Cardiovascular disease (CVD) is the leading cause of death in the United States, where up to 60% of adults will have a myocardial infarction, stroke, or incident of heart failure in their lifetime. Despite these striking numbers, research data suggest that CVD is largely preventable. Individuals with optimal risk profile—collectively named “Life’s Simple 7” by the American Heart Association—have as much as an 80% reduction in risk of CVD.

Cholesterol and CVD Risk
Six of Life’s Simple 7 (healthy diet, physical activity, no smoking, and well-controlled blood pressure, blood glucose, and body weight) can be universally recommended by clinicians. However, the seventh item (cholesterol level) is a challenge because the optimal level is primarily determined by an individual’s risk for CVD.

National guidelines recommend the use of population-based risk algorithms, such as the Pooled Cohort ASCVD (Atherosclerotic Cardiovascular Disease) Risk Equations. “These risk algorithms are remarkably effective in predicting risk in populations, but have limitations in predicting individual risk,” says R. Todd Hurst, MD, director of the Heart Health and Performance Clinic at Mayo Clinic in Arizona. “The best illustration of these limitations is that the majority of CVD events (up to 75%) occur in low- and intermediate-risk populations.”

Because more accurate means of determining individual CVD risk are needed, a search is ongoing for better tools to identify high-risk individuals before clinical events occur. One such tool is imaging for subclinical atherosclerosis, most commonly accomplished by quantifying the amount of calcium in the coronary arteries by computed tomography.

Subclinical Atherosclerosis and CVD Risk Prediction
The coronary artery calcium score (CACS) is strongly correlated with future risk for myocardial infarction and stroke, making it a potentially attractive tool to further clarify individual risk for CVD. Several large studies with long-term follow-up have shown that CACS adds incremental information in CVD risk identification and provides more accurate CVD risk prediction compared with traditional risk factors in about 25% of individuals.

Despite the potential utility of these data, it is not known if identifying individuals who are at higher risk by CACS—and intensifying the prevention regimen—lowers the risk for CVD events. That question has not been adequately studied.

A Case: Statin or No Statin?
Mr. Smith is a 50-year-old African American man with concerns regarding cardiovascular risk. He has no personal history of CVD. He is active and asymptomatic and takes no medication. He is not a current smoker. His blood pressure is 134/82 mm Hg, and he has total cholesterol level of 212 mg/dL, high-density...
lipoprotein cholesterol of 54 mg/dL, triglycerides of 92 mg/dL, and calculated low-density lipoprotein cholesterol of 140 mg/dL. His Pooled Cohort ASCVD 10-year risk is 5.7%.

He notes that his 52-year-old brother recently had coronary artery bypass graft surgery and his father died of a myocardial infarction at 55 years of age but feels their health problems were primarily due to long-term tobacco abuse.

Mr Smith leads a healthy lifestyle but is wondering if he should consider taking a statin medication to further lower his risk for CVD.

“The 2013 American Heart Association/American College of Cardiology Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults” recommends shared decision-making about the benefits and risks of a statin medication when the 10-year risk is 7.5% or higher in a primary prevention, nondiabetic adult. In addition, the guidelines state that CACS, as well as ankle-brachial index (ABI), high-sensitivity C-reactive protein (hs-CRP), and family history of premature CVD may be considered (Class IIb) to “inform treatment decision making.” However, the guidelines do not make specific recommendations on how these tools should be used. Thus, according to the guidelines, in the case of Mr Smith, it would be reasonable for a clinician to take one of the following actions:

1. Not recommend a statin because the patient’s 10-year ASCVD risk is less than 7.5%.
2. Recommend a statin on the basis of the patient’s family history of premature CVD and his moderately elevated 10-year risk score.
3. Seek further information such as CACS, ABI, or hs-CRP to help guide the decision.

Clinicians who seek additional information want to know whether Mr Smith is at higher risk than would be predicted by risk factors due to genetic disposition for atherosclerosis. Following this line of thought, a high-risk CACS result indicates that a statin medication should be considered. If a low-risk result is obtained, reassurance and continued emphasis on lifestyle measures should be recommended.

What Patient Should Not Have a CACS?
The appropriate patient for CACS is still debated, and the answer to this question will likely continue to evolve as data accumulate. However, there is more agreement among experts in CVD prevention concerning patients for whom CACS is rarely indicated:

1. Patients with clinical CVD or those already taking a statin medication.
2. Patient scenarios where both the clinician and the patient agree that a statin is indicated.
3. Patient scenarios where both the clinician and the patient agree that a statin is not indicated.
4. Patients who have had previous CACS to assess the response to treatment.

What Patient Should Have a CACS?
While there is not enough evidence to make a recommendation without reservation to perform CACS in any patient, many clinicians who specialize in CVD prevention (including those at Mayo Clinic) believe that CACS can add valuable clinical information in selected patients.

In our practice, the most common indication for CACS is lack of a decision by the patient, the clinician, or both about whether to start a statin for CVD risk reduction. In such a situation, the imaging study can further clarify the patient’s risk and, by extension, whether a statin medication should be considered. There are several common clinical scenarios where the individual’s risk for future CVD is uncertain:

- Family history of CVD

Family history is often the most difficult CVD risk factor to assess. Although it is clear that family history is an important determinant of
risk, the complex interplay between genetic factors, environmental exposure, and lifestyle choices often makes confident assessment of an individual’s risk impossible. In this situation, CACS may help determine if the patient has a genetic disposition to atherosclerosis.

**Striking risk factor in a young patient**

Because age is the most heavily weighted factor in population-based risk algorithms, younger patients (<60 years) are less likely to be high risk, even if they have significant risk factors. The guidelines recommend considering a lifetime risk score in such patients. However, many clinicians use CACS to guide prevention recommendations.

**“Gray zone” (5%-7.5%) ASCVD 10-year risk score**

An imaging study may place the patient in either a lower or a higher risk category which would then impact clinical recommendations.

**What Is a High-Risk Imaging Result?**

The generally accepted definition of high risk with CACS is a reading higher than 300 Agatston units or a CACS at or above the 75th percentile when adjusted for age, sex, and race (Figure).

**Too Much or Too Little?**

The answer to the question “Are we doing too many CACS studies or too few?” is primarily dependent on the clinical judgment of each clinician. “It is clear that there is great need to more accurately identify individuals who are at high risk of CVD prior to clinical events, yet the role of CACS in CVD risk prediction, if any, is not clearly defined from the current data,” says Dr Hurst. Until more definitive data become available, most experts in prevention of CVD favor a strategy that limits use of CACS to those patients for whom the result would have the most impact on treatment recommendations.

For more information, see Life’s Simple 7 at http://www.heart.org/HEARTORG /Conditions/My-Life-Check---Lifes-Simple-7 _UCM_471453_Article.jsp#.VjKBHNiFNaQ and Pooled Cohort ASCVD (Atherosclerotic Cardiovascular Disease) Risk Equations at http://clincalc.com/Cardiology/ASCVD /PooledCohort.aspx

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**RECOGNITION**

**Mayo Clinic Distinguished Alumni Award**

Bernard J. Gersh, MB, ChB, DPhil, a member of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester, Minnesota, has been awarded the Mayo Clinic 2015 Distinguished Alumni Award. The Mayo Clinic Board of Trustees established the award in 1981 to recognize the exceptional contributions of Mayo alumni to the field of medicine. Individuals who receive the award have been recognized nationally and often internationally in their fields and exemplify Mayo Clinic’s ideals and mission. Dr Gersh (left) is pictured with Charanjit S. Rihal, MD, MBA, chair of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester, Minnesota.
Spontaneous Coronary Artery Dissection: Hidden in Plain Sight

Individuals presenting to the emergency department with chest pain first undergo risk assessment and diagnostic testing to rule out life-threatening entities such as acute coronary syndromes (ACS), pulmonary embolism, and aortic dissection. Among patients with suspected ACS, spontaneous coronary artery dissection (SCAD) is an increasingly important nonatherosclerotic cause of acute myocardial infarction (MI) and sudden cardiac death. Increased awareness and improved imaging modalities suggest that this condition, previously considered rare, is more common than appreciated. Novel use of online patient communities to catalyze research efforts and recruit SCAD patients to the Mayo Clinic SCAD Registry has substantially increased understanding of this condition, which is the most common cause of MI in pregnancy and peripartum and may account for up to 40% of MI in women younger than 40 years.

The development of atherosclerotic coronary artery disease (CAD) is understood to be due to the interplay of genetic and lifestyle factors that lead to endothelial plaques that may become unstable or occlusive, whereas the pathogenesis of SCAD is distinct from CAD. The demographic profile of individuals with SCAD markedly differs from those with atherosclerotic disease in that these patients are typically young women without conventional risk factors for CAD, according to Sharonne N. Hayes, MD, a cardiologist at Mayo Clinic in Rochester, Minnesota. More than 80% of SCAD patients are female, with a mean age of 42 years at the index event, up to a quarter of which occur in the peripartum period. Associated factors include nonatherosclerotic systemic vasculopathies, especially fibromuscular dysplasia; extreme stress, emotion, or exercise; connective tissue disorders; and, less commonly, monogenic mutations such as Ehlers-Danlos type IV or Marfan syndrome. SCAD patients at Mayo Clinic undergo comprehensive vascular imaging; 66% of this population has evidence of extracoronary vascular abnormalities.

The presentation of SCAD mimics that of other acute coronary events; therefore, a high index of suspicion is required to make the diagnosis. Like other ACS, symptoms and signs of SCAD include electrocardiographic findings of non-ST or ST elevation myocardial infarction, elevated cardiac biomarkers, regional wall motion abnormalities, ventricular arrhythmias, and sudden cardiac death. Coronary angiography should be performed immediately if SCAD is suspected.

“SCAD may present angiographically with the appearance of a false lumen created by intimal dissection,” says Rajiv Gulati, MD, PhD, an interventional cardiologist at Mayo Clinic in Rochester. “However, more commonly, SCAD presents with intramural hematoma, which causes luminal compression.” This appearance may mimic vasospasm, mild atherosclerosis, or “normal coronary artery tortuosity.” It is difficult to visualize with angiography alone. Therefore, it is critical in these patients to consider intravascular ultrasound or optical coherence tomography to make the diagnosis (Figure). Correct diagnosis is essential, as management differs from recommended management of ACS due to atherosclerotic disease. Other angiographic clues to SCAD include the absence of atherosclerosis or the presence of coronary artery tortuosity. “Coronary tortuosity is markedly more common in patients with SCAD compared with controls,” says Dr Gulati. Additionally, more severe tortuosity is associated with higher rates of recurrent SCAD.

Intriguingly, individuals with ACS due to SCAD who undergo percutaneous interventions (PCIs) have markedly higher rates of complications compared with those with CAD. In retrospective series, 13% of patients with SCAD presenting with normal or near-normal blood flow required emergency coronary artery bypass graft surgery due to catastrophic complications from PCIs. This observation combined with the substantial rate of spontaneous vascular healing suggests a role for conservative management in stable SCAD patients who have preserved coronary flow. Empiric medical management (single
antiplatelet agent, β-blocker, angiotensin-converting enzyme inhibitor therapy if appropriate) and close observation are recommended in these individuals. Because dissection may progress early in otherwise stable patients, 4 to 5 days of inpatient monitoring is recommended.

Recurrence rates of up to 20% at 10 years underscore the need for long-term management and follow-up. While specific SCAD recommendations cannot be made because long-term data are lacking, individuals benefit physically and emotionally from participation in cardiac rehabilitation programs. Depression and anxiety are common after an event and should be recognized and treated. Nitrate-responsive chest pain is also common and often responds favorably to long-acting nitrates or calcium channel blockers. As many SCAD patients have a history of extreme physical activity immediately prior to their index event, it seems prudent to advise against high-level competitive athletics, extreme exertion, or body building. The high incidence of events associated with the peripartum period implicates a hormonal role, and women are advised to avoid pregnancy and hormonal contraceptives. Empiric low-dose aspirin is recommended in these individuals. Patients who have received a stent should receive dual antiplatelet therapy. Additional pharmacologic therapy should target non-SCAD conditions if present such as hypertension or hyperlipidemia. Routine statin therapy is not recommended, as it has been associated with increased risk of recurrent SCAD.

Medical genetics evaluation is advised in these patients. “Although several monogenic mutations associated with vascular pathology have been identified in SCAD patients, no mutations specific to SCAD (or fibromuscular dysplasia) have been identified to date,” says Timothy M. Olson, MD, a pediatric cardiologist at Mayo Clinic in Rochester. The Mayo Clinic SCAD Registry has developed a Virtual Multicenter SCAD Registry, which includes a DNA biorepository of blood samples from patients and first-degree relatives. Of the over 525 consented female SCAD participants, 98% have provided DNA samples.

Preliminary whole exome sequencing data from a pilot study of 28 sporadic SCAD family trios and an affected sibling pair have revealed that 1) SCAD is a genetically heterogeneous disorder; 2) mutations in genes for thoracic aortic aneurysm and dissection do not appear to be a common cause for SCAD; and 3) 4 plausible candidate genes implicate perturbed Rho signaling, angiogenesis, and actin cytoskeletal integrity as potential underlying factors in SCAD susceptibility. This sequencing endeavor is a key component in the investigation of cardiac disease in young women.

For further information about SCAD and the Mayo Clinic Virtual Multicenter SCAD Registry, visit www.mayo.edu/research/SCAD.

**Figure.** Top, Coronary angiogram of a 49-year-old woman who presented with an acute coronary syndrome in the absence of atherosclerotic risk factors. The arrow indicates focal smooth stenosis in the mid left anterior descending artery. Bottom, Intravascular optical coherence tomography (OCT) reveals intramural hematoma causing compression of the coronary lumen as the reason for stenosis (asterisks, lower left panel), with an absence of intraluminal plaque. Sequential OCT frames moving distally indicate separation of the intima from the media (arrow, lower right panel).
Follow-up data from the West of Scotland Coronary Prevention Study (WOSCOPS) suggests that even 5 years of statin therapy provides lifetime benefit in reducing the risk of disease.

WOSCOPS was an early, large, primary prevention trial that randomized almost 6,600 Scots with elevated low-density lipoprotein cholesterol (mean baseline, 190 mg/dL; mean age, 55 years) to treatment with pravastatin (40 mg/d) or placebo. At 5 years of follow-up, the treatment arm demonstrated a 31% reduction in the relative risk of myocardial infarction or cardiovascular death (N Engl J Med. 1995;333:1301-8). The results of this pivotal trial were critical to the formulation of recommendations to include aggressive treatment of hyperlipidemia with statin therapy as part of a primary prevention strategy. Despite recommendations, only 31% of participants in each arm of the study were placed on statin therapy at completion of the trial, likely because at the time primary prevention was not widely emphasized and statin drugs were relatively expensive compared with alternatives.

Because all health care utilization in Scotland is captured by the National Health Service, researchers were able to gather data on the original study participants. At 20 years, the only treatment difference between the 2 original groups was the extra 5 years of statin therapy that individuals in the treatment arm received during the study. The treatment group demonstrated impressive benefits, including relative risk reductions of 31% in hospital admissions for heart failure, 27% in coronary artery disease mortality, 19% in rate of coronary interventions, and 13% in all-cause mortality. Patients in the treatment arm who did experience cardiac events spent 25% fewer days in the hospital for treatment compared with those in the placebo group. Importantly, there was no increase in the incidence of cancer or noncardiac deaths in the treatment arm.

The mechanism of this treatment effect is unknown but may be attributable to statin-related slowing or stabilization of arterial plaque. Researchers concede that important caveats need to be considered. Study participants were relatively young at the beginning of the trial compared with the population in many other primary and secondary prevention trials, and other statin drugs may not demonstrate the same long-term effect. Nevertheless, this report suggests that early treatment with statin therapy as part of a primary prevention strategy is effective in both the short and long term.

**NEW STAFF**

Simon Maltais, MD, PhD, has joined the staff of the Division of Cardiovascular Surgery at Mayo Clinic in Rochester, Minnesota. He completed medical school at Sherbrooke University in Quebec and did his cardiothoracic training and his doctorate in biomedical sciences at the University of Montreal. He has been surgical director of the mechanical circulatory support and heart transplantation programs at the Vanderbilt Heart and Vascular Institute since 2011. Dr. Maltais’s clinical interests are surgery for heart failure, including heart transplantation and ventricular assist device therapy, and minimally invasive valve interventions. His research focuses on the management of patients with heart failure, alternative and less invasive options for mechanical circulatory support placement, and translational research, including cardiac cell-based therapies.

Sameh M. Said, MD, has joined the staff of the Division of Cardiovascular Surgery at Mayo Clinic in Rochester, Minnesota. He received his medical education at the University of Alexandria in Egypt. He completed training in adult and pediatric cardiovascular surgery at Mayo Clinic Graduate School of Medicine and in congenital cardiac surgery at Stanford University.
Innovation Award

John C. Burnett Jr, MD, and Seethalakshmi Iyer, members of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester, Minnesota, are recipients of the Department of Medicine 2016 Innovation Award for their project, Urinary Angiotensinogen: A Novel and Advanced Renal Biomarker to Enhance Outcomes of Patients Hospitalized for Heart Failure: Accelerating Discovery to the Bedside. Innovation awards are given to those projects designed to fulfill the strategic goals identified by the Mayo Clinic Department of Medicine to stimulate innovation in health care.

Named Professorship

Joseph A. Dearani, MD, chair of the Division of Cardiovascular Surgery at Mayo Clinic in Rochester, Minnesota, has been named the Sheikh Zayed Professor in Cardiovascular Diseases Honoring George M. Gura MD. The late Sheikh Zayed bin Sultan Al Nahyan was the founder of the United Arab Emirates, and his family has led the Emirate of Abu Dhabi for over 300 years. George M. Gura, MD, a cardiologist at Mayo Clinic in Rochester, maintains a close relationship with the Al Nahyan family.

Kirsten and Freddy Johansen Foundation Award

John C. Burnett Jr, MD, a member of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester, Minnesota, received the 2015 International Rigshospitalet Kirsten and Freddy Johansen Foundation Award, presented on November 30, 2015, in Copenhagen, Denmark. This prize is awarded annually to a medical researcher of international prominence to foster international, collaborative, research efforts. Dr. Burnett has devoted his research career to the study of the endocrine role played by the heart in cardiorenal homeostasis, with a focus on the function of natriuretic peptides in heart failure, hypertension, myocardial infarction, arrhythmias, and vascular tone.

Department of Medicine Research and Education Recognition

The Department of Medicine at Mayo Clinic in Rochester, Minnesota, presented 2015 Education and Research Recognition Awards on November 10, 2015. Awardees from the Division of Cardiovascular Diseases are Sunil V. Mankad, MD, who received the Teaching Excellence Award, and Veronique L. Roger, MD, director of the Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, who received the Research Career Achievement Award.

Laennec Award

Carole A. Warnes, MD, a cardiologist at Mayo Clinic in Rochester, Minnesota, is the recipient of the 2015 Laennec Master Clinician Award. This prestigious American Heart Association award honors academic cardiologists who have made outstanding contributions to clinical cardiovascular medicine through their clinical and teaching acumen.

Department of Medicine Faculty Recognition Awards

The Mayo Clinic Department of Medicine has announced recipients of the 2015 Faculty Recognition Awards. Honored members of the Division of Cardiovascular Diseases are Robert L. Frye, MD, who received the Henry S. Plummer Distinguished Physician Award; Amir Lerman, MD, who received the Outstanding Mentor Award; and Douglas L. Wood, MD, who received the Cardiology Laureate Award.
Continuing Medical Education, Mayo Clinic
For additional information:
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Email: cvcmce@mayo.edu
Phone: 800-283-6296, 507-266-0677, or 507-266-6703

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Feb 1-5, 2016, Maui, HI

Hawaii Heart 2016: Case-Based Clinical Decision Making Using Echocardiography and Multimodality Imaging
Feb 8-12, 2016, Kauai, HI

41st Annual Cardiovascular Conference at Snowbird
Feb 12-15, 2016, Snowbird, UT

21st Annual Cardiology at Cancun
Feb 22-26, 2016, Cancun, Mexico

23rd Annual Echocardiographic Workshop on 2-D and Doppler Echocardiography at Vail
Mar 7-10, 2016, Vail, CO

Echo Revolution: Adult Echocardiography for Physicians and Sonographers
Mar 11-13, 2016, Boston, MA

Heart Failure Management for Nurse Practitioners, Physician Assistants, and Primary Care Providers
Mar 17-19, 2016, Lake Buena Vista, FL

ACC Symposium—Pericardial Diseases: Myth and Truth in Diagnosis and Treatment
Apr 3-5, 2016, Chicago, IL

State-of-the-Art Cardiovascular Update: A Case-Based Approach From the Heart of Manhattan
Apr 7-9, 2016, New York, NY

Echo Fiesta: An In-Depth Review of Adult Echocardiography for Sonographers and Physicians
Apr 7-10, 2016, San Antonio, TX

Innovations in Atrial Fibrillation: Detection and Management
Sep 24-25, 2016, Seattle, WA

Internal Medicine Review for Nurse Practitioners, Physician Assistants, and Primary Care Providers
Sep 28-30, 2016, Rochester, MN

Heart Disease in Women: A New Era of Understanding, Recognition, Prevention, Diagnosis, and Treatment
Oct 8-9, 2016, Rochester, MN

26th Annual Cases in Echocardiography, Cardiac CT and MRI
Oct 19-22, 2016, Napa, CA

Cardiovascular Medicine 2016: Updates for Practitioners From Brigham and Women’s Hospital and Mayo Clinic
Oct 21-22, 2016, Boston, MA

7th Annual Cardiology Conference for Health Care Professionals
Oct 22-23, 2016, Wisconsin Dells, WI

The Genetics of Heart and Vascular Disease
Oct 28-29, 2016, Amelia Island, FL

Mayo Clinic Update in Echocardiography: Role of Echo From Prevention to Intervention
Nov 3-6, 2016, Phoenix, AZ

32nd Annual Echocardiography in Pediatric and Adult Congenital Heart Disease
Nov 3-6, 2016, Phoenix, AZ

Coronary Artery Disease: Prevention, Detection, and Treatment
Nov 18-20, 2016, Las Vegas, NV

5th Annual ECG and Heart Rhythm: A Case-Based Approach
Dec 1-4, 2016, Scottsdale, AZ

Echo on Marco Island: Case-Based Approach
Dec 1-4, 2016, Marco Island, FL

9th Annual The Heart Beat of Cardiology: Practical Application of Echocardiography
Dec 8-10, 2016, Chicago, IL

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