

UNIT NO. 3

**DIAGNOSIS & EVALUATION OF
ATHEROTHROMBOSIS PATIENTS**

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ABSTRACT

Cardiovascular disease and cerebrovascular disease together are the leading causes of morbidity and mortality in Singapore. Primary and secondary prevention of atherosclerosis play major roles in minimising these complications in the community. Many epidemiological studies have shown that peripheral arterial disease (PAD) is a marker for systemic vascular disease. PAD can be diagnosed accurately, quickly, and non-invasively in most patients in the office setting through Ankle – Brachial Index (ABI). The ABI has emerged as one of the most useful markers of diffuse atherosclerosis, cardiovascular (CV) risk, and overall survival in various patient populations. Measurement of the arterial circulation using ABI is thus considered mandatory. Most patients with significant peripheral vascular disease are symptom-free and have the same increased risk of cardiovascular events and death as in patients with symptomatic disease. The true prevalence of peripheral vascular disease is under-recognised in primary care.

The evidence for screening for asymptomatic peripheral vascular disease is compelling. The currently acceptable method of determining atherothrombosis consists of a historical review of patient symptoms and atherosclerotic risk factors, a physical examination including auscultation for carotid bruit, palpation of peripheral pulses and measurement of the ABI. The physical examination will include looking for evidence of sequelae of atherothrombotic disease namely, cerebrovascular disease, cardiovascular disease and PAD.

INTRODUCTION

Cardiovascular (CV) disease remains a leading cause of morbidity and mortality in Singapore. Hence, detection of atherothrombotic events is important, as is primary and secondary prevention of atherosclerosis aimed to minimize the onset of these complications in the community.

The following discussion draws on Western epidemiological data. Our local data is limited. Nevertheless, variance in the pattern of atherothrombosis in the different ethnic groups in Singapore is well recognised.

**DETECTION OF ATHEROTHROMBOTIC DISEASE
IN THE COMMUNITY**

Epidemiological studies show that peripheral arterial disease (PAD) is a marker for systemic vascular disease. Coronary artery disease and cerebrovascular disease are present in a large proportion of individuals with PAD. Also, PAD by itself confers sharply increased risks for cardiac and cerebral atherothrombotic events. Ten-year CV disease mortality in PAD patients is 6.6-fold higher than in age-matched controls.¹

Estimates of cerebrovascular disease prevalence in PAD patients vary widely from 0.5% to 52%, depending on the sophistication of the detection method used. While clinical history revealed cerebrovascular disease in 0.5% to 15% of PAD patients, cervical bruit or abnormal Doppler testing found it in 44% to 52%.^{2,3}

The commonest presentation of peripheral vascular disease in primary care is intermittent claudication. Epidemiological studies have shown that symptomatic peripheral vascular disease confers a higher risk of fatal and non-fatal CV ischaemic events. Half of the patients presenting with peripheral vascular disease have symptoms of coronary heart disease or electrocardiographic abnormalities, and 90% have abnormalities on coronary angiography. Prompt diagnosis and treatment to stop the progression of systemic atherosclerotic disease are of paramount importance.

DIAGNOSIS OF PAD

PAD can be diagnosed accurately, quickly and non-invasively in most patients in the office setting through measurement of the Ankle-Brachial Index (ABI), which is the ratio between the handheld continuous wave Doppler-recorded systolic blood pressures (SBP) in the lower and upper extremities (ankle SBP divided by brachial SBP). The value of ABI is heightened because it correlates with disease severity, CV and lower-extremity morbidity, and overall mortality.⁴

ABIs of 0.90 to 1.30 are considered normal; those under 0.90 are diagnostic for PAD, and ABIs of under 0.40 are characteristic of individuals with ischaemic rest pain or ulceration. For some diabetic patients with calcified, non-compressible arteries, ABI yields false readings with ankle pressure much higher than brachial pressure, in which case referral to a vascular lab is warranted, for an accurate diagnosis.

The ABI has emerged as one of the most potent markers of diffuse atherosclerosis, CV risk and overall survival in various patient populations; an abnormal ABI indicates a threefold increase in CV risk. In a study of 2,023 middle-

aged men screened with ABI,⁵ the relative risks for mortality from all causes, CV causes and coronary causes were significantly higher among patients with an ABI <0.90 than among patients with a normal ABI. Similarly, in a study of 1,492 women aged over 65 years,⁶ the relative risks for all-cause mortality, heart disease and CV disease were significantly greater when the baseline ABI was less than 0.90. Furthermore, in a study of >5,000 men and women aged 65 years or older,⁷ the results showed that the lower the ABI, the greater the incidence of CV risk factors and clinical CV disease.

The PARTNERS (PAD Detection, Awareness and Treatment in Primary Care) programme assessed the feasibility of detecting PAD in primary care clinics via ABI or history.⁸ ABI has been shown to be a simple, accurate diagnostic tool. PARTNERS enrolled 6,979 patients either aged 70 years or more, or aged 50 years or more with a history of cigarette smoking or diabetes. Analysis showed PAD prevalence to be 29%. Among these, 13% had PAD alone and 16% had both PAD and clinically apparent CV disease. Many of these patients had asymptomatic PAD.

ANKLE-BRACHIAL INDEX

The first and most important noninvasive test for PAD is the ankle-brachial index (ABI). This test may be performed in the physician's office and has only four requirements:

1. Basic understanding of how to perform an ABI.
2. Basic knowledge of arterial anatomy, namely brachial artery in the cubital fossa, posterior tibial artery in the ankle and dorsalis pedis artery in the foot.
3. Handheld continuous-wave Doppler ultrasonic probe 5 or 10 MHz and acoustic gel.
4. Sphygmomanometer.

The ABI compares the blood pressure obtained with the handheld Doppler in the dorsalis pedis or posterior tibial artery (whichever is higher) with the higher of the two brachial pressures. In general, an ABI of ≥ 0.90 is considered normal, between 0.40 and 0.90 reflects mild to moderate PAD, and <0.40 suggests severe arterial occlusive disease.

On the arterial side, the investigation is carried out as pedal pulse palpation followed by Doppler investigation. Doppler investigation is started by applying a sphygmomanometer cuff on the upper arm. The Doppler probe is placed over the antecubital fossa identifying the arterial pulse. The cuff is inflated until pulse disappearance and slowly deflated until reappearance of pulse, noting the corresponding pressure (brachial pressure). The cuff is then placed just above the ankle. The Doppler probe is placed over the dorsalis pedis artery identifying the pulse; the cuff is then inflated until pulse disappearance and slowly deflated until reappearance of pulse noting the corresponding pressure (ankle pressure). The procedure is repeated with

the probe over the posterior tibial artery. The higher of the ankle pressures is used. The ABI is calculated by dividing ankle pressure into the brachial pressure, approximating the value to two decimals.

Limitations of the ABI

A normal ABI in the face of abnormal peripheral arterial circulation (i.e., a false-negative result). In elderly patients or patients with end-stage renal disease or, more commonly, diabetes mellitus, the ankle arteries may have calcification in the medial layer. Therefore, when the physician compresses the sphygmomanometer and listens with the Doppler probe, a higher pressure is required to obliterate the Doppler signal, giving an artificially higher ankle pressure. This reading does not translate into a normal ABI but instead indicates vessel calcification, and more sophisticated non-invasive tests are required.

A normal ABI in patients with classic symptoms, suggesting intermittent claudication and PAD. Patients with moderate disease of the infrarenal aorta or iliac arteries may have normal arterial circulation at rest but when exercising, a decrease in ankle pressure may be noted. Therefore, a resting study is inadequate for patients with exertional symptoms of intermittent claudication. In this situation, an exercise arterial study should be performed in a vascular lab to determine the true etiology of exertional limb pain.

Pedal pulse palpation instead of Doppler ankle pressure measurement

The correlation between dorsal pedal pulse palpation and handheld Doppler measurement of ankle pressure has been studied by Mats Bjellerup in patients referred to a specialised leg and foot ulcer clinic at a dermatological department in Sweden.⁹ Complete data regarding palpable dorsal pulse and ABI were available for 510 patients. Palpable dorsal pedal pulse was present in 337 patients and absent in 173. Mean ABI in patients with palpable pulses was 1.07 (median 1.07, range 0.35 to 1.79). Mean ABI in patients without palpable pulses was 0.79 (median 0.80, range 0.22 to 1.31). The difference was significant ($P < .0001$).

In the group without palpable pedal pulses, 39.8% had an ABI >0.9. In the group with palpable pedal pulses, 52 patients (15.4%) had an ABI of 0.9 or less. While there is a strong association between ABI and palpable pedal pulse, the latter delivers 40% false-negative predictions in alerting professionals to the presence of arterial disease as defined by ABI of 0.9 or less. Measurement of the arterial circulation using a handheld Doppler is thus considered mandatory.

PROGNOSIS OF PAD

Most patients with significant peripheral vascular disease are symptom-free.¹⁰ Asymptomatic peripheral vascular disease is also associated with an increased risk of subsequent CV events

with a specificity of 83% and sensitivity of 30%.¹¹ The prevalence of asymptomatic peripheral vascular disease is estimated to be between 12% and 18% in Western populations.¹¹ The natural history of patients with asymptomatic peripheral vascular disease is also well documented.¹² Patients with asymptomatic peripheral vascular disease have the same increased risk of CV events and death as patients with symptomatic disease.¹² Asymptomatic patients with peripheral vascular disease can easily be detected by ABI (<0.9), which has a sensitivity of 97% and a specificity of 100% for angiographically defined stenosis.¹³

Furthermore, ABI has been shown to be a good predictor of subsequent CV events and has high patient acceptability.¹² Approximately 60% of patients will die of myocardial infarction and 10% will die of stroke.¹⁴ In a cross-sectional study in Edinburgh, UK, more than 18% of subjects aged 55 to 74 years had an ABI of <0.94 . The specificity of CV events for a lower index (<0.7) was approximately 95%.

Evidence for screening for PAD

The true prevalence of peripheral vascular disease is under recognized in primary care. Therefore, it seems logical to undertake primary care screening and targeted preventative therapy for patients with asymptomatic peripheral vascular disease with a view to improving CV morbidity and mortality. Almost one in five subjects would be identified at risk should a population of patients between the ages of 55 and 74 be screened.¹²

Should general practitioners screen and identify patients with asymptomatic peripheral vascular disease? As part of the quality framework for CV disease, the National Health Service in UK will require general practitioners to identify all patients with a diagnosis of coronary heart disease or occlusive arterial disease, including stroke and peripheral vascular disease, and offer them appropriate interventions.¹⁵

The evidence for screening for asymptomatic peripheral vascular disease using a simple, inexpensive and non-invasive measurement is strong. Large proportions of patients with peripheral vascular disease are asymptomatic, and are therefore not known to general practitioners as representing a higher risk group. Asymptomatic peripheral vascular disease is an independent risk factor for incident CV disease, recurrent CV disease and mortality.¹¹ If a screening programme is implemented, it would be best targeted at patients with a high risk of developing coronary heart disease, including patients with hypertension, diabetes mellitus, hyperlipidaemia, family history and patients who are smokers.

There is a strong consensus that patients with asymptomatic peripheral vascular disease should receive the same secondary prevention strategies as those with established coronary heart disease.^{8,16,17} However, there is currently a lack of evidence supporting the effectiveness of screening programmes¹⁸ for reducing CV morbidity and mortality in patients with asymptomatic disease. Previous surveys have shown that only

a few general practitioners are even providing secondary prevention to patients with established peripheral vascular disease.¹⁹

PAD is a clear marker for increased atherothrombotic risk and warrants more vigilant screening and prompt treatment.

DIAGNOSIS AND EVALUATION OF ATHEROTHROMBOSIS

The currently acceptable method of determining the presence of atherothrombosis consists of a historical review of patient symptoms and atherosclerotic risk factors, a physical examination including auscultation for carotid bruit, palpation of peripheral pulses and noninvasive vascular testing. The examination will also include looking for evidence of sequelae of atherothrombotic disease namely cerebrovascular and cardiovascular disease and PAD. As discussed above determination of ABI is a marker of atherothrombotic disease.

Lipid profile

The clinical Practice Guidelines 7/2001 on Lipids issued by Ministry of health states that a full lipid profile should be obtained in the following individuals:

- Patients with Coronary Heart Disease, Cerebrovascular disease or PAD
- Diabetic patients
- Individuals with a family history or clinical evidence of familial hyperlipidaemia
- Individuals with other risk factors for coronary heart disease.

Other investigations

Other investigations that would include for individuals at risk of atherothrombosis or who has atherothrombotic disease will include screening for diabetes (Urine for sugar and fasting blood sugar), electrocardiogram and chest x-ray. Those who are at risk of coronary heart disease, in addition will require treadmill exercise test. Troponin testing for diagnosis of acute coronary syndrome will soon be available in the form of rapid diagnostic kits to the primary physician. The value of troponin assay is discussed under module V.

Those patients detected to have atherothrombotic disease will require referral to respective specialists for further evaluation and these are discussed in the respective modules.

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LEARNING POINTS

1. **PAD is a marker of atherothrombosis.**
 2. **Asymptomatic PAD is more prevalent in the community than symptomatic PAD.**
 3. **ABI measurement using handheld Doppler is a sensitive index for detection of PAD.**
 4. **The true prevalence of PAD in the community is under recognised.**
 5. **Primary care screening and targeted preventive therapy for patients with asymptomatic PAD with a view to improving cardiovascular (CV) morbidity and mortality is important.**
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