BONUS DIGITAL CONTENT

U.S. Preventive Services Task Force

Risk Assessment for Cardiovascular Disease with Nontraditional Risk Factors: Recommendation Statement

Summary of Recommendation and Evidence

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of adding the ankle-brachial index (ABI), high-sensitivity C-reactive protein (hsCRP) level, or coronary artery calcium (CAC) score to traditional risk assessment for cardiovascular disease (CVD) in asymptomatic adults to prevent CVD events *(Table 1)*. **(I statement)**.

See the Clinical Considerations section for suggestions for practice regarding the I statement.

Rationale

IMPORTANCE

CVD is the most common cause of death among adults in the United States. Treatment to prevent CVD events by modifying risk factors is currently informed by the Framingham Risk Score, the Pooled Cohort Equations, or similar CVD risk assessment models. If current CVD risk assessment models could be improved by adding more risk factors, treatment might be better targeted, thereby maximizing the benefits and minimizing the harms.

DETECTION

The USPSTF found adequate evidence that adding the ABI, hsCRP level, or CAC score to existing CVD risk assessment models (Framingham Risk Score [which estimates a person's 10-year risk of coronary heart disease] or Pooled Cohort Equations [which estimate 10-year risk of myocardial infarction, death from coronary heart disease, or stroke]) may improve calibration (agreement between observed and predicted outcomes), discrimination (ability to distinguish between people who will and will not experience an event), and reclassification (ability to correctly reassign people into clinically meaningful risk strata). The USPSTF chose to review these 3 nontraditional risk factors because prior evidence reviews identified them as the most promising to improve on existing CVD risk assessment tools.

BENEFITS OF RISK ASSESSMENT AND INTERVENTION

The USPSTF found inadequate evidence to assess whether treatment decisions guided by ABI, hsCRP level, or CAC score test results, when added to existing CVD risk assessment models, lead to reduced incidence of CVD events or mortality.

HARMS OF RISK ASSESSMENT AND INTERVENTION

The USPSTF found adequate evidence to bound the harms of risk assessment and intervention as small. When direct evidence is limited, absent, or restricted to select populations or clinical scenarios, the USPSTF may place conceptual upper or lower bounds on the magnitude of benefit or harms. Harms can include abnormal test results, inappropriate risk reclassification, and incidental findings leading to additional testing and possible procedures, as well as anxiety.

USPSTF ASSESSMENT

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of adding the ABI, hsCRP level, or CAC score to traditional risk assessment for CVD in asymptomatic adults to prevent CVD events.

See related Putting Prevention into Practice on page 123.

As published by the U.S. Preventive Services Task Force.

This summary is one in a series excerpted from the Recommendation Statements released by the USPSTF. These statements address preventive health services for use in primary care clinical settings, including screening tests, counseling, and preventive medications.

The complete version of this statement, including supporting scientific evidence, evidence tables, grading system, members of the USPSTF at the time this recommendation was finalized, and references, is available on the USPSTF website at https://www.uspreventiveservicestaskforce.org/.

This series is coordinated by Kenny Lin, MD, MPH, Deputy Editor.

A collection of USPSTF recommendation statements published in *AFP* is available at https://www.aafp.org/afp/uspstf.

TABLE 1

Risk Assessment for CVD with Nontraditional Factors: Clinical Summary of the USPSTF Recommendation

Population	Adults
Recommendation	No recommendation. Grade: I (insufficient evidence)
Risk assessment	Several traditional risk factors are associated with higher risk for CVD events, including older age, male sex, high blood pressure, current smoking, abnormal cholesterol levels, diabetes mellitus, obesity, and physical inactivity. Risk factors can be combined in many ways to classify a person's risk for a CVD event. CVD risk assessment in the United States has been generally based on the Framingham Risk Score and the Pooled Cohort Equations.
Screening tests	ABI is the ratio of the systolic blood pressure at the ankle (measuring the pressure proximal to the dorsalis pedis or posterior tibial artery) to the systolic blood pressure at the brachial artery. A value ≤ 0.9 indicates peripheral artery disease. hsCRP is a serum protein involved in inflammatory and immune responses; the test involves a single blood sample and is widely available. A threshold of > 2 or 3 mg/L indicates increased cardiovascular risk. CAC score is obtained by electron-beam or multidetector CT, which measure the calcium content in the coronary arteries. Scoring systems and thresholds for an elevated CAC score vary, but the baseline comparison is often a score of 0.
Treatment and interventions	Asymptomatic adults at increased risk for CVD are usually treated with a combination of diet and exercise modifications, statins, aspirin, blood pressure management, and smoking cessation interventions.
Other relevant USPSTF recommendations	The USPSTF has made recommendations on many factors related to CVD prevention, including screening for high blood pressure, statin use, counseling on smoking cessation, counseling on healthful diet and physical activity, screening for peripheral artery disease and CVD risk assessment with the ABI, and low-dose aspirin use in certain persons at increased risk for CVD.

Note: For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, go to https://www.uspreventiveservicestaskforce.org/.

ABI = ankle-brachial index; CAC = coronary artery calcium; CT = computed tomography; CVD = cardiovascular disease; hsCRP = high-sensitivity C-reactive protein; USPSTF = U.S. Preventive Services Task Force.

Clinical Considerations

PATIENT POPULATION UNDER CONSIDERATION

This recommendation applies to asymptomatic adults without a history of CVD.

SUGGESTIONS FOR PRACTICE REGARDING THE I STATEMENT

Although in the United States both the Framingham Risk Score and the Pooled Cohort Equations are used in practice, the USPSTF recommends that clinicians use the Pooled Cohort Equations to assess CVD risk and to guide treatment decisions until further evidence shows additional benefit of adding other CVD risk factors.

POTENTIAL PREVENTABLE BURDEN

CVD comprises diseases of the heart and vascular system, including atherosclerosis, cerebrovascular disease, and peripheral artery disease. It is the most common cause of death among adults in the United States, accounting for 1 in 3 deaths each year.[1] Although CVD remains a significant cause of morbidity and mortality, CVD mortality has been decreasing over time in the United States. Currently, the annual incidence of new cases of myocardial infarction and cerebrovascular accident in the United States is 580,000 and 610,000, respectively.[1]

The incidence of CVD varies by sex. Men, on average, develop CVD about 10 years earlier than women.[2] The burden of CVD increases with age. In 2015, the age-adjusted prevalence of coronary artery disease among U.S. adults aged 45 to 64 years was 6.1%, compared with 16.4% among those aged 65 to 74 years and 23.3% among those 75 years or older.[3] In the same year, 2.7%, 5.6%, and 11.2% of U.S. adults in these age groups, respectively, experienced a stroke. Prevalence also varies by race/ethnicity; in 2015, the prevalence of coronary artery disease was 2 times greater among American Indian/Alaska Native adults than Asian adults (9.3% vs. 3.7%, respectively). Prevalence in Hispanic, African American, and white adults was similar, at 5.1%, 5.4%, and 5.6%, respectively.[3] However, strokes were most common among African American adults (3.7%), followed by white (2.4%), Hispanic (2.4%), American Indian/Alaska Native (2.2%), and Asian (1.4%) adults.

POTENTIAL HARMS

Testing for hsCRP level and the ABI is noninvasive, and there is little direct harm from the tests. Harms of testing for CAC score include exposure to radiation and incidental findings on computed tomography of the chest, such as pulmonary nodules, that may lead to further invasive testing and procedures. Abnormal test results may lead to further testing, procedures, and lifelong medication use without proof of benefit but with expense and potential adverse effects for the patient. Psychological harms may result from reclassification into a higher risk category for CVD events.

CURRENT PRACTICE

Only 1 of the risk assessment models currently used in the United States, the Reynolds Risk Score, incorporates hsCRP level into its risk calculation. A number of guidelines, including those from the American College of Cardiology and the American Heart Association, recommend considering hsCRP level, the ABI, or CAC score to clarify treatment decisions for patients whose risk assessment is borderline or unclear using a traditional risk assessment model.

ASSESSMENT OF RISK

Accurate identification of persons at high risk for CVD events, particularly nonfatal myocardial infarction or stroke, and CVD death provides the opportunity for more intensive risk factor management to reduce the likelihood of such an event. In addition, identifying persons at low risk may allow for a reduction in interventions with a low benefit to risk ratio for those not likely to benefit.

Several traditional risk factors are associated with higher risk for CVD events, including older age, male sex, high blood pressure, current smoking, abnormal cholesterol levels, diabetes mellitus, obesity, and physical inactivity. Risk factors can be combined in many ways to classify a person's risk for a CVD event as low, intermediate, or high. Several calculators and models are available to quantify a person's 10-year CVD event risk. The Framingham Risk Score (which estimates a person's 10-year risk of coronary heart disease) was 1 of the first widely used risk assessment tools. Persons with a 10-year CVD event risk greater than 20% are generally considered at high risk, those with a 10-year risk less than 10% are considered at low risk, and those in the 10% to 20% range are considered at intermediate risk. The Pooled Cohort Equations (which estimate 10-year risk of myocardial infarction, death from coronary heart disease, or stroke) were introduced in 2013 and were developed using more contemporary and diverse cohort data, with the inclusion of race/ethnicity and diabetes. Persons with a 10-year CVD event risk less than 7.5% are considered at low risk, and those with a 10-year risk of 7.5% or greater are considered at high risk.[4] The distribution of estimated CVD risk in the U.S. population is highly influenced by age and sex. Population estimates of the distribution of 10-year CVD event risk assessed by the Pooled Cohort Equations, which categorize risk using somewhat different thresholds, and using 2001-2010 data from the National Health and Nutrition Examination Survey show that the vast majority of U.S. adults aged 40 to 49 years have an estimated 10-year CVD event risk of 7% or less (93% of women and 81% of men). Among U.S. adults aged 50 to 59 years, 80% of women and 46% of men have an estimated 10-year CVD event risk of 7% or less; 42% of women and 7% of men aged 60 to 69 years have an estimated 10-year CVD event risk of 7% or less.[5]

SCREENING TESTS

CVD risk assessment in the United States has been generally based on the Framingham Risk Score and, more recently, the Pooled Cohort Equations. However, both have been documented to overestimate and underestimate risk in some persons. Therefore, identification of additional tests (for nontraditional risk factors) that could improve risk prediction, including the ABI, hsCRP level, and CAC score, is of interest.

The ABI is the ratio of the systolic blood pressure at the ankle (measuring the pressure proximal to the dorsalis pedis or posterior tibial artery) to the systolic blood pressure at the brachial artery. A value less than or equal to 0.9 indicates peripheral artery disease.[6]

High-sensitivity C-reactive protein is a serum protein involved in inflammatory and immune responses. Testing for hsCRP level involves a single blood sample, and the test is widely available. A threshold of greater than 2 or 3 mg per L is used in clinical practice to signify increased cardiovascular risk.[7-9]

Coronary artery calcium score is obtained by electron-beam or multidetector computed tomography, which measure the calcium content in the coronary arteries. Scoring systems and thresholds for an elevated CAC score vary across studies, but the baseline comparison is often a CAC score of 0.[10]

TREATMENT AND INTERVENTIONS

Asymptomatic adults at increased risk for CVD are usually treated with a combination of diet and exercise modifications, statins, aspirin, blood pressure management, and smoking cessation interventions.

ADDITIONAL APPROACHES TO PREVENTION

The National Heart, Lung, and Blood Institute provides resources on cardiovascular risk assessment, including a link to an online version of the Pooled Cohort Equations.[11] Healthy People 2020 provides a database of evidence-based resources for achieving Healthy People 2020 goals, including interventions to prevent CVD.[12]

USEFUL RESOURCES

The USPSTF has made recommendations on many factors related to CVD prevention, including screening for high blood pressure,[13] statin use,[14] counseling on smoking cessation,[15] counseling on healthful diet and physical activity,[16] and screening for peripheral artery disease and CVD risk assessment with the ABI.[17] In addition, the USPSTF recommends low-dose aspirin use in certain persons at increased risk for CVD.[18]

This recommendation statement was first published in *JAMA*. 2018;320(3):272-280.

The "Other Considerations," "Discussion," "Update of Previous USPSTF Recommendation," and "Recommendations of Others" sections of this recommendation statement are available at https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/cardiovascular-disease-screening-using-nontraditional-risk-assessment.

The USPSTF recommendations are independent of the U.S. government. They do not represent the views of the Agency for Healthcare Research and Quality, the U.S. Department of Health and Human Services, or the U.S. Public Health Service.

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