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Peripheral arterial disease

Screening in general practice

Background
As a manifestation of systemic atherosclerosis, peripheral arterial disease (PAD) signifies an increased risk of cardiovascular events. Peripheral arterial disease has received less attention than other atherosclerotic diseases, leading to under-diagnosis and under-treatment. Peripheral arterial disease affects approximately 10–15% of the general population, and approximately 50% of PAD patients are asymptomatic.

Objective
This article aims to review the literature on the rationale for screening for lower extremity PAD in the general practice setting, and to identify the barriers to screening for PAD experienced by general practitioners, with a focus on the Australian context.

Discussion
Screening for asymptomatic PAD among high risk groups has been recommended by major PAD authorities to increase early diagnosis. Screening for PAD using the ankle-brachial index can detect asymptomatic patients. Research into the effect of cardiovascular risk reduction therapies for asymptomatic patients is lacking, and available evidence is inconclusive. The prevalence of screening and barriers to screening experienced by Australian GPs has not yet been studied. Available data on the benefits of PAD screening is inconclusive, and further research is required to determine a survival benefit with treatment of asymptomatic PAD.

Keywords
screening; peripheral arterial disease

Cardiovascular disease is the leading cause of morbidity and mortality in the Western world, and is becoming increasingly common in developing nations.[1] A large body of data demonstrates that secondary prevention can reduce future cardiovascular morbidity and mortality indicating the potential value of early disease detection.[2] Atherosclerosis affects both coronary and peripheral arterial beds, typically developing in multiple vascular beds and remaining subclinical for many years before manifesting with clinical symptoms.[1] The risk factors for peripheral arterial disease (PAD) are similar to those for atherosclerosis in other beds with the strongest risk factors for PAD being increased age, smoking and diabetes.[3]

Approximately 20% of people over the age of 65 years have symptomatic or asymptomatic PAD.[4] The age standardised population prevalence in men aged 65–83 years of PAD in Australia is 15.6%.[5] A diagnosis of PAD holds important prognostic value as a marker of increased mortality and vascular event risk, but methods to identify PAD at an early stage are not widely used.[6]

A diagnosis of PAD presents the opportunity to initiate secondary prevention by instituting atherosclerosis risk factor modification, and thus reducing the risk of cardiovascular complications. A failure to diagnose PAD misses this opportunity.[4] Factors postulated to be responsible for the current under-diagnosis of PAD include the asymptomatic nature of most PAD, the inappropriate use of recommended screening and diagnostic tools, and poor awareness of the prevalence, natural history and prognostic significance of PAD among public and medical communities.[7]

This article aims to review the literature on the rationale for screening for lower extremity PAD in the general practice setting, and identify the barriers to screening for PAD experienced by general practitioners, with focus on the Australian context.

Methods

Databases searched included PubMed, Cochrane, EMBASE, Scopus, Web of Science and Informit Health Collection. The search was carried out in May 2012. The following search terms were used: 'peripheral arterial disease', 'screen', 'asymptomatic', 'detection', 'ankle brachial index', 'examination' and 'general practice'.

Rationale for screening

Asymptomatic PAD affects up to 12% of primary care patients aged 65 years and over.[4] Symptomatic PAD has been found in 8% of primary care patients aged more than 65 years, defined by an ankle-brachial index (ABI) of <0.9 in addition to intermittent claudication

(IC), ischaemic rest pain, ischaemic ulcers, or gangrene.[2,4] Typical characteristics of IC include exertional cramping or aching muscle discomfort, typically located in the calf, but may also include the buttock or thigh, that is not positional, has a reproducible onset, and is relieved within 10 minutes of rest. In addition to patients presenting with typical symptoms, it is increasingly recognised that a large portion of PAD patients have atypical leg symptoms and thus, many patients with PAD are easily missed in routine GP consultations.[8] Guidelines relating to PAD screening are presented in *Table 1*. Of note, there is no current Australian guideline relating to PAD screening. The World Health Organization criteria for an appropriate screening program are presented in *Table 2* and discussed below in the context of screening for PAD with the ABI.[9]

The condition

Asymptomatic PAD has long been disregarded because of the erroneous belief that it is benign. Contrary to this, asymptomatic and symptomatic PAD patients have a similarly increased cardiovascular mortality risk.[3,4] Compared to patients without PAD, asymptomatic patients without known cardiovascular disease in other arterial sites have a two-fold increased risk of premature death.[10]

Screening methods

Detection of PAD relying on history alone, or using a symptom based questionnaire, must necessarily miss all patients with asymptomatic PAD.[8] General practitioners commonly diagnose symptomatic and asymptomatic PAD using physical examination findings, such as absence of pulses, femoral bruit and trophic skin changes.[8] While specific for PAD, these findings have low sensitivity (*Table 3*).[11–13] The ABI is a simple test to effectively detect asymptomatic lower limb PAD.

ABI measurement as a screening test

The ABI is sensitive, symptom independent, non-invasive and cost effective, and has proven efficacy for community screening of high risk patients.[6] The ABI is calculated as the quotient of the higher of the posterior tibial or dorsalis pedis artery systolic pressures in the one leg, and the higher of the right and left brachial artery systolic pressures.[8]

The ACC/AHA 2011 guidelines define values between 1.0–1.4 as normal, 0.9–0.99 as borderline PAD, <0.9 as diagnostic of PAD, and >1.4 indicates non-compressible arteries.[2]

The diagnostic value of ABI is limited in diseases that cause arterial calcification and non-compressibility (eg. advanced diabetes, renal insufficiency and in the very elderly).[8]

Measurement of the ABI and arterial waveform analysis using a hand-held Doppler ultrasound device currently attracts a Medicare fee of $63.75 (MBS Item Number 11610) provided a hard copy trace and report are supplied.[14]

Treatment of asymptomatic PAD

The desired outcome of early detection of PAD is to identify patients at increased risk of cardiovascular events and mortality and to take action to reduce their risk. As many PAD patients have involvement of multiple arterial sites and are likely to already be receiving secondary prevention therapies, it has been questioned whether detection of early PAD will significantly alter management. However, half of those

Table 1. Guidelines relating to screening for PAD

Guidelines	Year of publication	Recommendation and rationale	
American College of Cardiologists and the American Heart Association (ACC/AHA)	2011	• Screen high risk patients with ABI • Symptoms: exertional leg pain, non-healing ulcers • Age >65 years • Age >50 years PLUS either smoking or diabetes	
TransAtlantic InterSociety Consensus (TASC-II)	2007	• Screen high risk patients with ABI • Symptoms: exertional leg pain • Age 50–69 years with cardiovascular risk factors • Age >70 years	
United States Preventive Services Task Force[10]	2006	Recommend against screening	Benefits of screening are outweighed by the harms; based on the outcome of PAD related morbidity, not cardiovascular risk
National Health and Medical Research Council[23] [rescinded 2004]	1996	Recommend against screening	Additional sensitivity and specificity data for detection tools required

Table 2. WHO principles of screening[21]

Condition	Important health problem
	Recognisable asymptomatic stage
	Known natural history of disease
Test	Suitable and acceptable test
Treatment	Treatment must be available
Program	Cost effective

Table 3. Sensitivities and specificities of PAD detection methods[11–13]

	Sensitivity	Specificity
Edinburgh Claudication Questionnaire	56%	>90%
Examination: absence of both pedal pulses	72%	>90%
Examination: femoral bruit	28%	>90%
Ankle-brachial index	77%	>95%
Duplex arterial ultrasound	96%	>95%

Table 4. National Heart Foundation recommendations for secondary prevention of cardiovascular disease[22]

Secondary prevention of cardiovascular disease	
Smoking	Complete cessation
Exercise	Moderate level activity (brisk walking) 30 min/day at least 5 days per week
Diet	Mediterranean diet: emphasis on fruits, vegetables, healthy oils, nuts/seeds and fish; limit sugar, saturated fats and salt
Weight	Target BMI <25 kg/m^2; waist measurement <94 cm for men and <80 cm for women; recommend weight loss 5–10% of starting weight or 1–4 kg/month
Alcohol	No more than two standard drinks per day for men and women, and no more than four standard drinks on a single occasion
Blood pressure	Lifestyle modification ± drug therapy to achieve BP <140/90 mmHg
Lipid management	Dietary modification and statin therapy is recommended for all people with clinical evidence of vascular disease. Targets: • LDL-C <2.5 mmol/L • HDL-C >1 mmol/L • TC <4 mmol/L • Triglycerides <1.5 mmol/L
Diabetes	HbA1c <7%; fasting blood glucose 4–8 mmol/L
Antiplatelet therapy	75–162 mg/day aspirin is advised for all patients with symptomatic cardiovascular disease

patients with undiagnosed, asymptomatic PAD have no known cardiovascular disease in other vascular beds.[1]

Secondary prevention of cardiovascular disease is detailed in *Table 4*. Despite the known benefit of these therapies in reducing cardiovascular risk in symptomatic coronary artery disease and stroke patients, limited data exists on the impact of early intervention on asymptomatic PAD patients.

There is little data supporting the use of aspirin for cardiovascular risk reduction amongst PAD patients.[2,8] Available evidence from two studies suggests that 100 mg of aspirin daily has no benefit in preventing fatal or non-fatal cardiovascular events among asymptomatic PAD patients (*Table 5*).[15,16] The Heart Outcomes Prevention Evaluation (HOPE) trial evaluated the impact of ramipril, an angiotensin converting enzyme inhibitor (ACEI), on the prevention of fatal or non-fatal myocardial infarction (MI) or stroke among patients with PAD, including those described as having subclinical PAD. The investigators demonstrated a reduction

Table 5. Summary of evidence for early intervention

Treatment	Study title	Year	Study type	Study size	Study population (inclusion)	Intervention	Finding/results
Aspirin	Aspirin for Asymptomatic Atherosclerosis (AAA) Trialists[15]	2010	Randomised controlled trial	3350	Age 50–75 years + ABI ≤0.95 + no history of CVD	100 mg vs placebo	HR=1.03 (0.84–1.27) for fatal or non-fatal MI or stroke or revascularisation
	Prevention Of Progression of Arterial Disease And Diabetes (POPADAD)[16]	2008	Randomised controlled trial	1276	Age >40 years + type 1 or 2 diabetes + ABI ≤0.99 + no symptomatic CVD	100 mg aspirin ± antioxidants vs placebo	HR=0.98 (0.76–1.26) for fatal or non-fatal MI or stroke or amputation
ACEI	HOPE[17]	2004	Randomised controlled trial	2118 with asymptomatic PAD	Age ≥55 years + existing CVD or other CV risk factors + ABI <0.9 + no clinical symptoms	10 mg ramipril vs placebo + vitamin E vs placebo	RR: 0.72 (0.56–0.92) for patients with asymptomatic PAD (ABI 0.6–0.9) for fatal or non-fatal MI or stroke
Multiple preventive therapies	NHANES[10]	2011	Cross-sectional	7458	General population aged ≥40 years included in NHANES without previously established CVD	Nil	Two or more preventive therapies (aspirin, ACEI, and/or statin) were associated with 65% reduced risk of all-cause mortality HR=0.35, 95% CI: 0.20–0.86, p=0.02

in vascular events amongst subjects with subclinical PAD randomised to ACEI.[17] The effect of lipid lowering therapy for PAD patients with asymptomatic disease has not been studied.

Data from the National Health and Nutrition Evaluation Survey (NHANES) suggested that secondary prevention in asymptomatic PAD patients without known atherosclerotic disease carries a survival benefit, with a 65% reduction in the risk of all cause mortality in the patients treated with multiple preventive therapies compared to no prevention.[10]

Screening program

No studies have been published to date regarding the cost effectiveness of PAD screening with an ABI or whether widespread implementation of a PAD screening program and appropriate treatment results in survival benefit.

Barriers to screening

In view of their position in the community as primary carers, GPs are best positioned to detect patients at high risk of PAD.[2] However, international studies indicate that screening is rarely practiced.[2] There is no literature concerning the prevalence of PAD screening in Australia. European and American reports suggest that this may be due to poor community and physician awareness of PAD, lack of familiarity with guidelines, and underutilisation of screening tools contribute.[7]

Studies have revealed suboptimal awareness of PAD and its consequences amongst both the public and medical community, with only half of GPs aware of their patient's PAD diagnosis.[18] Education interventions can effectively improve physician awareness of PAD and have resulted in significant changes to the number of GPs regularly measuring ABI.[18]

The ABI is underutilised, and research into the barriers to ABI use is lacking. A study of 886 American primary care physicians found that time constraints, lack of reimbursement and staff availability were identified as major barriers to ABI use.[19] Most GPs measure ABI within 15 minutes, however, over half regarded this as prohibitively too long.[19] The automated oscillometric measurement of ABI is a novel technology that is quick and easy to perform in the office setting and demonstrates high accuracy for detecting PAD.[23]

Conclusion

Cardiovascular disease remains the major cause of mortality in the developed world. Despite the attendant cardiovascular risk associated with even asymptomatic disease, PAD is under-diagnosed and under-treated. Early detection offers the advantage of early intervention to reduce the risk of future cardiovascular events.

While there are guidelines for screening for PAD in high risk groups in the United States and Europe, there are currently no Australian guidelines relating to PAD screening. Screening is rarely performed in general practice and there is a deficit in research on this subject in the Australian context. Data on the benefits of screening are inconclusive and more evidence of a survival benefit associated with treatment of asymptomatic PAD is needed in order to confidently recommend PAD screening. There is a clear need for further research and Australian guidelines in this area. At this time, in the absence of Australian guidelines, it may be reasonable to recommend screening for PAD with ABI measurement in Australia in high risk groups as outlined by the ACC/AHA; ie. in patients with symptoms of lower extremity PAD, age 65 years and over, or 50 years and over with a history of smoking or diabetes.[2]

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