Clinical Guideline

Annals of Internal Medicine

Screening for Peripheral Artery Disease and Cardiovascular Disease Risk Assessment With the Ankle–Brachial Index in Adults: U.S. Preventive Services Task Force Recommendation Statement

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Description: Update of the 2005 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for peripheral artery disease (PAD).

Methods: The USPSTF reviewed the evidence on the use of resting ankle–brachial index (ABI) as a screening test for PAD or as a risk predictor for cardiovascular disease (CVD). The review focused on resting ABI as the sole screening method; the diagnostic performance of ABI testing in primary care populations, unselected populations, and asymptomatic populations; the predictive value of ABI testing for major CVD outcomes in primary care or unselected populations; and the effect of treatment on general CVD and PAD-specific morbidity in patients with asymptomatic or minimally symptomatic PAD.

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

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Supplement CME quiz Consumer Fact Sheet **Population:** This recommendation applies to asymptomatic adults who do not have a known diagnosis of PAD, CVD, severe chronic kidney disease, or diabetes.

Recommendation: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for PAD and CVD risk assessment with the ABI in adults. (I statement)

Ann Intern Med. 2013;159:342-348.www.annals.orgFor author affiliation, see end of text.

* For a list of the members of the USPSTF, see the **Appendix** (available at www.annals.org).

SUMMARY OF RECOMMENDATION AND EVIDENCE

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for peripheral artery disease (PAD) and cardiovascular disease (CVD) risk assessment with the ankle– brachial index (ABI) in adults. (I statement)

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

See the **Figure** for a summary of the recommendation and suggestions for clinical practice.

Appendix Table 1 describes the USPSTF grades, and Appendix Table 2 describes the USPSTF classification of levels of certainty about net benefit (both tables are available at www.annals.org).

RATIONALE

Importance

In addition to morbidity directly caused by PAD, patients with PAD have an increased risk for CVD events because of concomitant coronary and cerebrovascular disease. Recent data from the National Health and Nutrition Examination Survey show that 5.9% of the U.S. population aged 40 years or older (7.1 million persons) has a low ABI (≤ 0.9) (1). More than half of these persons do not have typical symptoms of PAD.

Early detection of PAD in asymptomatic patients is primarily considered because subsequent treatment may re-

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U.S. Preventive Services TASK FORCE www.USPreventiveServicesTaskForce.org www.annals.org *Figure.* Screening for peripheral artery disease and cardiovascular disease risk assessment with the ankle–brachial index in adults: clinical summary of U.S. Preventive Services Task Force recommendation.

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SCREENING FOR PERIPHERAL ARTERY DISEASE AND CARDIOVASCULAR DISEASE RISK ASSESSMENT WITH THE ANKLE–BRACHIAL INDEX IN ADULTS CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic adults without a known diagnosis of peripheral artery disease (PAD), cardiovascular disease, severe chronic kidney disease, or diabetes	
Recommendation	nmendation No recommendation. Grade: I statement	
Risk Assessment	Important risk factors for PAD include older age, diabetes, smoking, hypertension, high cholesterol level, obesity, and physical inactivity. Peripheral artery disease is more common in men than in women and occurs at an earlier age in men.	
Screening Tests	Resting ankle-brachial index (ABI) is the most commonly used test in screening for and detection of PAD in clinical settings. It is calculated as the systolic blood pressure obtained at the ankle divided by the systolic blood pressure obtained at the brachial artery while the patient is lying down. Physical examination has low sensitivity for detecting mild PAD in asymptomatic persons.	
Balance of Benefits and Harms	Evidence on screening for PAD with the ABI in asymptomatic adults with no known diagnosis of cardiovascular disease or diabetes is insufficient; therefore, the balance of benefits and harms cannot be determined.	
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on using nontraditional risk factors, including the ABI, in screening for coronary heart disease. These recommendations are available at www.uspreventiveservicestaskforce.org.	

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

duce CVD in a potentially large group of persons who are otherwise not known to be at increased risk. Patients with known CVD or diabetes are already at high risk for CVD events, and risk reduction interventions (such as antiplatelet or lipid-lowering therapies) are recommended for these patients. Screening for PAD with the ABI in persons with diabetes or known CVD is unlikely to alter effective management decisions and is therefore outside the scope of this recommendation.

Detection

Although the USPSTF found few data on the reliability of the ABI as a screening test in asymptomatic persons, it was able to extrapolate from evidence in symptomatic adults and conclude that there is adequate evidence that the ABI is a reliable screening test for PAD.

Benefits of Detection and Early Treatment

The USPSTF found no evidence that screening for and treatment of PAD in asymptomatic patients leads to clinically important benefits. It also reviewed the potential benefits of adding the ABI to the Framingham Risk Score (FRS) and found evidence that this results in some patient risk reclassification; however, how often the reclassification is appropriate or whether it results in improved clinical outcomes is not known.

Determining the overall benefit of ABI testing requires not only evidence on appropriate risk reclassification but also evidence that this reclassification leads to treatments shown to improve clinical outcomes. One randomized trial found that aspirin did not reduce CVD events in patients with a low ABI (2). No studies assessed the effect of lipidlowering therapy or other cardiovascular risk reduction interventions in patients with asymptomatic PAD and no known diagnosis of CVD or diabetes. The USPSTF found inadequate evidence that early treatment of screen-detected PAD leads to improvement in clinical outcomes.

Harms of Detection and Early Treatment

The USPSTF found no studies addressing the magnitude of harms of screening for PAD with the ABI; however, the direct harms to the patient of screening itself, beyond the time needed for the test, are probably minimal. Other harms resulting from testing may include falsepositive results, exposure to gadolinium or contrast dye if magnetic resonance angiography (MRA) or computed tomography angiography (CTA) is used to confirm diagnosis, anxiety, labeling, and opportunity costs.

The USPSTF found inadequate evidence on the harms of early treatment of screen-detected PAD. One study showed that low-dose aspirin treatment in asymptomatic patients with a low ABI may increase bleeding (2). Additional harms associated with treatment include use of unnecessary medications (or higher doses) and their resulting adverse effects and discontinuation of medications known to be effective in patients with established coronary artery disease (CAD) if the patient is reclassified to a lower risk category on the basis of a normal ABI.

USPSTF Assessment

The USPSTF concludes that the evidence on screening for PAD with the ABI in asymptomatic adults with no known diagnosis of CVD or diabetes is insufficient and that the balance of benefits and harms therefore cannot be determined.

CLINICAL CONSIDERATIONS

Patient Population Under Consideration

This recommendation applies to asymptomatic adults who do not have a known diagnosis of PAD, CVD, severe chronic kidney disease, or diabetes.

Assessment of Risk

In addition to older age, major risk factors for PAD include diabetes, smoking, hypertension, high cholesterol level, obesity, and physical inactivity, with smoking and diabetes showing the strongest association (3). Peripheral artery disease is more common in men than in women and occurs at an earlier age in men, possibly in part because of the higher prevalence of smoking in men. Among healthy U.S. men aged 40 to 75 years without a history of CVD, the risk for PAD over 25 years in the absence of 4 conventional cardiovascular risk factors (smoking, hypertension, hypercholesterolemia, or type 2 diabetes) is rare (9 cases per 100 000 person-years) (4). These 4 risk factors account for 75% of all cases of PAD, and at least 1 of them is present at the time of PAD diagnosis in 96% of men. Therefore, if screening is determined to be beneficial, it would probably be most beneficial to persons who are at increased risk for PAD and are not already receiving cardiovascular risk reduction interventions.

Peripheral artery disease is a manifestation of systemic atherosclerosis and is typically considered a predictor for other types of CVD (CAD or cerebrovascular disease) and CVD events, such as myocardial infarction (MI), cerebrovascular accident, and death. Patients with PAD are at increased risk for CVD events because of concomitant coronary and cerebrovascular disease (5).

Screening Tests

Resting ABI is the most commonly used test in screening for and detection of PAD in clinical settings, although variation in measurement protocols may lead to differences in the ABI values obtained. The ABI is calculated as the systolic blood pressure obtained at the ankle divided by the systolic blood pressure obtained at the brachial artery while the patient is lying down. A ratio of less than 1 (typically defined as <0.9) is considered abnormal and is commonly used to define PAD. Physical examination has low sensitivity for detecting mild PAD in asymptomatic persons. Although femoral bruit, pulse abnormalities, or ischemic skin changes significantly increase the likelihood ratio for

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low ABI (≤ 0.9), these signs indicate moderate to severe obstruction or clinical signs of disease. Although often done, the clinical benefits and harms of screening for PAD with a physical examination have not been well-evaluated and are beyond the scope of this review (5).

In addition to its ability to detect PAD, an abnormal ABI may be a useful predictor of CVD morbidity and mortality. Ankle–brachial index measurement may increase the discrimination or calibration of existing CVD risk assessments apart from whether it accurately detects PAD. However, the number of patients with an abnormal ABI who also have other diseases or findings that would indicate treatment and whether there is value to these patients knowing they have an abnormal ABI is not clear.

Screening Intervals

No studies provided evidence about the intervals for screening for PAD with the ABI.

Treatment

Evidence shows that low-dose aspirin treatment in asymptomatic patients with a low ABI does not improve health outcomes and may increase bleeding (2). No trials provided evidence on other interventions to reduce CVD events or interventions that might delay the onset of lowerextremity symptoms.

Suggestions for Practice Regarding the I Statement

In deciding whether to screen for PAD with the ABI in asymptomatic adults, clinicians should consider the following factors.

Potential Preventable Burden

The true prevalence of PAD in the general population is not known. Recent data from the National Health and Nutrition Examination Survey show that 5.9% of the U.S. population aged 40 years or older (7.1 million persons) has a low ABI (≤ 0.9) (1). More than half of these persons do not have typical symptoms of PAD. The proportion of these patients who will go on to develop symptoms is not known; however, PAD is an indicator of CVD. Studies estimate that in persons with stable claudication but not critical ischemia, approximately 70% to 80% will remain stable over 5 years, whereas 10% to 20% will have worsening claudication and 1% to 2% will develop critical ischemia (6). Similar data are not available for asymptomatic patients with a low ABI.

Potential Harms

Although minimal harms are associated with the ABI test itself, downstream harms are possible. False-positive results, anxiety, labeling, and exposure to gadolinium or contrast dye if either MRA or CTA is used to confirm diagnosis may occur. Using the ABI in conjunction with FRS results may reclassify a patient's risk. Given the uncertainty of the appropriateness of such reclassifications, patients could either be reclassified to a higher risk category

and receive additional treatments with resulting adverse effects or be reclassified to a lower risk category and discontinue treatments that may be beneficial (5).

Cost

The cost of the ABI test is primarily in time and staff resources; performing the test in the office setting takes approximately 15 minutes (6). In addition, new equipment that performs pulse volume recordings or Doppler wave form tracings may need to be purchased (6). Providing this test to asymptomatic patients may divert time from other prevention activities that may be more beneficial to the patient.

Current Practice

In a survey of primary care practices across the United States, nearly 70% of providers reported never using the ABI in their practice settings, 6% to 8% reported using it once a year, and only 12% to 13% reported using it once a week or month (7).

OTHER CONSIDERATIONS

Research Needs and Gaps

Large, population-based, randomized trials are needed to determine whether screening for PAD with the ABI improves clinical outcomes. One ongoing study in Denmark expects to publish results after 2018. However, this study limited enrollment to men aged 65 to 74 years and includes screening for abdominal aortic aneurysm. Thus, the role of ABI screening alone or in women and younger men is not addressed by this study. Future studies should address the large population of persons who are at potentially increased risk for PAD and are not already receiving cardiovascular risk reduction interventions.

Clarity of the language used to describe PAD is important for researchers and clinicians. A low ABI seems to be a valid measure of PAD, although further verification studies with more diverse populations would be useful. More evidence is needed on the number of persons who will develop clinical signs or symptoms in their lifetime and the risk for overdiagnosis. In addition, it is not clear whether identifying and treating asymptomatic persons with screen-detected PAD is more worthwhile than targeting identification to those with signs or symptoms of disease or other manifestations of CVD or CVD risk equivalents (such as diabetes).

Intervention studies of persons with screen-detected PAD or those whose risk has been reclassified solely on the basis of their ABI are needed to determine whether treatment initiation, modification, or intensification improves clinical outcomes in patients with asymptomatic PAD who have no other indications for interventions (such as lipid levels, blood pressure, or antiplatelet therapy).

Because risk prediction for CAD and CVD continues to evolve, ongoing studies and reanalysis of existing

population-based cohorts will be critical to understanding the value of ABI screening to reclassify CAD and CVD risk within the current FRS system and other risk prediction models. An update of the ABI Collaboration analysis using the net reclassification index (NRI) is also currently under way.

Evaluating the relative value of ABI screening within certain subgroups (such as persons with higher underlying prevalence of low ABI, those in whom traditional risk prediction does not perform well, or those near thresholds of risk categories) may help in the discrimination and calibration of existing models.

Finally, further study is needed to determine whether aggressive modification of risk factors in patients with multiple atherosclerotic risk factors reduces the incidence of symptomatic PAD.

DISCUSSION

Burden of Disease

The most recent data from 1999 to 2004 show that 5.9% of U.S. adults aged 40 years or older have a low ABI. In the United States, a low ABI (typically <0.9) is considered a marker for PAD. However, evidence that the ABI is an accurate screening test in asymptomatic adults is limited, so the actual prevalence of PAD is unknown. When persons with known CAD or cerebrovascular disease are excluded, the prevalence of PAD is 4.7% (1). The burden of disease is higher in older populations; the prevalence of low ABI in adults aged 40 to 59 years is 1.9%. Prevalence increases to 8.1% in adults aged 60 to 74 years and to 17.5% in those aged 75 years or older. Peripheral artery disease is a manifestation of systemic atherosclerosis and is considered a predictor for other atherosclerotic CVD and CVD events. The natural history of screen-detected PAD, including the development of morbidity and mortality directly related to lower-extremity atherosclerosis, is not wellknown. Thus, the true burden of asymptomatic, screendetected PAD is difficult to determine.

Scope of Review

In 2005, the USPSTF recommended against screening for PAD (D recommendation), the same recommendation issued in 1996. The 2005 evidence review was limited, focusing only on lower-extremity symptoms and function. It did not address PAD as a predictor for CVD. In 2009, the USPSTF assessed the use of nontraditional risk factors, including the ABI, to predict coronary heart disease events and determined that the evidence was insufficient to assess the balance of benefits and harms (I statement) (8).

The current evidence review included broader CVD outcomes than previous reviews and specifically focused on resting ABI as the sole screening method; the diagnostic performance of ABI testing in primary care populations, unselected populations, and asymptomatic populations; the predictive value of ABI testing for major CVD outcomes in primary care or unselected populations; and the effect of treatment on general CVD and PAD-specific (lower-extremity) morbidity in patients with asymptomatic or minimally symptomatic PAD (5). The USPSTF reviewed studies published from 1996 through September 2012 that used resting ABI as a screening test for PAD or as a risk predictor for CVD. As described earlier, screening for PAD with the ABI in persons with diabetes or known CVD is unlikely to alter effective management decisions and is outside the scope of this recommendation. In addition, although often done, the clinical benefits and harms of screening for PAD with a physical examination have not been well-evaluated and are beyond the scope of this review.

Accuracy of Screening Tests

In practice, a low ABI is used as a surrogate marker for PAD; however, its accuracy as a screening tool for PAD in asymptomatic primary care populations is not known. Only 1 fair-quality study evaluated its use in a relevant population, but the study had some limitations (9). It was conducted in Sweden and included 306 participants, all of whom were aged 70 years on study entry. In addition, the mean interval between ABI and MRA was 16 months. When whole-body MRA showing at least 50% stenosis in the pelvic or lower-extremity arteries was used as the reference standard, an ABI of less than 0.9 had sensitivity of 15% to 20% but specificity of 99%. Despite its low sensitivity, the positive and negative predictive values for the ABI in this study were 82% to 83% and 80% to 84%, respectively. Although the study had significant limitations, the USPSTF, after extrapolating from evidence in symptomatic populations, concluded that there is adequate evidence that the ABI is a reliable screening test for PAD in asymptomatic populations.

Effectiveness of Early Detection and Treatment *Early Detection*

No studies directly addressed the effect of screening for PAD with the ABI on future cardiovascular morbidity or mortality or PAD-related outcomes. One meta-analysis and 14 additional fair- to good-quality studies addressed whether the ABI is predictive of CAD or CVD morbidity and mortality, independent of FRS risk factors (5). Included studies evaluated the added prognostic value of the ABI to FRS risk factors (age, sex, smoking status, systolic blood pressure, total cholesterol level, and high-density lipoprotein cholesterol level). One large, individual patient– level meta-analysis ($n = 48\ 294$) from the ABI Collaboration contributed the most evidence (10).

Overall, data from 52 510 persons across 18 population-based cohort studies showed that a low ABI (≤ 0.9) is associated with future CAD and CVD events, independent of FRS risk factors. The ABI Collaboration meta-analysis found that including the ABI with FRS risk factors resulted in the reclassification of 19% of men and 36% of women into different risk categories (10). In men, most reclassifications were from high risk to intermediate

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risk on the basis of a normal ABI, whereas most reclassifications in women were from low risk to intermediate and high risk on the basis of a low ABI.

Several issues, however, limit the interpretation of these findings. The proportion of persons who were appropriately reclassified is not known. The ABI Collaboration meta-analysis was done before the NRI became commonly used in research studies. The NRI is a measure of the proportion of cases that are appropriately reclassified to different risk categories on the basis of additional risk factors. Another limitation is that the ABI Collaboration reclassification is based on total CAD events (CAD death, MI, or angina), whereas the Adult Treatment Panel III FRS algorithm uses only hard CAD events (CAD death and MI). In addition, men were reclassified on the basis of small changes in their 10-year risk, which may not be clinically important if the risk measurement is imprecise or if different definitions are used for risk categories. The ABI Collaboration used a different definition of normal ABI (1.1 to 1.4 vs. 0.9 to 1.4) from the one typically used, which could exaggerate the risk compared with studies using the typical definition. The more common definition of 0.9 as a low ABI leads to a higher proportion of men (35%) and a lower proportion of women (7%) who are reclassified, although in the same direction.

Four cohort studies used the NRI to determine the appropriateness of reclassification using the ABI in addition to FRS risk factors and reported small or statistically nonsignificant NRIs (11–14). These 4 studies and the ABI Collaboration meta-analysis are difficult to compare because of differences in populations (age, sex, and race or ethnicity), choice of reference group (definition of normal ABI), definition of composite CAD outcomes (hard vs. total CAD) and risk categories (intermediate risk of 10% to 19%, 15% to 25%, or 5% to 20%), and measures of reclassification (number reclassified vs. NRI). These differences prevent analysis of consistency across the populations; however, the studies suggest that the NRI is relatively small, although it may be higher for older populations.

Treatment

Two studies addressed treatment of asymptomatic patients with a low ABI or PAD. The first, Aspirin for Asymptomatic Atherosclerosis, was a large, good-quality, randomized, controlled trial that addressed whether asymptomatic men and women aged 50 to 75 years with a screen-detected low ABI could benefit from daily aspirin therapy (2). The trial screened 28 980 participants, 17% of whom (n = 4914) had an ABI of 0.95 or less. Of those, 3350 were randomly assigned to aspirin therapy (100 mg/d) or placebo. The study had a mean follow-up of 8.2 years and did not show any significant difference in CVD events (MI, cerebrovascular accident, or revascularization) between the 2 groups (hazard ratio, 1.03 [95% CI, 0.84 to 1.27]). In the subset of patients with an ABI of 0.9 or less, there was also no significant difference between the aspirin and placebo groups. In addition, there were no significant differences in either secondary outcome—CVD events plus angina, intermittent claudication, or transient ischemic attack—or all-cause mortality.

The second study investigated whether patients with PAD and high levels of low-density lipoprotein (LDL) cholesterol could improve lipid control with an intensive telephone counseling intervention (15). Most patients in this trial, conducted at 2 U.S. medical centers, had no or atypical symptoms (20.3% and 54.5%, respectively), and some had intermittent claudication (15.2%). Patients had an average ABI of 0.68 and an average LDL cholesterol level of 4.7 mmol/L (183 mg/dL). Three groups were compared: intervention, attention control, and usual care. Patients in the intervention group received telephone calls every 6 weeks (total of 200 minutes) focusing on the importance of decreasing LDL cholesterol level, adherence to medication, communicating with their treating physician about needing more intensive therapy, and increasing walking activity; in addition, study staff sent a letter to the treating physician after each call. Patients in the attention control group received telephone calls with general PAD information, and those in the usual care group received no calls. At 12 months, the intervention group had a significantly greater decrease in LDL cholesterol level than the attention control group but not the usual care group; however, a greater proportion of participants in the intervention group achieved LDL cholesterol levels less than 2.6 mmol/L (<100 mg/dL) than in either of the other 2 groups.

After considering these 2 studies, as well as the lack of studies evaluating the effect of other cardiovascular risk reduction interventions (such as lipid-lowering therapy), the USPSTF determined that there is inadequate evidence that early treatment of screen-detected PAD leads to improvement in clinical outcomes.

Potential Harms of Screening and Treatment

No studies directly addressed the harms of screening for PAD with the ABI. The harms to the patient of screening itself, beyond the time needed to perform the test, are probably minimal. Other harms resulting from testing may include false-positive results, exposure to gadolinium or contrast dye if either MRA or CTA is used to confirm diagnosis, anxiety, labeling, and opportunity costs. The time and resources needed to screen a patient with the ABI in a primary care setting may detract from other prevention activities that may have more benefit.

The only study that addressed the harms of treatment of asymptomatic persons was the good-quality trial Aspirin for Asymptomatic Atherosclerosis, which compared daily aspirin therapy with a placebo control. In this trial, participants randomly assigned to the aspirin therapy group had a nonsignificant trend toward increased major bleeding events requiring hospitalization compared with those in the placebo group (hazard ratio, 1.71 [CI, 0.99 to 2.97]) (2). No studies addressed the harms of other potential treatments, such as cholesterol-lowering medications or smoking cessation.

Estimate of Magnitude of Net Benefit

The USPSTF found adequate evidence that the ABI is a reliable screening test for PAD (on the basis almost exclusively of information from symptomatic adults) and that a low ABI (≤ 0.9) is associated with future CAD and CVD events, independent of FRS risk factors. In addition, using the ABI with regular FRS risk factors resulted in patient risk reclassification, although the appropriateness of the reclassifications could not be assessed. Studies addressing the benefits of treatment are sparse, with 1 good-quality study showing no benefit of daily aspirin therapy compared with placebo control. No studies evaluated whether treatments initiated because of risk reclassification made on the basis of ABI findings result in benefit to reclassified asymptomatic patients. Also, no studies addressed harms of screening, although the potential exists for overdiagnosis, labeling, and opportunity costs. The study that addressed the harms of treatment evaluated daily aspirin therapy and showed a nonsignificant trend toward increased risk for major bleeding. Therefore, the USPSTF concludes that the evidence on the balance of benefits and harms of screening is lacking.

How Does Evidence Fit With Biological Understanding?

Peripheral artery disease is generally considered to be a manifestation of systemic atherosclerosis. Detection of this condition when a patient is asymptomatic may also suggest that the patient has significant atherosclerosis in other vessels, such as the heart or brain, and may therefore be at risk for types of CVD other than PAD. Early detection and intervention to reduce atherosclerotic progression and prevent future CVD events could improve health outcomes compared with intervention strategies used in the absence of PAD screening. However, a substantial number of persons with an asymptomatic low ABI may never develop clinical signs or symptoms of CVD but would still be subjected to the harms of testing and subsequent treatments.

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 19 March to 15 April 2013. The USPSTF received few comments, several of which agreed with the recommendation. Some comments provided additional studies and different interpretations of the evidence reviewed by the USPSTF. The USPSTF reviewed all of these studies and determined that they did not provide the necessary evidence to change its conclusions because the recommendation focuses on asymptomatic adults who do not have a known diagnosis of PAD, CVD, severe chronic kidney disease, or diabetes and are treated in a primary care setting.

UPDATE OF PREVIOUS USPSTF RECOMMENDATION

This is an update of the 2005 recommendation. Unlike the previous recommendation, which used evidence from a targeted review that only evaluated screening for PAD as it related to lower-extremity symptoms, this recommendation also considered evidence on the potential benefits of adding the ABI to FRS results. This change was in response to public comment on the research plan. In 2005, the USPSTF issued a D recommendation for screening for PAD with the ABI to reduce lower-extremity symptoms. The current recommendation, an I statement, notes that there is insufficient evidence to determine the balance of benefits and harms of screening for PAD with the ABI to prevent future CVD outcomes.

RECOMMENDATIONS OF OTHERS

The American College of Cardiology Foundation and the American Heart Association released joint practice guidelines recommending the use of resting ABI for detecting PAD in patients at increased risk, including adults aged 65 years or older, adults aged 50 years or older with a history of smoking or diabetes, and adults of any age with exertional leg symptoms or nonhealing wounds (16). In the 2010 "Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults," the American College of Cardiology Foundation and the American Heart Association also recommended the ABI as a reasonable tool for cardiovascular risk assessment in patients at intermediate risk (17).

From the U.S. Preventive Services Task Force, Rockville, Maryland.

Disclaimer: Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.uspreventiveservicestaskforce.org).

References

 Pande RL, Perlstein TS, Beckman JA, Creager MA. Secondary prevention and mortality in peripheral artery disease: National Health and Nutrition Examination Study, 1999 to 2004. Circulation. 2011;124:17-23. [PMID: 21690489]
 Fowkes FG, Price JF, Stewart MC, Butcher I, Leng GC, Pell AC, et al; Aspirin for Asymptomatic Atherosclerosis Trialists. Aspirin for prevention of cardiovascular events in a general population screened for a low ankle brachial 3. Cassar K. Peripheral arterial disease. Clin Evid (Online). 2011;2011. [PMID: 21477401]

4. Joosten MM, Pai JK, Bertoia ML, Rimm EB, Spiegelman D, Mittleman MA, et al. Associations between conventional cardiovascular risk factors and risk of peripheral artery disease in men. JAMA. 2012;308:1660-7. [PMID: 23093164]

5. Lin S, Olson C, Johnson E, Senger C, Williams C, Whitlock E. Screening for Peripheral Artery Disease With Ankle Brachial Index Testing: A Systematic Evidence Review for the U.S. Preventive Services Task Force. Evidence Synthesis no. 100. AHRQ Publication no. 12-05162-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2013.

6. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/ Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation. 2006;113:e463-654. [PMID: 16549646]

7. Mohler ER 3rd, Treat-Jacobson D, Reilly MP, Cunningham KE, Miani M, Criqui MH, et al. Utility and barriers to performance of the ankle-brachial index in primary care practice. Vasc Med. 2004;9:253-60. [PMID: 15678616]

8. **U.S. Preventive Services Task Force.** Screening for Peripheral Arterial Disease: Recommendation Statement. AHRQ Publication no. 05-0583-A-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2005.

9. Wikström J, Hansen T, Johansson L, Lind L, Ahlström H. Ankle brachial index <0.9 underestimates the prevalence of peripheral artery occlusive disease assessed with whole-body magnetic resonance angiography in the elderly. Acta Radiol. 2008;49:143-9. [PMID: 18300136]

10. Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, et al; Ankle Brachial Index Collaboration. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a metaanalysis. JAMA. 2008;300:197-208. [PMID: 18612117]

11. Rodondi N, Marques-Vidal P, Butler J, Sutton-Tyrrell K, Cornuz J, Satterfield S, et al; Health, Aging, and Body Composition Study. Markers of atherosclerosis and inflammation for prediction of coronary heart disease in older adults. Am J Epidemiol. 2010;171:540-9. [PMID: 20110287]

12. Kavousi M, Elias-Smale S, Rutten JH, Leening MJ, Vliegenthart R, Verwoert GC, et al. Evaluation of newer risk markers for coronary heart disease risk classification: a cohort study. Ann Intern Med. 2012;156:438-44. [PMID: 22431676]

13. Yeboah J, McClelland RL, Polonsky TS, Burke GL, Sibley CT, O'Leary D, et al. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. JAMA. 2012;308:788-95. [PMID: 22910756]

14. Lee AJ, Price JF, Russell MJ, Smith FB, van Wijk MC, Fowkes FG. Improved prediction of fatal myocardial infarction using the ankle brachial index in addition to conventional risk factors: the Edinburgh Artery Study. Circulation. 2004;110:3075-80. [PMID: 15477416]

15. McDermott MM, Reed G, Greenland P, Mazor KM, Pagoto S, Ockene JK, et al. Activating peripheral arterial disease patients to reduce cholesterol: a randomized trial. Am J Med. 2011;124:557-65. [PMID: 21605733]

16. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, et al; Society for Cardiovascular Angiography and Interventions. 2011 ACCF/ AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2011;58:2020-45. [PMID: 21963765] 17. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, et al; American College of Cardiology Foundation. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2010;56:e50-103. [PMID: 21144964]

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APPENDIX: U.S. PREVENTIVE SERVICES TASK FORCE

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized[†] are Virginia A. Moyer, MD, MPH, *Chair* (American Board of Pediatrics, Chapel Hill, North Carolina); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Francisco A.R. García, MD, MPH

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(Pima County Department of Health, Tucson, Arizona); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veterans Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); and Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina). Timothy Wilt, MD, MPH, a former USPSTF member, also contributed to the development of this recommendation.

[†] For a list of current Task Force members, go to www .uspreventiveservicestaskforce.org/members.htm.

Grade	Definition	Suggestions for Practice
А	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
В	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
С	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer/provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

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Appendix Table 2. USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	 The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; and lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	 The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings that are not generalizable to routine primary care practice; and a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level on the basis of the nature of the overall evidence available to assess the net benefit of a preventive service.