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Chapter II: Diagnostic Methods

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Abstract Non-invasive vascular studies can provide crucial information on the presence, location, and severity of critical limb ischaemia (CLI), as well as the initial assessment or treatment planning.

Ankle-brachial index with Doppler ultrasound, despite limitations in diabetic and end-stage renal failure patients, is the first-line evaluation of CLI. In this group of patients, toe-brachial index measurement may better establish the diagnosis. Other non-invasive measurements, such as segmental limb pressure, continuous-wave Doppler analysis and pulse volume recording, are of limited accuracy. Transcutaneous oxygen pressure ($TcPO_2$) measurement may be of value when rest pain and ulcerations of the foot are present. Duplex ultrasound is the most important non-invasive tool in CLI patients combining haemodynamic evaluation with imaging modality.

Computed tomography angiography (CTA) and magnetic resonance angiography (MRA) are the next imaging studies in the algorithm for CLI. Both CTA and MRA have been proven effective in aiding the decision-making of clinicians and accurate planning of intervention. The data acquired with CTA and MRA can be manipulated in a multiplanar and 3D fashion and can offer exquisite detail. CTA results are generally equivalent to MRA, and both compare favourably with contrast angiography. The individual use of different imaging modalities

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depends on local availability, experience, and costs. Contrast angiography represents the gold standard, provides detailed information about arterial anatomy, and is recommended when revascularisation is needed.

1. Non-invasive vascular laboratory tests

In patients with critical limb ischaemia (CLI) an accurate diagnosis can be established with modern non-invasive vascular diagnostic techniques to provide adequate information for creation of a therapeutic plan. When required, non-invasive physiological and anatomical data will be supplemented by the use of more accurate imaging techniques, such as computed tomography angiography (CTA) or magnetic resonance angiography (MRA), and selective use of lower extremity angiographic techniques.

The objectives of modern non-invasive testing of patients with peripheral arterial disease are:

- to confirm the presence of the disease
- to provide reproducible physiological data concerning disease severity
- to document the location and haemodynamic importance of vascular lesions
- to make a detailed plan in case intervention is needed.

These tests can be repeated over time to follow disease progression and results of treatment.

Non-invasive assessment of patients with CLI can be broadly grouped into three general categories of techniques:

- physiologic or haemodynamic measurements
- measurements of tissue perfusion
- anatomic imaging.

Each modality has advantages, disadvantages and limitations.

Non-invasive techniques assessing physiological parameters of pressure and flow can provide an initial assessment of the location and severity of arterial disease. Doppler ultrasonography and plethysmography, each with various forms and techniques, are the two most commonly used haemodynamic methods to evaluate patients with CLI.

Measurements of tissue perfusion include microcirculation techniques; the most commonly employed is transcutaneous partial pressure of oxygen ($TcPO_2$) measurements.

Non-invasive anatomic imaging is usually based on a combination of Doppler haemodynamic and B-mode ultrasonography imaging and will be detailed in the second part of this chapter ("Imaging techniques. Duplex ultrasound").

2. Physiological and haemodynamic measurements (Table 1)

2.1. Doppler ultrasonography

Doppler ultrasonography is the single most important modality in non-invasive evaluation of vascular disease extent. Ultrasound techniques are based on the principle that sound waves emitted from a probe are reflected at the interface of two surfaces; the observation that an ultrasound wave undergoes a frequency shift proportional to the velocity of any moving object encountered (e.g. red blood cells) is known as Doppler principle. Both quantitative and qualitative measurements of flow are allowed by Doppler ultrasonography. Quantitative analyses are based on pressure measurements and include ankle-brachial and toe-brachial indices and segmental pressure; qualitative measurements are based on the analysis of the shape and morphology of Doppler waveforms.

2.1.1. Ankle-brachial index (ABI)

The single most valuable and commonly used diagnostic test in the evaluation of peripheral arterial occlusive disease is measurement of the ankle-to-brachial systolic blood pressure ratio, termed ankle-brachial index (ABI). The ABI is a simple, inexpensive, non-invasive test that can be performed easily in most clinical settings; it is measured with a handheld continuous-wave Doppler ultrasound probe and a blood pressure cuff: the highest systolic pressure measured from either the posterior tibial or dorsalis pedis artery (in each leg) is divided by the highest brachial artery pressure taken from either arm. Optimal recordings are obtained with blood pressure cuffs that are appropriately sized to the patient's lower calf, immediately above the ankle. Systolic pressures are recorded with a Doppler probe after the patient has been at rest in supine position for 5 minutes. Pulse wave reflection in healthy individuals causes the ankle pressure to be 10–15 mmHg higher than the brachial artery systolic pressure.[2–4] If the arm blood pressures are not equal, a subclavian/axillary stenosis or occlusion might be present, and the arm with the highest blood pressure is used for subsequent blood pressure ratio calculations. In patients with ischaemic ulcers, the ankle pressure is typically 50–70 mmHg, and in patients with ischaemic rest pain it is typically 30–50 mmHg. However, falsely high values can be recorded in CLI patients, in whom the ABI test is not reliable due to incompressible calcified vessels as in patients with long-standing diabetes, advanced age or end-stage renal disease.

The ABI provides objective data that serve as the first-line assessment for the diagnosis of lower limb vascular disease and has been used either as a baseline diagnostic tool for patients with CLI (foot ulcer or rest pain) or to monitor the efficacy of therapeutic interventions. The normal range of ABI is quoted as 0.91–1.31.[4,5] The cut-off point for diagnosis of vascular disease is typically set at $\leqslant$0.90 at rest.[1] ABI values between 0.41 and 0.90 are considered "mildly to moderately" diminished and an ABI of 0.40 or less as "severely" decreased. Although it has been suggested that patients with an ABI <0.40 are more likely to develop ischaemic rest pain, ischaemic ulceration, or gangrene, compared to patients with an ABI $\geqslant$0.5, there is no general consensus regarding the prognostic value of these ABI categories for peripheral disease.[1,2,6–11] In diabetic patients, Clairotte et al. reported that the cut-off values for the highest sensitivity and specificity for vascular disease screening were between 1.0 and 1.1.[11]

ABI measurement is claimed to be a simple and reproducible test. Reporting standards require a change of 0.15 to be considered clinically relevant, or >0.10 if associated