Does screening for peripheral arterial disease improve risk stratification for patients at intermediate risk for coronary artery disease?

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MANY PATIENTS AT INTERMEDIATE RISK OF developing coronary artery disease (CAD) are seen in primary care. Intermediate risk is classified as a calculated Framingham 10-year risk of 10% to 20% for patients without a history of arteriosclerotic disease or diabetes. A recent audit showed that 14% of patients aged 35 to 75 years in my family practice meet this profile.

Recent Canadian dyslipidemia guidelines[1] have been criticized for promoting the overuse of statins for patients at low risk of developing CAD.[2] Statins decrease the relative risk of coronary events by approximately 30%.[3] If a patient has a 5% risk of developing CAD in the next 10 years, using a statin for 10 years would only reduce his or her absolute risk by 1.5% (0.3 x 5%); 67 patients would have to be treated for 10 years to prevent 1 myocardial infarction and 66 of these patients would not benefit from the treatment. With statins costing about $1 per day, treating 67 patients for 10 years would translate to $245 000 in drug costs alone. Patients at high risk of developing CAD (Framingham 10-year risk >20%) derive greater benefit from statins, and there is more evidence to support treating them.

Several ways to further stratify patients at intermediate risk have been proposed. A family history of early CAD (a first-degree relative who developed CAD at age 50 years or younger) doubles the calculated Framingham risk.[4] A plethora of biomarkers, including C-reactive protein, B-type natriuretic peptide, aldosterone, renin, fibrinogen, D-dimer, plasminogen-activator inhibitor type 1, homocysteine and urinary albumin-to-creatinine ratio, 5 have been suggested as candidates to improve risk stratification. However, the accuracy of these biomarkers and the resulting risk adjustment is not clear, and a recent study found that even the use of multiple markers adds little to the Framingham score.[5] Using at least two high-sensitivity C-reactive protein measurements has been found to be a reliable marker for a new risk calculator in women (the Reynolds score)[6] but the additional complexity and expense of implementing this new score may limit its use in primary care. I am not using these biomarkers in my practice.

There are other tests that can be used for risk stratification. The US Preventive Services Task Force recently reviewed CAD screening; the Task Force gave electrocardiography, cardiac stress exercise testing, and electron beam computed tomography (EBCT) an "I" rating (insufficient evidence to make a recommendation for or against) for patients at intermediate Framingham risk.[7] EBCT is expensive and as there are already long waiting lists for CT scans in Canada this is not an ideal test to use for screening at this time.

Recommendations have been made that all patients aged 50 years and over with at least 1 cardiovascular risk factor and all patients aged 70 years and over should be screened for peripheral arterial disease (PAD) using the ankle-brachial index (ABI)(Figure 1).[8,9] PAD is a known risk factor for underlying cardiovascular disease, but neither history taking nor clinical examination is sensitive or specific enough for PAD screening.[10] The US Preventive Services Task Force does not currently recommend PAD screening in the general population (grade D recommendation), because there is the potential for a small degree of harm resulting from false-positive results and unnecessary investigations for PAD.[11] Perhaps we should think of ABI as a tool for risk stratification for cardiovascular disease rather than solely as a screening or diagnostic test for PAD.

The prevalence of abnormal ABIs (0.9 or less) is 18% to 29% in patients aged 50 years and over; 75% of those patients are asymptomatic.[11] A systematic review found that with an ABI of 0.9 or less, the likelihood ratio of CAD is 2.5 and the likelihood ratio for death from coronary causes is 5.6.[12] Using a nomogram, one
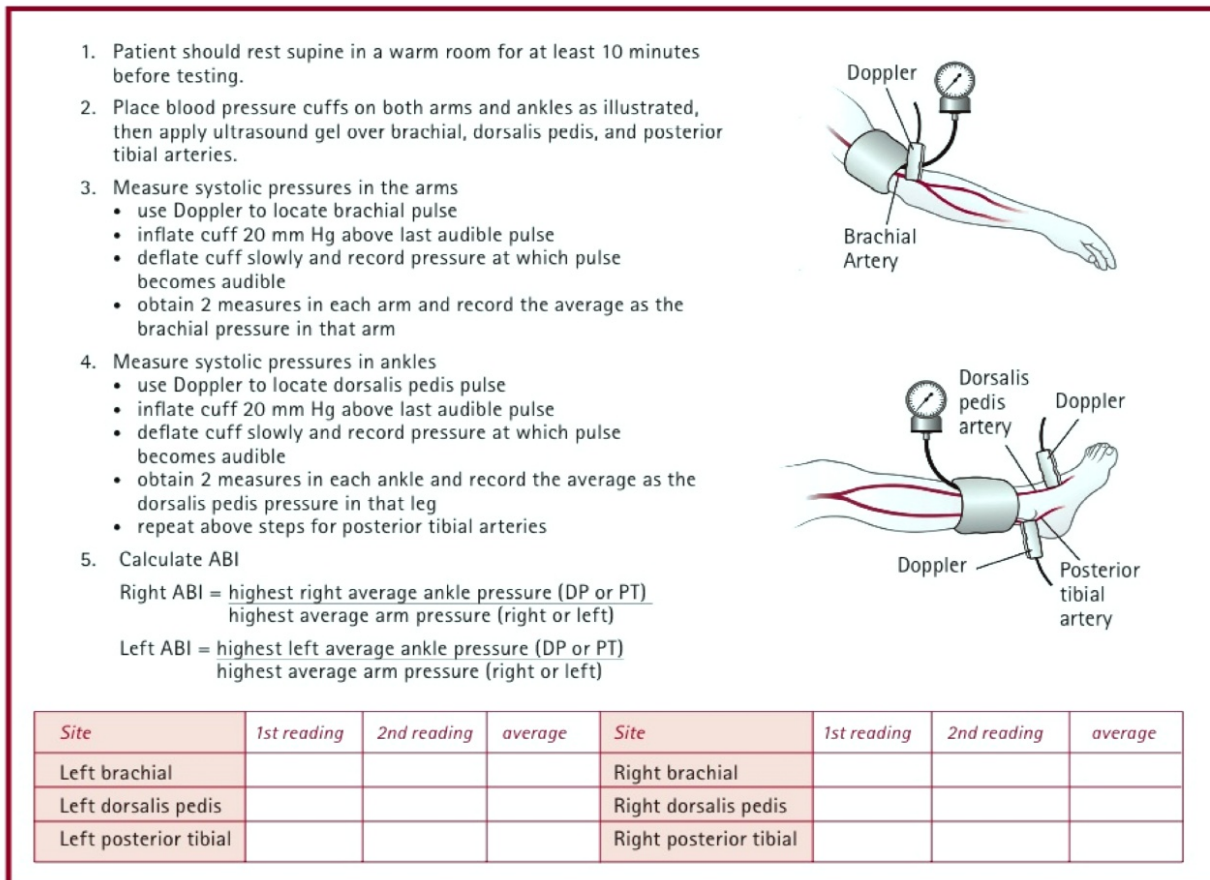
1. Patient should rest supine in a warm room for at least 10 minutes before testing.

2. Place blood pressure cuffs on both arms and ankles as illustrated, then apply ultrasound gel over brachial, dorsalis pedis, and posterior tibial arteries.

3. Measure systolic pressures in the arms
   - use Doppler to locate brachial pulse
   - inflate cuff 20 mm Hg above last audible pulse
   - deflate cuff slowly and record pressure at which pulse becomes audible
   - obtain 2 measures in each arm and record the average as the brachial pressure in that arm

4. Measure systolic pressures in ankles
   - use Doppler to locate dorsalis pedis pulse
   - inflate cuff 20 mm Hg above last audible pulse
   - deflate cuff slowly and record pressure at which pulse becomes audible
   - obtain 2 measures in each ankle and record the average as the dorsalis pedis pressure in that leg
   - repeat above steps for posterior tibial arteries

5. Calculate ABI

$$\text{Right ABI} = \frac{\text{highest right average ankle pressure (DP or PT)}}{\text{highest average arm pressure (right or left)}}$$

$$\text{Left ABI} = \frac{\text{highest left average ankle pressure (DP or PT)}}{\text{highest average arm pressure (right or left)}}$$

Site	1st reading	2nd reading	average	Site	1st reading	2nd reading	average
Left brachial				Right brachial			
Left dorsalis pedis				Right dorsalis pedis			
Left posterior tibial				Right posterior tibial			

Fig. 1. How to measure the ankle-brachial index (ABI).
DP = dorsalis pedis. PT = posterior tibial. Reprinted with permission from Laine et al.[9]

can calculate that if a patient has a 15% Framingham risk and a positive ABI, their risk of developing CAD is approximately 30%. This puts him or her in the high-risk category and he or she should be offered treatment with a statin.

The cost of testing ABI in Ontario at a vascular or ultrasound laboratory is $22.60 for the technical component and $13.70 for the professional component. However, the test can be performed easily and accurately in an office setting with a handheld Doppler probe and a blood pressure cuff.

The fee per test is $10.05, but the cost of the Doppler probe is approximately $700. It is unclear whether it is practical to perform the test in the primary care setting, given the current reimbursement rates and the additional time required for providers to perform the test.

A prospective randomized controlled trial enrolling patients at intermediate risk of developing CAD who are randomly assigned to be screened or not screened with ABI would provide the best assessment of this test's usefulness. The trial registry clinicaltrials.gov does not currently list any studies addressing the use of ABI in patients at intermediate risk, although it includes a randomized controlled trial using the expensive and more invasive EBCT. Guidelines produced by specialty groups appear to recommend the use of ABI to screen for PAD in patients at intermediate risk of developing CAD,[13,14] but the producers of these guidelines are perhaps more likely to be biased toward intervention in their area of interest rather than routine screening in the general population. It would be helpful to practitioners if the US Preventive Services Task Force or the revitalized Canadian Task Force on Preventive Health Care reviewed the subject. Meanwhile, we are each left to weigh the evidence to decide if it is strong enough to start using ABI for risk stratification of patients at intermediate Framingham risk of developing CAD.

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