Cardiovascular Medicine

Epidemiology and Risk Factors

Overview

Cardiovascular disease (CVD) encompasses many conditions, including coronary artery disease (CAD), heart failure, valvular heart disease, stroke, congenital heart defects, heart rhythm disorders, and sudden cardiac arrest. CVD is the leading cause of death in the United States; however, from 2004 to 2014, the mortality rate attributable to CVD fell approximately 25%, likely as a result of improved primary and secondary prevention. Despite this improvement, CVD was responsible for nearly 31% of all deaths in the United States in 2014 (roughly 800,000 people). Globally, CVD resulted in more than 17.3 million deaths in 2013, representing 31% of all deaths.

More than one in three U.S. adults currently have some form of CVD. Prevalence increases with age, and more than 70% of persons aged 60 to 79 years have CVD. The American Heart Association projects that 44% of the U.S. population will have some form of CVD by 2030. Lifetime risk for CVD is estimated to be one in three for women and two in three for men according to data from the Framingham Heart Study.

Hospitalizations for cardiovascular-related diseases continue to increase. In 2011, heart failure and heart rhythm problems were among the top 10 diagnoses associated with hospital admission in the United States, accounting for approximately 1.7 million hospital stays. The number of inpatient cardiovascular operations and procedures increased 28% to more than 7.5 million from 2000 to 2010. CVD, including stroke, was associated with a cost of $316.6 billion in 2011.

An estimated 5.7 million U.S. adults older than 20 years have a diagnosis of heart failure, a final common pathway for many cardiovascular conditions. The prevalence of heart failure is projected to increase by 46% between 2012 and 2030, and the current annual incidence is 1 in 1000 persons in those older than 65 years. Most patients with heart failure (75%) have a history of hypertension. The overall mortality rate after the diagnosis of heart failure is roughly 50% at 5 years, with about half of those deaths due to cardiovascular causes.

Risk Factors for Cardiovascular Disease

Lifestyle

Cardiovascular risk can be mostly attributed to modifiable risk factors. Very few persons meet the seven metrics of cardiovascular health: optimal lipid, blood pressure, and glucose levels; healthy diet; appropriate energy intake; physical activity; and avoidance of tobacco. Elevated cholesterol levels impart the highest risk for myocardial infarction (MI), followed by current smoking, diabetes mellitus, hypertension, abdominal obesity, no alcohol intake, inadequate exercise, and suboptimal consumption of fruits and vegetables.

Elevations in serum cholesterol levels are associated with increased cardiovascular risk, and reductions in cholesterol levels can reduce overall risk. Thirteen percent of adults older than age 20 years, or 31 million persons, have total cholesterol levels greater than 240 mg/dL (6.22 mmol/L), and 6% of adults are estimated to have undiagnosed hypercholesterolemia. Elevated LDL cholesterol and low HDL cholesterol levels are also independently associated with increased risk for CVD. A 1% reduction in LDL cholesterol level decreases risk for CAD by 1%. Risk for CAD decreases 2% to 3% for every 1% increase in HDL cholesterol level; however, pharmacologic therapies that increase HDL cholesterol levels in patients with acceptable LDL cholesterol levels do not reduce cardiovascular events. Current cholesterol treatment guidelines are based on cardiovascular risk rather than absolute lipid levels. For primary prevention of cardiovascular events, the treatment goal is at least a 50% reduction in LDL cholesterol level in high-risk patients and a 30% to 50% reduction in moderate-risk patients (see MKSAP 18 General Internal Medicine).

Tobacco exposure is a significant risk factor for CVD, including CAD, stroke, and peripheral vascular disease. In 2010, smoking was the second leading risk factor for death in the United States, exceeded only by dietary risks. The prevalence of tobacco use continues to decline; 18.8% of men and 15.1% of women were current smokers in 2014. The percentage of adolescents who smoke tobacco daily has also decreased significantly, from 15.2% in 2003 to 7.8% in 2013. In patients who smoke, overall mortality is increased two to three times, and risk for stroke is increased two to four times. The use of tobacco increases the risk for CAD by 25% in women. Secondhand smoke increases the risk for CVD by 25% to 30%. Smoking cessation substantially reduces cardiovascular risk within 2 years, with risk returning to the level of a nonsmoker after approximately 10 years. Smokers who quit extend their life expectancy by several years. Smoking status should be assessed at every visit, and cessation counseling should be offered to active smokers (see MKSAP 18 General Internal Medicine).

Psychosocial stressors, including depression, anger, and anxiety, are associated with worse cardiovascular

outcomes. Depression has been linked with higher risk for cardiovascular events, and psychosocial stressors also affect the course of treatment and adherence to healthy lifestyles after an event.

Sedentary lifestyle, poor diet, and obesity contribute to increased cardiovascular risk and increase the risk for diabetes. According to the Centers for Disease Control and Prevention, 23.7% of adults report no leisure time physical activity, and only 20.2% of adults meet aerobic and strengthening recommendations. Average fruit and vegetable consumption in the United States is less than 1 cup of fruit daily (recommended is 1.5-2 cups daily) and less than 1.5 cups of vegetables daily (recommended is 2-3 cups daily). On the basis of adherence to 2010 U.S. dietary guidelines, average diet quality is worse in men than in women, in younger adults than in older adults, and in smokers than in nonsmokers. The National Diabetes Prevention Program found that in persons at high risk for diabetes, interventions such as changes in diet, exercise, and moderate weight loss of 5% to 7% reduced the risk for developing diabetes by 58% but did not reduce CVD events.

Genetics

Although CVD risk is mainly attributable to traditional risk factors, additional risk may be caused by other factors, including genetic predisposition. A history of premature CAD (male younger than 55 years, female younger than 65 years) in parents doubles risk for MI in men and increases risk in women by 70%. CVD in a sibling increases risk for CVD by 45%, and stroke in a first-degree relative increases risk for stroke by 50%. A parental history of atrial fibrillation increases odds of this condition by 80%. In addition to genetics, the shared environment (that is, lifestyle) may contribute to increased risk in family members.

Ethnicity

There are significant racial and ethnic differences in the risk and prevalence for CVD in the United States. The prevalence of heart disease, including MI, chest pain, heart failure, and stroke, is highest among Hawaiians and Pacific Islanders (19.1%), followed by American Indians and Alaska Natives (13.7%), non-Hispanic whites (11.1%), blacks (10.3%), Hispanics and Latinos (7.8%), and Asians (6.0%).

Risk factor prevalence varies by ethnicity, location, income, and education level. Prevalence of hypertension (blood pressure ≥130/80 mm Hg) is highest among non-Hispanic black men (59%) and non-Hispanic black women (56%) and lowest among Hispanic men (44%) and non-Hispanic Asian women (36%). In contrast, the risk for diabetes is highest among American Indians and Alaska Natives (15.9%), followed by non-Hispanic blacks (13.2%) and Hispanics (12.8%). Tobacco use is highest among non-Hispanic blacks (19.9%) and lowest among Asian men (13.8%) and Hispanics (13.8%).

Globally, the prevalence of cardiovascular risk factors and subsequent CVD is increasing as a result of changes in eating habits, tobacco use, and lifestyle factors.

KEY POINT

- Risk for cardiovascular disease is mostly attributed to modifiable risk factors, including dyslipidemia, smoking, diabetes mellitus, hypertension, obesity, inadequate exercise, and diet.

Calculating Cardiovascular Risk

Cardiovascular risk scores and calculators can be used to assess a patient's future risk for major cardiovascular events and to identify which interventions are most effective for prevention. Traditionally, the Framingham risk score, which includes age, systolic blood pressure, total cholesterol level, HDL cholesterol level, smoking status, and presence of diabetes, was used to estimate the 10-year risk for a major coronary heart disease event (MI or coronary death). The Framingham risk score classifies a 10-year risk for coronary heart disease of less than 10% as low risk, 10% to 20% as intermediate risk, and greater than 20% as high risk (considered a CVD risk equivalent). A limitation of the Framingham risk score is its underestimation of risk in women and minority populations. The Reynolds risk score, which was developed in an effort to create a more accurate risk assessment tool, is a sex-specific score for both men and women that includes family history and high-sensitivity C-reactive protein level.

The American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equations are a risk assessment instrument derived from several community-based cohorts that included large minority populations in addition to the cohort included in the Framingham Heart Study. The Pooled Cohort Equations include the cardiovascular endpoints of MI, angina, ischemic or hemorrhagic stroke, transient ischemic attack, claudication, and heart failure. The ACC/AHA CVD risk calculator based on the Pooled Cohort Equations (available at http://tools.acc.org/ASCVD-Risk-Estimator/) may be used to identify persons at risk for the development of CVD who would benefit from preventive measures, including statin therapy. The risk calculator can also be used to risk-stratify patients with diabetes to determine the appropriate intensity of statin therapy. However, there are concerns that the Pooled Cohort Equations overestimate risk in certain populations, including women and some minorities.

The ACC/AHA and U.S. Preventive Services Task Force do not recommend routinely using several previously considered cardiovascular risk factors, including a history of premature cardiovascular disease in a first-degree relative, elevated lifetime ASCVD risk, and LDL cholesterol level of 160 mg/dL (4.14 mmol/L) or higher, for cardiovascular risk calculation. Other nontraditional risk factors,

such as high-sensitivity C-reactive protein level of 2 mg/L or greater, coronary artery calcium score of 300 or higher or in the 75th percentile or greater, and ankle-brachial index below 0.90, have been associated with an increased risk of cardiovascular events; however, the value of these measurements, and whether they should affect treatment decisions, is unclear.

KEY POINT

- The American College of Cardiology/American Heart Association Pooled Cohort Equations are used to identify persons at risk for the development of cardiovascular disease who would benefit from preventive measures, including statin therapy.

Specific Risk Groups

Hypertension

Hypertension, defined as a blood pressure of 130/80 mm Hg or higher, affects approximately 46% of individuals aged 20 years and older. Before age 45 years, the prevalence of hypertension is higher in men than in women; however, after age 65 years, the prevalence is higher in women than in men. The population attributable risk of hypertension for first MI is 18%. Among the modifiable risk factors, hypertension is the leading cause of death in women. Treatment of hypertension reduces risk for stroke, heart failure, and kidney disease.

Women

Although mortality from CVD has decreased in the past decade, the death rate remains higher in women than in men. CVD remains the leading cause of death in women, resulting in more deaths than caused by cancer, diabetes, and kidney disease combined. In 2013, heart disease caused 398,086, or 1 in 3.2, deaths in women. Mortality within the first year after first MI is higher in women (26%) than in men (19%), and younger women are particularly at risk for death. Within 5 years of MI, nearly 50% of women will die, develop heart failure, or have a stroke, compared with 36% of men. Women have a higher risk for stroke than men throughout their lifetime as well.

The prevalence of and risk for CVD are higher in nonwhite women than in white women. Prevalence of acute MI and mortality are highest among black women. Black women also have a higher prevalence of heart disease (7.0%) compared with Hispanic women (5.9%) and white women (4.6%). Hispanic women develop heart disease nearly 10 years earlier than white women. In the past decade, heart disease mortality has increased in Asian Indian women.

Hyperlipidemia, type 2 diabetes, obesity, and tobacco use confer greater risk for CAD in women compared with men. Additional factors associated with increased risk for CVD include depression; preterm labor; and less aggressive management of recognized CVD risk factors, such as hypertension. Significant anatomic obstruction in coronary arteries is less predictive of clinical CAD in women than in men.

Approximately two thirds of women who die of MI have no previous symptoms or have symptoms that were unrecognized as cardiac in origin. Many women have symptoms described as chest discomfort, indigestion, shortness of breath, or unusual fatigue, but less than 50% of women seek medical attention for these symptoms. Because of the atypical presentation of angina, diagnosis and treatment in women are delayed when compared with men.

Treatments and outcomes also differ between men and women. After an acute coronary syndrome, women undergo fewer interventions, have more complications, and have higher unadjusted mortality. Women with non-ST-elevation MI have worse outcomes, with higher rates of bleeding, heart failure, shock, kidney failure, stroke, and reinfarction.

Obesity and Metabolic Syndrome

In the United States, 33.1% of adults older than 20 years are overweight (BMI, 25-29.9), 35.7% are obese (BMI >30), and 6.3% are extremely obese (BMI >40). Rates are increased in nonwhite adults. Obesity may increase the risk for CVD events, even in the absence of metabolic risk factors.

Metabolic syndrome is characterized by the presence of at least three of the following conditions: elevated glucose level, central obesity, low HDL cholesterol level, elevated triglyceride level, and elevated blood pressure. The hallmark feature of metabolic syndrome is glucose intolerance. Approximately 23% of adults older than 20 years meet the criteria for metabolic syndrome, but the prevalence varies considerably among different ethnicities. The highest prevalence is among Mexican American men (35%) and lowest among non–Mexican American black men (19%). Metabolic syndrome is associated with increased risk for CVD, with risk increasing as the number of component conditions increases. The cardiovascular risk associated with metabolic syndrome also appears to be higher among women.

Diabetes Mellitus

Diabetes has been diagnosed in approximately 23.4 million U.S. adults, and an estimated 7.6 million U.S. adults have undiagnosed diabetes. The prevalence of diabetes and prediabetes is increasing among adolescents aged 12 to 19 years and in those older than 65 years. Additionally, diabetes prevalence is disproportionately higher in nonwhite ethnic groups, including African Americans and Hispanics/Latinos.

Diabetes increases cardiovascular risk, especially in women, and is considered a CVD risk equivalent. Persons with diabetes have a two to four times increased risk for CVD; 68% of those with diabetes eventually die of heart disease, and 16% die of stroke. In persons with diabetes, the risk for stroke is increased 1.8- to 6-fold. Additionally, CAD is more extensive in persons with diabetes, and the incidence of multivessel disease is increased. Patients with diabetes are more

likely to have undiagnosed CAD and have worse outcomes when hospitalized for other CVDs, such as heart failure. Undiagnosed diabetes may be recognized at the time of an acute event, such as MI.

Aggressive treatment of cardiovascular risk factors, such as elevated cholesterol levels, is associated with reduced cardiovascular risk in patients with diabetes. Early recognition and treatment are important in reducing the burden of CVD and the morbidity and mortality associated with diabetes.

Systemic Inflammatory Conditions

The prevalence of atherosclerosis is increased and the risk for CVD is higher in patients with systemic inflammatory conditions, such as systemic lupus erythematosus and rheumatoid arthritis. The risk for CAD is nearly 60% higher in patients with rheumatoid arthritis and is doubled in patients with systemic lupus erythematosus. Patients with systemic lupus erythematosus and antiphospholipid antibodies have a higher prevalence of CAD and MI; the relative risk for MI is higher in younger patients with systemic lupus erythematosus than in age-matched controls. The risk for CVD in patients with rheumatoid arthritis increases from twofold at baseline to threefold over 10 years when compared with the general population. The increased risk is likely a result of the inflammatory process, including a prothrombic state, in addition to traditional cardiovascular risk factors.

Chronic Kidney Disease

Chronic kidney disease, defined as reduced estimated glomerular filtration rate, is associated with higher incidence of CVD and worse cardiovascular outcomes. Beyond the risk attributable to traditional risk factors, the risk for cardiovascular events is higher in patients with kidney dysfunction. CVD is the leading cause of death in patients with end-stage kidney disease, and the risk for CVD-related death is 5 to 30 times higher in patients undergoing dialysis than in those with similar risk factors and preserved kidney function. The presence of moderately increased albuminuria (microalbuminuria) independently increases the risk for cardiovascular events.

Despite excessive cardiovascular risk, there is evidence that patients with chronic kidney disease do not receive appropriate preventive therapies, such as statins. Data indicate that patients undergoing hemodialysis do not benefit from secondary prevention with statins.

HIV

Increased survival of patients infected with HIV due to effective antiretroviral therapy has resulted in the increased development of non–AIDS-related complications, including CVD. Patients with HIV have a 1.5 times increased risk for CVD, and cardiovascular mortality is increasing in the HIV-infected population. The increased risk is likely multifactorial, related to antiretroviral therapy–associated dyslipidemia, insulin resistance, medications associated with CVD events (such as protease inhibitors), viral load, and disease-related increases in risk factors (dyslipidemia, diabetes).

KEY POINTS

- Hyperlipidemia, type 2 diabetes mellitus, obesity, and tobacco use confer greater risk for coronary artery disease in women than in men.
- Delayed diagnosis of coronary artery disease in women is often due to the presentation of atypical chest pain.
- Cardiovascular disease risk is increased in patients with diabetes mellitus, systemic inflammatory conditions, HIV, and chronic kidney disease.
- Statin therapy should not be used for secondary prevention of cardiovascular disease in patients on hemodialysis. HVC

Diagnostic Testing in Cardiology

Clinical History and Physical Examination

The clinical history and physical examination are cornerstones in the diagnosis of cardiovascular disease. A careful history that includes symptom characteristics, timing, and duration; factors that exacerbate or relieve symptoms; and functional capacity is critical to ensure a focused and appropriate diagnostic evaluation. Abnormal findings on the cardiovascular examination may also raise suspicion for specific cardiac conditions and guide the selection of tests.

Cardiovascular testing provides both diagnostic and prognostic information, and its use should be guided by symptoms, the pretest likelihood of heart disease, and whether testing results will alter patient management.

Diagnostic Testing for Atherosclerotic Coronary Artery Disease

Diagnostic testing for coronary artery disease (CAD) can be categorized as providing functional and/or anatomic information regarding atherosclerotic disease burden. Functional studies reveal the presence of ischemia (exercise electrocardiography [ECG], single-photon emission CT [SPECT], PET), the extent and severity of ischemia (SPECT, PET), information on coronary blood flow (PET, fractional flow reserve (FFR)–CT), and development of wall motion abnormalities (echocardiography, cardiac magnetic resonance [CMR] imaging). Anatomic information is obtained from invasive angiography, coronary CT angiography (CTA), and coronary artery calcium (CAC) scoring. Cardiac diagnostic testing modalities are summarized in **Table 1**.