In Brief

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in patients with diabetes. Consequently, proper screening and diagnosis of CAD is crucial for the prevention and early treatment of coronary events. This review explains the variety of diagnostic exams available for the identification of CAD in patients with diabetes and will assist health care providers in determining the appropriate diagnostic tool for each patient.

Screening for Coronary Artery Disease in Patients With Diabetes

Eve Roelker, MS, ANP-BC, CCRN

Diabetes is a metabolic disease that requires diligent management by patients and health care providers. Patients often present with serious comorbidities and risk factors that appear to occur in clusters. One of the most important goals in clinical practice is aggressive management of these risk factors to prevent complications that lead to disability and decreased survival.

The leading cause of mortality in patients with diabetes is cardiovascular disease (CVD). When it does occur, CVD in diabetic patients is more severe, more complex, and results in higher complication rates than in patients without diabetes.[1] Coronary artery disease (CAD) increases with advancing age but often occurs at a younger age in patients with diabetes. Occult CAD among asymptomatic patients with diabetes is common, ranging from 20 to > 50%.[2,3] The occurrence of silent myocardial ischemia, especially in the setting of autonomic neuropathy, may delay or mask the diagnosis of CAD, particularly at its early stages. High mortality rates are often associated with silent or asymptomatic myocardial infarction (MI).

Diabetes is considered a CAD risk equivalent according to the Adult Treatment Panel of the National Cholesterol Education Program guidelines; this means patients with diabetes have a risk for coronary events similar to that of patients without diabetes who have already had an event.[4] The risk is identified as low, intermediate, or high based on annual event rates for CVD death or MI.

This essentially places patients with diabetes at high risk for cardiovascular events, with an overall risk > 20% in 10 years. In acute coronary syndrome (ACS), diabetes confers a significant adverse prognosis, with mortality at 30 days and at 1 year significantly higher than in patients without diabetes.[5] This high risk was once again supported in a recent study from Denmark that confirmed that patients with diabetes are twice as likely to die from an MI as patients without diabetes.[6] Once a patient with diabetes has had an MI, the mortality risk is two to four times higher than in an individual without diabetes.[7]

Cardiovascular events are the leading cause of death and disability in women, with mortality nearly three times higher in diabetic women than in diabetic men. The onset of CAD in women is delayed by 10–15 years compared to men, yet more women than men die from CAD. Some of the factors involved in determining risk may include sex hormones, chronic inflammation, plaque burden, impaired flow reserve, and endothelial dysfunction.[8,9] Up to 65% of women, especially younger women, may have a different presentation or atypical symptoms that may include fatigue, dyspnea, or sleep disturbance. Additional factors that affect risk assessment in women include the complex and multifactorial nature of the disease process, the small

arterial size, and vascular/metabolic abnormalities.

Women with ACS have a worse prognosis than men. Some believe this may be related to gender bias within the medical community. The initial presentation of CAD in women is acute MI or sudden cardiac death in 60% of cases.[9] In acute MI, the 1-year death and reinfarction rates are higher in women. It is interesting to find, however, that at the time of angiography, women have a higher prevalence of nonobstructive coronary arteries, and this may lead to diagnostic uncertainty and therapeutic indecision and delays. In fact, nearly 60% of women from the Women's Ischemia Syndrome Evaluation study undergoing coronary angiography for evaluation of chest pain or an abnormal stress test did not have a flow-limiting stenosis.[10] In the absence of a flow-limiting stenosis, ischemia may be the result of microvascular disease and endothelial dysfunction affecting the production of nitric oxide.

Why Screen?

Screening for CAD may help to identify patients at highest risk within a population that has a high prevalence and risk of CAD. Some would argue that screening is not helpful or indicated because all patients with diabetes are already presumed to be at high risk and need to be treated aggressively. The American Diabetes Association (ADA) guidelines were developed to help identify patients at highest risk, but studies have shown that using the ADA guidelines yields poor identification of patients at risk for silent myocardial ischemia.[3,11]

In general, assessment of traditional risk factors alone fails to detect a significant percentage of patients with ischemia, especially silent ischemia. Screening certain patients would not only help to make the diagnosis but would also help to identify prognosis. The goal of screening would be to identify the presence and extent of myocardial ischemia in patients who may benefit from both medical therapy and revascularization, although this remains unproven. Confirming the diagnosis of CAD from a screening study may in fact alter medical therapy, such as by adding β-blocker therapy to the medical regimen. Treatment goals may also change; an example of this would be LDL cholesterol lowering, which has a lower goal of < 70 mg/dl in those at highest risk.[12]

Who to Screen?

Screening asymptomatic patients with diabetes is considered controversial, in part because there are no data to support improved outcomes with screening. In addition, screening every patient with diabetes is probably not cost-effective. There are some patients who could be categorized as higher risk, such as those with the triad of smoking, hypertension, and diabetes. The risk continues to increase if you add high LDL and low HDL cholesterol to these three factors. Obesity also increases risk, especially abdominal obesity, which is associated with insulin resistance and higher levels of C-reactive protein. Other risk factors include chronic kidney disease (CKD), as well as family history.

The major risk factors identified by the Framingham Risk Score include sex, total cholesterol, HDL cholesterol, systolic blood pressure (or treatment thereof), cigarette smoking, and age.[13] The ADA consensus statement on CAD[14] recommends screening in the following cases:

- typical or atypical chest pain
- abnormal electrocardiogram (ECG) suggestive of ischemia or infarction
- peripheral or carotid arterial occlusive disease
- > 35 years with sedentary lifestyle in a patient who plans a vigorous exercise program
- Two or more risk factors in addition to diabetes, such as dyslipidemia, hypertension, tobacco use, family history for premature CAD, or micro- or macroalbuminuria

However, studies have demonstrated that the burden of traditional risk factors does not predict inducible ischemia on testing.[3] We need to change our thinking from culprit lesion to culprit patient, especially in women.[9] But how do we identify the culprit patient?

The recommendation in women is to assess overall risk for CVD. Women can be considered to be at optimal risk, at risk, or at high risk. Optimal risk refers to a woman with a healthy lifestyle and no cardiovascular risk factors. Women at risk have one or more cardiovascular risk factors, and women at high risk already have CAD, diabetes, peripheral arterial disease (PAD), or CKD.[15]

We recommend careful questioning about exertional symptoms in every patient. Anginal symptoms may be difficult to elicit in some patients.[11] Any patient with exertional symptoms, which may be described as generalized fatigue, shortness of breath, chest pain, nausea, or lightheadedness, should be screened for CAD and ischemia.

Other patients who may be considered for screening, despite being asymptomatic, include high-risk patients, such as those with PAD, CKD, abnormal resting ECG with changes suggestive of silent MI (Q waves, T wave inversion, or left bundle branch block), known history of autonomic neuropathy, retinopathy, hyperglycemia, advanced age, unexplained dyspnea, and the presence of multiple risk factors, such as smoking, hypertension, dyslipidemia, sedentary lifestyle, and abdominal obesity.[16] The greater the number of risk factors, the higher the pretest probability, and the more useful the test.[17,18]

Which Test for Which Patient?

Stress testing with exercise or imaging has the greatest value in patients with a pretest intermediate risk for CAD. Stress testing can be performed with several modalities that can provide different types of information regarding diagnosis and prognosis. Several studies may be considered, including coronary calcium calcification (CAC) scoring, coronary computed tomography angiogram (CCTA), stress test with and without an imaging modality, and cardiac catheterization (not usually the initial screening test).

Exercise treadmill test (ETT)

An ETT can be used to assess tolerance of increased activity with continuous ECG monitoring, as well as hemodynamic response and symptoms. This test is well established, inexpensive, and easily available. In addition to providing information about exercise-induced ischemia, ETT also offers information regarding exercise capacity and functional status. The stress portion of the test can be conducted with exercise or medical therapy, and an imaging modality may be appropriate for some patients.

Exercise capacity is a strong and independent predictor of all-cause mortality. In the Veterans Administration study, patients with the highest exer-

cise capacity had a 70% lower risk of all-cause mortality, and even moderate fitness had a 50% lower death rate.[19]

The ability to exercise is important when performing an ETT, and the need to reach target heart rate based on age may limit some patients. The test must be a measure of central ischemia, and some patients may be unable to complete the test before peripheral fatigue sets in, usually manifested in the legs. Consider this test without imaging in women who have a normal ECG tracing and can achieve 5 metabolic equivalents (METS) or higher in their daily routine. Begin the assessment by asking the woman if she can perform usual household chores. Use examples such as doing the dishes, house cleaning, and vacuuming. One tool that can be used to assess functional status before deciding if an ETT is the right test for a particular patient is the Duke Activity Status Index (DASI) questionnaire.[20] The DASI is a 12-item questionnaire for self-assessment of functional capacity.

Women who perform at < 5 METS might be better evaluated with pharmacological stress imaging[21] because they may not exercise adequately to provoke ischemia. Patients with lower exercise capacity are more likely to be female with comorbid conditions, such as diabetes and hypertension, and more likely to have chest pain, an abnormal heart rate recovery (HRR), and an abnormal chronotropic response with ETT.[22]

Although ST segment deviation is a significant finding in men, ST changes or even the presence of chest pain are not the best predictors of outcome in women. Functional capacity is a stronger predictor of outcome in women.[23] Prognostic values that signal poor outcomes derived from an adequately performed ETT include poor exercise capacity < 5 METS, exercise induced angina, low peak blood pressure or fall in systolic blood pressure, chronotropic incompetence, low HRR at 1–2 minutes after exercise, and ventricular arrhythmias, especially during the recovery phase.[17,24–26]

An abnormal HRR is failure to decrease the heart rate by a certain amount 1 minute after peak exercise. It may be seen in patients with autonomic dysfunction, which is common in patients with diabetes.

Exercise capacity is a strong and independent predictor of nonfatal cardiac events and mortality among patients referred for ETT. Failure to achieve 85% of predicted target heart rate is associated with higher risk of death from all causes.[22] Some studies, although small in size, support the use of ETT in asymptomatic women with diabetes to help identify unrecognized CAD.[1] Screening with imaging is recommended for symptomatic women with established CAD, abnormal ECG tracing, or an indeterminate ETT.[21]

Stress test with imaging

Examples of this modality include a treadmill or medical stress test with imaging via single-photon emission computed tomography (SPECT) or echocardiography. SPECT imaging is the most commonly used imaging study. Medical stress tests with SPECT imaging are valid and reliable methods to assess for myocardial ischemia with sensitivity of 91–96% and specificity of 75–82%. Results help to determine risk based on extent and severity of the size of the perfusion defect and reversibility signifying underlying obstructive CAD. A fixed defect without evidence of reversibility suggests a previous infarction or scar.

Imaging studies also provide information regarding left ventricular systolic function and wall motion. Medical stress tests with vasodilator therapy are recommended for patients who are not able to exercise or have an abnormal ECG, such as seen with left ventricular hypertrophy and strain pattern, a paced rhythm, a left bundle branch block, or sometimes scooping of the ST segments, as is sometimes seen with digoxin therapy.

Diabetic women with ischemia are at the highest risk for cardiac events and are usually candidates for testing with imaging. Indeed, SPECT imaging is recommended for symptomatic women with an intermediate to high pretest probability of CAD and abnormal ECG. If there is no evidence of ischemia on the study, the annual event rate in women is < 1%. There is always concern, however, that CAD is actually present despite negative results, and in women, false positive results may occur as a result of breast attenuation and small left ventricle chamber size.[21]

Stress testing may also be performed with echocardiography as the imaging modality. The stress portion of the study may be performed with exercise or with dobutamine if the patient is unable to exercise to an adequate level. This is referred to as a dobutamine stress echocardiogram (DSE). Stress echocardiography provides information about left ventricular systolic and diastolic function and valvular function and assesses for evidence of exercise-induced ischemia. It is also recommended for symptomatic women with an intermediate to high pretest probability of CAD. Both stress echocardiography and DSE appear to be gender neutral and equally accurate for men and women. They may also provide higher specificity and accuracy than standard ETT alone. Imaging might be limited in cases of obesity, pulmonary disease, breast implants, or large breasts.

CAC testing

The concept of CAC testing is based on the fact that calcification occurs early in atherosclerosis but it is not seen in normal arteries. The fast method scans to measure CAC are electron beam computed tomography or multidetector computed tomography. CAC is an assessment of total atherosclerotic plaque burden but does not necessarily identify the severity or vulnerability of a particular lesion. In fact, there is no relationship between a CAC score and outcome or location of stenosis.[27]

CAC is independently predictive of outcome over and above traditional risk factors. Studies have confirmed that higher CAC scores are associated with higher risk, and data suggest that any detectable calcium elevates the risk of CAD events nearly fourfold.[28] The association of CAC with adverse events was also recently confirmed in various ethnic groups where a doubling of CAC scores was associated with a 20% increase in risk of major event.[29] Scoring is based on the Agatston method using the CAC volume score; scoring is also age- and sex-dependent. There are five score categories as follows:

- Zero: no calcification
- 1–100: mild calcification
- 101–399: moderate calcification
- 400–999: severe calcification
- ≥ 1,000: extensive calcification

A negative result, or a calcium score of zero, is associated with a high level of confidence that an individual has no obstructive CAD with a very low rate of death or MI over 3–5 years (0.1% within next 2–5 years with a zero score).[27,28] Thus, a score of zero has a negative predictive value of 100%.

Scores of < 100 are usually associated with a low probability of abnormal perfusion on nuclear scan or significant obstruction on catheterization. Patients with scores ≥ 400 are likely to have event rates the same as patients at high risk because of known CAD or risk equivalent status (event rate ≥ 20% over 10 years). A positive result is 100% specific for atheromatous plaque but not specific for obstructive CAD because all lesions, obstructive and nonobstructive, have calcium. Asymptomatic women with a score ≥ 400 are considered at high risk.

CAC scoring can confirm or reclassify individual risk derived from the initial risk assessment.[27] It is an anatomic study; however, it is not a functional one and is usually considered second-line testing or for patients who are not able to exercise.[28] Consider CAC scoring as the initial test in patients when goals are not met with optimized medical therapy and for those with strong clinical suspicion of very high risk for CAD.[16]

Disadvantages involve cost; radiation exposure, especially in young patients; the absence of reimbursement strategies; and the lack of data showing that screening leads to improved outcomes. Currently, there are no data documenting improved survival or quality of life as a result of screening. Results are based mainly on referral populations and cannot be compared to population-based studies. Studies with larger numbers and longer follow-up periods are needed before CAC can be recommended to modify treatment goals in patients with diabetes.

Coronary computed tomography angiogram

This study is performed with a multislice or 64-slice computed tomography scanner to detect CAD. It is a noninvasive imaging test to evaluate fatty or calcium deposits in the coronary arteries. This technology can also detect both soft and hard plaque. It also provides additional information, such as the size of the aorta, location of plaque, anatomy of the coronary tree, and the presence of any congenital anomaly. The study usually takes about 10 minutes, and there is the risk of radiation exposure.

This test can be considered for asymptomatic patients who have significant risk factors or symptomatic patients with typical or atypical chest pain and for those with an equivocal stress test result. Patients who are significantly overweight or who have an abnormal rhythm, such as atrial fibrillation, are not good candidates for this study because imaging quality may be compromised. A functional study is recommended if the study reveals a > 50% lesion or a CAC score > 1,000.[30]

Cardiac catheterization

Coronary angiography is considered the gold standard for identifying obstructive lesions, but it also has its limitations. An angiogram is in reality a luminogram, and there may be outward remodeling in the vessel that does not show on the images. Women often have angina in the absence of coronary obstruction. This is likely related to microvascular ischemia resulting from impaired coronary flow reserve.[8] Cardiac catheterization is never used as an initial screening test. Instead, it is reserved for patients who have evidence of ischemia on a stress test or for further assessment of the coronary anatomy in patients with a negative stress test who continue to have symptoms (suspected false negative results).

Emerging studies

Cardiovascular magnetic resonance (CMR) imaging data are sparse but evolving rapidly. These studies can provide information regarding coronary stenoses and flow, evaluation of myocardial perfusion and metabolism, wall motion during stress, and evidence of infarction. The absence of ionizing radiation in CMR is an attractive feature because all imaging studies except echocardiography require exposure to ionizing radiation. There are limited data to support the use of CMR in aysmptomatic women, and claustrophobia in certain patients is sometimes seen.

The presence of plaque and thickness of intima and medial layers in carotid arteries, measured as carotid intima media thickness (CIMT), is considered a marker for CAD. The test is performed with high-frequency B-mode ultrasonography. It is simple and reproducible, widely available, well-validated, and does not expose patients to ionizing radiation. CIMT has an independent relationship to cardiovascular outcomes in women > 45 years of age. The relationship between CIMT and events is continuous, but testing has not shown improved outcomes. Limitations include lack of accepted technical standards for testing.[21]

Screening Recommendations

Begin the assessment by carefully interviewing patients to accurately assess for exertional symptoms. Understand that some patients may have begun limiting their activity levels to avoid provoking symptoms and may be unaware of this until questioned about changes in their activity level over time. In addition, some patients may have atypical anginal symptoms; this is particularly true in diabetic women. Patients with exertional symptoms, which may be variable in presentation, warrant screening.

Although it remains controversial to screen asymptomatic patients, screening patients with a limited functional status is probably a reasonable approach for people at moderate to high risk of underlying CAD. An ETT can be a safe and effective initial screening test in patients who can exercise and have a normal baseline ECG.

If, based on the assessment, a treadmill stress test is not the best study for a particular patient, an imaging study may be considered. In the Detection of Silent Myocardial Ischemia in Asymptomatic Diabetic Subjects study, the strongest predictors for silent myocardial ischemia were duration of diabetes, evidence of autonomic dysfunction, and male sex.[3] Patients with diabetes who are > 60 years of age or who have had diabetes for > 15 years warrant screening with an imaging study.[18] Screening should also be considered in patients with an abnormal ECG tracing suggestive of ischemia or infarction. If the results of an anatomical study, such as CAC or CCTA, are abnormal, a functional study, such as a nuclear stress or stress echocardiography study, is recommended to assess for the presence of ischemia.

When discussing options with patients, remember to consider the emotional and behavioral impact that screening and subsequent results, negative or positive, may have on them. There is also the issue of cost and possible disease labeling. Screening may have adverse effects on patients, including depression, anxiety, and stress, especially with positive results.[16] Negative results may lead to the mistaken belief that lifestyle changes are not indicated.[31] In planning a screening strategy with patients, it might help to

shift the focus from identifying risk to identifying benefit based on the findings to help guide therapy.[18]

Patients with diabetes are considered at high risk for cardiovascular events and mortality. Therefore, regardless of the results from any screening, aggressive treatment and management is imperative to prevent or delay the onset of vascular complications. Prevention is the first goal, especially in women with diabetes.

Cardiovascular risk reduction guidelines emphasize a team approach with a commitment from patients to make positive choices and self-management strategies. Therapeutic lifestyle modification, such as medical nutrition therapy, physical activity based on patients' willingness and ability, smoking cessation with counseling and behavioral therapy, and weight loss, remain the cornerstone of management. Of course, medical therapy to maintain systolic blood pressure < 130 mmHg, statins to reach an LDL goal < 100 mg/dl (or < 70 mg/dl in the setting of CAD), agents to treat hyperglycemia, and daily aspirin therapy are mandatory.[7] In terms of treatment, perhaps it is time to change our concept from "the lower the better" to "the sooner the better" for primary prevention of cardiovascular disease in patients with diabetes.[6]

Case Study

L.B. is a 48-year-old Hispanic woman who presents for a cardiovascular evaluation at the recommendation of her primary care provider. She has complaints of dyspnea with minimal activity, although she is quite sedentary. She denies any chest pain or pressure. She considers herself to have "borderline" diabetes but has no history of hypertension or dyspidemia. She stopped smoking 5 years ago. Her father died in his 70s from an MI. Her weight is 160 lb, and she is 5′4″ tall (BMI = 28 kg/m^2). On examination, her blood pressure is 136/80 mmHg with a heart rate of 88 bpm. The ECG reveals normal sinus rhythm with nonspecific ST changes.

Question: What would be the appropriate screening test for L.B.?

An exercise stress test would help to better assess her exercise tolerance, a strong predictor of mortality, as well as her hemodynamic response to activity. She would also be monitored for HRR and ventricular ectopy during the recovery phase. Her baseline ECG is abnormal, however, so an imaging modality is recommended. In this case, the stress test could be performed with SPECT or echocardiography. Imaging would also provide additional information regarding perfusion, systolic function, and wall motion.

Acknowledgment

The author wishes to thank Paula DeAnda, NP, for her editorial input and assistance.

References

[1]Albers AR, Krichavsky MZ, Balady GJ: Stress testing in patients with diabetes mellitus. *Circulation* 113:583–592, 2006

[2]Di Carli MF, Hachamovitch R: Should we screen for occult coronary artery disease among asymptomatic patients with diabetes? *J Am Coll Cardiol* 45:50–53, 2005

[3]Wackers FJT, Young LH, Inzucchi SE, Chyun DA, Davey JA, Barrett EJ, Taillefer R, Wittlin SD, Heller GV, Filipchuk N, Engel S, Ratner RE, Iskandrian AE: Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. *Diabetes Care* 27:1954–1961, 2004

[4]Haffner SM, Lehto S, Ronnemaa T: Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 339:229–234, 1998

[5]Donahoe SM, Stewart GC: Diabetes and mortality following acute coronary syndromes. *JAMA* 298:765–775, 2007

[6]Schramm TK, Gislason GH, Kober L, Rasmussen S, Rasmussen JN, Abildstrom SZ, Hansen ML, Folke F, Buch P, Madsen M, Vaag A, Torp-Pedersen C: Diabetes patients requiring glucose-lowering therapy and nondiabetics with a prior myocardial infarction carry the same cardiovascular risk. *Circulation* 117:1945–1954, 2008

[7]Blonde L, Dempster J, Gallivan JM, Warren-Boulton E: Reducing cardiovascular disease in patients with diabetes: a message from the National Diabetes Education Program. *J Am Acad Nurse Practs* 18:524–533, 2006

[8]Bellasi A, Paolo Raggi, Bairey Merz CN, Shaw LJ: New insights into ischemic heart disease in women. *Cleveland Clin J Med* 74:585–594, 2007

[9]Bairey Merz CN, Shaw LJ, Bittner V, Olson M, Pepine CJ, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Lerman A, Quyyumi AA, Sopko G: Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) study. *J Am Coll Cardiol* 47:21–29, 2006

[10]Merz CN, Kelsey SF, Pepine CJ, Reichek N, Reis SE, Rogers WJ, Sharaf BL, Sopko G: The Women's Ischemia Syndrome Evaluation (WISE) study: protocol, design, methodology and feasibility report. *J Am Coll Cardiol* 33:1453–1461, 1999

[11]Kharlip J, Ryan KA, Naglieri R, Donner TW, Mitchell BD: Screening for silent coronary heart disease in type 2 diabetes. *Diabetes Care* 29:692–694, 2006

[12]Grundy SM, Cleeman JI, Merz CN, Brewer Jr. HB, Clark LT, Hunninghake DB, Pasternak RC, Smith SC, Stone NJ: Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 110:227–239, 2004

[13]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* 285:2486–2497, 2001

[14]American Diabetes Association: Standards of medical care in diabetes. *Diabetes Care* 30:S4–S41, 2007

[15]Mosca L, Banka CL, Benjamin EJ, Berra K, Bushnell C, Dolor RJ, Ganiats TG, Gomes AS, Gornik HL, Gracia C, Gulati M, Haan CK, Judelson DR, Keenan N, Kelepouris E, Michos ED, Newby LK, Oparil S, Ouyang P, Oz MC, Petitti D, Pinn VW, Redberg RF, Scott R, Sherif K, Smith SC, Sopko G, Steinhorn RH, Stone NJ, Taubert KA, Todd BA, Urbina E, Wenger NK: Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update. *J Am Coll Cardiol* 49:1230–1250, 2007

[16]Bax JJ, Young LH, Frye RL, Bonow RO, Steinberg HO, Barrett EJ: Screening for coronary artery disease in patients with diabetes. *Diabetes Care* 30:2729–2736, 2007

[17]Lauer MS: What is the best test for a patient with classic angina? *Cleveland Clin J Med* 74:123–126, 2007

[18]Ali YS, Maron DJ: Screening for coronary disease in diabetes: when and how *Clin Diabetes* 24:169–173, 2006

[19]Kokkinos P, Myers J, Kokkinos JP, Pittaras A, Narayan P, Manolis A, Karasik P, Greenberg M, Papademetriou V, Singh S: Exercise capacity and mortality in black and white men. *Circulation* 117:614-622, 2008

[20]Hlatky MA, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, Cobb FR, Pryor DB: A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 64:651–644, 1989

[21]American Heart Association: Scientific statement: Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease. *Circulation* 111:682–696, 2005

[22]Peterson PN, Magid DJ, Ross C, Ho PM, Rumsfeld JS, Lauer MS, Lyons EE, Smith SS, Masoudi FA: Association of exercise capacity on treadmill with future cardiac events in patients referred for exercise testing. *Arch Intern Med* 168:174–179, 2008

[23]Shaw LJ, Olson MB, Kip K, Kelsey SF, Johnson BD, Mark DB, Reis SE, Mankad S, Rogers WJ, Pohost GM, Arant CB, Wessel TR, Chaitman BR, Sopko G, Handberg E, Pepine CJ, Bairez Merz CN: The value of estimated functional capacity in estimating outcome: results from the NHLBI-Sponsored WISE study. *J Am Coll Cardiol* 47:36–43, 2006

[24]Dewey FE, Kapoor JR, Williams RS, Lipinski MJ, Ashley EA, Hadley D, Myers J, Froelicher VF: Ventricular arrhythmias during clinical treadmill testing and prognosis. *Arch Intern Med* 168:225–234, 2008

[25]Curfman GD, Hillis LD: A new look at cardiac exercise testing. *N Engl J Med* 348:775–776, 2003

[26]Frolkis JP, Pothier CE, Blackstone EH, :auer MS: Frequent ventricular ectopy after exercise as a predictor of death. *N Engl J Med* 348:781–790, 2003

[27]Erbel R, Mohlenkamp S, Budde T, Schmermund A: Non-invasive screening for coronary artery disease: calcium scoring. *Heart* 93:1620–1629, 2007

[28]Greenland P, Bonow RO, Brundage BH, Budoff MJ, Eisenberg MJ, Grundy SM, Lauer MS, Post WS, Raggi P, Redberg RF, Rodgers GP, Shaw LJ, Taylor AJ, Weintraub WS: 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. *J Am Coll Cardiol* 49:378–402, 2007

[29]Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, O'Leary DH, Tracy R, Watson K, Wong ND, Kronmal RA: Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 358:1336–1345, 2008

[30]Lepor NE, Madyoon H, Friede G: The emerging use of 16- and 64-slice computed tomography coronary angiography in clinical cardiovascular practice. *Revs Cardiovasc Med* 6:47–53, 2005

[31]Chyun DA, Katten DM, Melkus, GD, Talley S, Davey JA, Wackers FJT: The impact of screening for asymptomatic myocardial ischemia in individuals with type 2 diabetes. *J Cardiovasc Nurs* 21:E1–E7, 2006

Eve Roelker, MS, ANP-BC, CCRN, is a nurse practitioner with Pima Heart Associates in Tucson, Ariz.