Screening for Peripheral Arterial Disease: A Brief Evidence Update for the U.S. Preventive Services Task Force

Introduction

Systematic reviews of the literature serve as the basis for the U.S. Preventive Services Task Force (USPSTF) recommendations on clinical prevention topics. In 1996, the USPSTF addressed the utility of routine screening for peripheral arterial disease (PAD):

> Routine screening for peripheral arterial disease in asymptomatic persons is not recommended ("D" recommendation). Clinicians should be alert to symptoms of PAD in persons at increased risk (persons over age 50, smokers, diabetics) and evaluate patients who have clinical evidence of vascular disease.[1]

The USPSTF tailors the scope of these reviews to each topic. The USPSTF determined that a brief, focused evidence review was needed to update its 1996 recommendation on screening for PAD. AHRQ staff and the Lewin Group reviewed the literature published on this topic between 1994 and 2005, and AHRQ staff wrote this evidence update. The review was focused to search for direct evidence of decreased PAD-specific morbidity (improved health outcomes) from routine PAD screening, incremental benefit for patients (and subgroups) who received early treatment secondary to screen-detected PAD, and harms from PAD screening. The USPSTF reviewed and graded the evidence to draft its updated recommendations. This brief update and the updated USPSTF recommendations are available through the AHRQ Web site (http://www.preventiveservices.ahrq.gov). The recommendations are also available at the National Guideline Clearinghouse (http://www.guideline.gov).

Epidemiology and Background

PAD refers to atherosclerotic occlusive disease of the arterial system distal to the aortic bifurcation, and is a relatively common disorder in the elderly.[2] The American Heart Association estimates that as many as 8 to 12 million Americans have PAD and that nearly 75% of those with PAD are asymptomatic.[3] The prevalence of lower-extremity PAD based on ankle-brachial blood pressure ratios is approximately 10% to 20% of community-dwelling individuals aged 65 and older and 18% to 29% of patients aged 50 and older in general medicine practices.[4-8]

The prevalence of symptomatic claudication is less than half that of PAD. The disease spectrum ranges from mild, intermittent claudication resulting in calf pain, to severe, chronic leg ischemia requiring arterial bypass or amputation. Severe critical leg ischemia affects fewer than 1 million adults in the United States.[5] Risk factors associated with PAD include older age,

cigarette smoking, diabetes mellitus, hypercholesterolemia, hypertension, and (possibly) genetic factors.[2]

Screening for PAD may be conducted by instruments, such as history-taking or questionnaires, or by ankle-brachial index (ABI). Results from one study found that the sensitivity and positive predictive value of a classic history of claudication were only 54% and 9%, respectively, when compared with the results of formal noninvasive testing, such as the ankle-brachial index.[9] In general, less than 20% of persons with PAD are symptomatic,[7,10] exacerbating the unreliability of history in the diagnosis of PAD.

Aside from history-taking, a common screening measure is the Edinburgh Claudication Questionnaire (ECQ), which is a modification of the World Health Organization/Rose Questionnaire. The ECQ has been validated in a study of approximately 300 patients aged 55 and older who saw their physician for any complaint. When compared with the independent assessment of two blinded clinicians, the ECQ showed a sensitivity of 91% and a specificity of 99% for the diagnosis of intermittent claudication.[11]

The ABI is another common screening tool in determining the presence of PAD, and it has demonstrated better accuracy than other instruments. Hummel et al found that an ABI measurement of less than 0.9 (the accepted cut-off for the presence of PAD) is 95% sensitive and specific for detecting angiographic arterial disease.[12] The accuracy of this screening tool increases as the severity of lower extremity stenosis increases.

PAD is associated with increased risk of cardiovascular morbidity and mortality.[6,13,14] Early PAD is associated with several intermediate indicators for which the frequencies are higher and, therefore, lend themselves for further study. These include intermittent claudication (a clinical manifestation of atherosclerosis in the lower extremities), the maximum walking distance before onset of intermittent claudication, and the ankle-brachial index.[15]

Methodology

The literature search was guided by an analytical framework developed specifically for PAD by the USPSTF. Specifically, this review focused on PAD outcomes and did not examine PAD as a risk factor for coronary heart disease. Five Key Questions were identified from this framework:

1. Does screening for PAD lead to reduced morbidity from PAD (including claudication, amputation, impaired ambulation)?
2. What is the yield of screening (eg, prevalence, sensitivity, specificity) for PAD in primary care practice?
3. What are the harms of screening (eg, labeling, over-diagnosis, over-treatment)?
4. Does treatment of people with screening-detected PAD lead to improvement in the outcomes specified in Question #1 beyond the benefits of treatment at the time of symptoms?

a. Is there a subgroup of screening-detected PAD patients in whom detection of PAD results in more effective treatment of claudication beyond identification of conventional risk factors alone (eg, through earlier or more aggressive use of treatments, such as aspirin or other anti-platelet agents, lipid-lowering therapy, blood pressure treatment, or lifestyle intervention)?

5. What are the harms of earlier treatment for PAD (ie, side effects of treatment)?

The search strategy included a review of English language articles identified from PubMed, the Cochrane Library, and the National Guideline Clearinghouse published between 1994 and 2003. The search excluded letters, editorials, and narrative reviews. Studies of symptomatic (ie, PAD or intermittent claudication) populations were also excluded from this search. The following table summarizes the results:

Search Criteria	**Number**
Peripheral Vascular Diseases [mh] OR Intermittent Claudication [mh]	3,500

Limits	**Number**
AND Mass Screening [mh]	28
AND (Clinical Trial [pt] OR Randomized Controlled Trial [pt])	459
AND Practice Guideline [pt]	4
AND Meta-analysis [pt]	29
AND (Review [pt] AND systematic*[tw])	13
Total	**533**

Abstracts were reviewed to determine which articles addressed the Key Questions. One reviewer examined the abstracts with the instruction to retain all that were clearly in-scope and those with potential or ambiguous relevance. These abstracts were then reviewed by a senior staff member for relevance.

Upon finalizing this report, a subsequent bridge search was conducted of literature published between January 2004 and June 2005. No relevant studies were identified.

Key Questions and Results

Key Question 1: Does screening for PAD lead to reduced morbidity from PAD (including claudication, amputation, impaired ambulation)?

One fair-quality randomized controlled trial (RCT) addressed this overarching question. Fowler et al investigated the impact of increased physical activity and cessation of smoking on the natural history of early PAD identified through population-based screening.[15] Participants were identified through either the ECQ or the ABI. The study involved 882 men divided equally into a control group that received "usual care" from their general practitioner and an intervention

group that received a “stop smoking and keep walking” regime. Follow-up occurred at 2 and 12 months via self-reported physical activity questionnaires. Maximum walking distance was the outcome of interest. At 12 months, significantly more men allocated to the intervention group had improved their maximum walking distance and reported walking more than 3 times per week. More smokers in the intervention group had stopped smoking than had smokers in the control group, but this difference was not statistically significant. The study results indicated that a combination of simple and safe interventions that are readily available in the community has the potential to improve outcomes in early PAD. The study determined that ambulation did improve as a result of the interventions applied. These interventions (smoking cessation and increased physical activity) are recommended to most patients with or without health concerns, regardless of the presence of PAD, as counseling measures to encourage healthy lifestyles.

Key Question 2: What is the yield of screening (eg, prevalence, sensitivity, specificity) for PAD in primary care practice?

No new evidence meeting search criteria was identified.

Key Question 3: What are the harms of screening (eg, labeling, over-diagnosis, over-treatment)?

No new evidence meeting search criteria was identified.

Key Question 4: Does treatment of people with screening-detected PAD lead to improvement in the outcomes specified in Question #1 beyond the benefits of treatment at the time of symptoms?

One cross-sectional study addresses this question. McDermott et al investigated the association of statin use with improved lower-extremity function in a population of persons with and without PAD.[16] Three hundred ninety-two men and women with PAD (defined as ABI<0.9) and 249 without PAD (defined as 0.9<ABI<1.5) participated in the study. Participants were recruited from noninvasive vascular laboratories and general medicine clinics. Names of prescription drugs and over-the-counter medicines (but not their doses or duration of use) were recorded. Outcome measures included 6-minute walking distance and 4-meter walking velocity. The summary performance score—an accepted summary metric that indicates lower-extremity functioning and predicts mobility loss, nursing home placement, and mortality among community-dwelling older men and women—was calculated.

The study concluded that statin use, independent of cholesterol level and other confounding variables, is significantly associated with superior lower-extremity leg functioning in patients with and without PAD. There was no association between the outcome measures and aspirin, angiotensin-converting enzyme (ACE) inhibitors, vasodilators, or beta-blockers. The authors postulated that statin use favorably influenced functioning in patients with and without PAD due to the medication’s non-cholesterol-lowering properties.

Key Question 4a: Is there a subgroup of screening-detected PAD patients in whom detection of PAD results in more effective treatment of claudication beyond identification of conventional

risk factors alone (eg, through earlier or more aggressive use of treatments, such as aspirin or other anti-platelet agents, lipid-lowering therapy, blood pressure treatment, or lifestyle intervention)?

One fair-quality study addressed this question for a subgroup of smokers. The outcome of interest was first occurrence of intermittent claudication, which is an intermediate outcome of interest in the Key Question. Tornwall et al performed a subgroup analysis of an RCT that involved 26,289 male smokers aged 50 to 69 with no history or symptoms of intermittent claudication.[17] The Rose Questionnaire was administered annually to identify incident cases of typical intermittent claudication. Subjects were randomly assigned to receive long-term supplementation with vitamin E, beta-carotene, both, or placebo. There were 2,704 cases of first occurrence of typical intermittent claudication during a median follow-up time of 4 years. The adjusted relative risk (RR) for development of intermittent claudication among those who received vitamin E only was 1.11 (95% confidence interval, 1.00-1.24); for those who received both vitamin E and beta-carotene, adjusted RR was 1.02 (0.91-1.13); and among those who received beta-carotene only, it was 1.02 (0.92-1.14). When compared with those who received no vitamin E, the adjusted RR was 1.05 (0.98-1.14). Therefore, the analysis found that vitamin E and beta-carotene have no primary preventive effects on intermittent claudication among middle-aged males.

Key Question 5: What are the harms of earlier treatment for PAD (ie, side effects of treatment)?

No new evidence meeting the search criteria was identified.

Summary

Although there is substantial literature on PAD, most recent evidence pertains to symptomatic patients, including use of diagnostic tests (eg, magnetic resonance angiography) or treatments for intermittent claudication (eg, exercise therapy, naftidrofuryl) or leg ischemia (eg, revascularization via bypass surgery or angioplasty), and is therefore outside the scope of this analysis.

Evidence does exist to support the use of increased physical activity and smoking cessation to improve the outcomes from early PAD. These interventions, however, are already offered to all patients to encourage healthy lifestyles and do not necessarily offer additional benefit for persons with screen-identified PAD.

A cross-sectional study found that statin use was associated with superior lower-extremity functioning in patients with and without PAD. No conclusions could be made regarding statin dose or duration of use and the outcome of asymptomatic versus symptomatic PAD.

Recommendations of Professional Organizations

The American Diabetes Association currently recommends annual screening for PAD in people with diabetes that includes a history of claudication and palpation of pedal pulses.[18] The

American Academy of Family Physicians recommends against the use of Doppler or duplex ultrasound or other vascular laboratory testing in asymptomatic persons for PAD.[19] A few organizations, such as the American Heart Association and the Society of Interventional Radiology, support the use of ABI in the evaluation of suspected PAD. For further information, please refer to the following Web sites:

- American Heart Association, http://www.americanheart.org.
- American College of Surgeons, http://www.facs.org/index.html.
- Society of Interventional Radiology, http://www.sirweb.org/.

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