EVALUATION OF CLINICAL OUTCOME POST LOWER LIMB ANGIOPLASTY IN PERIPHERAL ARTERIAL DISEASE PATIENT

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PAD	Peripheral Arterial Disease
CLI	Critical Limb Ischemia
ABI	Ankle-brachial index
IC	Intermittent Claudication
DSA	Digital Subtraction Angiography
CTA	Computed Tomographic Angiography
MRA	Magnetic Resonance Angiography
PTA	Percutaneous Transluminal Angioplasty

DEFINITION OF TERMINOLOGY

Technical success/efficacy – The efficacy of lower limb angioplasty is best on its technical success. An angioplasty is considered technically successful when recanalization of the stenosed/occluded arterial segment achieved antegrade flow into the pedal arch (Lazaris et al., 2004).

Limb salvage – successful limb salvage was defined as able to preserved talus and calcaneus after amputation at the Chopart level or distal to it. (Lee et al., 2014).

Number of stenosed vessels – it was defined as major vessels (common femoral, superficial femoral, popliteal, anterior tibialis, posterior tibialis or peroneal arteries(Lee et al., 2014)) with more than 50% stenosed.(Met et al., 2009).

Number of occluded vessels – it involved major vessels which were totally occluded (100%) (Lee et al., 2014).

Level of angioplasty – The level of angioplasty was divided into 2 groups, which was femoropopliteal group(common femoral, superficial femoral, popliteal arteries), and infrapopliteal arteries(anterior tibialis, posterior tibialis and peroneal arteries)(Pua and Wong, 2008). The distal most level was recorded when angioplasty done more than 1 level.

Complication/Safety – Safety of lower limb angioplasty was determined by complication rate. All complication that occurred within 30 days post angioplasty will be recorded. It was divided into bleeding, thromboembolic events, and medical related complication. Bleeding complication included hematomas, arteriovenous fistulae, and pseudoaneurysms that require surgical intervention. Thromboembolic events included those who need thrombolysis or amputation at/proximal to level of angioplasty (Shrikhande et al., 2011). Medical complications included bronchopneumonia, stroke/TIA, renal failure requiring dialysis and myocardial infarction (Meves et al., 2010, Conrad et al., 2011).

Abstrak

Pengenalan

Penyakit arteri periferal disebabkan oleh proses aterosklerosis atau thromboembolic yang mengubah struktur dan fungsi arteri tungkai. Kebanyakan pesakit mendapatkan rawatan selepas mereka mengalami claudication, masalah penyembuhan luka, atau gangren kaki yang telah meningkat risiko pemotongan kaki. Tujuan rawatan PAD dan komplikasinya adalah mengekalkan pengaliran salur darah dan memelihara anggota kaki yang berfungsi. Rawatan angioplasty tungkai bermula sejak tahun 2012 di Hospital Universiti Sains Malaysia. Tujuan kajian ini adalah untuk menilai keselamatan dan keberkesanan rawatan angioplasty tungkai.

Objektif

Objektif utama kajian ini adalah untuk menilai keselamatan dan keberkesanan rawatan angioplasty tungkai dalam merawat penyakit arteri periferal selama 6 bulan sehingga 1 tahun. Hasil klinikal adalah berdasarkan kejayaan dalam menyelamatkan tungkai bawah pesakit dengan mengekalkan tulang talus dan calcaneus selepas pemotongan di peringkat Chopart atau ke bawahnya. Di samping itu, kajian ini akan mengenalpasti faktor-faktor untuk menyelamatkan anggota kaki yang berfungsi.

Kaedah

Seramai 35 pesakit (37 tungkai) yang berumur antara 40 hingga 82 tahun yang telah dirawat dengan angioplasty tungkai untuk PAD dipilih dari unit Advanced Minimally Invasive Endovascular and Neurointerventional (AMIEN) Hospital Universiti Sains Malaysia. Pesakit telah dikenal pasti mengikut kriteria yang ditetapkan dengan menggunakan HUSM PACS. Semua angioplasty tungkai dirawat oleh pakar radiologi intervensi dan laporan angiogram telah disahkan. Laporan angiogram di mana data tidak mencukupi telah dikaji semula. Hasil klinikal angioplasty selepas 6 bulan dan 1 tahun dikesan melalui folder pesakit. Data yang telah dikumpul dan dianalisis dengan menggunakan perisian IBM® Sains Sosial dan perisian Pakej Statistik (SPSS).

Keputusan dan rumusan

Kadar kejayaan teknikal bagi angioplasty tungkai di pusat kami adalah 89%, tetapi anggota kaki yang selamat dalam tempoh 6 bulan dan 12 bulan adalah hanya 67.5%. Kajian ini telah menunjukkan bahawa kejayaan teknikal angioplasty tungkai tidak bersamaan dengan kadar penyelamtan anggota kaki yang berfungsi. Angioplasty tungkai adalah selamat dan berkesan dengan komplikasi serta kegagalan teknikal yang minima. Kami tidak dapat menunjukkan faktor yang mempengaruhi kejayaan klinikal angioplasty tungkai. Kajian menyeluruh dan melibatkan sampel yang lebih besar dari lain-lain negeri di negara Malaysia adalah disyorkan untuk mendapatkan data yang lebih lanjut untuk penduduk Malaysia.

Abstract

Introduction

Peripheral arterial disease is caused by atherosclerosis or thromboembolic processes that alter the structure and function of the arteries of the lower extremity. Most of the patients presented to medical personnel after they experience claudication, non-healing wound, or foot gangrene which increases the risk of amputation. The aim of treatment in PAD with its complication is to maintain the vascular patency and preserve a functional limb. Lower limb angioplasty service was started since year 2012 in this centre and referral were received from various unit in this facility (vascular, orthopaedics, plastic etc.) and other nearer health centers. The purpose of this study was to evaluate the safety and efficacy of lower limb angioplasty procedure in term of lower limb salvage.

Objective

The main objective of this study was to evaluate the safety and efficacy of lower limb angioplasty in treating peripheral arterial disease patients at intervals of 6months and 1-year interval. Clinical outcome was based on successful limb salvage where patients able to preserve talus and calcaneus after amputation at the Chopart level or distal to it. In addition, this study will help to identify the factors for successful limb salvage.

Methods

35 patients (37 lower limbs) aged between 40 to 82 years old who had been treated with lower limb angioplasty for peripheral arterial disease were selected from Advanced Minimally Invasive Endovascular and Neurointerventional (AMIEN) Unit registry in Hospital Universiti Sains Malaysia. The patients were identified according to the pre-determined inclusion and exclusion criteria by using Hospital PACS system. All lower limb angioplasty was performed by an interventional radiologist and the angiogram result prior to angioplasty was validated. Angiogram films were studied when the data provided in the previous report were insufficient. 6 months and 1-year clinical outcome of angioplasty was accessed by tracing the patient folder. The data were diligently collected and were analysed using the IBM® Social Science and Statistical Packaged (SPSS) software.

Results and conclusion

The technical success rate for lower limb angioplasty in this centre was 89%, however, the limb salvage rate at 6 months and 12 months was only 67.5%. This study had shown that the technical success of lower limb angioplasty does not equal to successful limb salvage. Lower limb angioplasty was considered a safe and efficient procedure with minimal complication and low technical failure rate. The study failed to demonstrate the factors that influence the clinical outcome of lower limb angioplasty. An extensive study involving larger samples from various regions in the country is recommended for a more conclusive and representative data for our Malaysian populations.

Chapter 1: Introduction

Peripheral arterial disease (PAD) is defined as vascular diseases caused by atherosclerosis or thromboembolic processes that alter the structure and function of the aorta, and the arteries of the lower extremity (Hirsch et al., 2006). Aetiologies that predispose to PAD include smoking, hypertension, diabetes mellitus, hypercholesterolemia, and hyperhomocysteinemia.

Majority patients with lower limb PAD are asymptomatic. Most of the patients only presented to medical personnel after they experience claudication, non-healing wound, or foot gangrene which has increased the risk of amputation. Pulse examination is one of the most critical but has limited sensitivity and specificity. A more accurate anatomic diagnosis can be made with non-invasive vascular diagnostic techniques (e.g., ankle- and toe-brachial indices (ABI). These physiological and anatomic data can be supplemented by the use of computed tomography angiogram (CTA) or magnetic resonance angiogram.

The aim of treatment in PAD with its complication is to maintain the vascular patency. It can be achieved by vascular bypass surgery or angioplasty. There is no different in limb salvage comparing both methods (Darling et al., 2014). However, there is reduced in length of hospital stay, wound complication and lower morbidity in patients treated with angioplasty (Aihara et al., 2014). Meanwhile, the patient with more advance stages of the disease may benefit from bypass surgery.

From patient perspective, limb salvage is more important compared to arterial patency as it leaves patient with a functional limb (Reekers, 2002). Amputees have significantly higher morbidity and mortality rate compares with those with functional limb. A pre-existing study showed that even the technical success rate was reported as 89% but limb salvage rate was only 82% at 6 months and 78% at 1 years post angioplasty (Pua, 2008). Hence, technically success cases in PTA does not necessarily preserve functional limb for PAD patients.

The lower limb angioplasty service in radiology department started since year 2012. To date, it has provided services to multiple disciplines from this hospital and nearby health centers. It also has established a good networking at national and international level. This study was to evaluate the safety and efficacy of lower limb angioplasty in limb salvage.

Chapter 2: Literature Reviews

2.1: Definition

Peripheral arterial disease (PAD) is a vascular disease caused by atherosclerosis or thromboembolic event that alter the structure and function of the aorta, and the arteries of the lower extremity (Hirsch et al., 2006). Other interchangeable terms for this condition include peripheral arterial occlusive disease, peripheral vascular disease, and lower extremity arterial disease (Criqui and Aboyans, 2015).

Critical limb ischemia (CLI) is the most severe form of peripheral arterial disease (PAD) where inadequate blood supply to meet the metabolic demand of the limb even at rest(Hirsch et al., 2006). Limb loss is the most feared sequelae of CLI. The TransAtlantic Inter-Society Consensus (TASC) defines CLI as persistently recurring ischaemic rest pain requiring opiates for at least 14 days, foot or toe ulceration or gangrene and ankle-brachial index (ABI)<0.40, toe pressure (TP) <30 mmHg, systolic ankle pressure <50 mmHg, flat pulse volume waveform and absent pedal pulses (Group, 2000).

2.2: Epidemiology

PAD is estimated to affect more than 200 million people globally (Fowkes et al., 2013). This prevalence is expected to increase throughout the world as the population ages, cigarette smoking persists, and increase the prevalence of diabetes mellitus and obesity (Hirsch et al., 2008).

The prevalence of asymptomatic PAD is difficult to estimate. A non-invasive method using ankle-brachial systolic pressure index (ABI) has been popularized in general population. A structured review showed that resting ABI of ≤0.90 is highly specific and accurate in identifying patient with serious stenosis ≥50% (Xu et al., 2010). PAD prevalence and incidence are both sharply age-related, rising >10% among patients more than 60 years old (Criqui and Aboyans, 2015). The Edinburgh Artery Study found that, using duplex scanning, a third of the patients with asymptomatic PAD had a complete occlusion of a major artery to the leg (Fowkes et al., 1991).

Symptomatic PAD, often referred to patient with intermittent claudication (IC) is reported in 7.5% to 33% of the patients (Schorr and Treat-Jacobson, 2013). Patients usually give a history of muscular leg pain on exercise that is relieved by a short rest. However, presence of IC does not always equate to the presence of PAD. For example, some patients with spinal stenosis can have symptoms like IC in the absence of PAD. On the other hand, patient with severe PAD may not have the symptom of IC because of present of concomitant osteoarthritis, back pain or sedentary lifestyle (Mcgrae Mcdermott et al., 2001).

In Malaysia, the only study that conducted among the high-risk population with PAD had found out that the prevalence of PAD was as high as 23%, of which only 27% were symptomatic (Amudha et al., 2003).

PAD, cardiovascular and cerebrovascular diseases are associated with common risk factors. As a result, patients with PAD are more likely to have these other disorders concomitantly and vice versa. The Global Reduction of Atherothrombosis for Continued Health registry has highlighted the high prevalence of patients with PAD who also have concomitant coronary or cerebrovascular disease (Bhatt et al., 2006). Given this association, patients with PAD is at high risk of cardiovascular events, stroke, major limb loss and death(Criqui et al., 1992).

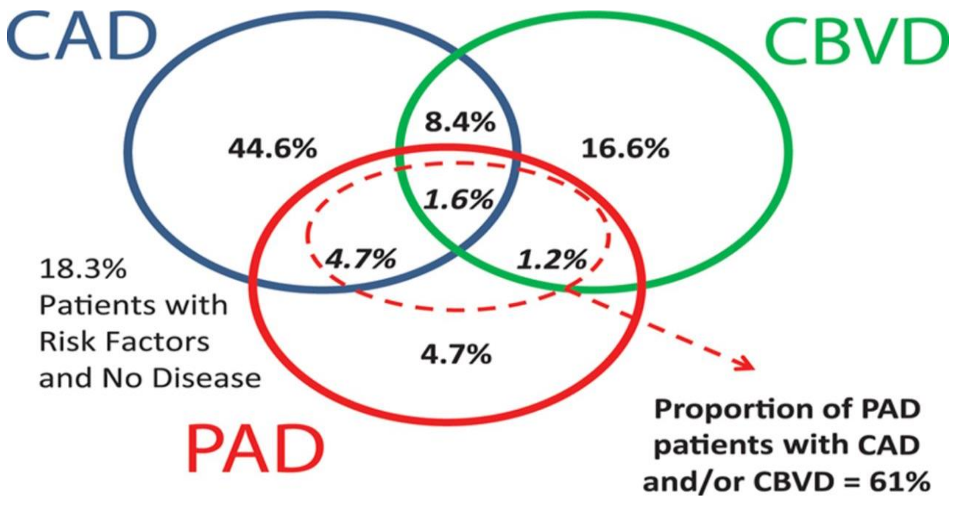

Figure 2.1: Prevalence and distribution of single-bed and polyvascular disease in reduction of Atherothrombosis for Continued Health registry. CAD indicates coronary artery disease; CBVD, cerebrovascular disease; and PAD, peripheral artery disease (Bhatt et al., 2006).

2.3: Risk Factors

2.3.1 Gender

Man posted a greater risk of PAD compare to women, especially in the younger age groups. In symptomatic PAD, the ratio of men to women is between 1:1 and 2:1. Meanwhile, in the more severe stage of the disease, this ratio increases to at least 3:1 (Norgren et al., 2007). Recent study shown that men have higher amputation but lower mortality rates than women (Lo et al., 2014).

2.3.2 Age

Increasing in age in a well-known risk factor for PAD and coronary artery disease. Its relationship can be demonstrated by Figure 2.2.

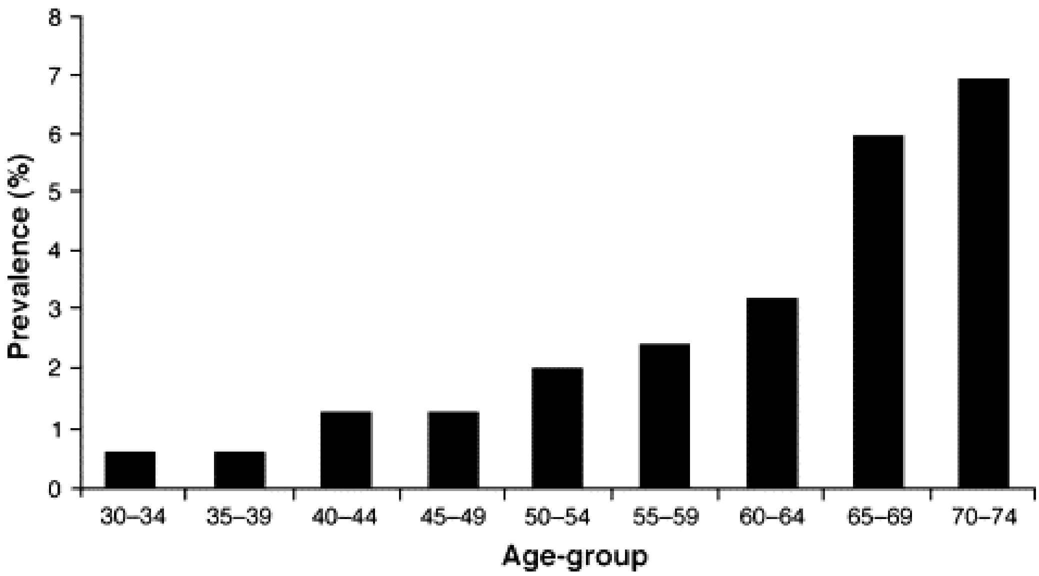

Figure 2.2 : Weighted mean prevalence of intermittent claudication (symptomatic PAD) in large population-based studies (Norgren et al., 2007).

2.3.3 Smoking

Smoking has been a long established risk factors to PAD. Its magnitude of association is greater as compared to coronary heart disease (Lu et al., 2014). Diagnosis of PAD is made approximately a decade earlier in smokers than in non-smokers. Number of cigarettes smoked has associated with the severity of PAD. The Edinburgh Artery Study found out that the relative risk of IC was 3.7 in smokers as compared with 3.0 in ex-smokers (who had discontinued smoking for less than 5 years) (Fowkes et al., 1991). This result highlight that intervention should be taken among smokers to lower mortality rate and improved amputation-free survival (Armstrong et al., 2014).

2.3.4 Diabetes Mellitus

The PAD prevalence is reported to be higher, ranging from 10-42% in diabetes patients (Tseng, 2003, Rabia and Khoo, 2007). In patients with diabetes, for every 1% increase in hemoglobin A1c, there is a corresponding 26% increased risk of PAD (Selvin et al., 2004). The disease progression in the diabetic patient is more aggressive as opposed to non-diabetics, with early large vessel involvement and distal symmetrical neuropathy leading to higher rate of major amputation (Jude et al., 2010). This is contributed by sensory neuropathy and decreased resistance to infection.

2.3.5 Hypertension

Hypertension is associated with all forms of atherosclerosis, including PAD and cardiovascular disease. However, its relative risk for developing PAD is less than diabetes or smoking (Norgren et al., 2007). Even so, European society of hypertension had emphasized the important of intensive blood pressure control to reduces the risk of cardiovascular events in PAD and diabetes patients (Mancia et al., 2013).

2.3.6 Dyslipidaemia

In the Framingham study, a fasting cholesterol level greater than 7 mmol/L (270 mg/dL) was associated with a doubling of the incidence of IC but the ratio of total to high-density lipoprotein (HDL) cholesterol was the best predictor of the occurrence of PAD (Norgren et al., 2007). Senti et al. demonstrated that high levels of serum triglycerides, very low-density lipoprotein (VLDL) cholesterol, VLDL triglycerides, VLDL proteins, intermediate density lipoprotein (IDL) cholesterol, and IDL triglycerides and lower levels of HDL are associated with higher incidence of PAD (Sentí et al., 1992). Lipid lowering medication has proved to improve pain-free walking distance and community-based physical activity in patients with intermittent claudication (Mohler et al., 2003).

2.4: Clinical Presentation of PAD

The clinical presentation of PAD depend upon the anatomical location and degree of arterial stenosis or occlusion, and range from asymptomatic to limb-threatening ischemia. Smokers, diabetes or renal insufficiency are at risk of rapid disease progression and devastating outcome (Harris, 2015). The diagnosis of PAD remains a challenge as diagnosis often being made after permanent damage, resulting in high rate of amputation (Norgren et al., 2007).

2.4.1 Intermittent Claudication (IC)

Intermittent claudication (IC), as discussed earlier is the classic manifestation of symptomatic PAD (Rose, 1962). It manifests as exercise induced lower limb discomfort that relieved by rest within 10 minutes. The symptoms are most commonly localized to the calf, but may also affect the thigh or buttocks (Harris, 2015). However, typical claudication symptoms may not occur in patients who mobilize poorly due to underlying co-morbidities (i.e. congestive heart failure, severe pulmonary disease, musculoskeletal disease).

PAD is caused by atherosclerosis that leads to arterial stenosis and occlusions in the major vessels supplying the lower extremities. Patients with intermittent claudication have normal blood flow at rest (and, therefore, have no limb symptoms at rest). With exercise, occlusive lesions in the arterial supply of the leg muscles limit the increase in blood flow, resulting in a mismatch between oxygen supply and muscle metabolic demand that is associated with the symptom of claudication (Hiatt et al., 2015).

2.4.2 Gangrene

Total loss of circulation to the lower limb will result in gangrene and eventually loss of a limb. Gangrene usually affects the digits or, in a bedridden patient, the heel (as this is a pressure point). In more severe case, gangrene may involve the forefoot. Gangrenous tissue, if not infected, can form an eschar, shrink and eventually mummify and result in spontaneous amputation. Amputation should be considered if tissue loss has progressed beyond the point of salvage, if the anesthetic risk is too high, or if functional limitations obviate the benefit of limb salvage (Aronow, 2004).

Dilemma often occurs in deciding the best amputation level of the lower limb (Sarin et al., 1991). In cases of forefoot gangrene, Transmetatarsal or Chopart's amputations had high ambulatory levels and longer durability as compared to below knee amputation (Brown et al., 2012). However, it poses the risk of poor healing of the amputation stump. Hence, this requires a multidisciplinary approach in determining the level of amputation and future rehabilitation program.

In our society, we still lack user friendly facilities in most of the public area. This has limited the amputee to mobilize independently during his/her daily activity. Rehabilitation center in this country are focused mainly in the city and is unable to meet the demand of increasing amputees.

2.4.3 Non-healing Ulcer

Optimum wound healing requires a well-orchestrated of biological and molecular events of cell migration and proliferation, and of extracellular matrix deposition and remodeling. However, this healing process is impaired in chronic wounds. Several contributory factors include reduced blood supply, angiogenesis, and matrix turnover due to infection and repetitive trauma (Falanga, 2005).

However, in those with diabetic neuropathy, the initial presentation is with a neuroischemic ulcer. Risk factors for ulcer formation include peripheral neuropathy, which leads to an insensate foot and structural foot deformity. Peripheral vascular involvement is diffuse and particularly severe in the tibial arteries, with a high prevalence of long occlusions (Graziani et al., 2007). There are significant differences between patients with and without diabetes at this stage of CLI. Importantly, PAD in patients with diabetes is usually accompanied by peripheral neuropathy with impaired sensory feedback, enabling the silent progression of the ischemic process.

While CLI is a significant risk factor for non-healing of diabetic foot ulcers, it is not the sole major factor associated with the development of diabetic foot lesions. Diabetic foot complications are the most common cause of nontraumatic lower extremity amputations in the world. The rates of recurrence of diabetic foot ulcers are very high, being greater than 50% after 3 years (Boulton et al., 2005). Hence, an integrated care approach is important with regular screening and education of patients at risk.

2.5: Diagnostic Evaluation of PAD

2.5.1 Ankle Brachial Index (ABI)

Ankle Brachial Index (ABI) is a highly sensitive (>90%) non-invasive method widely used to screen asymptomatic patients, diagnose patients with clinical symptoms, and to monitor patients who have had radiological or surgical intervention (Carter, 1968). A 10-12cm sphygmomanometer cuff placed just above the ankle and a Doppler instrument used to measure the systolic pressure of the posterior tibial and dorsalis pedis arteries of each leg (Figure 2.3).

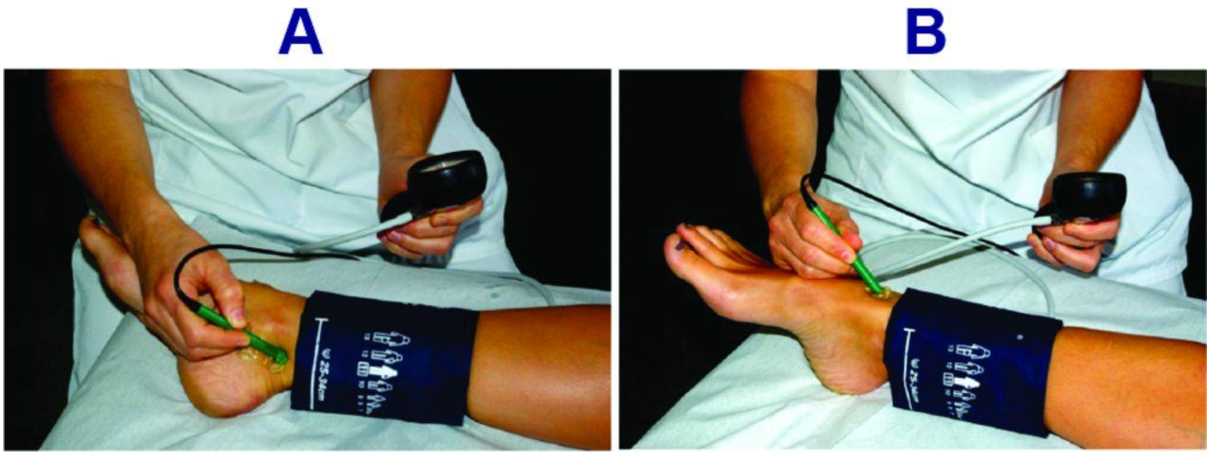

Figure 2.3 Ankle pressure measurement with a Doppler probe: posterior tibial (A) and dorsalis pedis (B) arteries (Aboyans et al., 2012)

These pressures are then normalized to the higher brachial pressure of either arm to form the ankle-brachial index (ABI). The index leg is often defined as the leg with the lower ABI.

The ABI provides considerable information as shown in Table 2.1. A reduced ABI in symptomatic patients confirms the existence of hemodynamically significant occlusive disease between the heart and the ankle. The lower the patient's ABPI, the more severe the disease, with an ABI < 0.4 indicating critical limb ischemia (Blecha, 2013). In some circumstances, the ABI result might be abnormally high, >1.4. This is related to calcification of the arterial wall in patients with medial calcinosis, diabetes mellitus, or end-stage renal disease. When vascular calcification is present the stenotic vessels cannot be detected by the ABI (Aboyans et al., 2008).

Ankle-brachial index (ABI)	**Clinical interpretation**
> 1.4	Inconclusive due to non-compressible blood vessels
1.0 – 1.4	Normal; peripheral artery disease can be excluded in most patients
0.9	Borderline; discussion with a vascular surgeon may be appropriate depending on the patient's symptoms and risk factors
< 0.9	Abnormal and diagnostic of peripheral artery disease
< 0.4	Critical limb ischemia

Table 2.1 : Clinical interpretation of the ankle-brachial index (ABI) (Kim et al., 2012)

From a systemic perspective, a reduced ABI is a potent predictor of the risk of future cardiovascular events(Kim et al., 2012). This risk is related to the degree of reduction of the

ABI (lower ABI predicts higher risk) and is independent of other standard risk factors. The ABI thus has the potential to provide additional risk stratification in patients with Framingham risk between 10% and 20% in 10 years, in that an abnormal ABI in this intermediate- risk group would move the patient to high risk in need of secondary prevention whereas a normal ABI would lower the estimate of risk indicating the need for primary prevention strategies (Ankle Brachial Index, 2008).

The ABI measurement has become a routine practice in primary care setting. Patients aged 50-69 years who also had diabetes, hypertension, dyslipidemia, smoking history, or those over the age of 70 should be screened as the prevalence of PAD in this group is up to 13% (Savji et al., 2013).

2.5.2 Ankle and Toe Pressure Measurement

The Trans-Atlantic Inter-Society Consensus (TASC)-recommended absolute toe pressure < 30 mm Hg and ankle systolic pressure <50mm Hg for the definition of chronic critical limb ischemia (CLI) (Group, 2000). Absolute toe pressure had an average sensitivity and specificity of 85% and 88% for asymptomatic limbs and 89% and 86% for ischemic limbs. A toe pressure greater than 30 mmHg was indicative of a good healing potential, and ankle pressure less than 80 mmHg was associated with poor healing (Ramsey et al., 1983). In cases with abnormality high ABI, toe systolic pressures have been recommended as they are less likely to be affected by medial calcification (Romanos et al., 2010).

Portable continuous wave Doppler units is used to measure toe systolic pressures. However, when the toes are cold, Doppler-derived toe systolic pressure are unreliable due to vasoconstriction of digital arteries. Therefore, a low toe systolic pressure may be associated with PAD or vasoconstriction of the digital arteries (Bonham et al., 2007).

2.5.3 Transcutaneous oxygen tension (tcpO2)

Transcutaneous oxygen tension measurement has become a popular noninvasive tool and can be applied to all patients irrespective of Doppler signals, non-compressible vessels, or painful lesions. Tcpo2 helps to predict successful healing with accuracy and is useful in addition to clinical judgment in the selection of optimal amputation level (Ruangsetakit et al., 2010). In patient without any co morbidities, wounds are able to heal when the tcpo2 is >40 mmHg (Arsenault et al., 2011). Meanwhile, a higher value is likely needed in patient with diabetes or other comorbidities.

TcpO2 following exercise is sensitive in detecting the presence of peripheral arterial disease as it solely determined by stenosis of perfusing arteries. However, its sensitivity falls in a resting limb as it is affected by multiple factors (Ueno et al., 2010).

2.5.4 Treadmill Exercise Test

Treadmill exercise testing with and without pre-exercise and post-exercise ABIs helps differentiate claudication from pseudoclaudication in patients with exertional leg symptoms (Hirsch et al., 2006). Treadmill exercise testing may be useful to diagnose PAD with a normal resting ABI but a reduced post-exercise ABI. Treadmill exercise testing may objectively document the magnitude of symptom limitation in patients with claudication.

2.6 : Imaging Technique

Imaging helps to identify an arterial lesion that is suitable for revascularization with either an endovascular or open surgical technique. The current available imaging options are digital subtraction angiography, duplex ultrasound, computed tomography angiography and magnetic resonance angiography. Potential side effects and contraindications should be considered in choosing the imaging modality.

2.6.1 Color-assisted duplex ultrasonography

Color-assisted duplex imaging is a noninvasive method and has been proposed as an attractive alternative to angiography. In addition to being completely safe and less expensive, duplex ultrasonography can provide most of the essential anatomic information in an expert hand (Jandaghi et al., 2013). It has high sensitivity and specificity of 90% to detect hemodynamically significant lesions (>50% stenosis or occlusion) (Jandaghi et al., 2011).

2.6.2 Digital Subtraction Angiography (DSA)

Precise mapping of the affected lower limb arterial tree is the key for success revascularization. DSA utilizes computerized x-ray imaging equipment for image acquisition and subtraction, together with the used of highly radiosensitive contrast media, allow visualization of major blood vessels. It has traditionally been favored due to its ability to provide the operating surgeon with a precise visual display of the vascular system (Brody, 1982).

DSA are better in visualizing the collateral flow comparing to computed tomographic angiography (CTA) as the caliber of these vessels are typically small often reaching the limits of spatial resolution on CTA (Albrecht et al., 2007).

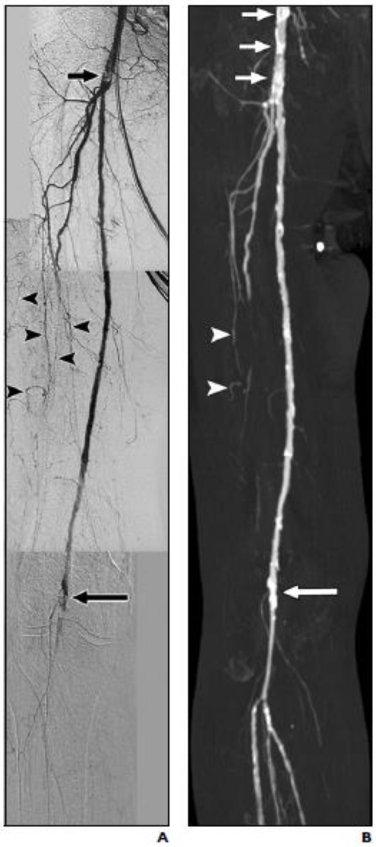

Figure 2.4 : Digital subtraction angiography (DSA) and CT angiography (CTA) of right leg in 51-year-old woman with critical lower leg ischemia.

A, DSA image (posteroanterior projection) shows grade 3 stenosis of common femoral artery (short arrow) and grade 3 stenosis of popliteal artery (long arrow) with grade 1 collaterals at thigh (arrowheads). Below-knee arteries are not visualized.

B, Corresponding CTA maximum-intensity-projection (MIP) reconstruction image shows extensive calcification of common femoral artery (short arrows) and area of calcification of popliteal artery (long arrow). Based on MIP reconstruction, it is unclear whether these calcifications cause stenosis. Grade 1 collaterals (arrowheads) are shown, but they are less extensive on CTA than on DSA. CTA depicts all three arteries of proximal lower leg that cannot be seen on DSA and shows them to be patent. (Albrecht et al., 2007)

Radiosensitive contrast media has become the main drawback of DSA. It leads to contrast induced nephropathy, especially in patient with preexisting renal insufficiency, diabetes mellitus, impaired liver function, and cardiovascular disease. The reported complications that associated with DSA are hematoma, anaphylaxis, arterial injury, and renal failure (Katsanos et al., 2014).

2.6.3 Computed tomographic angiography (CTA)

Lower limb CTA is increasing used to locate and detect the degree of stenosis of PAD. The image can be reconstructed and viewed in 3-dimensional (3D), thus is useful even in assessment of an early developmental of PAD.

Earlier, single detector technology allowed only 1 cross-sectional image to acquire at a time and thus limits the length of the imaged vessels. Advancement in new multi-detector technology can acquire as few as 4 and as many as 64 simultaneous cross-sectional images. This has permitted CTA to be performed faster, with less contrast material, and greater details (Cernic et al., 2009).

Several studies on CTA reported the sensitivity and specificity rates of around 98% in detecting PAD (Laswed et al., 2008, Schernthaner et al., 2008). However, overstaging may occur when a calcified patent vessel is mistaken for an occluded vessel due to the blooming effect of the calcium (Sarwar et al., 2008).

CTA has several potential advantages over MRA. Patients with pacemakers or defibrillators may be imaged safely with CTA. Metal clips, stents, and prostheses usually do not cause significant CTA artifacts. Time to acquire images is significantly faster with CTA than with MRA. Hence, claustrophobia is far less of a problem. However, CTA requires iodinated contrast, which may be nephrotoxic in azotemic patients (Kim et al., 2010).

2.6.4 Magnetic Resonance Angiography (MRA)

In many centers, MRA has become the preferred imaging technique for diagnosis and treatment planning in patients with PAD, especially those with nephropathy (Hodnett et al., 2011). MRA is relatively safe and able to provide rapid high-resolution three-dimensional (3D) imaging of the entire abdomen, pelvis and lower extremities in one setting. The 3D nature of magnetic resonance imaging implies that image volumes can be rotated and assessed in an infinite number of planes (Chan et al., 2010).

The high magnetic field strength in MRA excludes patients with defibrillators, spinal cord stimulators, intracerebral shunts, and cochlear implants etc (Dill, 2008). Metallic stents within segments of peripheral vessels may produce a susceptibility artifact and impair evaluation of these segments. Newer magnetic resonance compatible stent allow artifact free images (Buecker et al., 2002).

MRA techniques can be gadolinium contrast-based (contrast-enhanced MRA or CE-MRA) or non-contrast-based (time-of-flight techniques). In general, CEMRA techniques utilize a moving table (floating table) approach and sequentially following a bolus of contrast through multiple stations extending from the abdomen to the feet (Kruger et al., 2002). A meta-analysis of 32 studies found that CE-MRA has a sensitivity and specificity of >95% in diagnosis segmental steno-occlusion lesion (Menke and Larsen, 2010). Gadolinium contrast agents can lead to potentially life-threatening nephrogenic systemic fibrosis in patients with renal failure (Abu-Alfa, 2011). 3D Gd-enhanced MRA improves diagnostic performance compared with 2-D MRAv (Koelemay et al., 2001).

MRA is generally used in young patients and in patients with contrast allergy or renal insufficiency. MRA should not be used in patients with pacemaker and other implants. MRA is not effective in unstable and uncooperative patients.

2.7: Treatment

Limb salvage is the ultimate goal in treating patients with PAD. Studies have also shown that the most important aspect of life quality for PAD patient is actually limb salvage as compared to other markers such as resting pain and ulcer healing (Faglia et al., 2005).

The lower extremity amputation prevention (LEAP) is a comprehensive program aimed at reducing lower extremity amputations in individuals with PAD and diabetes mellitus (Tan et al., 2011). The main aims of LEAP are to:

1) detect and treat early chronic ischemic lesions

2) offer alternatives to amputations in surgically untreatable patients,

3) preserve the remaining limb after major amputation

4) reduce the global risk for cardiovascular disease.

A multidisciplinary approached from various levels is needed to achieve this. It starts from risk factors modification and patient education at the primary healthcare level, up to active treatment of critical limb ischemia (CLI) at tertiary institutions (Sumpio et al., 2010)