirely on a medical approach to prevention. As described by the famed epidemiologist Geoffrey Rose,[31] the "high-risk" strategy consists of identifying people at high risk and treating them. While these people benefit from this approach, from a societal viewpoint the overall impact on disease is small. Population-based approaches that specifically address risk factors may reduce disease burden to a much greater extent.[31] Rather than try to screen all adults, it might make more sense instead to try to improve the national diet and level of exercise and to discourage smoking. There is reasonable evidence that addressing these lifestyle factors may well reduce the prevalence of disease substantially.[32]

Screening helps individuals, but may have little impact on society as a whole

WHAT SHOULD BE DONE WITH OUR PATIENT?

As for the patient described at the beginning of this paper, I would explain to him that given his current situation, his risk of having a major coronary event in the next 10 years is low, less than 1% per year. Given this low risk, specific treatment of coronary disease would be unlikely to help him.[33]

I would also explain to him that while imaging tests might tell us whether he has disease or not, there is no evidence that we can use that information to reduce his risk of clinical disease or to prevent premature death.[19,21] In fact, were he interested enough, I might go so far as to explain how evidence-based medicine relies substantially on properly designed and implemented clinical trials.[17] I might point out to him that the only randomized trial of calcium scanning in coronary disease found that, compared with aggressive risk factor reduction, calcium scanning did not yield any reduction in disease risk or any increase in motivation to change risk-related behaviors.[34]

I would emphasize the importance of a proper diet and regular exercise, especially since his total cholesterol and HDL-C values are not ideal. Finally, I would recommend that his blood pressure and cholesterol values be followed on a periodic basis, according to current guidelines.[1,5]

REFERENCES

1. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486–2497.
2. **Naghavi M, Falk E, Hecht HS, et al.** From vulnerable plaque to vulnerable patient—part III: executive summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force report. Am J Cardiol 2006; 98:2H–15H.
3. **Elmore JG, Armstrong K, Lehman CD, Fletcher SW.** Screening for breast cancer. JAMA 2005; 293:1245–1256.
4. **Hartmann KE, Nanda K, Hall S, Myers E.** Technologic advances for evaluation of cervical cytology: is newer better? Obstet Gynecol Surv 2001; 56:765–774.
5. **Chobanian AV, Bakris GL, Black HR, et al.** The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289:2560–2672.
6. **US Preventive Services Task Force.** Guide to clinical preventive services, second edition. http://odphp.osophs.dhhs.gov/pubs/guidecps. Accessed August 1, 2007.
7. **Fleming C, Whitlock EP, Beil TL, Lederle FA.** Screening for abdominal aortic aneurysm: a best-evidence systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2005; 142:203–211.
8. **Greenland P, Smith S Jr, Grundy SM.** Improving coronary heart disease risk assessment in asymptomatic people: role of traditional risk factors and noninvasive cardiovascular tests. Circulation 2001; 104:1863–1867.
9. **D'Agostino RB Sr, Grundy S, Sullivan LM, Wilson P.** Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA 2001; 286:180–187.
10. **Greenland P, Bonow RO, Brundage BH, et al.** ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collabora-

tion with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2007; 49:378–402.
11. **Mozaffarian D.** Electron-beam computed tomography for coronary calcium: a useful test to screen for coronary heart disease? JAMA 2005; 294:2897–2901.
12. **Patz EF Jr, Goodman PC, Bepler G.** Screening for lung cancer. N Engl J Med 2000; 343:1627–1633.
13. **Grimes DA, Schulz KF.** Uses and abuses of screening tests. Lancet 2002; 359:881–884.
14. **Ashton HA, Buxton MJ, Day NE, et al.** The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet 2002; 360:1531–1539.
15. **Yamamoto K, Ohta S, Ito E, et al.** Marginal decrease in mortality and marked increase in incidence as a result of neuroblastoma screening at 6 months of age: cohort study in seven prefectures in Japan. J Clin Oncol 2002; 20:1209–1214.
16. **Schilling FH, Spix C, Berthold F, et al.** Neuroblastoma screening at one year of age. N Engl J Med 2002; 346:1047–1053.
17. **Grimes DA, Atkins D.** The U.S. Preventive Services Task Force: putting evidence-based medicine to work. Clin Obstet Gynecol 1998; 41:332–342.
18. **Agency for Healthcare Research and Quality.** About USPSTF. http://www.ahrq.gov/clinic/uspstfab.htm. Accessed August 1, 2007.
19. **Lauer M, Froelicher ES, Williams M, Kligfield P.** Exercise testing in asymptomatic adults: a statement for professionals from the American Heart Association Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention. Circulation 2005; 112:771–776.
20. **Fowler-Brown A, Pignone M, Pletcher M, Tice JA, Sutton SF, Lohr KN.** Exercise tolerance testing to screen for coronary heart disease: a systematic review for the technical support for the U.S. Preventive Services Task Force. Ann Intern Med 2004; 140:19–24.
21. **U.S. Preventive Services Task Force.** Screening for coronary heart disease: recommendation statement. Ann Intern Med 2004; 140:569–572.
22. **Pasternak RC, Abrams J, Greenland P, Smaha LA, Wilson PW, Houston-Miller N.** 34th Bethesda Conference: Task force #1—Identification of coronary heart disease risk: is there a detection gap? J Am Coll Cardiol 2003; 41:1863–1874.
23. **Aktas MK, Ozduran V, Pothier CE, Lang R, Lauer MS.** Global risk scores and exercise testing for predicting all-cause mortality in a preventive medicine program. JAMA 2004; 292:1462–1468.
24. **Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC.** Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004; 291:210–215.
25. **Gibbons RJ, Balady GJ, Bricker JT, et al.** ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation 2002; 106:1883–1892.
26. **Gibbons RJ, Abrams J, Chatterjee K, et al.** ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on the Management of Patients With Chronic Stable Angina). J Am Coll Cardiol 2003; 41:159–168.
27. **Grundy SM, Cleeman JI, Merz CN, et al.** Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. Circulation 2004; 110:227–239.
28. **Smith S.** Article urging heart exams shows conflicting interests: Drug firm funded printing in journal. Boston Globe. Boston, 2006.
29. **Lee TH, Brennan TA.** Direct-to-consumer marketing of high-technology screening tests. N Engl J Med 2002; 346:529–531.
30. **McFalls EO, Ward HB, Moritz TE, et al.** Coronary-artery revascularization before elective major vascular surgery. N Engl J Med 2004; 351:2795–2804.
31. **Rose G.** The Strategy of Preventive Medicine. New York: Oxford University Press, 1992.
32. **Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC.** Primary prevention of coronary heart disease in women through diet and lifestyle. N Engl J Med 2000; 343:16–22.
33. **Califf RM, Armstrong PW, Carver JR, D'Agostino RB, Strauss WE.** 27th Bethesda Conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 5. Stratification of patients into high, medium and low risk subgroups for purposes of risk factor management. J Am Coll Cardiol 1996; 27:1007–1019.
34. **O'Malley PG, Feuerstein IM, Taylor AJ.** Impact of electron beam tomography, with or without case management, on motivation, behavioral change, and cardiovascular risk profile: a randomized controlled trial. JAMA 2003; 289:2215–2223.

ADDRESS: *Michael S. Lauer, MD, Division of Prevention and Population Science, National Heart, Lung, and Blood Institute, 6701 Rockledge Drive, room 10122, Bethesda, MD 20892; e-mail lauerm@nhlbi.nih.gov.*