Screening for Coronary Artery Disease in Patients With Diabetes

JEROEN J. BAX, MD, PHD[1]
LAWRENCE H. YOUNG, MD[2]
ROBERT L. FRYE, MD[3]
ROBERT O. BONOW, MD[4]
HELMUT O. STEINBERG, MD[5]
EUGENE J. BARRETT, MD, PHD[6]

Coronary artery disease (CAD) accounts for a large fraction of the morbidity, mortality, and cost of diabetes. Recognizing this, nearly 10 years ago the American Diabetes Association published a consensus recommendation that clinicians consider a risk factor–guided screening approach to early diagnosis of CAD in both symptomatic and asymptomatic patients. Subsequent clinical trial results have not supported those recommendations. Since the prior consensus statement, newer imaging methods, such as coronary artery calcium scoring and noninvasive angiography with computed tomography (CT) techniques, have come into use. These technologies, which allow quantitation of atherosclerotic burden and can predict risk of cardiac events, might provide an approach to more widespread coronary atherosclerosis screening. However, over this same time interval, there has been recognition of diabetes as a cardiovascular disease (CVD) equivalent, clear demonstration that medical interventions should provide primary and secondary CVD risk reduction in diabetic populations, and suggestive evidence that percutaneous coronary revascularization may not provide additive survival benefit to intensive medical management in patients with stable CAD. This additional evidence raises the question of whether documenting asymptomatic atherosclerosis or ischemia in people with diabetes is warranted. More data addressing this issue will be forthcoming from the BARI 2-D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial. Until then, for patients with type 2 diabetes who are asymptomatic for CAD, we recommend that testing for atherosclerosis or ischemia, perhaps with cardiac CT as the initial test, be reserved for those in whom medical treatment goals cannot be met and for selected individuals in whom there is strong clinical suspicion of very-high-risk CAD. Better approaches to identify such individuals based on readily obtained clinical variables are sorely needed.

Diabetes Care 30:2729–2736, 2007

As coronary artery disease (CAD) is the major cause of morbidity, mortality, and medical cost of diabetes (1), early diagnosis of CAD to prevent progression and clinical events has intuitive appeal. In February 1998, the American Diabetes Association (ADA) convened an expert panel to develop consensus positions addressing a series of questions related to coronary heart disease in both symptomatic and asymptomatic patients with diabetes (2). After discussing the potential value of early diagnosis, the types and frequency of testing, and most critically, which patients are particularly appropriate to be tested, the consensus panel recommended specialized CAD screening for patients thought to be at high risk. For the CAD asymptomatic diabetic patient, the panel particularly focused on risk factor burden (i.e., the number of risk factors, not the severity of any one), baseline electrocardiogram (ECG), and whether there was clinical evidence of vascular disease at other sites. The panel recognized that the positions articulated represented expert opinion, since evidence from well-controlled trials was lacking. However, the perceived high prevalence of adverse cardiac outcomes underscored the need for considering diagnostic testing. The panel also suggested that additional research should be conducted to evaluate the recommendations articulated.

Over the past 10 years, there has been a greatly increased recognition, both in the medical community and among patients, of the prevalence and impact of CAD among patients with diabetes. The complicity of both conventional and inflammatory risk markers in this increased risk has been extensively explored (3). Perhaps most importantly, the benefit of both primary and secondary CVD risk factor modification on cardiac outcomes has been proven in prospective interventional studies (4–9), and these results have driven new guidelines for care in diabetes (10). This may now be favorably affecting population risks for events, at least in those with adequate access to care. In clinical practice, the improved outcomes of aggressive medical therapy (11) are modifying the approach to treatment of patients with symptomatically less severe CAD.

Several studies of asymptomatic type 2 diabetic patients have specifically examined whether risk factor burden (i.e., number of risk factors) is predictive of inducible ischemia (as determined by myocardial perfusion imaging), and these have not supported the recommendation of the 1998 consensus panel for screening asymptomatic patients with two or more risk factors (12–14). At the same time, evidence has accumulated regarding newer CAD diagnostic modalities, e.g., CT angiography (15), coronary artery calcium scoring (16,17), and cardiac magnetic resonance imaging (18), that are being implemented in strategies to diagnose and stage CAD. These modalities likely have implications for diabetic as well as nondiabetic patients (2). However, data that could provide a robust "evidence-based" recommendation for CAD testing in diabetic patients are not available. Recognizing these issues, the ADA recently convened an expert panel that revisited the issue of screening for CAD in diabetic patients. The panel approached this by addressing four specific questions:

From the [1]Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands; the [2]Departments of Medicine and Physiology, Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, Connecticut; the [3]Department of Medicine, Cardiovascular Division, Mayo Clinic College of Medicine, Rochester, Minnesota; the [4]Department of Medicine, Division of Cardiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois; the [5]Department of Medicine, Division of Endocrinology and Metabolism, Indiana University, Indianapolis, Indiana; and the [6]Department of Medicine, Division of Endocrinology and Metabolism, University of Virginia, Charlottesville, Virginia.

Address correspondence and reprint requests to Eugene Barrett, MD, PhD, University of Virginia, Box 801410, Charlottesville, VA 22903. E-mail: ejb8x@virginia.edu.

Abbreviations: ADA, American Diabetes Association; CAD, coronary artery disease; CT, computed tomography; CVD, cardiovascular disease; ECG, electrocardiogram; MI, myocardial infarction.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc07-9927.

1. Which patients with diabetes are at increased risk for adverse cardiovascular outcomes?
2. What are the implications of an early diagnosis of coronary ischemia or atherosclerosis?
3. What tests, or sequence of tests, should be considered? With what frequencies should testing be done?
4. What further research is needed to evaluate the effectiveness of these recommendations?

The goal was to provide practitioners with information on the role of specialized cardiac testing in their CAD asymptomatic diabetic patients, recognizing that diabetic patients with CAD symptoms are typically referred for cardiac testing. The panel recognized that some patients, who may be at high risk for CAD, do not have access to care that would allow them to benefit from this guidance or from the proven benefits of risk modification. Clearly, priority resources are needed to address these access disparities. The panel also recognized the need for educational interventions, directed toward diabetic patients and their families, dealing with early symptom recognition and response, as well as lifestyle modifications that diminish CVD risk.

Finally, in these discussions, it was recognized that the preponderance of data regarding both testing and risk factor modification derive from studies of type 2 diabetes. However, there is evidence from epidemiological studies that people with type 1 diabetes have significantly higher CAD event rates than age-matched control subjects; these rates exceed 1% per year after age 45 years and 3% per year after age 55 years (19). These estimates likely do not reflect the impact of newer risk-reduction interventions, but there is no reason to suspect that this population would respond less well to these than either the type 2 diabetic or nondiabetic populations. When appropriate, we point out how positions articulated herein may apply to people with type 1 diabetes.

1. Which patients with diabetes are at increased risk for adverse cardiovascular outcomes and should be screened?

The strategy of screening patients with diabetes for advanced asymptomatic CAD is motivated by the goal of identifying patients with high cardiac risk whose outcomes might be improved through more aggressive risk factor modification, medical surveillance, or revascularization of their CAD. However, clinical factors that confer risk for adverse cardiac outcomes do not always predict which patients will have abnormal screening tests (13,14), and negative screening tests in patients with diabetes do not uniformly confer a benign prognosis (20,21). Tests that detect inducible ischemia or assess atherosclerotic burden do not always identify those patients at risk for plaque rupture and thrombosis, which typically leads to acute coronary events. Further research focusing on the biological properties of the vessel wall is needed to identify individuals at high risk for acute coronary events, and such evidence might in the future guide treatment in asymptomatic individuals.

Patients with clinical CAD are generally classified into three categories: low risk, with a cardiac mortality risk <1% per year; high risk, with a cardiac mortality risk >3% per year; or intermediate risk, with a cardiac mortality risk between 1 and 3% per year. The overall population of asymptomatic patients with type 2 diabetes falls into the intermediate cardiac risk category. In UK Prospective Diabetes Study (UKPDS), relatively healthy patients recently diagnosed with type 2 diabetes had a 10-year mortality rate of 18.9%, with an incidence of myocardial infarction (MI) of 17.4%, including fatal MI of 8.9% (22). In middle-aged subjects with newly detected diet-controlled diabetes in the Diabetes Intervention Study, 15% had evidence of myocardial infarction by 11 years of follow-up (23). However, within such groups, there is a range of risk that would be helpful to further understand.

The 1998 Consensus Development Conference proposed a group of patients with diabetes who might have the highest yield from cardiac testing, those with multiple CVD risk factors. Unfortunately, recent studies have shown that the burden of traditional categorical risk factors does not predict inducible ischemia on nuclear or echocardiographic myocardial perfusion imaging (13,14).

In the absence of symptomatic CAD, clinical features that help to identify the patient with increased risk for myocardial infarction or cardiac death include evidence of other atherosclerotic vascular disease, renal disease, abnormal resting electrocardiogram, diabetes complications including autonomic neuropathy, age, sex, and both traditional and novel cardiac risk factors. Although these factors might not specifically predict the presence of inducible ischemia, they still warrant careful consideration for identifying patients at risk for events.

Other atherosclerotic vascular disease. Clinically evident atherosclerotic disease involving lower-extremity, cerebral, renal, or mesenteric arteries identifies a patient with diabetes who is at increased risk for adverse cardiovascular outcomes and might have advanced coronary atherosclerosis (24). In patients with claudication or asymptomatic peripheral arterial disease, 90% of deaths are attributable to CAD (25). Clinical history is important to determine the presence of vascular symptoms (transient ischemic attack, mesenteric ischemia, or claudication), as is the physical exam for bruits and peripheral pulses. A diminished ankle-brachial index is a sensitive indicator of increased risk for future CVD events (26).

Microalbuminuria and chronic kidney disease. Microalbuminuria predicts increased risk for vascular disease complications (15,17,27,28), as well as for the progression to overt nephropathy, in patients with type 1 or type 2 diabetes. Patients with type 1 diabetes and diminished renal function often develop extensive atherosclerosis. Patients with type 2 diabetes with chronic kidney disease due to diabetic nephropathy have a very high risk for MI and cardiac death, with 40% experiencing a cardiac complication over a 5-year period (25). Microalbuminuria has been a predictor of inducible ischemia in some (29), but not all (14), studies of asymptomatic patients with diabetes.

Abnormal resting ECG. Asymptomatic patients with type 2 diabetes occasionally have evidence of previously unrecognized MI on resting ECG, including abnormal Q-waves or deep T-wave inversions. These findings or the presence of a left-bundle branch block usually trigger evaluation for CAD and inducible ischemia, as would be pursued in a patient with angina. Testing in these patients should probably not be considered "screening," but rather evaluation of an objective abnormality for clinical reasons. However, nonspecific ST-T wave changes also are a strong predictor of inducible ischemia in asymptomatic diabetic patients (12).

Autonomic neuropathy. Cardiovascular autonomic neuropathy is associated with a poor overall prognosis in patients with type 2 diabetes (30). The mechanisms that confer the high risk are poorly understood but may include impairment in ischemia awareness, delaying the diagnosis of CAD, or hemodynamic lability due to blunted parasympathetic activa-

tion. Autonomic neuropathy might also be a parallel consequence of cardiac risk factors, including hyperglycemia, dyslipidemia, and renal disease. Autonomic neuropathy was a major predictor of inducible ischemia in the DIAD (Detection of Ischemia in Asymptomatic Diabetics) study (14) and has been associated with abnormal cardiac test findings in other (31), but not all (32), studies. The ADA has recently recommended screening for cardiac autonomic neuropathy, at least with a history and an examination for signs of autonomic dysfunction, beginning at diagnosis of type 2 diabetes or 5 years after the diagnosis of type 1 diabetes (33). The possibility of cardiac autonomic neuropathy should be considered in the presence of unexplained tachycardia, orthostatic hypertension and/or hypotension, and other autonomic or peripheral neuropathies.

Retinopathy. Although a manifestation of microvascular disease, diabetic retinopathy is also an indicator of risk for CAD in both type 1 and type 2 diabetes (34,35). In clinical studies, retinopathy has been associated with inducible ischemia in some (36), but not all, screening studies.

Hyperglycemia. Hyperglycemia is a stronger predictor of microvascular disease than atherosclerotic macrovascular disease in people with diabetes (37,38). In clinical trials, interventions to improve glycemic control reduced coronary events in type 1 and type 2 populations (37,39) and mortality in a type 1 population (39). Hence, chronic undertreated hyperglycemia could be viewed as a risk factor for CVD.

Age and sex. Although diabetes increases relative cardiovascular risk more in women than men, the absolute risk of cardiovascular events is still higher in men than women (40). Age is an important determinant of cardiovascular risk, and the prevalence of inducible ischemia is significantly higher in patients with type 2 diabetes over the age of 65 years (41).

Unexplained dyspnea. Frequently providers are uncertain as to whether a patient's complaint of shortness of breath is attributable to myocardial ischemia (an angina equivalent) or simply to obesity and deconditioning. However, it is important to recognize that, irrespective of cause, patients who are unable to exercise are at increased cardiac risk. The incidence of inducible ischemia is increased in these patients and when present portends a very poor prognosis (42).

Multiple cardiac risk factors. Patients with type 2 diabetes often have multiple cardiac risk factors, including hypertension in ~50–60% of individuals, dyslipidemia, inactivity, smoking, and abdominal obesity. Multiple risk factors in the same patient substantially increase the overall cardiovascular risk (43). Furthermore, intervention directed at multiple risk factors significantly improves cardiovascular prognosis (44). Despite the rationale that these patients are logical candidates for screening, recent CAD screening studies in type 2 diabetes have been unable to link the number of risk factors to inducible ischemia on perfusion imaging (14). This may reflect the inability of these studies to account for the severity, duration, and effect of treatment of both lipid abnormalities and hypertension in patients with long-standing type 2 diabetes.

There remains a need to improve our ability to identify, on the basis of readily available clinical data, those patients at highest risk for CVD events who would be priority candidates for additional diagnostic and/or therapeutic interventions. While simple categorical risk factor burden has not proven to effectively discriminate which asymptomatic diabetic patients will or will not have ischemia on stress testing (14), it is still possible that risk factor burden might predict risk of CVD events in individual patients. Efforts have been made using data from Framingham (which included fewer than 400 diabetic subjects), the UKPDS (which included only newly diagnosed diabetic subjects and excluded patients with significant comorbidities), and other populations (45) to develop models that identify individuals at highest risk for cardiovascular events. These efforts have been only modestly successful (45,46). Another prediction model, Archimedes, available on the ADA Web site as Diabetes PHD, has proved useful in predicting population clinical outcomes in response to specific interventions used in clinical trials (47,48). Such tools may provide useful probabilistic guidance for diagnostic algorithms.

2. What are the implications of an early diagnosis of coronary ischemia or atherosclerosis?

Several noninvasive imaging techniques are evolving that enhance the anatomic diagnosis of CAD. Demonstration of atherosclerotic involvement of the coronary arteries may now be made with measurement of the amount of coronary calcification. CT coronary angiography is also being used to define the atherosclerotic burden, including noncalcified atherosclerotic disease, and to estimate the degree of narrowing of individual lesions. Documentation of coronary atherosclerosis with noninvasive imaging has attracted the attention of patients, physicians, and the general public. While the images are quite impressive and provide objective evidence of coronary atherosclerosis, how these tests should influence management decisions is uncertain. For example, in the asymptomatic middle-aged or older diabetic patient who already receives intensive atherosclerotic risk factor therapy, "routine" imaging of the coronary arteries is not necessary to make decisions regarding treatment for well-established risk factors.

Coronary atherosclerosis may exist with or without flow limitation in the epicardial coronary arteries. Flow limitation is a major consequence of epicardial coronary atherosclerosis and is the basis of "ischemic heart disease." There is a large body of evidence documenting the relationship between indexes of myocardial ischemia by noninvasive testing and the presence of high-risk coronary anatomy. Autopsy studies have documented a greater prevalence of severe multivessel CAD among patients with diabetes compared with those without diabetes, even in the absence of prior symptoms or clinical evidence of disease (49). Ischemic abnormalities on noninvasive testing predict outcomes better than presence or absence of angina (21). Thus, the presumed benefit to the individual asymptomatic patient of assessing the presence and extent of myocardial ischemia is to identify those patients who would have a survival benefit from coronary artery revascularization, specifically those with left main or severe multivessel disease with a large area of jeopardized myocardium.

Patients with diabetes have significant risk for atherosclerotic vascular disease, and aggressive treatment of risk factors is recommended in the absence of symptomatic or known CAD. Therefore, the role of coronary imaging in diabetic patients is not to document the presence of coronary atherosclerosis but to identify those with more extensive disease in whom further testing may be warranted in order to identify those with significant inducible myocardial ischemia. This is

based on the assumption (and the widespread clinical practice) that patients with severe myocardial ischemia involving a large segment of the left ventricular myocardium are candidates for coronary angiography and subsequent revascularization. The exact definition of "severe" ischemia is unknown and has not been tested prospectively, but the available data (50) suggest that patients with ischemia involving 10% or more of the left ventricle have a better outcome after myocardial revascularization compared with the results of medical therapy alone. Retrospective studies have shown similar results in patients with diabetes (51).

The recently completed COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive DruG Evaluation) trial (52) reported that among 2,287 patients with stable angina, many of whom had multivessel or proximal left anterior descending coronary artery disease, intensive medical treatment was as effective as percutaneous intervention combined with intensive medical treatment in preventing overall mortality or myocardial infarction. Results were similar in the approximate one-third of subjects with diabetes. It may not be appropriate to extrapolate the results of this trial in symptomatic patients (in which the event rate for diabetic subjects approached 5% per year) to somewhat lower-risk asymptomatic patients. The hypothesis that asymptomatic patients with severe ischemia benefit from revascularization over and above aggressive medical management remains unproven and is currently the subject of several prospective randomized trials, some specifically targeted to the diabetic population. The results of these trials will either support or disprove the validity of testing for myocardial ischemia.

Are there other advantages to establishing the diagnosis of "ischemic heart disease," including definition of coronary atherosclerotic burden? Some would argue that compliance to medical therapy is enhanced with definition of the presence of disease, although this has not been established by controlled studies. Negative implications of diagnosing CAD in the absence of symptoms may include anxiety, compromised insurability, false-positive and negative tests, and more. The cost implications must also be considered given the constraints on health care resources (53).

In summary, accurate and early diagnosis of coronary atherosclerotic/ischemic heart disease is likely of benefit primarily to those patients with severe anatomic disease, where revascularization has particular benefits. However, extensive and expensive diagnostic testing to define the presence of CAD is not required before deciding to implement medical therapy for established risk factors in most diabetic patients. There may be exceptions; an example is a patient with type 1 diabetes under 40 years of age who may have a 20- to 25-year history of diabetes but does not fall within current guidelines for aggressive statin or aspirin therapy (10).

3. What tests, or sequence of tests, should be considered? With what frequencies should testing be done?

The 1998 ADA Consensus Development Conference recommended exercise electrocardiography to screen patients felt to be high risk due to risk factor burden or presence of atherosclerosis at other sites. Imaging for ischemia was recommended as the initial strategy only in patients with abnormal resting electrocardiograms. Over the course of the last several years, a number of important developments in cardiovascular imaging technology have evolved, together with a growing database regarding the role of imaging in detecting CAD in asymptomatic patients with risk factors, including diabetes. For example, we note recent studies of cardiac CT demonstrating prognostic value of such imaging (54,55). Moreover, professional societies have updated their recommendations for the use of CT imaging (56) and have developed appropriateness criteria for the use of nuclear cardiology procedures, cardiac CT, and cardiac magnetic resonance (57). These new recommendations and appropriateness criteria have important implications for screening asymptomatic patients with and without diabetes.

The broad strategy for screening asymptomatic patients remains uncertain, based on the very limited database and the lack of prospective clinical trials. If in the judgment of the clinician an asymptomatic patient is a candidate for CAD testing, it is reasonable to apply cardiac CT for detection of coronary artery calcification, using either electron beam or multislice technology, as the first step. The coronary calcium score is an excellent marker for the overall coronary atherosclerotic burden and identifies asymptomatic individuals at higher risk for inducible ischemia. The calcium score may also identify those at risk of subsequent coronary events but should be used with full knowledge of the patient's complete cardiovascular risk profile. The updated American Heart Association scientific statement (58) states that coronary calcium testing is not valuable in individuals at low Framingham risk but may be useful as a screening tool in those at intermediate risk, which would include patients with diabetes. However, there was only limited support for coronary calcium testing of patients at intermediate risk, with a class IIb recommendation (level of evidence B). Moreover, the American College of Cardiology appropriateness criteria for cardiac CT (57) indicate that the usefulness of screening asymptomatic intermediate-risk populations with this technology is currently unknown (56).

Several studies have shown that the coronary artery calcium score is valuable in identifying patients with a high likelihood of inducible myocardial ischemia (59,60). These studies have consistently observed that the likelihood of ischemia in patients with a calcium score <100 is negligible, whereas those with a score of ≥ 400 have a relatively high likelihood of inducible ischemia. It should be noted that these studies evaluated patients undergoing stress testing for clinical indications, in whom the likelihood of CAD would be higher than in the population that might be selected for screening, and did not specifically study patients with diabetes. However, Anand et al. (17) studied asymptomatic patients with diabetes and confirmed the higher incidence of inducible ischemia in patients with higher calcium scores. Nearly one-third of those patients had a calcium score >400, and 28% of which had large ischemic defects.

The decision to undertake coronary artery calcium screening should be based on sound clinical judgment and the test performed only if the results have the potential to change patient management. There are populations, including the elderly and those with renal insufficiency, with a very high prevalence of coronary calcification but in whom calcium scores are less predictive of ischemia, which limits the value of such testing. In such patients, any screening test might be considered inappropriate. Alternatively, one might proceed directly to stress imaging to assess myocardial ischemia.

If coronary calcium testing is performed, it appears reasonable to proceed with further testing in diabetic patients with calcium scores >400, considering factors such as age and renal function.

The threshold of 400 for further testing is consistent with the 2006 American College of Cardiology appropriateness criteria (57). Further testing could be performed using single photon emission tomography to assess myocardial perfusion or stress echocardiography to assess ischemic wall motion abnormalities. Cardiac magnetic resonance is now able to assess perfusion, wall motion, or both during pharmacologic stress but is less widely available and in most situations more expensive.

The timing of serial stress imaging studies in patients with initially normal stress tests is also uncertain. The issue of the "warranty" period of a normal study was addressed by Hachamovich et al. (61) in a general population using myocardial perfusion imaging and Elhendy et al. (62) in patients with diabetes with exercise echocardiography, both suggesting that the cardiac event rate is low within 2 years after normal stress myocardial perfusion or echo studies but that events may subsequently occur, presumably due to progressive atherosclerosis.

4. What further research is needed to evaluate the effectiveness of these recommendations?

Several considerations suggest that better approaches to patient selection for CAD screening would be of considerable value. CARDS (Collaborative Atorvastatin Diabetes Study) included individuals with type 2 diabetes and no history of cardiovascular disease. In that study, the active treatment group, in whom LDL cholesterol was lowered to ~80 mg/dl, still had a 1.5% per year major cardiovascular event rate. While other, non-LDL risk factors were not optimally treated in this study, its findings serve to emphasize that type 2 diabetic patients being treated according to intensive treatment guidelines likely have a residual "intermediate risk" (1–2% per year) for cardiac events. In the recently completed COURAGE trial (63,64), overall event rates among diabetic patients were nearly 5% per year, again indicating a significant residual risk in intensively medically treated patients as well as those undergoing percutaneous intervention. These findings would seem to highlight the need for improved methods to stratify residual risk within populations undergoing intensive medical management.

As a first step, development and testing of improved risk prediction models against data available from national registries would be particularly helpful in capturing general population risk data (65). There is a significant need to be inclusive in the populations assessed, so that adequate representation of both sexes and all racial groups is captured. Such data are not readily available in the U.S., where, for the present, we would likely rely on analyses of populations studied during clinical trials. Integration of the efforts at the National Heart, Blood, and Lung Institute and the National Institute of Diabetes and Digestive and Kidney Diseases to facilitate analyses of this sort could potentially fill much of this need. While it would be desirable to prospectively study a large cohort of individuals with type 2 diabetes without CVD symptoms to test such predictive models, a more intense analysis of pooled data from completed studies offers the attractive advantage of being available in a much more timely fashion.

The BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial, focused entirely on patients with type 2 diabetes, will provide a next step in outcomes. In this trial, patients with documented CAD have been randomized to immediate revascularization combined with aggressive medical management or to a program of aggressive medical management with delayed or no revascularization. The trial will provide a perspective on the benefits of revascularization in the era of modern medical therapy and important information for developing strategies for the treatment of asymptomatic patients. Proper trials testing the new imaging modalities, such as those called for in recent American College of Cardiology consensus recommendations, are a particularly important area of investigation. The results of these trials will have a major impact on the implementation of the recommendations outlined in the current article and will provide a basis for further revisions in the future.

Future studies should include innovative new approaches to characterization of plaque structure and stability, consider use of biomarkers, and perhaps incorporate genetic testing in combination with imaging strategies. These trials should specifically include strong representation of women and minorities who bear a disproportionate burden of disease and mortality from diabetes. It will be critical as part of future trials to determine whether screening for CAD is cost effective and helps to improve patient adherence to risk-reducing therapies. Partnership between the National Heart, Blood, and Lung Institute, the National Institute of Diabetes and Digestive and Kidney Diseases, the Centers for Medicare and Medicaid Services, and the industry would help facilitate the application of newer technologies to diabetes cardiovascular research. Beyond that, the establishment of an international clinical research network devoted to the study of cardiovascular disease in diabetes would help further our understanding. The need for such a network is clear with the current worldwide epidemic of obesity and type 2 diabetes.

Closing comments

Although the CAD asymptomatic patient with diabetes is by definition at least at intermediate risk for CVD events, it is difficult to support routine CAD screening for these patients. As previous recommendations for stratifying diabetic patients based upon the number of risk factors have not proven effective, the question remains whether there are individuals with diabetes in whom coronary artery imaging would seem particularly appropriate. Presumably, the motivation for such testing would be the clinical suspicion that the individual is at high risk for having a CVD event in the short term. Further development and testing of diabetes-specific "risk engines" may be helpful in identifying these subjects. In patients deemed on clinical grounds to be at particularly high risk, coronary artery calcium scoring may be the reasonable first test, with subsequent functional imaging performed if the calcium scoring indicates a substantial atherosclerotic burden.

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