Editorials

Noninvasive Detection of Atherosclerosis

Atherosclerosis has been a serious health epidemic in developed countries in the late 20th century, and its rising prevalence in developing nations suggests that it will become the chief cause of morbidity and mortality worldwide by early in the next century.[1] Although the principal clinical complications of atherosclerosis, such as myocardial infarction and stroke, usually occur in middle-aged or older people, the atherogenic process actually begins in childhood and early adult life, with a preclinical phase lasting many decades.[2] This pattern provides a window of opportunity for the presymptomatic detection of the disease, the identification of high-risk subjects, and the application of appropriate preventive strategies.

Recent advances have defined many of the early molecular and cellular changes that occur during atherogenesis.[3] Some of these processes provide a focus for diagnostic assays. Oxidative modification of lipoproteins, adhesion of monocytes to vascular endothelium, foam-cell formation, and arterial-wall thickening occur during childhood or young adult life in persons at high risk. Dysfunction of the arterial endothelium is also an important early event, with decreased local availability of nitric oxide and thus impaired vasodilator capacity.[4] Inflammation and calcification of plaques may be slightly later events, but they still usually precede luminal narrowing and the onset of symptoms.

Ideally, clinical testing for atherosclerosis should involve methods that are safe, inexpensive, noninvasive or minimally invasive, reliable, and reproducible; their results should correlate with the extent of atherosclerotic disease and have high positive and negative predictive values for clinical events. Although no such techniques are yet available, the areas currently of greatest interest include blood tests for atherosclerosis, vascular ultrasonography, magnetic resonance imaging (MRI), and electron-beam computed tomography (CT).

So far, blood tests for atherosclerosis have emphasized the measurement of predisposing risk factors, such as high levels of cholesterol, lipoprotein subfractions, and homocysteine. Newer tests may detect markers released from areas of early atheroma — for example, novel lipid or protein oxidation products or adhesion molecules specific for atherosclerosis. The levels of less specific markers of endothelial activation or inflammation, such as C-reactive protein and intercellular adhesion molecule 1, have recently been shown in population studies to correlate significantly with the risk of future vascular complications,[5] but assays for these markers cannot yet be recommended for use in individual patients.

Noninvasive ultrasonography has also been used to detect early signs of atherogenesis, such as impaired endothelial function[4] and arterial-wall thickening in peripheral arteries.[6] These tests are safe and quick; their results are reproducible and correlate with major cardiovascular risk factors, as well as with the extent of coronary atherosclerosis.[4,6] Recent studies have also demonstrated that greater carotid intima–media thickness predicts a greater likelihood of subsequent cardiovascular events in high-risk persons,[7] a finding that suggests that ultrasonography will have increasing value in the presymptomatic detection of early atherosclerosis.

MRI is already in clinical use for the detection of peripheral and cerebral atherosclerosis. MRI of the coronary circulation has proved more challenging because of cardiac and respiratory motion.[8] MRI has also recently been used to obtain images of plaque in the vessel wall, both in animals and in superficial human arteries, allowing measurements of plaque size as well as visualization of the fine structure of lesions, such as the fibrous cap and necrotic core.[9] Although costly, MRI therefore holds promise for future studies of plaque and its effects on the diameter of the lumen.

Electron-beam (or "ultrafast") CT is an exciting technique in coronary imaging. It differs from conventional CT in that the x-ray source does not need to be rotated around the patient, allowing much faster acquisition.[10] Because calcification is an early feature of atherosclerotic-plaque formation, measurement of coronary calcium by means of CT scanning of the heart may reflect the extent of atherosclerosis.

In general, calcium makes up approximately 20 percent of atherosclerotic-plaque volume and is significantly correlated with the total burden of plaque. Deposition of calcium hydroxyapatite in plaque is an active process, and atherosclerotic areas may express genes related to calcium metabolism, such as those for osteopontin and osteocalcin.[10] Nevertheless, some high-grade lesions and many smaller plaques lack calcium altogether.[11] High coronary calcium scores have good sensitivity for obstructive coronary disease (80 to 100 percent), but low specificity (40 to 60 percent). Some studies, but not all, that have prospectively examined the value of indexes of coronary calcium for predicting clinical events have documented low rates of complications among those with no coronary calcium and a relatively high risk among asymptomatic subjects with high calcium scores.[10]

In this issue of the *Journal,* Callister et al. describe the use of a new, reproducible calcium-volume score in assessing the coronary circulation in a cohort of asymptomatic subjects.[12] In a retrospective review, the authors found less progression of the calcium-volume score in patients who were treated with lipid-lowering agents than in untreated subjects (particularly if treatment resulted in a level of low-density lipoprotein cholesterol that was below 120 mg per deciliter [3.1 mmol per liter]). Although this suggests slower progression of plaque growth with effective lipid lowering, it is uncertain whether a change in the calcium-volume score represents a change in plaque size, in the composition of the lesion, in the degree of vulnerability to rupture, or a combination of these factors. Several other mechanisms that may explain the apparent benefit of lipid-lowering therapy in terms of arterial structure and vasomotion have recently been documented, including improved endothelial function with less coronary constriction and increased stability of plaques.[13] Reduction in coronary calcium, therefore, may also contribute to the observed clinical benefit of lipid-lowering treatment in high-risk subjects with hypercholesterolemia.

Elsewhere in this issue of the *Journal,* Achenbach and colleagues report the results of their examination of the role of contrast-enhanced electron-beam CT for the assessment of coronary luminal size in symptomatic patients who were undergoing conventional coronary angiography.[14] In approximately 65 percent of patients, technically adequate CT images of all the major coronary arteries were obtained. In these cases, the authors could accurately classify subjects according to whether they did or did not have high-grade coronary stenoses (>75 percent) or occlusions. Furthermore, the negative predictive value of the technique in patients without severe stenoses on CT was 98 percent. With the caveat that relatively minor plaques are often the culprit lesions in acute coronary syndromes,[15] contrast-enhanced CT may permit certain patients with chest pain to be evaluated and treated without cardiac catheterization. Conventional coronary angiography, however, remains relatively quick, entails a low risk, generally clarifies the severity of obstructive stenoses in all the major proximal and distal epicardial vessels, and allows immediate catheter-based intervention, if indicated. Further studies are now required to evaluate the clinical implications of this exciting new research for the diagnostic workup of patients with suspected coronary disease.

Coronary imaging with electron-beam CT is therefore a promising noninvasive method that may contribute to overall risk assessment. Calcium-volume scoring may provide information on the extent of atherosclerosis in the coronary arteries, and contrast-enhanced CT may determine the severity of the disease. Before the routine clinical use of coronary CT scanning can be recommended for screening of asymptomatic patients or for the evaluation of patients with chest pain, however, more work is needed. Basic studies are required to define the role of calcium in plaque stability and progression, and prospective studies are needed to demonstrate the cost effectiveness of these techniques and their potential impact on cardiovascular outcomes. As the prevalence of atherosclerosis increases worldwide, there is a pressing need for investigators to refine and evaluate these and other noninvasive techniques, in order to ensure reliable detection of atherosclerosis during the long presymptomatic phase of the disease.

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ROLE MODELS — GUIDING THE FUTURE OF MEDICINE

IN this issue of the *Journal,* Wright et al. present provocative evidence that many physician-teachers do not exhibit the professional characteristics that residents desire to emulate.[1] Assuming that this study's results, from two highly respected teaching programs, are representative of other institutions, these data indicate that less than half of teaching physicians are perceived as excellent role models. What does this mean? Do less than half of medical teachers have the skills and behavior of respected physicians? Do learners recognize the value of the professional roles of less than half of faculty members? Do less than half of clinical teachers currently work in an environment that fosters mastery and demonstration of the characteristics of excellent physicians? There may be truth in each of these hypotheses.

Many faculty members may not exhibit the skills and behavior that residents perceive as characteristic of excellent role models. In this study, faculty members who emphasized interactions between patients and physicians and the psychosocial aspects of medicine and who provided specific feedback to learners were more likely to be perceived as positive role models. Earlier work with students indicates that physicians who show insensitivity to or disrespect for patients, professional dissatisfaction, or a lack of camaraderie are judged to be negative role models.[2]

The good news is that physicians can improve their skills as teachers and possibly their effectiveness as role models. Even experienced teachers may have a limited awareness of their strengths, areas that can be improved, or trainees' perception of their behavior.[3] Philosophically and intellectually, such faculty members may understand and embrace relevant humanistic and educational principles. However, their behavior may not consistently reflect these values. In addition, many are unaware of the potential for improving their teaching skills. Faculty-development programs, which use methods such as videotape review, allow teachers to see what others see, thus providing a mechanism for both self-discovery and improvement.

In the study by Wright et al., generalists were more likely than medical subspecialists to be identified as desirable role models. This difference may reflect the current educational emphasis on general internal medicine. It may also reflect the full array of individual efforts, reallocated resources, and programmatic innovations in general internal medicine over the past 15 years. Funding from both governmental sources and private foundations has supported a wide variety of faculty-development programs,[4] enabling many generalist faculty members to improve their communication and teaching skills — characteristics that were specifically identified as important in this study. Such efforts have focused on generalist teachers in an effort to expand the number of faculty members to that needed for training generalists. However, the desire to develop excellent skills in teaching and improve patient–physician communication is not unique to these physicians. Thus, it is possible that specialists may also benefit from attention to these areas.

Why might medical residents identify this particular group as excellent role models? Residents spend the majority of their time caring for patients and teaching; therefore, it is likely that they will focus on aspects of teachers' behavior that have the greatest congruence with their daily work. At this point in their education, residents, understandably, may model themselves on physicians whose careers focus on patient care and teaching. This explanation may lessen the concern that 60 percent of faculty members in this study were not deemed to be excellent role models.

At the same time, the findings arouse concern about the learners' futures. Trainees may not recognize that faculty members who embody characteristics other than those identified in this study can be important career guides and role models. As adult learners, trainees may reject role models who do not fit the expectations shaped by their experiences as residents and thus may overlook opportunities to broaden their views. Many physicians can retrospectively identify teachers with strengths in arenas outside the daily activities of clinical training who catalyzed a change in the direction of their careers. Such physicians may be possible role models in other areas of medicine, such as research or less popular subspecialties. Thus, educational institutions should present residents with a wide variety of role models.[5]

Faculty members not generally identified as role models can still be important in reshaping and broadening learners' views of their future careers. To do so, these physicians must first attempt to reflect core attributes of physicians — for example, by demonstrating effective patient–physician interactions. Although it is sometimes difficult to highlight these attributes in the face of hectic schedules and increased pressures for productivity, they are essential components of physicians' roles that should not be compromised. Second, to be maximally effective as guides, teachers must be aware of learners' viewpoints and, when necessary, help them understand the merits of ideas and models that may not fit their expectations. Knowing that residents may focus on issues of immediate relevance, faculty members may have to create a "need to learn" about seemingly less relevant material and other professional roles. Such instruction requires commitment, confidence, and skill on the part of the faculty to convey enthusiastically and effectively the importance and applicability of fields unfamiliar to learners. In the study by Wright et al., faculty members who were not identified by residents as excellent role models also did not see themselves as role models. Thus, they may have been unconvincing in their attempts to convey the attractiveness of their work to learners.

Teachers, even those who are motivated and highly skilled, cannot accomplish these goals without institutional support. Today, academic medical centers face great challenges. Financial constraint has become a predominant force. Faculty members are being asked to teach and care for patients more efficiently.

This requirement may translate into spending less time with learners, something that had a negative influence on physicians' ability to serve as positive role models in this study. In addition, faculty members may need support to be able to offer support to trainees. In this study, excellent role models reported feeling more support than their counterparts. By the same token, residents perceived the most supportive faculty members as excellent role models. Not surprisingly, all the players share common needs. Just as patients need and respond to supportive care, so house staff and faculty members need skills, time, and care to enable them to display exemplary behavior.

Academic institutions have an obligation to society to produce competent and sensitive clinicians, physician-scientists, physician-teachers, and physician-administrators. As academic medical institutions attempt to match the efficiency of their nonacademic counterparts, finding time for teachers to participate in faculty-development programs and even to teach becomes a major challenge. Unless institutions provide time for a greater number of faculty members to demonstrate their professional roles effectively and convincingly, institutional leaders may have to accept that fewer than half of their teachers will be perceived as effective role models by those they teach. These institutions may provide society with an adequate number of qualified physicians in the short term. In the long run, however, the restriction on the number of available role models may lead to a diminished science and practice of medicine.

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Sounding Board

Self-Referral of Patients for Electron-Beam Computed Tomography to Screen for Coronary Artery Disease

ELECTRON-BEAM computed tomography (CT) is a new, increasingly widely promoted technique for the detection of calcification within coronary atherosclerotic lesions. Evidence supporting the use of this test in screening for coronary artery disease is gradually accumulating, but there is considerable controversy about the role of electron-beam CT in identifying patients at risk for cardiovascular events.[1,2] Despite the controversy among experts, centers performing electron-beam CT advertise for and generate business on the basis of patients' referring themselves for the test. Is electron-beam CT ready for widespread use through the mechanism of self-referral? This question can be answered only after proper consideration of the potential hidden costs and risks of patients' decisions to seek the test.

THE GROWTH OF ELECTRON-BEAM CT

The detection of coronary-artery calcification with electron-beam CT began as a part of research protocols in the mid-1980s, but the technique is now spreading rapidly into clinical use in the United States. There are currently about 50 electron-beam CT scanners in the United States. Most are operated in association with hospitals, but the industry projects that the number of scanners in clinical use will double within the next one to two years. The test is appealing because it is noninvasive (radiation exposure is an order of magnitude less than with coronary angiography[3]), fast (the entire procedure lasts approximately 15 minutes), and simple. The cost of scanning with electron-beam CT is approximately $475.

There are various potential uses of electron-beam CT, notably as a replacement for conventional CT and in emerging approaches such as electron-beam CT angiography (as reported by Achenbach et al. in this issue of the *Journal*[4]). But the current growth of electron-beam CT is being fueled by its use as a screening procedure for coronary calcification associated with coronary atherosclerosis. As a diagnostic test for obstructive coronary artery disease, its cost and accuracy approximate those of the treadmill exercise test.[5] It is less invasive than coronary angiography, yet it provides diagnostic data that are related to the extent of coronary disease.[6,7] As a screening tool, whether its prognostic capability surpasses[8] or equals[9] that of conventional risk-factor–based screening methods is controversial. Because of "insufficient data," the American Heart Association has discouraged both the use of electron-beam CT as a screening procedure in low-risk asymptomatic patients and the "widespread proliferation of screening programs for coronary calcium as a single, isolated diagnostic modality" until more data are available.[10]

PATIENT SELF-REFERRAL FOR ELECTRON-BEAM CT

Despite the American Heart Association's call for patience, news reports in the lay press as well as mass-media advertising (on radio, in newspapers, on the Internet, and even on billboards) have promoted the test to the general public.[8] Most centers performing electron-beam CT permit patients to refer themselves (i.e., the patients schedule the tests for themselves and receive the results directly, without consulting with a physician). Many electron-beam CT centers (both hospital-affiliated and free-standing) rely on self-referred patients for the majority of their volume of procedures (for example, approximately three of every four patients at Walter Reed Army Medical Center, as at many civilian centers, are self-referred). Is electron-beam CT screening for coronary calcium scientifically mature enough to warrant such a practice, or has the profit motive circumvented the best clinical practice? Does a positive test provide incremental information, derived in a cost-effective manner, that can meaningfully alter decisions about management? Does a negative test result carry hidden risks?

Self-referral for electron-beam CT is based on the premise that conventional cardiovascular risk factors inadequately quantify risk. In this framework, electron-beam CT is viewed as a physiologic "litmus test" for cardiac risk factors. For example, the test might identify patients with borderline cholesterol values who should or should not receive drug treatment to lower their cholesterol levels. Self-referral for electron-beam CT may also help lead patients toward potentially beneficial treatments to modify cardiovascular risk. However, many patients are well served by existing guidelines for the evaluation and treatment of risk factors for cardiovascular disease, as implemented by physicians. Furthermore, because the ultimate focus for any patient will be on modifiable coronary risk factors, it remains unclear whether electron-beam CT will provide useful information to guide the choice and intensity of strategies to modify risk. The observational data presented by Callister et al. in this issue of the *Journal*[11] provide a glimpse into this potential application of electron-beam CT with respect to lipid-lowering therapy.

THE HIDDEN COSTS OF ELECTRON-BEAM CT

The discovery of coronary calcification on electron-beam CT scanning will undoubtedly result in additional testing for many patients who undergo the screening procedure. An array of tests can be envisioned, beginning with a lipid profile. Many patients with a positive electron-beam CT scan showing coronary calcification will undergo additional physiologic evaluation (for example, stress testing) or even anatomical assessment (for example, by cardiac catheterization). How many exercise treadmill tests and additional imaging procedures, as well as potentially harmful invasive diagnostic and revascularization procedures, will result from abnormal findings on electron-beam CT? In a middle-aged and elderly group of self-referred patients, rates of detection of calcification on electron-beam CT of 50 percent or more could reasonably be anticipated.[12] The potential for a gathering snowball of tests — some warranted, some not — is immense. Such further testing can be limited only by restraint on the part of physicians in a position to assess the implications of an abnormal screening test.

Although patients may personally "purchase" an electron-beam CT scan in many cases through self-referral, insurers and health plans are more likely to bear the costs of subsequent evaluations after an abnormal scan. Studies that clarify the relation of electron-beam CT to other diagnostic screening tests and that examine the cost-effectiveness of electron-beam CT are clearly needed.

Self-referral for electron-beam CT may also have hidden psychological costs. The balance between creating a group of "worried well" patients and justifiably increasing their awareness of behavior that increases their risk of cardiovascular disease must be more closely examined.[13] We must also recognize the potential for patients to be further removed by such self-referral from a relationship with a personal physician.

THE RISKS OF SELF-REFERRAL FOR ELECTRON-BEAM CT

Even though electron-beam CT is a simple, noninvasive radiographic test that entails limited exposure to radiation, does it stand up to the Hippocratic principle of "first, do no harm"? This issue is particularly important for a self-referred screening test. It is reasonable to assume that a patient with an electron-beam CT scan showing coronary calcification will be strongly motivated to consult his or her physician.[13] This response is appropriate, since the available data indicate that the risk of a future cardiovascular event (the positive predictive value of the test) is related to increasing degrees of coronary calcification.[8,9] But is the negative predictive value of electron-beam CT high enough to guard against false reassurance? In follow-up studies of electron-beam CT, even middle-aged and elderly patients with little or no coronary calcification have had ischemic events.[9] Complacency on the part of the patient or the physician after a negative electron-beam CT scan or one indicating a low risk could result in a failure to modify risk factors for coronary disease or risk-related behavior. Even worse, patients might delay seeking attention for symptoms of cardiac ischemia because of the presumption that they are in good cardiovascular health. The balance between the perceived benefits (any incremental value over that associated with standard care) and the costs (primarily the occurrence of potentially preventable events in falsely reassured patients) must be considered. The basic assumptions underlying the use of electron-beam CT for screening should be subjected to two-sided hypothesis testing in appropriately designed studies (including randomized trials) that can measure both the positive and the negative effects of the test.[14]

SUMMARY

As the availability of electron-beam CT increases, it is appropriate to question the balance among medical science, patient care, and profits. Broadening patients' sense of empowerment and promoting their autonomy are worthy goals within medicine. Breast-cancer screening with mammography is an example of a radiographic test used successfully in a diagnostic program based on self-referral. But the lessons of such a program, in which the distinction between the disease and the disease-free state is more easily recognized than is the case for age-dependent calcific arterial changes, are not easily extrapolated to screening for coronary disease. Currently, we are facing the possibility that market forces may increase interest in electron-beam CT beyond what is justified by its potential medical benefit. Well-designed clinical trials are required to define fully the appropriate indications for and limitations of electron-beam CT. Such trials will eventually clarify the medical applications of the technique and determine its suitability as a screening procedure for cardiovascular disease. Until then, the use of electron-beam CT, like that of all tests in medicine, should be based on a clearly defined rationale and should be coupled with a medical evaluation by a physician.

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