Peripheral Arterial Disease

Editor: Nadraj G Naidoo

The concept of best medical, interventional or surgical vascular practice pertaining to peripheral arterial disease (PAD) is best informed by: the level of available clinical evidence, local expertise and practices, availability of resources and affordability. While it is generally accepted that the scientific basis for any practice guideline or clinical recommendation is level 1 evidence supported by multiple large prospective randomized controlled trials (RCT) and meta-analyses of RCTs, such evidence is surprisingly rare in a condition as common as PAD

In an effort to develop practice guidelines for the management of patients with PAD in South Africa, a meeting of South African vascular surgeons was convened in November 2011 in Johannesburg. These vascular surgeons (listed at the end of this documented) are all registered members of the Vascular Society of Southern Africa (VASSA). In attempting to compile these guidelines contributing authors at this consensus meeting were requested to review existing international practice guidelines for PAD developed by various vascular societies and consensus groups, to supplement these guidelines with an updated literature review of the latest publications and recommendations, and to consider local expertise and resources when providing recommendations adapted for local conditions.

These guidelines when published will be the official guidelines of VASSA. In this regard they are intended to guide vascular surgical practice and inform other interested parties. As mentioned in previous practice guidelines developed by VASSA "It is essential to note that these guidelines are not intended to be absolute dictates, but should provide a framework within which the reasonable physician can and should practice. Undoubtedly future technological, pharmaceutical and other therapeutic developments and progress in the understanding of the diseases will become available. These guidelines will therefore have to be revised on a regular basis and it is envisaged that similar meetings will be held on a regular basis for this purpose".

Existing practice guidelines for PAD are available and have been deliberated upon and compiled by various societies and consensus groups. Some of these publications are listed below as additional supplemental references for perusal.

1. TASC. Management of peripheral arterial disease (PAD). Trans-Atlantic Inter-Society Consensus (TASC). Eur J Vasc Endovasc Surg 2000; 19(Suppl A):S1-S250

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Table of contents

Levels of evidence and class of recommendations Page 3

PAD – Epidemiology and disease stratification **(NG Naidoo)** Page 4

PAD – Clinical definitions and natural history **(ATO Abdool-Carrim)** Page 6

PAD – Clinical and basic diagnostic appraisal **(JV Robbs)** Page 11

PAD – Vascular imaging **(T Mulaudzi**) Page 13

Smoking cessation strategies for patients with PAD **(C Vermaak)** Page 15

Exercise therapy for patients with PAD **(T Fernandes)** Page 17

PAD – Medical treatment (Part 1) **(P Mistry)** Page 19

PAD – Medical treatment (Part 11) (**J Kowalczyk)** Page 21

Claudication: Principles of management **(MV Veller)** Page 24

PAD – Surgical treatment (Aorto-iliac disease) **(T Mulaudzi)** Page 29

PAD – Surgical treatment (Femoro-popliteal disease) **(A Kadwa / NG Naidoo)** Page 31

PAD – Surgical treatment (Infra-popliteal disease) **(R Botha)** Page 34

The rationale for primary amputation **(G Weir)** Page 37

PAD – Endovascular treatment for aorto-iliac disease **(P Matley)** Page 39

PAD – Endovascular treatment for femoro-popliteal disease (**JV Robbs)** Page 42

PAD – Endovascular treatment for infra-popliteal disease **(J Pillai)** Page 44

PAD – Drug eluting treatment strategies (**B Pillay)** Page 46

PAD – Other novel interventional, debulking and CTO crossing strategies **(P Mouton)** Page 49

PAD – Multi-level surgical revascularization **(B Natha)** Page 50

PAD – Multi-level endovascular revascularization **(D le Roux)** Page 52

PAD – Hybrid revascularization strategies **(L Redman)** Page 54

PAD – Limb salvaging strategies for non-reconstructable disease (**C Dreyer**) Page 61

PAD – Predicting outcomes for revascularization (**NG Naidoo)** Page 65

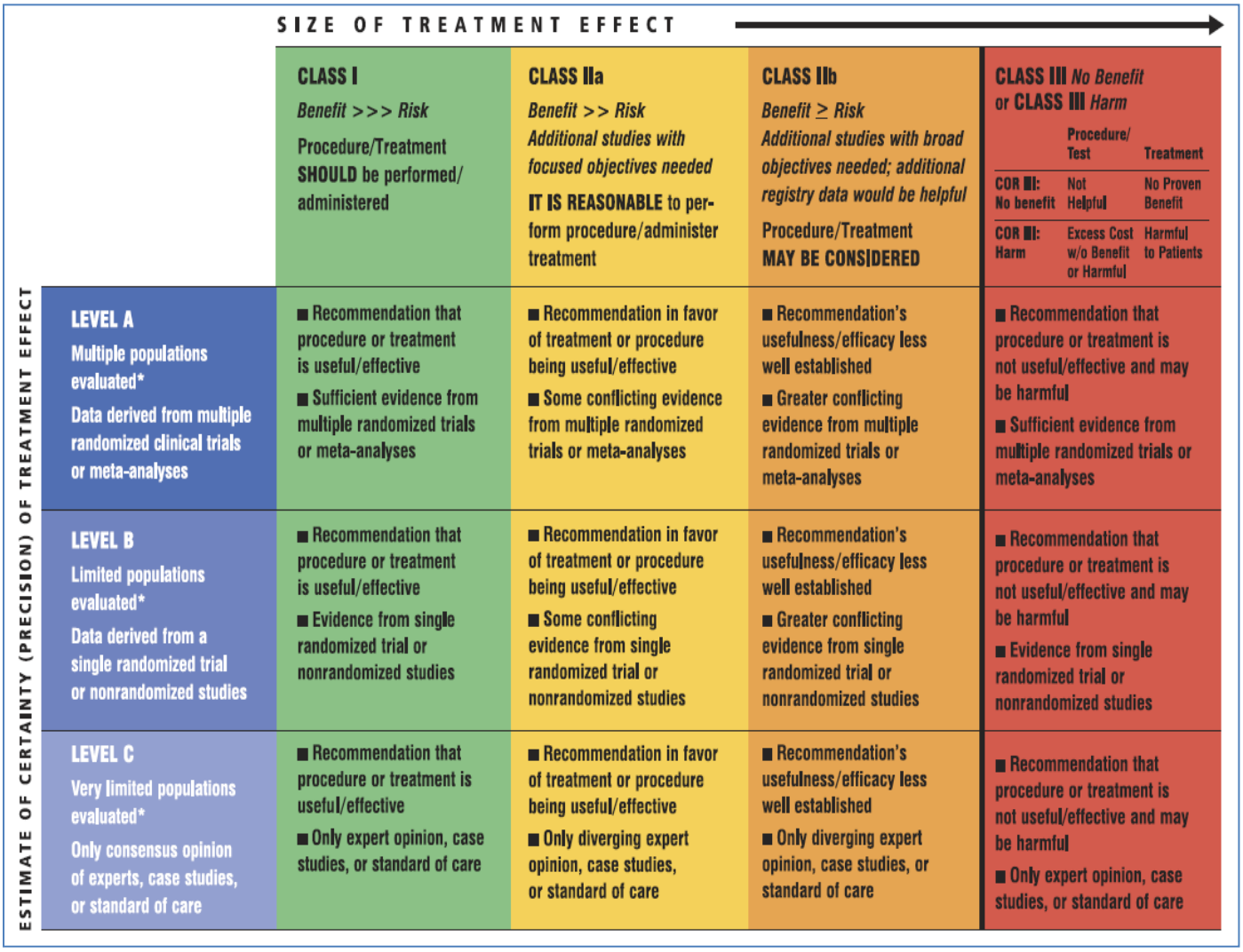
PAD – Post-operative surveillance and pharmacotherapy **(J Islam)** Page 68

PAD – Post-interventional surveillance and pharmacotherapy **(R Botha)** Page 73

PAD - Screening and follow-up (**EJ Honiball)** Page 74

Grading system: Level of Evidence and Class of Recommendation

It was agreed by the participants that many methods of evaluating the quality of data and making guideline recommendations on the basis of this information exist. A consistent easily applicable system is essential and as a consequence the method currently being used in most American cardiovascular guidelines would be adopted by VASSA.[1]



ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT →			
	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *No Benefit* or **CLASS III** *Harm* Procedure/ Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care

From: TG Brott, JL Halperin, S Abbara, et al. Guideline on the management of patients with extracranial carotid and vertebral artery disease. J Am Coll Cardiol. 2011; 57: e16-94.

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1. TG Brott, JL Halperin, S Abbara, et al. Guideline on the management of patients with extracranial carotid and vertebral artery disease. J Am Coll Cardiol. 2011; 57:e16-94.

PERIPHERAL ARTERIAL DISEASE – Prevalence & disease stratification

Nadraj G Naidoo

The community prevalence of peripheral arterial disease (PAD) averages ~ 10% -12% in most studies[1, 2, 3] The prevalence is age-related being low in patients between 50 – 59 years (2.5% - 5%) and increasing with advancing age. The prevalence exceeds 20% for patients over 70 years. A prevalence of 12% was found in 1 South African study of a high prevalence stroke community.[4]The ratio of asymptomatic PAD vs. symptomatic PAD ranges from 2:1 – 4:1. The prevalence of claudication is also age –related and ranges from 3% in young patients over 40 years to > 6% in patients older than 60 years. Approximately 10% - 50% of claudicants do not consult their doctor. More than 50% of patients with PAD have no symptoms or have

atypical claudication. The PARTNERS study [5] revealed that PAD afflicted 29% of all patients > 70 years, aged 50 – 69 years with > 10 year history of smoking, and aged 50 – 69 with a history of diabetes. More than 70 % of treating physicians in this study was unaware of established PAD in their patients. The prevalence of critical limb ischaemia (CLI) is more difficult to determine. In general for every 100 claudicants 1 patient will have CLI.

The risk factors for PAD are comprehensively addressed in the TASC II [6] document. Potent risk factors for PAD include smoking, diabetes mellitus, advancing age, hypertension and hypercholesterolemia. Other risk factors include black ethnicity, obesity, sedentary lifestyles, hyperfibrinogenaemia, hyperhomocysteinaemia, elevated C-reactive protein (CRP) and chronic kidney disease.

The dominant pathology in PAD is atherosclerosis which affects multiple vascular beds. The poly-vascular implications related to PAD are comprehensively addressed in the TASC II document. Approximately 40% - 60% of patients with PAD have associated coronary artery disease (CAD) or cerebrovascular disease (CVD). The REACH registry [7] provides compelling data on 1 year outcomes (death, myocardial infarction or stroke) in outpatients at risk (i.e. patients with CAD, CVD, PAD or patients with at least 3 risk factors for atherosclerosis). Patients with established PAD have a 1 year death, MI or stroke rate approaching 5,35%. Patients with CAD, CVD & PAD have a 1 year death, MI and stroke rate approaching 26,2%. PAD is a potent surrogate marker for cardiovascular death, MI or stroke. Currently PAD is regarded as a coronary artery disease (CAD) risk equivalent. A low ankle-brachial index (< 0.9) is an independent predictor of mortality.

The clinical severity of PAD can be categorized using the Fontaine or Rutherford grading systems [6]. PAD can be categorized into 3 segmental types based clinically on pulse status: aorto-iliac disease, femoro-popliteal disease and tibio-peroneal disease. The profile of occlusive disease varies according to risk factors e.g. tibio-peroneal disease is a common profile in diabetic patients. The lesional characteristics and extent of PAD can be categorized according to the TASC II classification into 4 types (A – D) for supra-inguinal and infra-inguinal PAD. Patients with TASC A lesions appear suitable for endovascular treatment and patients with TASC D lesion will require surgery in general. TASC B and C lesions need to be rationalized. Infra-inguinal and infra-popliteal runoff is known to impact on outcomes of revascularization but appear difficult to quantify. Methods used have been the SVS (Society of Vascular Surgeons) runoff score, the Bollinger score (in the BASIL trial), etc. However none appear to be user friendly. In general 2 or more patent crural vessels suggest good runoff, 1 crural vessel – reasonable runoff and 0 crural vessels – poor runoff.

PAD prevalence data are based on US, UK and European data in general (Level A and B evidence). The evidence for risk factors for PAD has also evolved from good observational data (Level A and B evidence). The involvement of other vascular territories in patients with PAD is also derived from observational studies (Level B evidence). PAD disease extent stratification is based on multi-disciplinary consensus. PAD is an independent predictor of cardiovascular death, MI or stroke (Level A evidence)

PAD prevalence in the community still remains to be adequately defined in South Africa. While some estimates exists for diabetic Indians in Durban & HIV positive patients, more rigorous quantification is needed in large community-based studies. Compelling major amputation rates locally are glossed over

because it`s impact on overall health care costs are not appreciated. This needs to be defined in order to drive a more comprehensive programme aimed at patient identification, education and treatment.

Future directions

A more concerted effort should be made to identify patients with PAD earlier so that disease altering evidence based medical therapies may be instituted to reduce the incidence of cardio-vascular deaths, MI and stroke. This may take the form of more aggressive and sustained PAD awareness campaigns, physician education, community workshops, etc.

Recommendations

- PAD must be recognized as an independent predictor of mortality and a potent surrogate marker of future cardiovascular events. (Class 1 recommendation / Level A evidence)
- Aggressive screening for PAD in patients at risk (Class 1 recommendation / Level B evidence)
- A more comprehensive workup of patients with PAD, considering the multiple risk factors for atherosclerosis and the polyvascular nature of the disease (Class 1 recommendation / Level B evidence)

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PERIPHERAL ARTERIAL DISEASE (PAD) - Definitions and Natural History

ATO Abdool-Carrim

Cardio vascular disease is responsible for approximately 30% of all mortality world-wide. Peripheral arterial disease (PAD) is one component of cardiovascular disease affecting mainly the lower limbs and, less

commonly, the upper limbs. The prevalence of PAD is in the range of 3 – 10%, increasing to 15 – 20% in persons above 70 years. The most widely used test to diagnose PAD is the ankle-brachial pressure index (ABI) measurement. An ABI of < 0.9 (resting) is caused by haemodynamically significant arterial stenosis and is the often used as a haemodynamic definition of PAD.

Patients with PAD can have asymptomatic disease or symptomatic disease. The ratio of the two is independent of age and is usually in the range of 3:1 to 4:1 respectively. It is important to define the population at risk for PAD. These are:

1. Age < 50 years with diabetes mellitus and one additional risk factor (e.g. smoking, dyslipidaemia and hypertension)
2. Age 50 – 69 years with history of smoking and diabetes
3. Age 70 years or more
4. Leg symptoms with exertional symptoms (suggestive of claudication) or rest pain (ischaemic foot pain)
5. Abnormal lower extremity pulse examination
6. Known atherosclerotic coronary, renal and carotid disease

The most common pathology associated with PAD is atherosclerosis. There are other causes, especially in young black South Africans where there is a high prevalence of arteritis. Young PAD patients (< 55 year old) may present with accelerated or precocious atherosclerotic PAD. These are generally high-volume smokers with or without other risk factors for atherosclerosis. However, they may have other non-atherosclerotic pathologies that may require an extensive diagnostic appraisal (by way of an expanded blood work, imaging and histological specimens) to confirm.

Individuals with PAD present in clinical practice in one of the following ways:

(A) Asymptomatic: without obvious complaint of functional impairment.

(B) Symptomatic:

1. those with classical exertional symptoms involving the calf, and less commonly the thigh and buttock, muscle groups (intermittent claudication)
2. “Atypical” leg pains: lower extremity pain that may or may not be exertional, and may be associated with a host of other aetiologies

(C) Complicated:

1. Critical limb ischaemia without tissue loss
2. Critical limb ischaemia with tissue loss
3. Acute lower extremity limb ischaemia

Asymptomatic Patients

These patients do not present with recognizable ischaemic limb symptoms but have objective evidence of PAD (absent pulses and/or ABI< 0.9). The asymptomatic patient, when objectively assessed by duplex criteria in one study, one third had occlusion of a major artery. It is also important to keep in mind that asymptomatic patients have higher cardiovascular mortality/morbidity when compared to normal population.

Symptomatic Patients

These patients present with classical leg claudication involving a muscle group that comes on with exercise and is relieved by rest. Clinical assessment is essential, palpation of pulses is not sensitive (Class 2b recommendation / Level C evidence) but objective test viz, ABI < 0.9, more sensitive and specific (Class 1 recommendation / level C evidence) to make diagnosis. (In diabetes ABI < 1.3 is more helpful / or alternatively measure toe pressures).

There are 2 clinical classifications of Peripheral Arterial Disease: Fontaine and Rutherford. This guideline recommends either one to be used - the Fontaine classification being more user-friendly.

Fontaine		**Rutherford**		
Stage	**Clinical**	**Grade**	**Category**	**Clinical**
I	Asymptomatic	0	0	Asymptomatic
IIa	Mild claudication	I	1	Mild claudication
IIb	Moderate to severe claudication	I	2	Moderate claudication
		I	3	Severe claudication
III	Ischaemic rest pain	II	4	Ischaemic rest
		III	5	Minor tissue loss
IV	Ulceration or gangrene	III	6	Major tissue loss

Critical Limb Ischaemia (CLI)

This term refers to those patients whose arterial disease has resulted in breakdown of skin (ulceration/gangrene) or pain at rest without tissue loss and require narcotic analgesics for approximately two weeks. This coincides with Fontaine stages III and IVB, and Rutherford categories 4, 5 and 6. CLI is a clinical diagnosis but must be confirmed by objective testing, viz ABI /toe pressure measurement/Transcutaneous oxygen tension measurement (TcP02). Reduced ankle systolic pressures (< 50 – 70mmHg); toe pressure (< 30 – 50mmHg) or reduced TcPo2 (< 30 – 50mmHg) are highly indicative of CLI.

Due to calcification of arteries in diabetic patients the systolic pressures maybe higher and therefore these guidelines recommend that all patients with diabetes mellitus with skin breakdown be evaluated as patient with critical ischaemia and seek rapid vascular surgical opinion. In diabetic patients with tissue loss an ABI > 0.6 is not reliable. These patients may be further assessed with toe pressure measurements or transcutaneous oxygen tension measurements when available.

Acute Limb Ischaemia (ALI):

These patients present with a sudden decrease in limb perfusion causing a threat to the limb viability. Presentation is up to 2 weeks following an acute event. Clinical presentation may include a spectrum of presenting signs and symptoms including the 6 P's, viz, pain, pulselessness, pallor, paraesthesia, paralysis and poikilothermia. The following points need to be emphasized:

1) Assessment of acute limb ischaemia must include Doppler pressure measurements due to the inaccuracy of pulse palpation (Class 2a / C)
2) Proper severity grading of ALI is fundamental to management:
    - Is the limb viable?
    - Is limb viability immediately threatened?
    - Are there irreversible changes that preclude limb salvage?

Rutherford criteria to grade severity of ALI:

- Grade 1: Viable - not immediately threatened, no sensory loss or muscle weakness, arterial Doppler signals often audible
- Grade 2a: Marginally threatened - salvageable if promptly treated, minimal sensory loss, no muscle weakness, arterial Doppler signal often inaudible.
- Grade 2b: Immediately threatened - salvageable with immediate revascularization, sensory loss associated with rest pain in more than the toes, mild to moderate muscle weakness, arterial Doppler signals usually inaudible.
- Grade 3: Irreversible - major tissue loss or permanent nerve damage inevitable if delay before intervention, profound limb anaesthesia and paralysis, arterial and venous Doppler signals inaudible.

Urgency of diagnosis of acute limb ischaemia and its cause is a matter of extreme importance and has a bearing on outcome; therefore this guideline recommends urgent rapid diagnosis and treatment (Class 1 recommendation / Level A evidence) and urgent referral to a Vascular Surgeon (Class 2a recommendation / Level C evidence).

Fate of the leg in PAD

PAD is a progressive disease. However as far as the leg is concerned the clinical course is quite stable in most cases. PAD is progressive for both the symptomatic and asymptomatic disease profiles. Only a quarter of patients with intermittent claudication will significantly deteriorate. This is most frequent after the first year after diagnosis (7 – 9% compared to 2 – 3% per year thereafter).

Major amputation is relatively rare in patients with intermittent claudication (1 - 3.3% of patients in this group will, over a 5 year period, require major amputation). A changing ABI is the best predictor of progression. Also these with a low ankle systolic pressure (40 – 60mmHg) are at risk of progression to severe ischaemia or limb loss (~8.5% per year).

Most patients with CLI will today receive some form of revascularization. In the subgroup with non-reconstructable disease or where reconstruction has failed, 40% will lose their legs within 6 months and up to 20% will die.

Fate of the patient in PAD

The increased risk of cardiovascular events in patients with PAD is related to the severity of the disease in the legs as defined by ABI. Atherosclerosis tends to affect all vascular territories. The annual overall major cardiovascular event rate (MI, Stroke and vascular death) is approximately 5 – 7%.

Excluding CLI, patients with PAD have a 2 – 3% annual incidence of non-fatal MI. The 5, 10 and 15 year morbidity and mortality rates are 30%, 50% and 70% respectively. Coronary Artery Disease (CAD) is the most common cause of death in PAD patients (40 – 60%).

The ABI is a good predicator of mortality. There is a linear relationship between ABI and fatal, and non-fatal, cardiovascular events. Each decrease in ABI of 0.1 is associated with a 10% increase in a relative risk of a major vascular event. In diabetic patients, in particular, the lower the ABI the higher the 5 year risk of a cardiovascular event.

Summary

PAD is a marker and predictor of cardiovascular events. They have multiple atherosclerotic risk factors and extensive atherosclerotic disease placing them at an increased risk for cardiovascular events.

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PERIPHERAL ARTERIAL DISEASE: Clinical and basic diagnostic appraisal

JV Robbs

The Guidelines embrace occlusive disease of the lower limbs involving the large, medium and small calibre vessels in the aorto-iliac, femoro-popliteal and tibio-peroneal distribution. In many cases, multiple segments are involved. Causes are atherosclerotic or non-atherosclerotic. The latter includes fibro-muscular dysplasia, Buerger's disease, arteritides (HIV related, etc), entrapment syndromes, cystic adventitial popliteal disease, etc. The basic clinical assessment entails staging the degree of severity of the disease which ranges from asymptomatic to ulceration or gangrene (Fontaine and Rutherford classifications).

Essentially there are three major clinical groups:

1. Claudication (no limb threat).

2. Critical limb ischaemia.

3. Unsalvageable limb.

The pattern of claudication depends on distribution of the disease.

- Aorto-i1iac: buttock, thigh and calf with or without impotence or erectile dysfunction.
- Femoro-popliteal: calf claudication
- Tibio-peroneal: foot claudication but this is rare.

Most important is the degree of severity or life-style limiting incapacity caused by claudication.

A differential diagnosis of leg pain with effort includes spinal stenosis, radiculopathy, compartment syndrome, chronic venous insufficiency, arthritis and other musculo-skeletal disorders. There is often co-existing peripheral arterial disease that often adds to the diagnostic dilemma.

Critical limb ischaemia often implies limb threat. By definition this entails rest pain of more than 2 weeks duration, with or without tissue loss, not responding to conventional analgesia, and a toe pressure of <30 - 50mm Hg and an ankle pressure of <50 - 70mm Hg (depending on the presence tissue loss).

Limb salvagability: if the gangrene extends beyond the insertions of the ankle extensor (tibialis anterior) or the invertors and evertors of the ankle (peroneal muscles) it will not be possible to salvage the foot.

A special consideration in diabetics with PAD is peripheral neuropathy which includes motor, sympathetic and sensory components with or without associated ischaemia. Neuropathy should be assessed in all patients.

Risk factors for atherosclerosis include smoking, diabetes, hypertension, hyperlipidaemia, family history, hyperhomocysteinaemia and elevated C-reactive protein levels. Patients with coronary and carotid artery disease have a two to fourfold increase in peripheral arterial insufficiency.

Investigations for PAD

1) Continuous wave Doppler
    - ankle brachial index
    - exercise stress testing (this is essential in patients with exertional symptoms)
    - toe pressures measurements

2. Duplex Doppler: has a 90% specificity and sensitivity for assessment of level of disease. Limitations include the presence of bowel gas, calcification, down-stream stenosis and tortuous vessels.

3) Transcutaneous oxygen pressure measurement has a place in selected patients.

4) For non-atherosclerotic disease the diagnosis depends upon the clinical presentation, age, gender, the pattern and distribution of the disease, and specific features.

SUMMARY

Clinical assessment includes history, claudication, pattern, distribution, degree of disability and question whether this is vasculogenic and not pseudo claudication.

A proper evaluation should enable one to identify risk factors and associated comorbidities including cardiac, cerebral, and renal disease.

Examination should define the level of disease, establish whether critical limb ischaemia is present or not, and establish whether the limb is salvageable or not. If the patient is diabetic - do full test of sensation and examine pressure areas.

Investigation - routine ABI testing in all patients with established PAD. In claudicants stress ABIs are important (treadmill testing: 10 degrees inclination at 10 kph). In selected patients, where revascularization is being considered, a Duplex Doppler to establish level and distribution of disease is a useful first line vascular imaging modality.

Standard blood-work in all patients with PAD should incorporate a full blood count; creatinine, urea and electrolytes; blood glucose estimation, HbA1C levels in diabetics and a fasting lipid profile. Homocysteine and C-reactive protein should be requested selectively.

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Vascular imaging in PAD

Dr TV Mulaudzi

Imaging in vascular disease is dictated by disease type, anatomical location, renal function and availability. These imaging could be non-invasive or invasive. Non-invasive investigations include duplex ultrasound (DUS), computed tomographic angiography (CTA), magnetic resonance angiography (MRA). Invasive investigation is a digital subtraction angiography (DSA).

Duplex ultrasound

Duplex ultrasound is a useful first line imaging modality in patients with PAD. For aorto-iliac imaging DUS is limited overlaying bowel gas and obesity. Imaging in this area may be improved by performing a fasting DUS. Peak systolic velocity (PSV) ratio has very accurate diagnostic criteria. A ratio of more than 2 is indicative of an iliac stenosis of more than 50%. [1] It has a sensitivity and specificity of 90% and 95% respectively. Duplex ultrasound imaging may be affected by severe calcification of the arteries.

Computed tomographic angiography

The use of multi-detector CTA (MDCTA) has greatly improved the diagnostic accuracy of CTA. It is now widely used as an initial diagnostic tool. It has the advantage of a much shorter procedure time than both MRA and DSA and less radiation exposure than DSA. Its disadvantage is that it requires the use of iodinated contrast and radiation exposure.

CTA has an excellent accuracy in detecting occlusions with the sensitivity and specificity of almost 100%[2]. Multi-detector CTA has improved the accuracy of detecting stenosis. Several small studies have shown a

sensitivity of 89 to 100% and a specificity of 92 to 100% in detecting stenosis of more than 50% [3/4]. CTA should be considered an initial imaging tool in patients with aorto-iliac disease (Class IIa recommendation / Level B evidence).

Magnetic resonance angiography

Many centres still use MRA for the diagnosis and management planning in PAD. Its advantages are its safety and ability to provide a three dimensional image. The use of 3D imaging and contrast enhancement has improved the diagnostic accuracy of MRA. Because of the high magnetic field it excludes patients with defibrillators, spinal cord stimulators, and other implants. It also excludes those with claustrophobia.

The sensitivity and specificity of MRA when compared to DSA in detecting stenosis of more than 50% was 90% to 100%; accuracy improved with gadolinium enhancement [2/3/5]. MRA is limited by the fact that it overestimates the degree of stenosis and occluded segment. MRA is an accurate diagnostic and management planning tool for patients with aorto-iliac disease and should considered in the armamentarium of aorto-iliac disease management (Class I recommendation / Level A evidence).

Digital subtraction angiography

Digital subtraction angiography is currently still considered a gold start. It is able to define normal and pathological arteries and it is easy to interpret for most physicians. The use of DSA as an investigation tool is now largely being replaced by duplex ultrasound, CTA and MRA due to marked improvement in their imaging techniques. Angiography offers the advantage of intra-arterial pressure measurement across a stenosis to assess its significance. Peak systolic pressure differences of 5mmHg to 10mmHg without vasodilation and 10mmHg to 15mmHg with vasodilation are significant.

Due to its invasive nature DSA can be complicated by pseudoaneurysm, arteriovenous fistula and haematomas. Other risks associated with DSA are severe reaction to contrast media in 0.1% of patients; it carries a mortality risk of 0.16% and is significantly expensive[5].

Digital subtraction angiography provides good arterial anatomy and should be recommended for imaging in aorto-iliac disease before surgical intervention (Class I recommendation / Level B evidence)

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Smoking cessation strategies for patients with PAD

Jacobus S Vermaak

Smoking carries a stronger association with peripheral arterial disease (PAD) than coronary artery disease.[1]The severity of PAD also tends to increase with the number of cigarettes smoked. With the exception of Buerger's disease, nicotine plays a minor role in smoking-induced disease. Nicotine is one of the factors that drives tobacco addiction, which in turn allows numerous carcinogens and pro-inflammatory atherogenic toxins to cause PAD, cancer, cardiovascular disease, pulmonary disease, infections, poor wound healing, etc.[2] The probability that a lifelong smoker will die prematurely from complications directly related to smoking is roughly a mere "flip of the coin", i.e. 50%.[3]

Smoking still carries a high global burden, especially in African and Asian countries. The addiction involves a complex interplay of pharmacological, conditioned behavioural, genetic, social and environmental factors. Even though most smokers perceive that smoking improves their reaction time, concentration and reduces stress, the reality is that they are more likely to smoke to avoid withdrawal symptoms. Light smokers who pride themselves in smoking less than 5 cigarettes per day also demonstrate a high level of dependence. Even though up to 70% of smokers verbalize that they would like to quit, only 0.1% of smokers will quit successfully at one year when going 'cold turkey'.

Counselling is an important, yet often neglected, aspect of smoking cessation. Even a 3 minute counselling session doubles the cessation rate. We recommend the same counselling strategy outlined in the Journal of Vascular Surgery by James Black.[4]

Current tobacco users willing to quit should be counselled using the five A's:

- **Ask** about their willingness to quit at every visit
- **Advise** on the benefits of complete cessation
- **Assess** their ability and commitment to quit
- **Assistance** should be provided with pharmacotherapy, and
- **Arrangement** of regular follow-up should be provided

Tobacco users not willing to quit may be frustrated by previous quitting failures or lack information about the harmful effects. They require a different approach and will respond poorly to direct confrontation. Counselling techniques involves informing them about the **five R's:**

- **Relevance** (why it is important to quit smoking?)
- **Risk** involved as a consequence of the on-going habit
- **Rewards** and benefit of cessation
- **Roadblocks** to quitting should be addressed (withdrawal, fear, weight gain and peer pressure)
- **Repetition** at every visit.

Tobacco users who managed to quit may have to be reminded that even a single puff increases the likelihood of a full relapse. The health care provider has to emphasize the benefits and address threats to abstinence.

Recent meta-analysis concur that the incidence of post-operative complications decrease with longer periods of cessation, but there is no evidence to suggest that health care professionals should not be advising smokers to quit even shortly before surgery.[5/6] Not only do the benefits of perioperative smoking cessation outweigh the risks, but the highest cessation rates are in patients whom have experienced a recent acute smoking related event: myocardial infarction, exacerbation of COPD or a threatened limb. This is the so-called **'teachable moment'**.[4]

Every patient should be offered pharmacotherapy, with rare exception. The current recommended pharmacological agent is Varenicline which targets the α4β2 nicotinic receptor and is specifically developed for the purpose of smoking cessation. One year smoking cessation rates of up to 23% can be achieved.[7] Side-effects of Varenicline include vivid dreams, nausea and 'psychiatric' symptoms like agitation, suicidal ideation and behavioural changes. The FDA specifically cautions against the use of Varenicline in pilots. Current recommendation by the FDA is that Varenicline should be used for 12 weeks and, should the patient abstain in that period, a further 12 week continuation course is advised. The sustained release formula of Bupropion at a 150mg twice daily is an alternative.[8/9] Bupropion is an anti-depressant drug. Patients should be screened for psychiatric issues before prescribing Varenicline or Bupropion. Monotherapy with nicotine replacement alone is not advised. We recommend regular counselling, nicotine replacement therapy and either Varenicline or Bupropion as the current accepted strategy to aid smoking cessation. Second line agents, not FDA approved for the purpose, include Nortriptyline and Clonidine. Still under investigation are: nicotine conjugate vaccines, other drugs targeting the α4β2 receptor (Dianicline), opioid antagonists (Naltrexone, Nalmefene hydrochloride) and cannabinoid receptor antagonists (Taranavant, Surivant).

Recommendations

- Smoking cessation strategies must form the corner stone of management in patients with peripheral arterial disease. (Class1 recommendation / Level A evidence)
- There is no 'bad time to quit'! Patients should not be advised to continue smoking, to minimize perioperative morbidity. (Class 1 recommendation / Level B evidence).
- A smoking cessation strategy must involve counselling and pharmacotherapy (Class I recommendation / Level B evidence)
- First line pharmacotherapy recommended is Bupropion or Varenicline. (Class 1 recommendation / Level B evidence)

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EXERCISE THERAPY IN PERIPHERAL ARTERIAL DISEASE

TIAGO FERNANDES

Peripheral arterial disease has a prevalence of between 3 and 10%. From this group 10-20% will go on to develop claudication and from this subgroup only 1-2% will develop critical ischemia. The current modalities of treatment for peripheral arterial disease have been well established. Firstly “best medical therapy” including smoking cessation, treatment of associated hypertension and diabetes as well as the use of HMG-CoA reductase inhibitors (statins). Secondly treatment of peripheral arterial disease with exercise therapy has been demonstrated to be of great benefit. Although it has been shown to be of great benefit there still remains some controversy in the methods of application of exercise that result in better outcomes or improvements. Overall exercise therapy has been shown to be cost effective, easy to apply and be of great benefit. The current TASC guidelines state that supervised exercise therapy should be made part of initial therapy, and this treatment should consist of treadmill walking sufficient to initiate claudication pain followed by rest over a 30-60 minute session, three times a week for 3-6 months. Multiple meta-analyses comparing exercise therapy to medical management consisting of either statins or rheological agents has clearly demonstrated far superior outcomes in combination with exercise therapy.

We know that exercise therapy is of benefit in the treatment of claudication. A recent Cochrane meta-analysis comparing exercise therapy versus angioplasty demonstrated better outcomes for patients in the exercise group at 6 months. Overall exercise therapy has shown an improvement of 150% in symptoms and maximum walking distances. It has also been clearly demonstrated that those patients who continue to smoke and don’t exercise will not show any improvement. The physiological effect of exercise includes better endothelial function, reduced local inflammation, increased exercise pain tolerance, induction of vascular angiogenesis with formation of collaterals, improved muscle metabolism and finally reduced blood viscosity and red cell aggregation. Exercise therapy improves reactive hyperaemic blood flow by 27% and increases blood flow by 30% during exercise, but during rest these values return to pre-exercise levels with no actual improvement in ABI’s, but walking distances do improve! This point was compared in studies

demonstrating similar outcomes in patients with claudication treated with exercise therapy alone versus exercise and surgery combined.

A recent review on exercise therapy looked at a number of trials examining different exercise therapies in claudication. Most of these trials continued medical care. Aerobic exercise was the most common form of exercise in these trials with walking and lower extremity aerobic exercise (LEA) being the most methods used. Other aerobic exercise included lower limb cycling, arm cranking, pole striding and stair climbing. The frequency of exercise ranged from 2-7 times per week, most commonly three times a week. The patient's pain was used to assess walking distance as tolerated. Symptomatic outcome measures and the relationship between prescriptive elements and claudication symptoms were assessed. Symptomatic outcome measures were divided into initial claudication time, initial claudication distance, absolute claudication time (ACT) and absolute claudication distance (ACD) as well.

In the initial claudication time group the exercise with most statistical power to show an improvement was walking to moderate or maximum claudication pain. In the initial claudication distance group the largest statistically significant exercise was walking exercise without inducing pain. Adding arm crank exercises to this group did not show a statistical benefit to this group. It was interesting to note in this subgroup that there was also no difference between low and high intensity exercise walking that was of statistical value.

In the absolute claudication time group the exercise that showed greatest improvement was pole striding exercises. In the absolute claudication distance group the exercise to demonstrate greatest improvement was lower extremity aerobic exercise (LEA). Collectively most forms of exercises improved claudication as a whole.

With regards to the prescriptive elements and claudication symptoms, modality, induction of claudication, frequency and supervision were examined. All modalities of exercise bring about an improvement but lower limb exercises produced the greatest improvement overall with regards to ACD/ACT. It is important to note that exercise of the limb is not always required to bring about an improvement in ACD. Alternatively a combination of upper and lower extremity exercises can bring about an improvement. So therefore the current evidence supports walking as the main exercise but that other modalities of exercise in smaller studies do also demonstrate a benefit and that there is room for adding these exercise therapies to existing treatment regimens.

Induction of claudication remains ill-defined. Some studies demonstrate that walking without inducing pain actually improves walking distances, but similarly walking to pain also demonstrated improvement in walking distances. Overall though walking without inducing pain seems to be just as effective in bringing about improvement and that pain might be detrimental.

Frequency and duration are important parameters. There are no direct trials examining dose-response relationships, but most trials conducted used exercise regimens 2-4 times per week demonstrating a clear improvement in walking times and distances. Therefore exercise regimens of at least three times a week, each lasting ~ 30 minutes and gradually increasing to one hour, is generally recommended.

Supervision has clearly been demonstrated to have better outcomes with a difference of at least 20% between supervised and unsupervised study groups.

The role of exercise therapy as a treatment modality or risk factor modifier in critical ischemia has not been studied extensively. The safety of exercise therapy in has been questioned and actually been seen to be

harmful in this sub group of patients. At this stage exercise therapy in critical ischemia is currently not indicated.

Exercise therapies regarding diabetic patients deserve special mention here. Neuropathic testing is mandatory in these patients. Foot deformities must be clearly documented and corrected in these patients. Adequate counselling regarding sport footwear and care of the foot during exercise sessions is absolutely essential in these patients.

Recommendation

In conclusion exercise therapy is currently strongly recommended in the management of claudication (Class 1 recommendation / Level B evidence). An exercise regimen which is supervised and which has been shown to be of benefit at least three times a week in an escalation pattern is still the current recommendation. Exercise therapy for critical ischemia is currently not recommended and is seen as being harmful.

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PAD: Medical management (Part I)

Pradeep Mistry

Diabetes Mellitus

Diabetes Mellitus (DM) and insulin resistance are both strong risk factors for PAD and critical limb ischaemia (CLI). There is an increased morbidity and mortality in patients with established atherosclerosis and DM.[1] There is also a definite correlation between glycaemic control and clinical outcomes in patients with PAD. Tight glycaemic control reduces micro-vascular complications but trials involving tight glycaemic control and macro-vascular complications have been disappointing. The strongest evidence for risk reduction in DM is via aggressive control of blood pressure and lipids. Diabetes associated dyslipidaemia is a potent atherogenic stimulus (↑Triglycerides, ↓HDL-C, small dense LDL-C particles).[2]

Arterial Hypertension

Patients, who maintained a diastolic blood pressure of 82.3mmHg or below, reached maximal cardiovascular protection in the HOT Study Group. However, achieving target blood pressures have proven to be low, even in specialist centres.[3] The effects of ACE – inhibitors on plaque, intimal-medial thickness, endothelium, smooth muscle and platelets are now well documented. The HOPE Study confirmed these effects demonstrating a 22% decrease in cardiovascular events in patients with PAD treated with ramilpril.[4] Thiazide diuretics have had similar outcomes when compared to ACE-inhibitors and calcium channel blockers. Thiazides, have however, demonstrated a significant decrease in hospitalization for cardiac failure.

B- Blockers

The use of B Blockers has previously been discouraged in PAD owing to the fear of worsening claudication. RCTs have shown that B Blockers can be safely utilized in patients with claudication.[5]There is also an added benefit of cardio-protection in patients with PAD and coronary disease. B Blockers can also be considered when treating hypertension in patients with PAD.

A meta-analysis of over 2000 patients randomised in 8 trials between B Blockers and placebo in major non cardiac vascular surgery showed no overall benefit for the use of perioperative B- blockade.[6]In the PREVENT III study B Blockers did not have any effect on survival at 1 year. Only statin use proved to be of any benefit in this trial.[7] Current data suggests that liberal use of B Blockers are of no benefit and can be potentially harmfull. However, withdrawal of beta-blockers prior to major surgery is associated with an increased incidence of cardiovascular morbidity and mortality.[8]

Recommendations

- Blood glucose should be monitored in patients with PAD (Recommended HbA1C target of < 7 %) (Class I recommendation / Level A evidence)
- More aggressive HbA1C targets (4-6 %) is not recommended (Class III recommendation / Level B evidence)
- Patients with PAD with arterial hypertension should be treated with an anti-hypertensive agent (Class I recommendation / Level B evidence)
- Target blood pressure should be < 130/90mmHg in non-diabetics and < 130/80mmHg in diabetics and renal insufficiency patients (Class IIa recommendation / Level C evidence)

- First line agents should include a thiazide diuretic and/or ACE-inhibitor (Class IIa recommendation / Level B evidence)
- Calcium channel blockers should be used for difficult to control hypertension (Class IIb recommendation / Level C evidence)
- Beta blockers should be continued in patients with CLI undergoing surgery who are receiving beta-blockers to treat angina, symptomatic arrhythmias, hypertension or other suitable medical indication (Class I recommendation / Level B evidence)
- Beta blockers should be given to patients with CLI undergoing vascular surgery with proven cardiac ischemia on preoperative testing (Class IIb recommendation / Level B evidence)
- Patients with a primary indication for beta-blockade regardless of surgery should be considered for beta-blockade on the strength of this medical indication (Class IIa recommendation / Level B evidence)

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PAD: Antiplatelet and lipid lowering therapy (Medical Management - Part II)

Jarek Kowalczyk

Aspirin as an agent inhibiting platelets aggregation was introduced for PAD treatment in early 1980s. The first large meta-analysis of ASA and/or Dipyridamole as antiplatelet medication in patients with PAD was published by Antiplatelet Trialists' Collaboration in 1994. This study incorporated 11 randomized controlled trials with about 70 000 participants. The primary outcome measure was the decreased rate of non-fatal MI, stroke or vascular death in the antiplatelet group. The final conclusion was that 75-325 mg of aspirin or any other antiplatelet drug offers a 25% decrease in major vascular events and 18 % decrease in vascular death.[1]

Beneficial action of 75-150 mg aspirin as a protective agent against MI, Stroke and vascular death was confirmed in high risk patients with PAD by Antithrombotic Trialists' Collaboration in 2002.[2]

However, in 2009 a meta-analysis by the Antithrombotic Trialists' Collaboration was published. The analysis looked at 90 000 patients at risk treated with aspirin exclusively for primary prevention against MI, stroke and vascular death. The authors concluded that in primary prevention without previous disease aspirin is of uncertain net value.[3]

Clopidogrel, an inhibitor of the Glycoprotein IIb-IIIa platelet receptor complex, was studied in 3 large trials. The CAPRI study with 19 185 patients showed clear 8.7 % overall relative risk reduction of MI, stroke and vascular death in favour of Clopidogrel in the PAD subgroup analysis.[4] The CHARISMA study (Clopidogrel and aspirin vs. aspirin alone for the prevention of atherothrombotic events) was published 2006. A total of 15 603 patients were randomly assigned to clopidogrel 75mg + aspirin 75-150 mg group or aspirin 75-150 mg alone. Follow-up was 2.5 years. The composite end-point (MI, stroke and vascular death) was 6.8% in clopidogrel group vs. 7.3% in ASA. Vascular mortality was 3.9% vs. 2.2%. Major bleeding complication rate was higher in the clopidogrel group: 1.7% vs. 1.3%. The trial concluded that clopidogrel and aspirin was not significantly more effective in reducing the rate of MI, stroke or cardiovascular death than aspirin alone.[5]
Recently two new oral antiplatelet agents have been introduced: prasugrel and ticagrelor (inhibitors of the P2Y12 platelet receptor). Both were studied in large randomized trials against clopidogrel in patients with acute coronary syndrome and MI. Both showed significant benefit in protection against MI stroke, cardiovascular death and stent thrombosis. However, to date there are no trials involving patients with PAD.

It is worth mentioning that in patients who are allergic to aspirin, have a high risk of upper GIT bleeding, or have aspirin resistance, dipyridamole alone may be considered as an antiplatelet agent. Pentoxyphilline, a drug that also inhibits platelet aggregation, generally is not recommended for use as an antiplatelet agent in patients with PAD.

The vitamin K inhibitor, warfarin, was studied against aspirin in 2007 in small trial comprising 2161 patients. The outcome indicated that there was no difference in cardiovascular events but bleeding was significantly higher in warfarin group. Therefore warfarin could not be recommended for routine use in PAD patients.[6]

The first statin was synthetized by Dr. Akira Endo in 1971. Statins have both lipid lowering and pleiotropic effects viz. decrease inflammation, plaque stabilisation, decreases thrombosis, decreases platelets adhesiveness and improvement in endothelial dysfunction. Recent large meta-analyses looking at incidence

of coronary heart disease (CHD), stroke and major vascular events in patients with peripheral artery disease have shown the clear benefit of treatment with statins.

The Cholesterol Treatment Trialists' Collaborators study analysed data from 14 randomized trials comprising 90,056 patients. Statins used were: simvastatin, pravastatin, lovastatin, fluvastatin and atorvastatin. The end-points were: coronary heart disease, stroke and other vascular events. The conclusion was that statin therapy can safely reduce the 5-year incidence of major coronary events, stroke and coronary artery revascularization by about 20% per 1 mmol/l reduction in LDL-cholesterol.[7]

The Heart Protection Study Collaborative Group data, published in 2007, randomized 6748 PAD patients to treatment with 40 mg of simvastatin vs. placebo. Treatment group was associated with a highly significant 22% (95% Cl: 15-29) relative reduction in the rate of the first major vascular event (MI, coronary death, stroke or revascularization). The conclusion of the authors was that statin therapy demonstrates the benefit in patients with PAD reducing the rate of first major vascular event by one-quarter. Therefore, statin therapy should be considered routinely for all patients with PAD.[8]

The Institute of Clinical Systems Improvement guidelines for lipid management in adults published in 2007, as well as the American Heart Association/American College of Cardiology guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease recommend LDL-cholesterol target levels of below 2.6 mmol/l, and aiming for level of below 1.8 mmol/l in high risk patients.[9]

Ezetimibe, inhibits the absorption of cholesterol from the intestine, and lowers LDL-cholesterol by 18 % alone. However, it significantly improves lowering of LDL-cholesterol in combination with statins. No large randomized trials could be found to evaluate the effect of this combination vs. statins alone.[10]

Recommendations

- As atherosclerotic disease is a systemic condition it is very difficult in clinical practice to differentiate patients with PAD only vs. high risk PAD complicated with CAD, carotid artery disease or N-STEMI. Therefore, it seems to be appropriate to treat all patients with PAD as high risk patients with antiplatelet agent (aspirin 75-150 mg or clopidogrel 75 mg) (Class1 recommendation / Level B evidence)
- Statin therapy to target level of LDL-cholesterol < 2.6 mmol/l in low - intermediate risk group (class 1 recommendation / Level A evidence); and target level < 1.8 mmol/l in high risk individuals* (Class 2a / Level A evidence).

*High risk individuals: - established atherosclerosis (PAD; CAD and cerebrovascular disease)

- Diabetes type 2 OR diabetes type 1 with proteinuria

- Familial hypercholesterolaemia

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Intermittent claudication – principles of management

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Intermittent claudication (IC) as a result of peripheral arterial disease is common, affecting up to 15% of the population over the age of 70 years.[1] This syndrome results in significant reduction in the quality of life and life expectancy (10% mortality within 2 years).[2] The most common cause of the arterial occlusive disease manifesting as PAD, in a typical elderly population, is atherosclerosis. In individuals under the age of 50 years other pathologies such as thromboangiitis obliterans, vasculitic diseases, fibromuscular dysplasias, entrapment syndromes – particularly popliteal artery entrapment – and compartment syndromes (including venous) are more common. Other non-vascular pathologies frequently have symptoms that mimic

intermittent claudication – including nerve compression syndromes, myopathies, neuropathies, arthritis and chronic musculoskeletal injuries.

Diagnosis

Intermittent claudication is usually recognised on the basis of the typical symptoms which are specific and reproducible – related to the level of lower limb muscular activity and relieved by rest – with absent distal pulses usually noted in the affected lower limb. Additional diagnostic tests – mostly duplex Doppler or some form of angiography – are usually not indicated unless:

- interventional treatment is being considered (Class 1 recommendation / Level A evidence) or
- uncertainty exists if endovascular intervention is feasible (Class 2a recommendation / Level B evidence)

When typical symptoms of intermittent claudication are found in the presence of normal pulses, which may occur in young athletic individuals, post-ambulation ankle brachial indices (ABI) should be compared to the resting ABI. A drop of more than 10% in the ABI or more than 15mmHg in the systolic pressures is highly suggestive of an underlying localised arterial stenosis (Class 2a recommendation / Level B evidence). Measurement of compartment pressures is also useful in this group of individuals.

In patients in whom entrapment syndromes are considered in the differential diagnosis, angiographic diagnostic imaging studies with stress views are required (Class 2a recommendation / Level B evidence). Duplex ultrasound is of limited value in making the diagnosis of this condition.[3]

Treatment

Many treatment modalities have been described in the management of intermittent claudication caused by atherosclerotic peripheral arterial disease.

Treadmill exercise versus placebo / usual care

Watson et al. in a 2008 Cochrane meta-analysis of 22 high-quality trials[4], including 1200 participants who were either subjected to 2 supervised sessions of treadmill walking per week or to usual care, found that such exercise resulted in:

- An increase in the pain free walking time by 2.9min (95%CI 2.5-3.3min)
- An increase in the maximum walking time by 5.1min (95%CI 4.5-5.7min)
- An increase in the pain free walking distance by 82m (95%CI 71-92m)
- An increase in the maximum walking distance by 113m (95%CI 94-13m)
- Without resulting in an increase in the peak exercise calf blood flow or the ABI.

Supervised versus unsupervised treadmill exercise

Bendermacher et al. in a 2009 Cochrane meta-analysis of 8 high-quality trials[5], including 319 participants who were either subjected to 3 supervised sessions of treadmill walking per week or only given advice that they should walk, demonstrated that supervised exercise resulted in:

- An increase in the pain free walking distance at 3 months with a treatment effect size of 0.61 (95%CI 0.31-0.91) which equates to approximately 125m.

- An increase in the maximum walking distance at 3 months with a treatment effect size of 0.58 (95%CI 0.31-0.85) which equates to approximately 150m.

Adjuncts or alternatives to treadmill exercise

The use of Nordic poles while walking on a treadmill increases the maximum walking distance by approximately 80m.[6]

A home based exercise program, using a step activity monitor to evaluate adherence, is as effective in improving claudication distances when it is compared to a standard supervised exercise program.[7] Such home-based exercise also appears to be more effective in increasing daily ambulatory activity.

Cardio-respiratory function and walking distances are improved equally after arm-ergometry or treadmill exercising.[8] These observations are considered to support the hypothesis that exercise induced improvements in walking distance are as a result of systemic effects.

This hypothesis is supported by studies that have found that all forms of aerobic exercise including progressive resistance training or graduated weight lifting exercise improve walking distances in a manner similar to treadmill training.[9]

Brief psychological intervention in patients with intermittent claudication increases daily walking distances.[10]

Pharmaco-therapy and claudication

Many drugs have been used in the management of intermittent claudication. Some such as the chelating agents are frankly contraindicated while many others such as Pentoxyfylline have very limited effects that make them cost ineffective. The following have a clinically significant effect:

- The HMG CoA reductase inhibitors (statins) significantly improve all parameters of intermittent claudication by between 90 and 150m without altering the ABI.11
- Buflomedil, Cilostazol and some prostaglandins (PGE1 and prostacyclin) modestly improve maximum walking distance by approximately 80m, 30m and 50m respectively.[12-14]

There is little or no evidence that smoking cessation improves intermittent claudication symptoms, or has an effect on claudication distances.

Percutaneous transluminal balloon angioplasty (PTA)

A number of trials have recently evaluated the use of endovascular intervention in the management of patients with intermittent claudication.

The mild to moderate intermittent claudication trial (MIMIC) evaluated 93 patients with femoropopliteal disease (48 undergoing PTA) and 34 with aorto-iliac disease (19 undergoing PTA).[15] The PTA treated patients at 24 months demonstrated statistically significant improvements in the initial claudication distance and in the absolute walking distance – 38% (95%CI 1-90% equivalent to 50-70m) in the femoro-popliteal

subgroup and 78% (95%CI 0-216%) in the aortoiliac subgroup. Improvement in the ABI was also noted but no benefits in quality of life were found in the groups treated with PTA.

A meta-analysis by Ahimastos et al. evaluating nine studies with 873 participants found significant heterogeneity between the studies.[16] In patients with intermittent claudication the evidence suggests that endovascular therapy improves the ABI and treadmill walking distance if added to medical and supervised exercise programme but that there is no evidence that endovascular therapy alone provides improved outcomes compared to supervised exercise. They concluded that the data is weak and that larger studies with longer follow-up are required.

- Mazari et al. evaluated 178 patients using three arms: PTA, supervised exercise and PTA, & supervised exercise alone. All treatment arms were equally effective at improving walking distance and quality of life after 12 months of follow-up.[17]
- Nordanstig et al. in a Swedish trial of a primary invasive versus a primary non-invasive treatment strategy in unselected patients presenting with intermittent claudication (100 patients in each arm) found that the walking performance parameters after 2 years were similar in both groups. The only difference that was found between the two groups was in the quality of life parameters of bodily pain and role physical which scored better in the primary intervention group. On the other hand, only 7% of the patients in the primary non-invasive treatment group crossed over to the treatment group.[18]

Recommendations:

- All patients presenting with intermittent claudication as a consequence of atherosclerosis should be subjected to intensive vascular risk factor modification (Class 1 recommendation / Level A evidence).
- The use of HMG CoA reductase inhibitors has been demonstrated to improve the ability to walk by approximately 150m (Class 1 recommendation / Level A evidence).
- While substantial other health benefits have been demonstrated, stopping smoking does not improve symptoms related to intermittent claudication.
- In patients in whom intermittent claudication causes no limitation to their quality of life, no additional therapy is recommended (Class 1 recommendation / Level B evidence).
- Patients in whom intermittent claudication does cause a limitation to their quality of life, an exercise programme is the first line of therapy as this is expected to improve their walking distance by approximately 100m (Class 1 recommendation / Level A evidence). Supervised exercise and various other adjuncts described above improve the symptoms related to intermittent claudication (Class 2a recommendation / Level B evidence). The primary use of drugs such as Buflomedil and prostaglandins should only be considered as an adjunct to exercise in patients who have had an inadequate response to exercise and where the expected improvement in walking distance is considered to be cost effective (Class 2b recommendation / Level B evidence).
- Endovascular intervention in the management of intermittent claudication should only be considered when other modalities of treatment have not achieved adequate improvements in the quality of life and when such treatment can be offered with a low risk of morbidity and mortality (Class 2a recommendation / Level B evidence).

- Open operative procedures for mild to moderate intermittent claudication are only rarely indicated (Class 2b recommendation / Level C evidence).

Future directions

Studies further evaluating the utility of PTA versus other forms of treatment are required.

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Surgical treatment of aorto-iliac disease

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Aorto-iliac disease is referred to as inflow disease that limits blood flow to the common femoral artery. It may present with buttock and thigh claudication, vasculogenic erectile dysfunction in males if internal iliac arteries are involved, and may present with critical limb ischaemia. Open surgery is generally indicated for diffuse aorto-iliac disease.

Surgery is indicated in those with critical limb ischaemia to relieve the rest pain and prevent limb loss (Class I recommendation / Level B Evidence). Only patients with lifestyle-limiting, medically refractory, claudication should be considered for surgery as only two percent will require amputation for ischaemia (Class I recommendation / Level B Evidence).

Patients should have a preoperative assessment to establish the operative risk and assist in deciding on type of surgical intervention. Atherosclerosis is a systemic disease and these patients usually have coronary artery disease which may be symptomatic or asymptomatic. Perioperative risk of myocardial ischaemic events is increased in lower limb revascularization procedures. Other causes of morbidity and mortality are renal and respiratory complications. The mortality and morbidity associated with aortobifemoral bypass is 3.3% and 8.3% respectively.[1] Myocardial infarction and renal failure is the course of major morbidity.[2]

Recommendation

- All patients for aortic surgery should have optimum preoperative evaluation of their cardiac, renal and pulmonary functions (Class I recommendation / Level B Evidence).

Computerized tomogram angiography (CTA) scan is the imaging modality of choice for patients with aorto-iliac disease. Magnetic resonance angiography is usually reserved for those with contraindications to CTA. Today digital subtraction angiography is rarely used as a diagnostic tool due its invasiveness and associated complications, and also due to marked improvements in CTA imaging.

Aortobifemoral bypass is the surgical procedure of choice for patients with diffuse aorto-iliac disease. It has a mortality rate of 3.3% with very good 5 and 10 year patency rates of 88% and 81% respectively.[3] Patients with diffuse aorto-iliac disease who present with disabling claudication or critical limb ischaemia and are fit for a major procedure should be offered an aorto-bifemoral bypass surgery (Class 1 recommendation / Level B Evidence).

Axillo-bifemoral bypass has a five year patency rate of 67.7% which is much less than that of aorto-bifemoral bypass. It also carries a mortality rate of 4.9%.[4]This procedure should be offered to patients with diffuse aortoiliac disease who present with critical limb ischaemia who cannot be managed with other surgical procedures (Class 1 recommendation / Level B Evidence)

In patients with symptoms associated with unilateral iliac disease, an ilio-femoral bypass procedure is an option with a good five year patency rate of 90%.[5]This procedure has largely been replaced by endovascular intervention. Ilio-femoral bypass surgery should be offered to patients with unilateral symptoms from iliac disease that cannot be managed with endovascular intervention or are not suitable candidates for aorto-bifemoral bypass (Class 1 recommendation / Level B Evidence)

Femoro-femoral bypass surgery has largely been replaced by endovascular surgery. It has a five year patency rate of 71%.[6]This procedure should be reserved for symptomatic uni-iliac disease in patients who cannot be managed with endovascular intervention or are not suitable candidates for aorto-bifemoral bypass.

Other procedures like aortic endarterectomy for type 1 aortoiliac disease, even though they have excellent results, are almost not being performed today. This has been replaced by endovascular intervention.

With the advancement of endovascular therapy most open surgical procedures will be replaced by endovascular surgery in the future.

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PAD – Surgical treatment (Femoro-popliteal disease)

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Femoro-popliteal disease represents the commonest segmental type of PAD in vascular practice. The surgical options for femoro-popliteal disease include:

- Common femoral endarterectomy and patch-plasty (vein / prosthetic)
- Profundaplasty (as an adjunct or as an isolated procedure)
- Above-knee femoro-popliteal bypass (vein / prosthetic graft)
- Below-knee femoro-popliteal bypass (vein / prosthetic graft)

The dominant indication for surgery is CLI with or without tissue loss. Surgery is sometimes performed for sub – CLI (no rest pain or tissue loss but severely ischaemic foot e.g. elevation pallor in a neuropathic foot). Surgery here is seldom performed for severe, medically refractory claudication.

There are no randomized controlled studies (RCT) comparing bypass surgery with best medical treatment (such a study may be deemed unethical in patients with CLI). The success of femoro-popliteal bypass is influence by many factors:

- Patient factors: Risk profile, PAD burden, suitable vein, etc
- Surgeon factors: Experience, technical expertise, choice of graft, etc
- Post-operative adjuncts: Best medical therapy, anticoagulation, graft surveillance, etc

The type of vascular conduit is crucial for the success of femoro-bypass grafting:

1. Autogenous vein graft with a diameter > 3.5mm
    - Single segment great saphenous vein (GSV) – this is the gold standard
    - Small saphenous vein (SSV)
    - Cephalic vein
    - Spliced vein segments
2. Autogenous arterial graft (internal iliac artery) – not relevant for femoro-popliteal bypass.
3. Prosthetic graft
    - Fabricated (Dacron polyester)
    - Non-fabricated (PTFE – polyflouroethylene; polyurethane, etc)
4. Biological graft
    - Allografts (human umbilical vein; cryopreserved artery/vein, etc
    - Bioengineered collagen grafts, etc

When harvesting the GSV the balance of evidence show no difference between a single incision over vein or creating skin bridges between incisions. Endoscopic vein harvesting is safe and feasible. There is no difference between graft orientation (reversed GSV has the same patency as an in-situ vein bypass graft).

Evidence

A meta-analysis of femoro-popliteal bypass grafting [1, 2] identified 73 studies between 1986 and 2004 (including 6 RCTs). The 5-year pooled primary patency rates were superior for vein grafts vs. above knee (AK) prosthetic grafts (80% vs. 60%) for claudicants. For patients with CLI the 5-year pooled primary patency rates were: 70% - vein, 50% - AK prosthetic and 30% - below knee (BK) prosthetic grafts.

Whilst prosthetic grafts may be comparable to vein grafts for AK fem-pop bypass, and indeed may have various arguments for its utility, the argument for preservation of the GSV for future coronary artery bypass graft (CABG) is wearing thin. A study by Dirven et al [3] analysed the results of 100 patients with AK prosthetic grafts over 8 years. Eleven patients needed a second bypass (10% probability) and one patient needed a CABG (1% probability). A suitable GSV therefore remains a first line conduit for AK fem-pop bypass grafting.

A recent meta-analysis by Tagaki et al [4] comparing Dacron to PTFE for AK fem-pop bypass, documented superior long-term patency rates for Dacron. Dacron is superior and cheaper than PTFE for AK fem-pop bypass grafting.

PTFE vs. heparin-bonded PTFE

The Scandinavian Propaten (heparin bonded PTFE) study, [5] a multicentre study that treated 569 patients with a femoro-femoral bypass or femoro-popliteal bypass, documented a 40% reduction in thrombotic graft occlusion rates.

PTFE vs. heparin-bonded Dacron

The Northwest femoro-popliteal trial [6] documented superior overall primary patency rates for heparin-bonded Dacron grafts over 5 years (70% vs. 66%). The results were better for AK c.f. BK fem-popliteal bypass.

Distal vein augmentation of prosthetic grafts

The culprit lesion for prosthetic graft failure is invariably neo-intimal hyperplasia (NIH) involving the distal anastomosis. To improve prosthetic graft outcomes various vein augmentation techniques have evolved with the aim of reducing NIH and improving prosthetic graft patency:

- Vein patch (Linton, Taylor, etc)
- Vein collar (Miller, St. Mary`s boot, etc)
- Interposition short vein segment
- AV fistulisation of the distal anastomosis (Dardek procedure)

The Joint Vascular Research Group (2004) [7] found no difference in AK prosthetic grafting. They did, however, document a significant advantage for vein augmentation in BK prosthetic grafting.

The SCAMICOS (Scandinavian miller collar study - 2010), [8] however, found no performance advantage for vein augmented PTFE vs. standard PTFE BK fem-pop prosthetic bypass.

Pre-cuffed PTFE vs. PTFE with a vein cuff

A study by Panneton et al [9] found no difference in long-term graft performance when these two procedures were compared.

Bypass vs. Percutaneous Transluminal Angioplasty (PTA)

Various studies have been reported comparing bypass to PTA.[10, 11, 12, 13] The most compelling of these studies was the BASIL (bypass vs. angioplasty in the severely ischaemic leg) study. [14] The Basil RCT randomized 452 patients either to the angioplasty group (224 patients) or to the bypass group (228 patients). The interim (2005) intention to treat analysis (5 year follow-up) showed no difference in amputation free survival (AFS) and overall survival (OS) at 2 years. The early costing data documented a higher cost for bypass (~ 1/3 more expensive) compared to PTA. The final (2008) intention to treat analysis found a significant trend towards long-term AFS and OS. The treatment received analysis documented that patients having a bypass following a failed PTA fared badly, and that vein was a superior conduit compared to prosthetic grafts.

Recommendations:

1. In patients with CLI, with a life-expectancy of < 2 years and an endo-suitable lesion, a PTA first strategy is justified. [14] (Class1 recommendation / Level A evidence)
2. In patients with CLI, with a life-expectancy > 2 years, a bypass first approach is justified; provided that a suitable GSV is available. [14] (Class 1 recommendation / Level A evidence). In patients without a suitable vein graft, a PTA first approach is feasible (Class IIa recommendation / Level A evidence). A prosthetic graft should be reserved as a last resort, especially to the BK popliteal segment(Class IIa recommendation / Level A evidence)
3. Proximal anastomosis: Any segment of the SFA or CFA may serve as the donor vessel provided that inflow is not compromised. (Class IIa recommendation/ Level B evidence)
4. Conduit – vein has better long-term patency than prosthetic; no difference between "in situ" & reverse saphenous vein graft (RSVG) (Class I recommendation / Level A evidence)
5. Adjunctive procedures with below knee prosthetic bypass:
    - addition of distal fistula adds no benefit (Class III recommendation / Level B evidence)
    - use of a vein cuff or patch has been promising (Class IIa recommendation / Level B evidence)
6. Profundoplasty should be considered with SFA occlusion and a > 50% PFA (profunda femoris artery) stenosis & excellent collateral flow distally.
7. Bypasses to the AK popliteal segment should be constructed with autogenous vein where possible. (TASC II) (Class I recommendation / Level B evidence)
8. Bypasses to the BK popliteal segment should be constructed with autogenous vein where possible. (TASC II) (Class I recommendation / Level B evidence)

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PAD – Surgical treatment (Infra-popliteal disease)

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Recommendations for infra-popliteal bypass grafting

1. For individuals with combined inflow and outflow disease with critical limb ischemia, inflow lesions should be addressed first. (Class I recommendation / Level C Evidence) [1]

2. For individuals with combined inflow and outflow disease in whom symptoms of critical limb ischemia (with or without tissue loss) persist after inflow revascularization, an outflow revascularization procedure should be performed. (Class 1 recommendation / Level B Evidence) [1]
3. If it is unclear whether a haemodynamically significant inflow disease exists, intra-arterial pressure measurements across supra-inguinal lesions should be measured before and after the administration of a vasodilator. (Class 1 / Level of Evidence C) [1]
4. Any artery, regardless of level, with continuous flow from above and without a stenosis greater than 20% should be used as the point of origin for a distal bypass [provided flow to that artery and the origin of the graft is not compromised]. (Class 1 recommendation / Level B Evidence) [1/2/3/4/5]
5. The proximal anastomosis of an autogenous infrainguinal bypass in a patient with an ipsilateral prosthetic inflow should be placed on a distal native artery. (Class 1 recommendation / Level B Evidence) [3]
6. The tibial or pedal artery that is capable of providing continuous and uncompromised outflow to the ankle/foot should be used as the site of distal anastomosis [used for outflow regardless of location, provided there is adequate length of suitable vein]. (Class 1 recommendation / Level B Evidence) [1/2/6/7/8/9/10]
7. An adequate, complete / single, greater saphenous vein is the optimal conduit in femoral below-knee popliteal and distal bypass. In its absence other sources of good quality autogenous vein from the leg or arm should be used (spliced vein graft). (Class 1 recommendation / Level B Evidence) [1,2,11,12,13,14]
8. Composite sequential femoro-popliteal-tibial bypass and bypass to an isolated popliteal arterial segment that has collateral outflow to the foot are both acceptable methods of revascularization and should be considered when no other form of bypass with adequate autogenous conduit is possible. (Class 1 recommendation / Level B Evidence) [1/2/15/16/17]

Adjunct procedures

When a prosthetic bypass graft is placed into the below-knee popliteal or distal artery adjunctive procedures, such as arteriovenous fistula, at or distal to the bypass, and the use of a vein interposition/vein cuff, have been suggested.

1. If no autogenous vein is available, a prosthetic femoral-tibial bypass, and possibly an alternative/adjunctive procedure, such as endovascular intervention or arteriovenous fistula or a vein interposition or vein cuff, should be used when amputation is imminent. (Class 1 recommendation / Level B Evidence) [1/12]
2. Revascularisation procedures to the infra-popliteal and crural artery levels should be undertaken by experienced individuals or teams. (Class 1 recommendation / Level B Evidence) [18]
3. Diabetic patients with CLI benefit from early revascularization. To achieve this benefit, multiple revascularization procedures may be required, and close surveillance is therefore mandatory. Choice of initial revascularization modality seems not to influence clinical success. [1/19]
4. For patients with limb-threatening ischemia and an estimated life expectancy of more than 2 years, bypass surgery, when possible and when an autogenous vein conduit is available, is reasonable to perform as the initial treatment to improve distal blood flow. (Class 2a recommendation / Level B Evidence) [12/20]

5. Prosthetic material can be used effectively for bypasses to the below-knee popliteal artery when no autogenous vein from ipsilateral or contralateral leg or arms is available. (Class 2a recommendation / Level B Evidence) [1]

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The rationale for primary amputation

Gregory Weir

Primary amputation is defined as an amputation of the ischaemic lower extremity without an antecedent attempt at revascularisation. The incidence of major amputations from large population or nation-wide data varies from 120 to 500/million/year. The ratio of below-knee to above-knee amputations in large surveys is around 1:1.[1]

The concept that all patients who require an amputation have steadily progressed through increasingly severe claudication to rest pain, ulcers and, ultimately, amputation is incorrect. It has been shown that more than half of patients having a below-knee major amputation for ischemic disease had no symptoms of leg ischemia in the 6 months before. [2]

In a review of the evidence there were no randomized trials of reconstruction versus amputation and no case-matched studies. The only information comes from a few prospective trials of the outcome of reconstruction versus amputation in unmatched patients from single centres. The majority of the literature consists of retrospective reports from single centres or consensus documents. There is no good evidence that reconstruction is better than amputation, because the required trials have never been done.[3]

Cost, [4, 5, 6]patient age [1, 7] and renal failure[8] have been evaluated, and have been found not to be accepted indications for primary amputations.

According to the TASC II document[1] the primary goals of treatment in patients with critical limb ischaemia include relief of ischaemic pain, improvement of quality of life and prolonging survival, which can be accomplished with primary amputation in selected individuals. Secondary goals include pain control and infection control. Primary amputation should not be considered in patients where ulcer healing, functional improvement and limb salvage are possible.

Accepted indications for primary amputation in patients with critical limb ischaemia include: [1,9,10,11]

- Severe patient co-morbidities (pre-terminal / limited life expectancy)
- Non-reconstructable occlusive arterial disease
- Severe intractable rest pain
- Non-ambulatory status (wheelchair-confined / bed-ridden)
- Non-salvageable limb
- Extensive necrosis / gangrene involving weight bearing areas
- Overwhelming, life threatening foot sepsis
- Fixed, irremediable flexion contractures
- Severe neuropathy (insensate foot)

The goals of a primary amputation should be the expedient return of the patient to a useful quality of life and to obtain primary healing of the lower extremity at the most distal level possible.[12] Primary healing rates increased when clinical assessment was combined with TcPO2 levels. [1, 13]

There were no randomized trials of vascular reconstruction versus amputation and no case-matched studies (Level of evidence C). The only information comes from a few prospective trials of the outcome of reconstruction versus amputation in unmatched patients from single centres. The majority of the literature consists of retrospective reports from single centres or consensus documents.[1, 3]

It is unlikely that there will be any randomised trials of reconstruction versus amputation in select patients. Surgeon judgement and experience is paramount in deciding on primary amputation versus revascularization. More emphasis should be placed on the importance of prevention, early diagnosis and appropriate treatment of patients with peripheral arterial disease.

Recommendations

1. The decision to amputate and the choice of the level should take into consideration the potential for healing, rehabilitation and return of quality of life. (Grade 1 recommendation / Level C evidence) [1]
2. Primary amputation may be considered in patients with critical limb ischaemia with severe patient co-morbidities, non-reconstructable occlusive arterial disease, uncontrolled rest pain, non-ambulatory status or dementia, non-salvageable limb, fixed, irremediable flexion contractures, extensive necrosis or gangrene involving weight-bearing areas, severe neuropathy and or overwhelming, life-threatening foot infection. (Grade 1 recommendation / Level C evidence)

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PAD – Endovascular treatment for aorto-iliac disease

Philip Matley

Today, most aorto-iliac lesions are managed using endovascular, rather than open surgical techniques.

Interventions for Functional Ischaemia

Notwithstanding the fact that long-term studies in claudicants have demonstrated that supervised exercise programmes may give better long-term results than angioplasty, endovascular treatment of aorto-iliac lesions is usually only indicated in individuals with vocational or lifestyle-limiting claudication where the likelihood of symptomatic improvement is high and there has been an inadequate response to exercise or pharmacological therapy [1, 2].

Patients with aorto-iliac disease and intermittent claudication should undergo a period of medical treatment before revascularisation therapy is considered. (Class I recommendation / Level C evidence)

Interventions for Critical Limb Ischaemia

Patients with critical limb ischaemia (CLI) invariably have multi-level or infra-popliteal disease. Isolated aorto-iliac disease is very uncommon in these patients. Individuals with CLI require revascularisation if technically feasible in order to avoid the high risk of limb loss. In such patients, where a significant inflow problem at aorto-iliac level has been identified the inflow problem should be addressed first [1, 2]. For individuals with combined inflow and outflow disease with CLI, inflow lesions should be addressed first. If it is unclear whether haemodynamically significant inflow disease exists, intra-arterial pressure measurements should be performed both before and after the administration of vasodilators. (Class I recommendation / Level C evidence)

Angioplasty vs. Stenting

Whereas some interventionists routinely use stenting, rather than angioplasty alone for aorto-iliac lesions, most use stents selectively for complex lesions, eccentric lesions, ostial lesions, recurrent stenoses, occluded common iliac arteries and where the anatomical result from angioplasty is sub-optimal. Stents are also indicated for flow-limiting dissections following angioplasty. In the only large randomised trial of angioplasty versus stenting[3], no significant difference in 2-year patency could be demonstrated in 286

patients randomized to primary stenting versus angioplasty alone with stenting being reserved for lesions that, following angioplasty, had a residual gradient across them exceeding 10mmHg. However, as this trial was confined to claudicants with relatively short lesions the results cannot be extrapolated to more complex lesions (TASC C&D). In a meta-analysis of a broader spectrum of patients Bosch et al[4] found that the use of stents was associated with an overall 39% reduction in the need for re-intervention.

There is no convincing evidence that primary stenting is better than a good angioplasty result for short iliac stenoses. Common iliac occlusions are usually stented. Severe disease at the origin of the CIA or EIA, especially if heavily calcified and eccentric will usually require primary stenting and in this situation a balloon-expanded stent may offer advantages over a self-expandable nitinol stent. Haemodynamically significant dissections and residual stenoses > 30% requires stenting as do recurrent lesions following previous angioplasty.

Stent placement is indicated for use in iliac arteries as salvage therapy for sub-optimal results from angioplasty alone (e.g. persistent trans-lesional gradient, residual stenosis > 30% or flow-limiting dissection). (Class I recommendation / Level B evidence)

Stenting is effective as primary therapy for select common and external iliac artery occlusive disease. (Class I recommendation / Level B evidence)

Endovascular treatment vs. surgical treatment

The TASC classification[5] is useful for determining which patients are more suited to endovascular treatment rather than open surgical treatment. The primary therapy for most TASC A and B lesions is endovascular[6]. For TASC C and D lesions surgery is recommended, however some may contest that treatment needs to be individualized. Endovascular treatment is usually preferred for shorter lesions with good run-off status, particularly in poor-risk patients. Longer and more complex lesions with poor run-off may be better suited to surgery, particularly in good-risk patients. This is particularly so for bilateral occlusions of either the common or external iliac arteries. Infra-renal aortic occlusion is best treated by aorto-femoral bypass or an extra-anatomical bypass procedure. Good results of endovascular treatment in large series of consecutive TASC C and D patients have recently been reported[7, 8] and there is evidence that this approach reduces hospital stays and overall cost [9].

In the aorto-iliac segment, TASC A and B lesions and most TASC C lesions should initially be treated with endovascular therapy. Certain TASC C lesions and TASC D lesions may be treated by either endovascular or open (hybrid) procedures, depending on lesion complexity, patient condition and operator experience. (Class 1 recommendation / Level C recommendation)

Surgical revascularization should be used in selected patients with more complex anatomy (TASC D) or in case of endovascular failure. (Class IIa recommendation / Level C recommendation)

Severity of iliac lesions requiring treatment

It is generally accepted that aorto or iliac stenoses of 70% or greater are haemodynamically significant. For lesions that are thought to be in the 50-70% range, trans-lesional pressure gradients (with or without vasodilatation) should be obtained to evaluate the significance of angiographic iliac lesions [1, 2].

Aorto or iliac stenoses of 70% or greater are haemodynamically significant and deserve attention if an intervention is planned. Trans-lesional pressure gradients (with or without vasodilatation) should be

obtained to evaluate the significance of angiographic iliac lesions thought to be in the 50-70% range. (Class I recommendation / Level C evidence)

Endovascular treatment is not indicated if there is no significant pressure gradient across a stenosis despite flow augmentation with vasodilators. (Class III recommendation / Level C evidence)

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PAD – Endovascular treatment for femoro-popliteal disease

John V Robbs

The superficial femoral artery is a dynamic vessel, subjected to flexion, piston action, rotation, twist and there is also fixation at the adductor hiatus all of which place considerable shear stress on a stent.

Indications for intervention are critical limb ischaemia and possibly incapacitating claudication. The modalities to be discussed are angioplasty and stent insertion. Only non-industry-driven meta-analysis has been referred to.

Selection of procedure depends upon the TASC classification[1] for femoro-popliteal lesions.

TASC A

Single stenosis < 10cm in length

Single occlusion < 5cm in length

TASC B

Multiple lesions (stenoses or occlusions) each < 5cm

Single stenosis or occlusion < l5cm not involving the infra-geniculate popliteal artery

Single or multiple lesions without continuous tibial vessels

Calcified occlusion <5cm in length

Single popliteal stenosis

TASC C

Multiple stenoses or occlusions totalling > l5cm in length

Recurrent stenoses or occlusions that need treatment after two endovascular interventions

TASC D

Total occlusion of CFA or SFA (> 20 cm in length / involving the popliteal artery

Chronic total occlusion of the popliteal artery and proximal trifurcation vessels

General consensus is that TASC A and B should be treated primarily by endovascular therapy; C and D require surgical revascularization. If the patient has severe co-morbidities, consider TASC C for endovascular treatment.

The influence of TASC

In a retrospective study Dearing et al [2] showed significantly improved results for endovascular treatment of TASC A and B lesions with 79% twelve month patency and 57% 36 month patency rates. With C and D lesions, endovascular treatment was associated with a 52% twelve month patency and a 19% 36 month patency rate.

Percutaneous transluminal angioplasty (PTA) vs. PTA plus stent

Twine, Coulston et al [3] made a collective review of randomised controlled trials. They identified eight trials

(968 patients)

At six months PTA and stent had a better patency; after 12 months no significant difference was noted.

Regarding quality of life there were no differences.

The conclusion was that stents were marginally better.

PTA versus primary stenting

Perrio S et al (2001) [4] in a collective review looked at patency at one year, and found no difference. The conclusion was that stents should only be used as a "bail out" procedure. Stent design and performance may be a factor influencing patency. The major problems with the stents are fractures, thrombosis and neo-intimal hyperplasia (in-stent stenosis). Muller-Hulsbeck and colleagues (2010) [5] devised a machine which tested stent durability against bending, twisting and pistoning, and showed significant differences according to stent design.

CONCLUSIONS

All evidence is Level B at best. The endovascular procedures should be limited to TASC A and B lesions.

Angioplasty should be the initial procedure, with stents being used if this fails. Failure is related to lesion recoil, extensive calcification of the lesions and possibly in lesions of >5cm in length.

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PAD – Endovascular treatment for infra-popliteal disease

Jay Pillai

Tibial Angioplasty (TA) may be used to successfully treat selected patients with atherosclerotic tibial occlusive disease. Although patency rates of TA are lower than that of surgical bypass, it is widely regarded as a suitable alternative to open surgery in patients with limited life expectancy. Limb salvage rates in some patients however, may be comparable to open surgery.

Anatomical Heterogeneity and Clinical Outcomes

The TASC-II document is generally unhelpful to guide therapy towards positive outcomes. Critical issues in tibial arteries include, degree of calcification; diameter of arteries, pedal artery run-off; peroneal vs. tibial arteries; presence of diabetes and renal failure; angiosome revascularization and ischaemic category.[1]

Observational studies indicate:

a) Small toe ulcers and rest pain are associated with better outcomes than extensive tissue loss
b) Limb salvage rates may be improved with "angiosome revascularization" [2, 3]
c) Outcomes in renal failure patients are particularly poor [4]

The paucity of scientific data, patient heterogeneity and anatomical / morphological variability mandates that most critically ischaemic patients be managed in high volume centres.

Evidence

Only 30% of all patients in the randomized controlled BASIL trial had tibial artery involvement.[5] Therefore conclusions cannot be extrapolated. Clinical success between surgery and angioplasty was comparable at 1 year with a trend favouring surgery at 2 years.

A meta-analysis of 30 observational studies comparing TA with popliteal-distal bypass indicated that primary patency was better with bypass (72% vs. 49% at 3 years). [6] Limb salvage was the same (82%) at 3 years.

Other studies indicate primary patency rates of 50% to 80% (4-5 years) and limb salvage rates of approximately 80%.[7,8,9] Repeat angioplasty was performed in 18% of cases. However the results for tibial angioplasty may be confounded by treatment of multilevel disease in these studies.

The use of coronary stents in critically ischaemic patients with predominant tibial disease appears counter-intuitive. Lesions are typically complex and current stents are limited by length and rigidity. Nonetheless a meta-analysis of 640 patients reported primary patency rates of 79% and limb salvage rates of 96%.[10] Most

stents were placed for suboptimal angioplasty results, and critical limb ischaemia (especially extensive tissue loss) was not the main emphasis.

Recommendations

- Tibial angioplasty is the preferred treatment in patients with TASC A & B lesions and minor tissue loss or rest pain (Class I recommendation / Level B Evidence).
- Patients with complex long lesions and tissue loss (Rutherford 5 - 6) may be treated endovascularly by experienced teams (Class IIb recommendation / Level C evidence).
- "Angiosome Revascularization" and revascularization of more than 1 tibial artery may lead to better clinical outcomes (Class IIa recommendation / Level C evidence).
- Patients with extensive tissue loss, a suitable pedal outflow artery and a suitable vein conduit should be considered for bypass over endovascular treatment (Class IIa recommendation / Level B evidence).
- Coronary stents may be considered in CLI patients with suboptimal angioplasty of the proximal tibial arteries (Class IIb recommendation / Level B evidence).

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PAD – Drug eluting treatment strategies

B Pillay

Percutaneous interventions may be complicated by restenosis as a result of myointimal hyperplasia. Restenosis may adversely influence the patient's symptoms and long term patency rates of peripheral vascular interventional procedures. The rationale for using drug eluting strategies is based on their anti-inflammatory properties, which retards the process of myointimal proliferation.

Evidence

PubMed and Cochrane literature reviews confirms the availability of randomised trials to demonstrate the above properties. Currently available results are the SIROCCO trials (I & II), the Thunder trial, and other cohort studies. On-going studies are evaluating the role of drug eluting devices and non-drug eluting devices for infrainguinal disease. Evidence from the available data suggests that the use of drug eluting stents and balloons are safe and effective for reduction of restenosis following percutaneous interventions. Small patient numbers, heterogeneous study populations, expense and single usage seem to be major limitations to this novel technique. Results from on-going studies would allow for a meta-analysis, so that these results can be translated into an effective clinical strategy in reducing restenosis following percutaneous procedures. The concept of using a drug eluting strategy for peripheral interventions seems logical in the context of its antiproliferative characteristics. Emerging data tends to support this modality as an option for treating restenosis in peripheral vascular disease and may guide future use. Concerns with respect to prescription of these devices relates to allergy (rare - 0.15%), excessive vessel wall remodelling that culminates in long term ectasia or aneurysm formation.

The results from randomised studies, namely SIROCCO AND THUNDER, seem promising. However results from other studies are awaited. A meta-analysis of the data would scrutinise the clinical applicability of such strategies

Current trials:

AUTHOR/NAME Published	NOS	TARGET GROUP	ENDPOINT	Is DES better?
SIROCCO 1	36	IC,CI	In –stent restenosis	Not statistically better
SIROCCO 11	93	IC,CI	In-stent restenosis	Not statistically better
COOK-ZILVER PTX INTERIM RESULTS	60	IC,CI	In –stent restenosis And patency rate	Unknown
COOK ZILVER PTX STENT REGISTRY	791	IC,CI	Freedom from target lesion revascularisation@ 48months	Registry-no Comparisons
Bosiers	18	IC,CI	In-stent restenosis and limb salvage	No comparison
Scheirt	53	IC,CI	In-stent restenosis	Yes
Commeau	30	IC,CI	Clinical improvement and vessel patency	No
Siablis	103	IC,CI	Mortality, limb salvage, primary patency	Yes-patency
				Is DEB better?
THUNDER	154	IC,CI	Lumen loss @ 6 months	Yes
Werk	87	IC,CI	Lumen loss@ 6 months	Yes

Key: IC-Intermittent claudication; CI-critical ischaemia with rest pain or tissue necrosis**;** DES-Drug eluting stents; DEB-Drug eluting Balloons

Recommendations

Drug elution in the peripheral circulation cannot be universally applied. The data is not robust in terms of pharmacokinetics, applicability to long calcified lesions compounded by an element of "geographical miss". Drug- eluting balloon trials do not adequately address clinical endpoints and vessel remodelling characteristics. Furthermore some trials have reported failure of this technology. The current socio-economic climate maybe influenced by the cost implications of this modality compounded their single usage prescription. Although safe, and effective as a viable alternative, expense is a major limiting factor. Current evidence dictates usage within the confines of a clinical trial until such time more randomized trials are performed that may allow a logical meta-analysis that better defines the benefits of clinical applicability.

- Drug eluting stents may be used for focal (< 2cm length lesions) infrapopliteal lesions in patients with CLI and tissue loss, who are poor operative risk, or have no suitable vein for bypass (Class IIb recommendation / Level B evidence)
- Drug eluting balloons may be used selectively in patients with severely symptomatic in-stent restenosis. (Class IIb recommendation / Level B evidence)
- Drug eluting balloons may be used for in patients with CLI and tissue loss, who have diffuse femoro-popliteal or infra-popliteal disease, who are poor operative risk, or have no suitable vein for bypass. (Class IIb recommendation / Level B evidence)

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PAD – Other novel interventional, debulking and CTO crossing strategies

Pierre Mouton

Failure in re-entry is reported to be as high as 26% after sub-intimal tracking. Small series reports success of 95%-100% with the Pioneer and Outback catheters after initial failure. Other possible advantages are accurate re-entry site with preservation of collateral vessels and future surgical sites, as well as reduced procedure time and reduced number of vessel perforations.

Devices for example the "FrontRunner XP", "FlowCardia", "Wildcat" and "Cittycat" are design to assist in crossing wire resistant lesions and to cross a lesion in the centre of the lumen. This will produce improved results with stenting, balloon angioplasty and drug eluting balloons. The Connect trial (prospective, multicenter, non-randomized study of 250 patients) reported an 89.3% procedural success with the "Wildcat" in crossing guide-wire resistant lesions. The Patriot Trial illustrated a success of 81.2% with the "FlowCardia" in crossing guide-wire resistant lesions.

The "Excimer Laser" is applied as a device to traverse resistant lesions and to debulk a lesion, thereby gaining at least 50% of the lumen with initial therapy, improve results with balloon angioplasty and reduce the number of stent placements. The LACI 2 Trial (Laser Angioplasty for Critical limb Ischemia) enrolled 145 patients with 423 lesions who were poor candidates for surgery and had a procedural success rate of 85%. Eight percent of patients had guide wire resistant lesions. Only 45% of lesions needed stent placement after laser therapy and angioplasty. The PELA trial (Peripheral Excimer Laser Angioplasty Trial) reported similar results as well as a number of small series written up by various authors.

The SilverHawk Plaque excision system is developed as a debulking system. It improves results in long, eccentric and heavily calcified lesions near a bifurcation. The "Proof Trial" was the only randomized trial, but was abandoned. The TALON Registry (Treating Peripherals with the SilverHawk: Outcome Collection) is a multicenter registry of 601 patients and 1258 lesions, with a procedural success of 97.6% (26.7% adjunctive therapy with 20.3% angioplasty and 6.3% stenting), limb salvage of 93.1% at 12 months and 92.4% at 18 months. Only 87 of 601 patients were available for follow-up at 12 months.

Evidence

The level of evidence for these devices is weak, consisting mostly of small case series, case studies or registries, which classify the evidence as Level C.

The role of these devices remains unclear. They are expensive, in the development phase and have little evidence of efficacy. The most likely suitable patient is the patient unfit to be exposed to a prolonged surgical procedure or who has no surgical option due to a lack of conduit. There is a need for hard evidence of efficacy for these devices.

Recommendations

These devices can be used in a patient unfit for a surgical procedure or who has a lack of conduit. (Class IIb recommendation / Level C evidence)

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PAD – Multi-level surgical revascularization

B Natha

Until recently pure multi-level surgical revascularisation was not uncommonly required for the treatment of multi-level arterial disease (MLAD). However, with the progress made with endovascular treatment modalities regarding supra and infra-inguinal PAD, such pure surgical multi-level revascularization is rare.

The following points need to be noted:

- Studies are generally historical and all are retrospective case series
- Patients included in these studies have all have multilevel lower extremity arterial occlusive disease with Rutherford clinical category 3-6
- Revascularisation studies pertaining to MLAD can broadly be categorised into 2 traditional groups:
    - Aorto-iliac inflow procedure and profunda artery revascularisation as an isolated procedure
    - Synchronous multilevel revascularisation

Isolated profunda artery revascularisation

There are a few case series assessing the efficacy of isolated profunda artery inflow revascularisation in patients with MLAD.

Madiba, Robbs et al.[1] reported one of the largest retrospective comparative case series with 492 patients with aorto-iliac disease (93 patients with MLAD) who underwent aortic-iliac revascularisation. All 93 patients

(48% presented with critical limb ischaemia) with MLAD had profunda artery revascularisation only without an additional infra-inguinal bypass. At 5 years 80% of these patients had inflow patency and good symptomatic relief. However a subgroup analysis demonstrated that claudicants fared better than the CLI group, some patients in this group requiring an additional infra-inguinal revascularisation procedure.

Hill et al.[2] demonstrated similar inflow graft patencies however only 26% of their study group (56 patients) had good symptomatic relief from an isolated inflow profunda revacularisation procedure.

Synchronous multilevel revascularisation

During the 1960s Beson et al.[3] published a retrospective case series of 12 patients that underwent synchronous MLAD revascularisation. He demonstrated only 30% relief of symptoms and all 12 patients suffered complication. Similar findings were reported in contemporary studies during that period. Due to these findings they advocated that patients with MLAD should either have isolated inflow procedures or staged multi-level revascularisation if necessary.

Since the 1960s there have been many advances in medical, surgical and endovascular care for patients with MLAD. In patients with extensive burden of arterial disease (TASC C & D lesions) the role of surgical revascularisation in MLAD cannot be underestimated. Numerous trials evolved in the 1990s to assess the safety and efficacy of synchronous surgical MLAD revascularisation.

Various studies all reported single centre retrospective comparative case reviews comparing isolated aorto-iliac revascularization with either delayed or synchronous multi-segment revascularization for MLAD. [4, 5, 6] They all demonstrate equally low mortality (1.8%-7%), morbidity and good long term patency rates (70%-95.6%) in both the synchronous and inflow-only revascularisation groups. Dalman et al. also demonstrated that with two surgical teams the intra-operative time and complications were similar in both groups (240 minutes for the synchronous group vs. 210 minutes for the inflow-only group). Nayper et al.[6] also found that those patients who underwent inflow-only procedures fared worse if these patients required a delayed additional bypass procedures compared to those patients where these procedures were performed synchronously.

However in a study published by Harward et al.[7] they demonstrated significantly higher mortality rates (18.5%), longer theatre times (8.6 hours), significantly higher blood loss and higher complication rates in the group undergoing synchronous vs. inflow-only surgical revascularisation. These were attributed to the highly complex composite graft bypasses and single surgery team approach to the synchronous revascularisation group.

Pure surgical infra-inguinal multi-segment revascularization is exceptionally rare but has been reported in the literature.

Recommendations

Consider surgery multi-level surgical revascularization in patients with extensive MLAD not suitable to other forms of revascularization in select patients (Class IIa recommendation / Level B evidence)

- Severe claudication or CLI with rest pain with a poor quality profunda femoris artery as recipient vessel

- Aorto-iliac disease with tissue loss

Preferably two vascular surgical teams are recommended for these procedures (Class IIa recommendation / Level C evidence)

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PAD – Multi-level endovascular revascularization

Dirk le Roux

Guidelines for limb and cardiovascular natural history clinical outcomes for PAD suggest the following at 5 years:

- stable claudication in 70 - 80 %
- worsening claudication in 10 - 20 %
- CLI in 1 to 2 %
- Non-fatal myocardial infarction or stroke in 20 %, and death in 15 to 30 % (75%cardiovascular)

For CLI the guidelines report the following outcomes at one year:

- Alive with two limbs — 50%
- Amputation — 25 %
- Cardiovascular mortality — 25 %

The prognosis for both limb loss and survival is significantly worse in diabetic patients and those who continue to smoke. Long-term success of percutaneous transluminal (balloon) angioplasty (PTA) depends

upon the site and length of the lesion. Lesions which are unsuitable, and which might be better treated surgically, have one or more of the following features:

- Long segments
- Multifocal stenoses
- Long segment occlusions
- Eccentric, calcified stenoses

There are however new challenges to the above-mentioned recommendations. PTA has been traditionally limited to the treatment of focal, short segment stenoses or occlusions. However, with advancements in technology, PTA is now routinely applied to more extensively diseased segments to attempt limb salvage before a surgical bypass is needed. It is useful in patients who are poor surgical candidates and in older patients, particularly octogenarians.

Aorto-iliac occlusive disease
PTA of an uncomplicated iliac stenosis has an initial technical success rate of approximately 90 %. Long-term patency is directly influenced by the extent of disease. The 5 year patency rate is 70 %. However, the five-year patency drops to 51% when there is poor distal runoff. The threshold for percutaneous intervention in aorto-iliac disease is typically lower than for infrainguinal disease due to better expected outcomes. Thus it makes sense to improve outcomes by addressing multi-segment disease with poor infra-inguinal run-off.

Infra-inguinal occlusive disease
Patency and limb salvage rates for endovascular treatment of tibial vessel disease are comparable with prior reports and with historical surgical controls. Patients who undergo multilevel intervention involving the tibial vessels exhibit improved secondary patency compared with those who undergo intervention for lesions isolated to the tibial vessels. This may reflect increased distal disease burden for patients who undergo isolated tibial intervention. Study data suggest that the presence of multilevel disease should not preclude an attempt at percutaneous revascularization. Further study is required before formulating definitive recommendations for the endovascular treatment of tibial vessel disease. (Class IIa recommendation / Level B evidence)

Diabetes Mellitus
Diabetics undergoing infrainguinal EVT (endovascular treatment) are a heterogeneous group, and further investigation is required to more completely understand the impact of diabetes on outcomes. Patients undergoing EVT with diabetes are most likely to have higher rates of technical failure and subsequent amputation. Also, patients with diabetes probably have higher rates of restenosis after EVT in the femoropopliteal arteries. The data is less clear for tibial EVT. The impact of diabetes on patency and restenosis rates in the femoropopliteal arteries is probably less important than TASC classification and tibial artery runoff. Among patients with diabetes and CLI, those presenting with isolated tibial artery occlusive disease are more likely to have more advanced tissue loss, ESRD, and a worse prognosis.

The revised AHA guidelines (2011) include two new recommendations for PAD:
1. For patients with limb-threatening lower extremity ischemia and an estimated life expectancy of 2 years or less or in patients in whom an autogenous vein conduit is not available, balloon angioplasty is reasonable to perform when possible as the initial procedure to improve distal blood flow. (Class IIa recommendation / Level B Evidence)
2. For patients with limb-threatening ischemia and an estimated life expectancy of more than 2 years, bypass surgery, when possible and when an autogenous vein conduit is available, is reasonable to perform as the initial treatment to improve distal blood flow. (Class IIa recommendation / Level B Evidence)

Adequate rates of limb salvage can be achieved in patients undergoing multilevel interventions for CLI, and improved patency is seen with multilevel compared to isolated tibial interventions. Patients with isolated tibial disease appear to have a higher incidence of limb loss secondary to poor initial pedal runoff, more extensive distal disease, and severe comorbidities precluding surgical bypass. Other therapeutic strategies should be considered in these patients, including primary amputation or pedal bypass when applicable.

Conclusion

Patency and limb salvage rates for endovascular treatment of tibial vessel disease are comparable with prior reports and with historical surgical controls. Patients who undergo multilevel intervention involving the tibial vessels exhibit improved secondary patency compared with those who undergo intervention for lesions isolated to the tibial vessels.

This may reflect increased distal disease burden for patients who undergo isolated tibial intervention. Data suggest that the presence of multilevel disease should not preclude an attempt at percutaneous revascularization. Further study is required before formulating definitive recommendations for the endovascular treatment of tibial vessel disease.

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PAD – Hybrid revascularization strategies

Laura Redman

Introduction

Hybrid re-vascularisation – that is combined endovascular and open surgical techniques – has been undertaken for over 20 years, but no standard guidelines have been developed and no randomized controlled trials have been performed looking at this technique. Thus, the literature is sparse, containing mostly retrospective accounts that cannot be accurately compared to open procedures or pure endovascular intervention and there are no definitive recommendations, each unit using its own discretion.

All current guidelines focus on single level disease using either open surgical or endovascular intervention.

The TransAtlantic Inter-Society Consensus (TASC) does not provide definitive guidelines regarding hybrid procedures. The guidelines rather refer to the choice of either open or endovascular surgery: "If endovascular and open repair give equivalent short and long term results, endovascular intervention should be chosen".

Multi-level disease and management [1, 2, 3]

It is extremely important to appreciate that hybrid re-vascularisation is performed for multi-level disease, which automatically implies high-risk patients. Patients with multilevel disease have a higher atherosclerotic burden, are generally older and have more severe co-morbidities than patients with single level disease. [1]

Multilevel disease implies disease at 2 or more major arterial segments. Disease at 1-2 levels will at least result in disabling claudication if not critical limb ischaemia and disease at 2-3 levels will result in critical limb ischaemia (with / without tissue loss). This is due to basic physiology with additive lesions resulting in lower ankle-brachial indices (ABI's) and peripheral perfusion.

With regard to the above information, it can be seen that multilevel disease involves complex lesions in complex patients – regardless of the chosen treatments; outcomes are bound to be worse in this group than a patient with less disease burden at one level.

Basic principles of vascular surgery entail adequate inflow and adequate outflow. Creating adequate inflow and outflow may be achieved using hybrid techniques, avoiding multiple large procedures, and thus possibly increasing the number of patients amenable to re-vascularisation or to better outcomes.

It has been debated whether a patient with multilevel disease will benefit enough from merely addressing the inflow, as this is often the chosen form of treatment to avoid amputation. This is usually in the aorto-iliac region. It is generally thought that if the presenting symptom is claudication, addressing the inflow may be sufficient to alleviate symptoms, but it has subsequently been found that a significant proportion of these patients will have persistent claudication.

The profunda popliteal index may be useful in such a setting although it is not routinely used.

The American College of Cardiology/American Heart Association guidelines are as follows:

1. For individuals with combined inflow and outflow disease with CLI, inflow lesions should be addressed first. (Class 1 recommendation / Level C Evidence)

2. For individuals with combined inflow and outflow disease in whom symptoms of CLI or infection persist after inflow revascularization, an outflow revascularisation procedure should be performed. (Class IIa recommendation / Level B Evidence)

Scher et al [2] found that the level of amputation was dependant on the number of levels of disease rather than on age and co-morbidity – including diabetes. They found that there was a significant reduction in amputation rate when both inflow and outflow was addressed compared to outflow alone – 13% versus 56% at one year. Thus addressing the full spectrum of disease will have improved limb salvage rate. However, it may be at the expense of a higher mortality and cardiovascular morbidity [1]. Quality of life has not been

assessed. The TASC guidelines have stated that if endovascular and open repair give equivalent short and long term results, endovascular intervention should be chosen.

Results generally show surgery provides superior patency, but co-morbidities of the patient as well as avoidance of major surgery for acceptable outcomes influence the choice of management.

TASC A: Endovascular / TASC B: Endovascular preferred / TASC C: Surgery preferred / TASC D: Surgery

The options for suprainguinal and infrainguinal disease include:

- Iliac angioplasty with femoral bifurcation surgery
- Iliac angioplasty with femoro-femoro cross-over and
- Iliac angioplasty and infrainguinal bypass surgery.

Combined suprainguinal and infrainguinal disease

There are no direct comparisons with multilevel open surgery versus multilevel endovascular surgery versus hybrid techniques, but retrospective reports have been documented in various units of their experience with hybrid techniques.

Intervention	Technical success	1 year patency	3 year patency	5 year patency	10 year patency
PTA (Iliac)	96%	86%	82%	71%	
AFBG (claudication)				91%	81%
AFBG (CLI)				87%	72%
Axillo-unifemoral Graft				51%	
Axillo-bifemoral graft				71%	
Fem-fem crossover				75%	

Table 1: Outcomes in terms of graft patency (Figures taken from: Norgren et al; Inter-Society Consensus for the management of Peripheral Vascular Disease (TASCII); Journal of Vascular Surgery, Volume 45, Number 1, Supplement) [3]

Table 2: Hybrid procedure outcomes for suprainguinal and infrainguinal disease

Iliac stent & Femoral endarterectomy	Limb salvage	CLI	Clinical success	Initial success	1 year patency	3 year patency	5 year patency	Reintervention	30 d mortality
Chang [4] (171 patients)		64%	92%	98%			1: 60% 2: 98%	Endo: 14% Surgery: 10%	2.3%
Nelson [5] (34 patients)			97%	100%	1A: 97%				0%
Iliac OTA +/- stent & fem-fem cross over									
AbuRhama [6] (34 patients)		66%				72%			
Lopex-Galarza [7] (18 patients)		28%					1: 51% 2: 63%		
Iliac PTA & infrainguinal bypass									
Faries [8] (126 patients)	85.2% (3 yrs.)	100 %				72.8%			1%
Schneider [9] (49 patients)			98%	100%			78%		
Miyahara [10]	80% (5 year)								

(1= primary patency; 2= secondary patency; 1A= primary assisted patency)

Success was defined as a residual stenosis of < 30% or a systolic pressure gradient of <10mm Hg. Stentgrafts (covered peripheral stents) were significantly better than bare metal stents.

Table 2 reflects graft patency as the only comparable variable. This, clearly, is not ideal. Limb salvage, mortality and quality of life all actually need to be assessed and compared.

AbuRhama noted a recurrence of symptoms according to length of iliac occlusion/stenosis within 30 days, 0% of iliac lesions <5 cm needed revision compared to 54% with lesions > 5cm.

Faries only used percutaneous angioplasty. These were all staged procedures with an average interval of 3.1 days. Diabetic mortality was 1% whereas non-diabetics had 0% mortality. Schneider used a one-stage procedure. Miyahara compared iliac stent and infrainguinal bypass with suprainguinal surgery followed later by infrainguinal surgery – primary and secondary patency rates were similar at 5 years (71.2% versus 80.5% for primary and 76% versus 84% for secondary patency respectively). Survival and limb salvage were comparable.

Collectively, PTA / stent patency is inferior compared to open surgery. Cumulative patency rates may approach that of open surgery but the patient may require multiple interventions to achieve this, which is not ideal in the high-risk patient.

Infrainguinal disease

Once again, there are no direct comparisons between open surgery and endovascular surgery for infrainguinal disease – the only available comparison is the stated TASC graft patency and mainly retrospective reviews.

The options for hybrid procedures of infrainguinal disease are:

- Femoral PTA and distal origin bypass grafts
- Supragenicular bypass and crural PTA
- Femoral endarterectomy and PTA of distal vessels

Table 3: Patency rates for infrainguinal disease.[3]

Procedure	**1 year patency**	**3 year patency**	**5 year patency**
PTA (occlusion)	65%	48%	42%
PTA + stent (occlusion)	73%	64%	
PTA (stenosis)	77%	61%	55%
PTA + stent (stenosis)	75%	66%	
Surgical bypass			
AK: Vein			75%
AK: PTFE			39-52%
BK: Vein			65%
BK: PTFE			30%

Table 4: Outcomes of hybrid procedures for infrainguinal disease

	CLI	1 year patency	3 year patency	Mortality	Re-intervention	Limb salvage
Femoral PTA + Distal SFA origin grafts						
Schanzer [11] (23)	95%		58%	0%	30%	100% (early)
Lantis [12] (22)	100%		1: 95% 2: 100% (3/12-4 years)			
Supragenicular bypass & crural PTA						
Volpe [13]		77%				95%(1 year)

Schanzer included staged procedures and 48% of the patient group had TASC A lesions.

Lantis excluded TASC D lesions. The origin of bypass was infra-genicular in 14 and supra-genicular in 8 patients. Volpe concluded that patency for supra-genicular bypasses can be improved if outflow is improved simultaneously.

Once again, overall technical success was excellent with reasonable results usually after 2 or more interventions, but not equating to open surgery.

Recent literature reporting on hybrid procedures document the following: [14, 15, 16]

- Initial success excellent: 93-100%
- Primary patency at 1 year: 53-79%
- Morbidity & mortality rates relatively good
- Risk factors for failure:
    - Disease extent, DM, dyslipidaemia
    - TASC lesion treated with endovascular means

Stent-assisted remote endarterectomy of iliac arteries[17]

This combines iliac stenting with endoluminal debulking of TASC D lesions of the common femoral and external iliac arteries. Results are comparable with endovascular techniques. There is a high re-stenosis rate and a high learning curve.

Conclusion

Hybrid techniques do appear to have a valuable role in high-risk patients with multilevel disease. They have reasonable patency and limb salvage rates and although surgery may be superior, in this group of high-risk patients with severe disease, these rates are acceptable, if not good. These are high-risk patients who complicate despite lesser procedures. Re-intervention rates are high. The morbidity and mortality is higher than isolated endovascular procedures. Quality of life has not been assessed.

Recommendations

- The presenting symptom (claudication versus critical limb ischaemia) is important when considering outcome and natural history of the disease. The debate of whether to address inflow alone or both inflow and outflow needs to be individualized for claudication, but once there is tissue loss both inflow and outflow should be addressed. (Class IIa recommendation / Level B evidence)
- Endovascular intervention should be considered for TASC A, B and sometimes C lesions and open surgery for D and sometimes C lesions. (Class IIa recommendation / Level B evidence)
- In patients with multi-level disease, a hybrid procedure is an acceptable intervention and if the patient is considered high-risk, should be the first choice of procedure if endovascular intervention alone would not be feasible. (Class IIa recommendation / Level B evidence)

The physiological risk of the patient needs to be fully assessed as a hybrid procedure is a greater undertaking than an endovascular procedure alone and in addition re-intervention is frequently needed. In certain high-risk patients, initial amputation may be the best option to improve quality of a usually shortened life, rather than risking a life for a limb.

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PAD – Limb salvaging strategies for non-reconstructable disease

Charl Dreyer

From trial data it is often quoted that 25% to 30% of CLI is non-reconstructable, of which there will be a 40% limb loss at six months and about 20% mortality at six months. This does not always reflect the clinical practice where higher than expected survival without amputation in specialized vascular centres is achieved.

The rationale for non-operative management of CLI is based on studies showing that patients managed without surgery do not inevitably progress to limb-loss and that in large placebo-controlled trials 50% of rest pain and ulcers improve on placebo alone

The natural history of limbs affected by ischaemic ulceration is poorly understood. In a study of chronic stable leg ulcers and CLI [1] treated without revascularization and a dedicated wound management plan 52% of limb ulcers healed one year, with a 23% limb amputation rate. Therefore it is argued that patients who

cannot undergo revascularization should have a trial of careful wound management before primary amputation is considered.

Research into the functional outcome of critical limb ischaemia is in its infancy, but more and more it is realized that patient-orientated end points such as health related quality of life and functional status are essential in defining optimal treatment options for the population of patients with CLI. Therefore, the focus should not only be on the physician-orientated parameters like graft patency, limb salvage and survival. It is in fact a minority (14%) of patients who truly have the ideal surgical outcome.[2]

There is a call for new scoring systems to help predict outcomes and the management of patients with CLI such as the FINNVASC risk stratification. [3]

Spinal cord stimulation for non-reconstructable chronic critical limb ischaemia

An updated Cochrane review has concluded that in utilizing spinal cord stimulation for the improvement of limb salvage and pain relief in the setting of non-reconstructable chronic critical leg ischaemia there is evidence to favour spinal cord stimulation over standard conservative treatment alone. However, the benefits must be considered against the possible harm of relatively mild complications and the costs. [4] The problem in utilizing this relatively expensive modality is in patient selection. Using a trial period of external stimulation combined with TcpO2 assessment is suggested as a tool to select appropriate patients. [5, 6]

Prostanoids for critical limb ischaemia

Again, the most recent Cochrane review of 2010, in which 20 trials were included for review, the final conclusion was that despite positive results regarding rest pain relief, ulcer healing and amputation there was no conclusive evidence of long-term effectiveness and safety of different prostanoids in patients with CLI and suggested that further high quality studies are necessary. [7]

However, there are several studies supporting some benefit in the short term use of PGE1 (Alprostadil) [8, 9] The problem, once again, is the difficulty in predicting a response as no such predictors have been found.

Hyperbaric Oxygen therapy for chronic wounds (HBOT)

The Cochrane review (2009) assessed utilization of Hyperbaric Oxygen therapy (HBOT) for treating chronic ulcers of the lower limb (diabetic foot, venous, arterial and pressure ulcers). Five trials contributed to this review.

The conclusions were that Hyperbaric Oxygen therapy significantly reduced the risk of major amputations and may improve the chance of healing at one year in diabetic foot ulcers and therefore may be justified where a facility is available. There are several shortcomings in these studies and the results should be interpreted cautiously. [10]

A more recent study in 2010 [11] added weight to the use of Hyperbaric Oxygen therapy as an adjunct in healing chronic foot ulcers in selected patients with diabetes. In this single centre randomized double-blinded placebo-controlled clinical trial 52% ulcer healing in HBOT versus 29% in placebo was achieved in

a select group of patients with foot ulcers. Selection mainly on the basis of transcutaneous oxygen measurement is once again recommended.

Emerging therapies

Stem cell, progenitor cell and gene therapy using growth factors have shown initial promise and many early studies have recently been published in this regard. In a large collaborative randomized placebo-controlled trial of gene therapy in CLI no evidence for reduction in amputation or death was found. [12] Nor did stem cell or progenitor cell therapy reveal any clinical benefit in patients with peripheral arterial disease. [13] So for the moment these avenues remain experimental.

Intermittent pneumatic compression

In small studies some promise has been shown as an adjunct to wound care and limb salvage but large-scale studies are still required to validate the benefits. [14, 15]

Lumbar sympathectomy

A recent systematic review in the Spanish literature did not show significant difference in mortality, amputation rate and grade of intermittent claudication in the subjects treated with sympathectomy. [16] Although in several cohort studies subjective improvement has been shown for pain relief and healing of ulcers, provided that Ankle Brachial Index is > 0.3. [17, 18]

Pentoxyfylline

Pentoxyfylline has vasodilatory and haemorheological properties. However, trial assessment has not shown any benefits in patients with CLI.

Cilostazol

Potentially useful in intermittent claudication, this has however not been adequately evaluated in CLI.

Compressed air massage

In the diabetic foot initial results appear to enhance ulcer healing but further studies are needed to verify the use thereof. [19]

Recommendations

- Parenteral administration of Pentoxyfylline is not useful for the treatment of CLI (Class III recommendation / Level B evidence)

- Parenteral administration of PGE-1 or iloprost for 7 to 28 days may be considered to reduce ischaemic pain and facilitate ulcer healing in patients with CLI, but its efficacy is likely to be limited to a small percentage of patients. (Class IIb recommendation / Level A evidence)
- Oral iloprost is not an effective therapy to reduce the risk of amputation or death in patients with CLI. (Class III recommendation / Level B evidence)
- Adjunctive hyperbaric oxygen therapy may be beneficial in healing chronic foot ulcers in selected diabetic patients. (Class IIb recommendation / Level B evidence)
- Spinal cord stimulation can be considered for limb salvage in management of non-re-constructible CLI. Benefits must be evaluated against possible harm and cost. (Class IIb recommendation / Level B evidence)

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PAD – Predicting outcomes for revascularization

Nadraj G Naidoo

The revascularization options for peripheral arterial disease (PAD) are: open surgery, endovascular or hybrid procedures. The benefits of "situational perfusion enhancement", e.g. balloon angioplasty for an ischaemic ulcer, as an alternative to definitive therapy remains to be defined. Traditional endpoints of revascularization (graft patency, overall survival, amputation-free survival) need to be expanded to reflect more tangible benefits (peri-operative mortality, major adverse limb events, major adverse cardiovascular events, major reintervention rates, minor reintervention rates, independence and ambulation, operative and ischaemic wound healing, and cost efficacy). The goals of revascularization (representing the "ideal result") are: to preserve life and limb, to maintain function (independence, ambulation and employment), to relieve ischaemia (pain and wound healing) and to minimize the frequency and magnitude of repeat interventions (safety and cost-efficacay).

What has evolved from the literature is that not all patients benefit from revascularization. Patient recovery after infrainguinal bypass grafting for limb salvage in one large series [1] with a mean follow-up of 42 months revealed: overall survival of 49% (despite graft patency rate of 77% and limb salvage rate of 87%), 73% still ambulant, 70% still independent, 54% repeat operations, mean wound healing time (operative and ischaemic) of 42 months, wound non-healing rate of 22%, and overall major amputation rate of 23%. **Only 14.3% achieved "THE IDEAL RESULT".**

Traditional reporting standards systematically underestimate the expenditure of effort required to attain limb salvage. In a study by Goshima et al (2004), [2] 48.9% of patients required reoperation within 3 months, 49.3% required readmission in 6 months, wound healing exceeded 3 months in 54%, and the mean 5-year mortality was 45% - 50%. The authors concluded that tissue loss was a significant factor for re-operation and that a significant portion of patients spend the remainder of their lives attending to their ischaemic limb needs.

A large series [3] using patient-orientated outcome measures (revascularization procedure patent until wound healing, limb salvage for 1 year, maintenance of ambulation for 1 year and survival for 6 months) following lower extremity bypass and endovascular intervention for ischaemic tissue loss had an overall clinical success rate of 40.9% with better, but not significantly so, results for bypass vs. endovascular treatment (44.3% vs. 37%, p=0.06). Independent predictors of failure (irrespective of treatment) were: impaired ambulatory status at presentation, diabetes, end-stage renal failure, presence of gangrene and prior vascular intervention. The probability of failure is cumulative ranging from 35.4% if no independent factors are present to 92.8% failure rate if all 5 independent predictors were present.

Clinical presentation influences outcomes following revascularization. In one large series [4] the results were uniformly better for claudication compared to rest pain compared to tissue loss (p=0.001 for trends). It cannot be emphasized strongly enough that the blending of clinical categories when reporting on outcomes need to be aggressively discouraged.

Any risk factor, however favourable, cannot overcome a poor technical result. Technical, anatomical and procedural factors trump all others [5]. Factors independently influencing endovascular interventions are: multilevel interventions, tibial interventions, poor tibial runoff scores, TASC II lesion stratification and femoro-popliteal stenting. Factors affecting bypass grafting include: infra-inguinal prosthetic grafts, small calibre vein grafts, non-great saphenous vein grafts (GSV) and spliced vein grafts. GSV orientation does not influence patency. GSV length influences primary, not secondary, patency.

The influence of race and gender on revascularization still remains elusive. A review of US registry and PREVENT III data [6] suggest that young black females may be at highest risk. These patients are generally diabetic or may have renal impairment. Tight blood pressure control, blood sugar control and lipid lowering strategies may influence cardiovascular event rates but do not influence the natural history of lower extremity revascularization[7]. The reduced graft patencies associated with continued smoking are well described. Well-controlled, epidemiologic studies, to date, have not conclusively implicated novel biomarkers or emerging risk factors in the causal pathway of restenosis[8].

The Lower Extremity Grading System (LEGS) score has been proposed to rationalize revascularization modality or amputation in patients with PAD[9]. It utilizes 5 objective criteria (angiographic findings, clinical presentation, functional status, co-morbidities and technical factors). A total score of 0 – 9 favours surgery; 10 – 19 favours endovascular interventions and > 20 favours amputation. The LEGS score has been validated retrospectively and prospectively[9.10] and it`s utility in treatment planning needs to be encouraged.

The PIII CLI risk score[11] (for critical limb ischaemia) is derived from the PREVENT III study. It employs 5 binary variables, to predict 1 year amputation free survival, each with a weighted score: Dialysis-dependent ESRF (4), presence of tissue loss (3), age > 75 (2), haematocrit < 30 (2) and history of advanced coronary artery disease (1). A total score 0 – 3 is associated with a 1 year amputation free survival rate of 86%, whereas a total score of 8 or more is associated with a rate of 45%. The PIII CLI risk score has been internally and externally validated[11.12].

The FINNVASC risk score has been proposed to predict 30-day post-operative outcomes in patients undergoing lower extremity revascularization[13]. It is based on 4 variables; each assigned 1 point (diabetes, coronary artery disease, gangrene and urgent operation). The FINNVASC score has been validated, with a lower 30-day mortality and amputation rates associated with lower FINNVASC scores (0 – 2) compared to higher FINNVASC scores (3 – 4)[13]. The FINNVASC score has also been validated for infrainguinal balloon angioplasty in patients with CLI. Patients with a FINNVASC score 3 – 4 have a 30-day mortality of 12.8%, an amputation rate of 25.5% and a combined mortality/amputation rate of 35.9%. A recent update show that

patients with a FINNVASC score 3 – 4 with a creatinine level > 150umol/L have a 1 year amputation free survival of 53.1% (vs. 12.5% for creatinine levels < 150 umol/L).

Evidence

The evidence base comprises predominantly large single center and multicentre observational studies (Level B evidence) with a few randomised controlled studies such as the BASIL and PREVENT III studies (Level A evidence)

There are obviously areas of uncertainty and these clearly need to be defined:

- Better definition of the role of established, novel and new emerging risk factor control in the natural history of revascularization procedures for PAD.
- The role of HIV / AIDS in risk prediction models remain to be defined.
- Predictive scoring systems are still to be validated beyond a single country`s experience.
- The role of race and gender in South Africa still needs to be defined in good quality studies.

Recommendations

To improve revascularization outcomes in patients with PAD the following recommendations apply:

- More intensive treatment planning is essential prior to revascularization (Class I recommendation / Level B evidence)
- Predictive scoring systems should be utilized in decision making (Class 1 recommendation / Level B evidence)
- Revascularization procedures should be considered only in patients who are independent and ambulatory (Class IIa recommendation / Level A evidence)
- Operative and endovascular strategies are complimentary and not competitive, and treatment needs to be individualized
- Diabetics should not be automatically excluded from revascularization, but cases need to be individualized
- Anatomical and technical factors need to be considered before proceeding to revascularization
- Patients with CLI (especially tissue necrosis) need to be informed of the high mortality, morbidity and amputation rates associated with revascularization.

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PAD – Post-operative surveillance and pharmacotherapy

J Islam

Infrainguinal bypass using autogenous vein is an established treatment for leg ischaemia and prosthetic grafts are used rarely. Vein grafts are prone to develop stenosis, which may lead to bypass failure. Duplex

ultrasound DUS) scanning has been used widely for infrainguinal vein graft surveillance to identify and treat the stenotic lesions to improve graft patency and limb salvage rates. The role of DUS surveillance for infrainguinal prosthetic bypass remains controversial. Currently there is absolutely no evidence to support DUS surveillance for suprainguinal prosthetic bypass grafts.

Vein grafts

Vein graft occlusion can be categorized into three types:

1) Early (30 days): due to technical failure, vein valves leaflets or pre-existing vein abnormality
2) Intermediate (30 days to one year): due to neo-intimal hyperplasia
3) Late (>1 year): due to progression of disease in the native arteries proximal and distal to the graft

Grafts stenoses are identifiable in 25% to 30% of vein bypass grafts within the first year.

The following factors are predictive of graft failure after infrainguinal vein bypass [1]

- Demographic factors:
  - African-American race
  - Female gender
- Technical factors:
  - Vein diameter <3.5 mm
  - Non- long saphenous vein conduit
  - Vein graft length >50 cm
- Other factors:
  - Intraoperative graft revision
  - Early duplex surveillance
  - Mean graft flow velocity <45 cm/s
  - Graft stenosis with peak systolic velocity (PSV) >180 cm/s, velocity ratio >4

Graft stenosis can be divided into four categories according to the velocity criteria of duplex scanning;

Low risk grafts / Mild flow disturbance / Intermediate stenosis / Critical stenosis

Table 1: Velocity criteria of duplex scanning[2] (ABI = ankle brachial index)

Category	**PSV at the site of stenosis (cm/s)**		**Post stenotic PSV (cm/s)**	**Drop in ABI**
	Absolute value	**PSV ratio**		
Critical stenosis	>350	3.5	<40	>0.15
Intermediate stenosis	250-350	3	40-45	<0.15
Mild flow disturbance	200-250	2	>45	<0.15
Low risk grafts	<200	<2	>45	<0.15

Table 2: Correlation between the velocity criteria & degree of stenosis [1, 2]

Category	**PSV (cm/s)**	**Degree of stenosis**	**Risk**
Critical stenosis	>350	>70% with low graft flow	*Imminent failure
Intermediate stenosis	250-350	>70% with normal graft flow	*High risk
Mild flow disturbance	200-250	50-70% with normal graft flow	#Moderate risk
Low risk grafts	<200	<50% with normal graft flow	Low risk

* 40-50% likelihood of stenosis progression or graft thrombosis within 3-4 months

20-30% lesions regress, 10-20% remain stable, 40-50% progress to >70%

Table 3: Management according to the risk[1]

Category	**Treatment**	**Surveillance duplex at**
Imminent failure	Prompt repair	1-2 weeks
High risk	Elective repair in 2-3 weeks	1-2 weeks
Moderate risk	No repair	4-6 weeks, repair if progress to >70%
Low risk	No intervention	6-12 months

Optimal surveillance program

There is no sufficient data to support a specific surveillance program. Cronenwett JL et al[3] have recommended performing the 1st DUS at four weeks, then every three months for one year, every six months for two years and annually thereafter.

Mofidi et al[2] followed-up 364 grafts for a median of 23 months. They concluded that duplex at six weeks predicts the graft at risk and that these grafts only should be subjected to continued duplex surveillance. Sub-critical stenosis does not progress to higher grade and may actually regress with time. For the grafts with no flow abnormality at six weeks, the yield from continuing duplex surveillance is low and probably equivalent to clinical examination. They do not recommend duplex surveillance for all grafts.

Lane et al [4] reported a Meta-analysis of 42 papers with post-operative vein graft surveillance and their recommendations were:

- Routine post-operative duplex surveillance does not improve limb salvage rate (Grade 1 recommendation)
- Duplex at six weeks helps predict failing grafts (Grade 2a recommendation)
- Three monthly clinical review with ABI for one year (Grade 1 recommendation)

Davies et al[5] randomized 594 patients into clinical examination and duplex surveillance at six weeks, then at 3, 6, 9, 12, and 18 months. Their conclusions were:

- There was no clinical benefit or quality of life improvement associated with continuous duplex scanning
- There are increased financial costs associated with duplex scanning
- Widespread duplex scanning cannot be recommended

The TASC II document supports these findings.

Prosthetic grafts

Prosthetic grafts are not used routinely for infrainguinal bypass graft and the role of duplex surveillance of infrainguinal prosthetic bypass grafts remains controversial.

Lane et al [4] reported that there is no evidence to support routine duplex scan or ABI measurement for prosthetic infrainguinal bypass

Hoballah et al [6] followed up 102 infrainguinal PTFE bypass grafts for six years and concluded that duplex surveillance of infra inguinal PTFE bypass grafts has a low yield and is inadequate at predicting continued bypass patency.

Pharmacotherapy

Following bypass the patients should be maintained on their preoperative medical therapy for the control of angina, arrhythmia, heart failure, hypertension and diabetes. In the absence of contraindications, preoperative β-blocker and statin also should be continued.

Antiplatelet therapy:

There is enough evidence to support the use of either aspirin 81-325 mg daily or Clopidogrel 75 mg daily, though clopidogrel is more effective than aspirin in reducing the combined risk of ischaemic stroke, myocardial infarction, or vascular death in patients with PAD. [7]

Anticoagulation

There is insufficient data to support the use of anticoagulation after bypass graft.

Tangelder et al [8] followed-up 2690 patients with infrainguinal bypass grafts in a randomized trial comparing oral anticoagulation to aspirin. Their conclusions were:

- Anticoagulants improved vein graft patency
- Aspirin improved prosthetic graft patency

- Anticoagulation was associated with a doubling of the risk of major bleeding

Warfarin +aspirin vs. aspirin

The University of Florida group[9] randomized infrainguinal bypass graft patients to either warfarin and aspirin or aspirin only. They found that graft patency and limb salvage rates were higher in the combination group than the aspirin group (74% vs. 51%) and (81% vs. 31%) respectably, but there was much more bleeding in group with warfarin.

Anand et al[10] expressed a different opinion. Combination of anticoagulant and antiplatelet therapy was not more effective than antiplatelet therapy alone; rather combination was associated with increase in life threatening bleeding.

Recommendations

- Routine: aspirin (81-325 mg daily) (Grade1recommendation / Level B evidence)
- Add warfarin in selected high risk group:
  - Prosthetic below the knee bypass grafts
  - Poor runoff
  - Re-operative cases
  - Poor or alternative vein conduit

  (Grade 2b recommendation / Level B evidence)

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PAD – Post-interventional surveillance and pharmacotherapy

Ruan Botha

Patients undergoing aortoiliac and infrainguinal transluminal angioplasty for lower extremity revascularization should be entered into a surveillance program, which consists of:

- Interval history (new symptoms)
- Vascular examination of the leg with palpation of proximal and outflow vessel pulses
- Resting and, if possible, post-exercise ABI recording

Surveillance programs should be performed in the immediate post- percutaneous transluminal angioplasty (PTA) period and at intervals for at least 2 years. [1, 3]

Recommendations

- Duplex ultrasound criteria, combining peak systolic velocities (PSV) >275 cm/s and PSV ratios >3.50, should be used to predict >80% stenosis / in-stent stenosis. (Class 1 recommendation / Level of A Evidence) [4,5]
- It is reasonable to employ duplex ultrasound criteria of restenosis >70% (PSV ratio >2.4) + recurrent symptoms / worsening or increasing ulcer / no wound area reduction within 1 month to predict the need for redo angioplasty to improve long-term patency of endovascular sites (Class IIa recommendation / Level B Evidence) [6]
- The usefulness of an abnormal duplex ultrasound (PSV >180 cm/s or PSV ratios >2.0) in the first 30 days after an intervention is less well established to indicate an increased risk of amputation. (Class IIb recommendation / Level B Evidence) [3]
- Unless contraindicated, all patients undergoing revascularization for CLI should be placed on antiplatelet therapy, and this treatment should be continued indefinitely. (Class I recommendation / Level A Evidence) [1]
- Long-term antiplatelet therapy with ASA 75 to 162 mg daily should be given to patients who undergo lower-extremity balloon angioplasty with or without stenting for chronic symptomatic PAD (Class IIa recommendation / Level C Evidence).[7]
- Anticoagulation with heparin or vitamin K antagonists should be avoided in this setting (Class III recommendation / Level of Evidence: B) [8]

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PAD - Screening and follow-up

Edward J Honiball

Why screen?

There is a high incidence of peripheral arterial disease (PAD) in the at risk population. The incidence ranges from 3% and increases to 20% in the population older than 70.[1] These patients are mainly asymptomatic. Patients with PAD are at increased risk for stroke, myocardial infarction and vascular death. For every 0.1% decrease in the ankle brachial index (ABI) there is a 10% increase in the relative risk of a cardiovascular event. Furthermore, 20% of patients with asymptomatic disease will have a non-fatal cardiovascular event within 5 years. Seventy-five percent of the overall mortality during this period will be attributable to cardiovascular causes. Patients with PAD are a high risk group that needs to be identified with a view towards aggressive risk factor modification.

How to screen?

Measurement of ABI is by far the most accurate screening tool. The ABI has been validated against lower extremity contrast angiography to determine its accuracy as a lower extremity PAD diagnostic tool. Fowkes, using a comparable ABI of less than 0, 9 showed that the ABI has a sensitivity of 95% and a specificity of 100% compared to angiography to detect a stenosis of at least 50%. [2] It also has a negative predictive value of 96%. The Edinburgh claudication questionnaire is another possible screening method. It consists of 6 questions. It has a sensitivity and specificity of above 90%. [3] Clinical screening by palpation of pedal pulses and the presence of a history of claudication is too unreliable to be used as screening tools.

Who to screen?

The American Heart Association (AHA) recommends screening for patients older than 65, for patients older than 50 with a history of smoking or diabetes, and for those younger than 50 with diabetes and another risk factor. (Class I recommendation / Level B evidence). Patients with abnormal pulse examinations should also be screened. The AHA also recommends that patients with asymptomatic PAD should be identified by ABI measurement so that interventions known to decrease their increased risk of myocardial infarction, stroke and death may be offered. Smoking cessation, lipid lowering and diabetes and hypertension treatment

according to national treatment guidelines are recommended for individuals with asymptomatic lower extremity PAD (Class I recommendation / Level A evidence) [4]

The TASC II [1] document suggest ABI screening in all patients with exertional leg symptoms, patients between age 50-69 and all patients older than 70 (Class I recommendation / Level B evidence). The American Diabetes Association also recommends screening in all diabetics older than 50 and in those with diabetes younger than 50 with any other risk factor. [5]

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