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Below The Knee Endovascular Intervention in Ischemic Diabetic Foot in Kurdistan Region of Iraq.

A thesis Submitted to the Council of Collage of Medicine -University of Sulaimani as Partial Fulfillment of the Requirements for the Degree of Doctor in Philosophy in Interventional Radiology.

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We certify that this thesis was prepared under our supervision at Departments of Medicine &General surgery , College of Medicine-University of Sulaimani as partial fulfillment of the requirements for the Degree of Doctor of Philosophy in Interventional Radiology.

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This Thesis is dedicated to

The soul of my father ….

My Family …..

My thanks is endless to my family member: dear Mom, lovely husband, sisters & brother sweat kids Ania, Zhir &Avi for their patience for not being their when they need me.

My Colleagues…..

To all those who take part in scientific development & education……

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Coronary Care Unit &Imaging Centre staffs in Sulaimani Teaching Hospital.

Abstract

Background: Management of ischemic diabetic foot (DF) due to infra-popliteal arterial disease is challenging and controversial. Observation, bypass surgery and endovascular intervention are the three available options. Outcome of percutaneous transluminal angioplasty (PTA) vs. conservative therapy is evaluated in this prospective study from Sulaymaniyah, Iraq.

Aim: To evaluate the outcome of endovascular intervention namely PTA in patient with ischemic diabetic foot ulcers.

Methodology: Over 2 years starting at Jan 2018, 40 patients with ischemic DF underwent PTA and compared with a control group (n=78) of ischemic DF managed conservatively. Besides clinical assessment all patients underwent Doppler ultrasonography (DUS) and CT angiography (CTA) while conventional angiography was reserved for PTA group. Patients who fulfilled the standard angiographic findings underwent standard PTA and their outcomes were compared with the control group.

Results: Mean age was 64; 70% (n=28) were males with a male: female ratio of 2.3: 1. Renal function was impaired in (n=11, 27.5%) and 7 (17.5%) patients were smokers. The commonest clinical presentation was non-healing ulcers (n=39, 97.5%) and most patients (n=39, 97.5%) had Fontaine IV and Rutherford V-VI grades. Most lesions were anatomically complex; TASC C and D types, Graziani class ≥ 4 (75%), long segment (n=28, 70%) and chronic total occlusion (CTO) (n=26, 65%). Success rate was (n=38, 95%) and no patient died. Ulcer healing was higher (67.5% vs. 34.6%) and ulcer recurrence was lower (20% vs. 47.4%) in PTA group but amputation rate wasn't significantly different (12.5% vs. 12.8%) ($p<0.05\%$).

Conclusion: although amputation & death rates were not significantly different endovascular intervention achieved better ulcer healing in ischemic diabetic foot compared to the conservative approach.

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3D	Three dimensions
ABI	Ankle brachial index
ATK	Above the knee
BASIL	Bypass versus angioplasty in sever ischemia of the limb
BTK	Below the knee
CLI	Critical limb ischemia
CRI	Chronic renal insufficiency
CRP	C-reactive protein
CTA	Computed tomo-angiography
CV	Cardiovascular
DFU	Diabetic foot ulcer
DUS	Doppler ultrasound
DSA	Digital subtraction angiography
DP	Dorsalis pedes
IWGDF	International Working Group on the Diabetic Foot
LEAD	Lower extremity artery disease
MI	Myocardial infarction
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
NICE	National Institute For Clinical Excellence
PAD	Peripheral artery disease
PVR	Pulse volume recording
PN	Peripheral neuropathy
PT	Posterior tibial
TASC	Trans Atlantic inter-society consensus
TBI	Toe brachial index
UK	United Kingdom

CHAPTER ONE

LITERATURE REVIEW

Introduction:

The dramatic increase in the worldwide prevalence of type2 diabetes mellitus (DM) has resulted in an inevitable rise in diabetes-related complications.[1] Diabetic foot (DF) is one of them which is chronic and highly disabling complication of diabetes leading to limb loss and diabetes mellitus is most common cause of non-traumatic amputation. The prevalence of peripheral arterial disease (PAD) is high in diabetic patients which is the clinical term describing stenosis or occlusion of upper- or lower-extremity arteries due to atherosclerotic or thromboembolic disease.[2,3]

PAD in diabetic patient commonly associated with peripheral neuropathy (PN), can be found in 50% of cases of DF, The presence of PN may mask the typical clinical symptoms of PAD, such as claudication and pain at rest, and so an ulcer that fails to heal and/or more or less extensive gangrenous areas of the foot may be the first signs of previously unknown PAD. [3]

Amputation is a largely preventable complication of diabetes and >85% of major amputations in patients with diabetes are preceded by foot ulceration.[1] Whilst the number and incidence of amputations have fallen in an ageing population without diabetes, those in patients with type2 diabetes have risen in some countries.[4] Many PAD diabetic patients are not revascularised due to lack of technical expertise or, even worse, negative beliefs because of poor experience.[3]

These patiens are restricted in physical function & may have depression & significant portion of patients undergoing major amputation do not have vascular evaluation in the year before their amputation.[5]And many patients with CLI experience prolong waiting lists before any intervention.[6]

This despite the progress obtained in the techniques of distal revascularisation that nowadays allow reopening distal arteries of the leg and foot. High rate of(especially cardiovascular) co-morbidities means that attention should not be exclusively focussed on the foot with an ulcer, but takes into account the patient as a whole and the various clinical conditions that can jeopardise his or her life and have a negative impact on treatment of DF itself.[3]

Diabetic Foot lesions carry high morbidity and mortality and represent the most common cause of hospitalization in patients with diabetes.The lifetime risk of foot ulceration in patients with diabetes lies between 15% and 25%.[7,8] The risk of a person with diabetes undergoing a lower extremity amputation is estimated to be 23 times that of a person without diabetes.[9]

Another aspect that needs to be considered is the complexity of the manifestations of DF, which include ischaemia, neuropathy, biomechanical problems, infection, and wound healing. This complexity practically rules out any single specialist approach and requires the assistance of a multidisciplinary team capable of guaranteeing functional rehabilitation of the foot and, whenever possible, optimising the patient's clinical condition. The team should include a diabetologist, a vascular surgeon, an interventional radiologist, and an orthopaedic surgeon, a specialist in infectious diseases,wound specialist, a cardiologist, an orthopaedic technician and a podiatrist. A multidisciplinary approach has proved to be the winning formula in many published experience.[10,11]

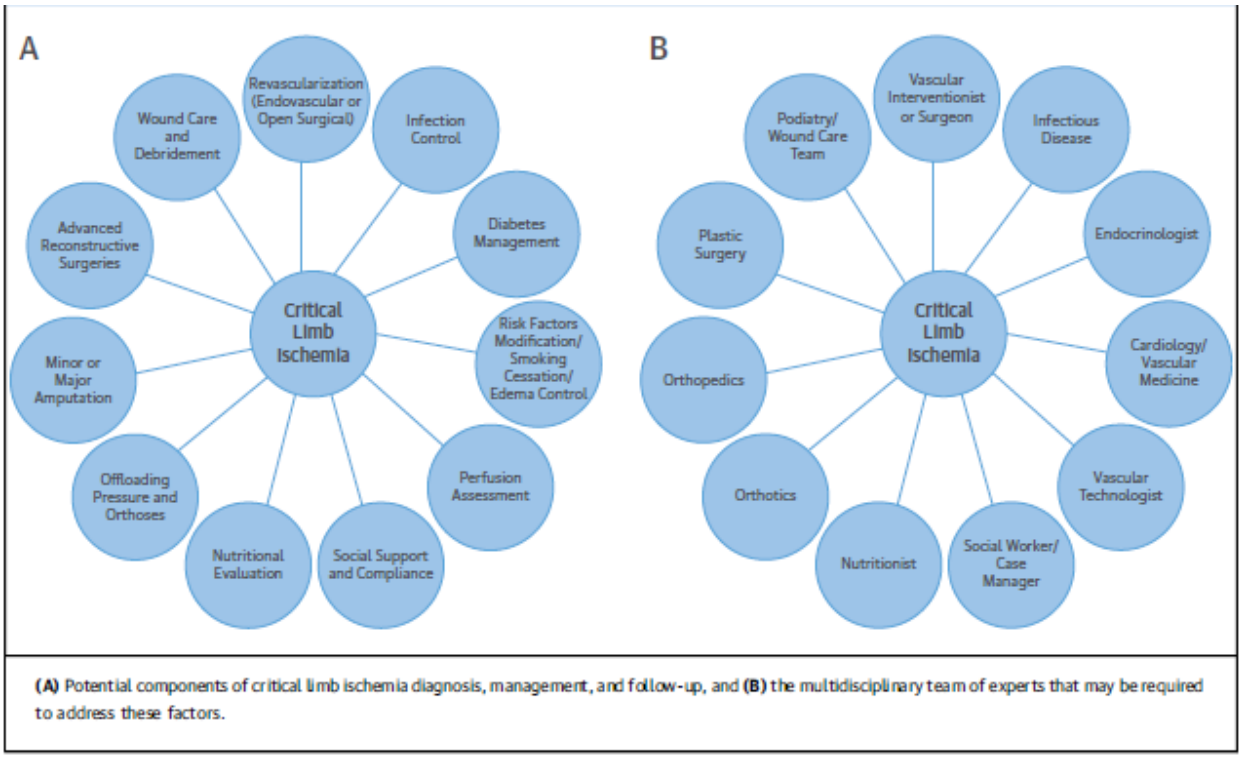


Figure1.1 Potential Components and Required Specialists for the Diagnosis and Treatment of Critical Limb Ischemia. [(12)]

The high prevalence of PAD in diabetic patients in general is due to the nature of the disease itself, but other factors such as the longer average life span, longer disease duration and in diabetics with end-stage renal failure the role of dialytic treatment should not be underestimated. This indicates the burden that the complication may have for individual patients and society as a whole, given its chronic nature and the relatively frequent recourse to major lower limb amputations. However, it is worth pointing out that, despite the progressive increase in the prevalence of PAD in diabetic patients, the number of major amputations has decreased because of the growing use of distal revascularization.[(3)]

Aim To evaluate the effect percutaneous transleuminal angioplasty short out comes in patient with ischemic diabetic foot ulcers .regarding limb salvage , wound healing &prevention of their complications .

Litrechure review:

1.1 Pathology in DFU

The aetiology of DFU is multifactorial and involves a complex interplay between distal polyneuropathy (motor, sensory and autonomic), abnormal foot anatomy, functional changes in the microcirculation and PAD. The pathway to ulceration typically follows abnormal loading or trauma of the painless neuropathic foot, which may be poorly perfused due to PAD, rendering it less able to heal. Both ulceration and infection in the foot will increase the demand for oxygen and, as such, vascular intervention may be required to achieve healing in cases where objective measures of perfusion suggest that PAD is only of mild severity. The wound repair process may be further impaired by virtue of various biological factors inherent to diabetes, including impaired humoral immunity and abnormal inflammatory response.[12,13] In patients with type 2 diabetes these changes occur in younger age group than non diabetic with PAD & then this lead to capillary hypoperfusion, probably further impairing wound healing.[14] Furthermore, the development of collateral vessels is impaired in patients with diabetes which are also affected by stenosis.[3,15]consequently arterial occlusions may result in more severe perfusion deficits in those with diabetes compared to those without diabetes.The distribution of PAD in patients with diabetes is characteristically distal and diffuse, multisegmental its rapid progression and prevalently bilateral topographical expression, with a greater prevalence of crural disease and long arterial occlusions rather than stenosis.The distribution of PAD in diabetes may relate to the presence of somatic neuropathy, which has been implicated in the development of medial arterial calcification.[3,16] This Large calcium burden is known to increase the risk of embolization with intervention, increase difficulty of crossing total occlusions, and increase the incidence of restenosis in treated segments.In addition, severe medial calcinosis makes standard measures of severity of disease unreliable and complicates the follow-up of lesions.[16]

1.2 Correlation Between Pathophysiology and Evolution of the Disease.

Patients with an ABI <0.5 have a 2-fold higher risk of requiring revascularization surgery or major amputation as compared with patients whose Ankle Arm Index (AAI) is >0.5. The systolic blood pressure (SBP) measured at the ankle is also a predictive factor of greater disease progression for patients with values <50 mm Hg. Nevertheless, it is important to note that patients with diabetes, due to their high prevalence of calcification in distal vessels, may have abnormally high SBP values in the malleolar region, with indices even above 1 in the presence of PAD. These 2 parameters, therefore, have limited validity in noninvasive evaluation. Individual analysis has shown that the presence of diabetes mellitus multiplies by 4 the risk of critical ischemia, smoking multiplies it by 3, and an ABI <0.5 does so by 2.5 times. Accordingly, it is of the utmost importance to make the earliest possible diagnosis of arterial disease in order to initiate treatment and modify the risk factors, thereby reducing the risk of disease progression.[(17)]

1.3 Prognosis

About 27% of diabetic subjects with PAD experience progressive disease in the following 5 years, and 4% undergo major amputation; about 20% manifest a cardiovascular event (myocardial infarction or stroke). The prognosis of diabetic patients with chronic limb threatening ischaemia (CLTI) is even more serious as 30% may require a major amputation and 20% die of cardiovascular disease within 1 year. Non-revascularisation of PAD diabetic patients is an independent predictive factor of amputation and also an independent determinant of poor survival.The risk of co-existing ischaemic heart disease in diabetic patients with PAD is 50%.The simultaneous presence of silent and non-silent myocardial ischaemia is significantly more frequent in diabetic than in nondiabetic subjects,which means that all diabetic patients with PAD should undergo diagnostic investigations of the coronary arteries in-order to identify any previously unknown coronary disease.[3,16]

Diabetic patients with PAD have frequently a concomitant chronic renal insufficiency (CRI) requiring haemodialysis, which means that the vascular damage is more severe and progresses more rapidly than in diabetic patients without end-stage renal disease that is very difficult to treat.[3,16]

1.4 Diagnosis of PAD:

Identification of PAD in patients with diabetes may be difficult because symptoms and signs are frequently masked by co-existing distal symmetrical polyneuropathy.Furthermore, most patients with DFU present to primary care, podiatry or internal medicine clinicians who are not experts in the diagnosis of PAD. IWGDF guidelines suggest that,in addition to a thorough history for symptoms of arterial insufficiency, all patients with a diabetic foot ulcer should undergo hand-held Doppler evaluation of both pedal pulses, measurement of ABI and, in cases of diagnostic uncertainty, measurement of toe-brachial index (TBI) or transcutaneous pressure of oxygen (TcPO2).[18]Importantly these screening tools, whilst highly sensitive in the nondiabetic population, may be less efficacious in diabetes, especially in the presence of peripheral and autonomic neuropathy.[16]

This complexity practically rules out any single specialist approach and requires the assistance of a multidisciplinary team.A multidisciplinary approach has proved to be the winning formula in many published experiences.[3]

1.4.1 Diagnostic approach of PAD

1. Clinical history: Personal and family clinical history should always be assessed. Family history includes coronary artery disease, cerebrovascular disease, and aortic aneurysm. Lifestyle habits, dietary patterns, smoking ,walking performances and physical activity need to be systematically interrogated.[19]
2. Those patients with signs and symptoms of PAD, including claudication which may be absent due to PN , rest pain , absent foot pulses, and more frequently characterised by the ischaemic lesions and gangrene typical of more advanced disease stages. For this reason, the current clinical classifications of PAD are not really applicable in the

presence of diabetes and foot ulcers, and it is more appropriate to use the University of Texas Wound Classification System. [20]

3. Individuals with carotid bruits have twice the risk of MI and CV deathas compared with those without. Interarm blood pressure (BP) asymmetry (≥15mmHg) is a marker of vascular disease risk and death.A femoral bruit is an independent marker for ischaemic cardiac events.[19,21]
4. Diagnostic methods` for PAD
    a. Ankle-brachial index (ABI) and toebrachial (TBI) indices or transcutaneous pressure of oxygen (TcPO2) are non-invasive tools useful for screening whilst highly sensitive in the nondiabetic population, may be less efficacious in diabetes, especially in the presence of peripheral and autonomic neuropathy.[16,18] they may not be obtainable in many patients due to calcified digital vessels or missing digits from prior amputation.[19,22]
    b. Duplex ultrasonography (echo Doppler) is considered to be the most important and, in many centres, is the only technique used before revascularisation procedures. One of its main advantages is that it provides information concerning the haemodynamics of the obstructive arteriopathy and the state of run-off. allows the morphological/functional study of the vascular tree .[19] Monophasic Doppler signals, ABI <0.9 or TBI <0.7 should be referred for imaging of the vascular tree and to consider revascularisation options as part of an interdisciplinary approach. Guidelines published by the National Institute for Clinical Excellence (NICE) in the UK recommend offering duplex ultrasound as first-line imaging to all people with PAD where revascularisation is being considered.[16] Evaluation of the below-knee vessels is particularly important in patients with diabetes and the sensitivity of DUS for

detecting a high-grade stenosis > (50%) are 90 % for the anterior and posterior tibial arteries and 82% for the peroneal artery.Although DUS is non-invasive and relatively inexpensive compared with other imaging modalities, its reliability is dependent on operator expertise.The evaluation of belowknee vessels with haemodynamic parameters alone does not provide adequate information for preoperative planning, but may serve as a useful and intermediate adjunct to other, more invasive modalities. More recent techniques, such as flow imaging or live three-dimensional (3D) echography, as well as the use of ultrasound contrast agents, further improve DUS performances, although their use is still limited. DUS can detect subclinical artery disease**.** [(19)]

c. Imagings such as magnetic resonance angiography (MRA) or computed tomography angiography (CTA) are necessary. It needs to be underlined that the American College of Cardiology/American Heart Association guidelines recommend the use of MRA rather than CTA because it allows better definition and leads to fewer technique-related risks.[(23)] The use of CTAand MRA has made it possible to obtain repeatable and panoramic images that not only assist the planning of the revascularisation procedure but also allow the simultaneous evaluation of any other area of vascular disease in just a few minutes.[(24)] However, they have the drawbacks of being expensive and not widely available.Advantages of CTA include rapid non-invasive acquisition, high resolution and 3D reformatting. Similar to DSA and MRA, CTA displays a ‘roadmap’ of the vascularization, essential for determining interventional strategies (lesion localization and severity, upstream/downstream status). The drawbacks of CTA include the lack of functional and haemodynamic data, the use of the iodinated contrast media: these

may be nephrotoxic in this category of patients, especially as it is followed by endovascular treatment using arteriography, which uses the same type of contrast. The benefit of acetylcysteine to limit nephrotoxicity is uncertain. Recent studies have suggested that statins or sodium bicarbonate could prevent contrast agent nephrotoxicity. [25,26]

Magnetic Resonance Angiography (MRA) is used for peripheral artery imaging using contrast (i.e. gadolinium) and non-contrast techniques (i.e. phase contrast and time-offlight sequences).These latter techniques have inferior resolution and are susceptible to artefacts, limiting their interpretation.They are avaluable alternative for use in patients with mild to moderate CKD. Compared with CTA, MRA does not need iodine contrast and has higher soft tissue resolution; however, motion artefacts are more frequent. Contraindications include pacemakers and implantable cardioverter defibrillators (ICDs) [except magnetic resonance imaging (MRI)-conditional and compatible pacemakers, ICDs and leads], claustrophobia and severe CKD.In the latter case, the risk of nephrogenic systemic fibrosis following gadolinium administration should not be underestimated. [19] Main MRA limitations are related to venous contamination of the foot, the lack of information concerning the type of plaque causing the stenosis/ obstruction (calcified, lipid or fibrous), the absence of signal in the presence of ferromagnetic artefacts (metal stents and arthroprostheses) , the occurrence of stent artefacts in MRA limit its use for the detection of in-stent stenosis.[16]

d. conventional arteriography is never considered a diagnostic technique per se, however it is the gold standerd imaging modality it represents the first step in endovascular therapy; it can only be

proposed for diagnostic purposes in cases in which the other methods have failed to define the extent and topography of stenotic/obstructive arterial disease.The advantage of allowing simultaneous endovascular intervention.Its main drawback in patients with diabetes and a high prevalence of renal insufficiency is the risk of contrast-induced nephropathy.As a precaution, patients with renal impairment should receive peri-procedural intravenous volume expansion and metformin should be stopped prior to DSA as it may cause a lactic acidosis. [27]

Or a substitie is **Carbon dioxide (CO_2) which** is an excellent negative contrast agent . Due to its high solubility rate and rapid diffusibility via the lungs, CO2 is safe for intravascular usage and it is an inexpensive, highly compressible, and low viscosity gas. Toxicity is not an issue when used correctly. It does not mix with blood and hence cannot be diluted, it pushes away the blood column within the vascular bed.Its very low viscosity allows injection via small (22G) needles/3F catheters even when there is a guidewire in situ and results in filling of the smallest branches regardless of blood flow rate and degree of stenosis. It is indicated in cases of

- allergy to iodinated contrast media
- poor renal function
- superior in:
  - detection of bleeding
  - opacification of small collaterals in occlusive disease
  - arteriovenous (AV) shunting in tumors

Contraindications

- **absolute**
  - CO_2 has potential neurotoxic and cardiotoxic effects hence it should not be used for cerebral or coronary artery (above diaphragm aorta) angiograms.

- prone position injection should be avoided due to possible spinal ischemia
  - arterial limb of dialysis AVF
- **relative**
  - COPD patients
  - patients on nitrous oxide anesthesia: may increase the volume of the CO2 bubbles leading to pulmonary artery vapor lock which may be fatal. [28]

e. Exercise test: In patients who complain of symptoms only on exercise, it is rewarding to examine the leg following an exercise challenge. This can be done quite simply in the consulting room or by asking the patient to walk up and down the corridor (or on a treadmill if available). Even elderly patients find it easy to exercise the calf muscle by a repeated 'tiptoe' while leaning on the couch. The patient returns to the couch so that the pulses can be examined immediately after exercising for 1 minute. More important, the post-exercise ABPI is measured.[19]

Table1.1 Lower extremity arterial disease diagnosis. [19]

LEAD diagnosis		
Screening for LEAD is indicated on a yearly basis, with clinical assessment and/or ABI measurement.	I	C
Patient education about foot care is recommended in patients with DM, and especially those with LEAD, even if asymptomatic. Early recognition of tissue loss and/or infection, and referral to a multidisciplinary team,[c] is mandatory to improve limb salvage.	I	C
An ABI <0.90 is diagnostic for LEAD, irrespective of symptoms. In case of symptoms, further assessment, including duplex ultrasound, is indicated.	I	C
In case of elevated ABI (>1.40), other non-invasive tests, including TBI or duplex ultrasound, are indicated.	I	C
Duplex ultrasound is indicated as the first-line imaging method to assess the anatomy and haemodynamic status of lower extremity arteries.	I	C
CT angiography or magnetic resonance angiography is indicated in case of LEAD when revascularization is considered.	I	C
In case of symptoms suggestive of intermittent claudication with normal ABI, a treadmill test and post-exercise ABI should be considered.	IIa	C
In patients with DM with CLTI with below-the-knee lesions, angiography, including foot run-off, should be considered before revascularization.	IIa	C

I,II class of recommendation

C level of evidence

1.5 General Risk factors for PAD

Sex

The prevalence of PAD, both symptomatic and asymptomatic,is greater in men than in women,especially in young persons.At very advanced ages almost no differences exist between the two genders .[17]

Age

Age is the main marker of PAD risk.The estimated prevalence of intermittent claudication in persons aged 60-65 years is 35%. However, the prevalence in persons 10 years older (70-75 years) rises to 70%.[17]

Smoking

Some studies have found a stronger association between tobacco abuse and PAD than between tobacco abuse and ischemic heart disease. Moreover, the heavier smokers not only have a greater risk for PAD, they also have the more severe forms that cause critical ischemia.Cessation of smoking is associated with reduction risk of PAD and, although the risk for PAD in ex-smokers is 7 times greater than in non-smokers, the risk in active smokers is 16 times greater.Additionally; the permeability of both venous coronary bypass and prosthetic grafts is reduced in patients who smoke.The rates of amputations and mortality are also greater in smokers.[17,23]

Diabetes

Diabetes is not only a qualitative risk factor; it is also a quantitative risk factor as each 1% increase in glycosylated hemoglobin is associated with a 25% increase in the risk for PAD.The involvement of distal vessels in the extremities is typical and, together with microangiopathy and neuropathy, which imply a poor response to infection and a specific healing disorder, diabetes is associated with a risk of amputation 10 folds that of non-diabetic patients.Of importance is the fact that diabetic patients may have abnormally

high pressure values in the ankle and,consequently,have a false negative evaluation of the ABI.[17,29]

Hypertension

The importance of hypertension as a risk factor is less than that of diabetes or smoking.Nevertheless, the risk for PAD is considered to be double in patients with hypertension as compared with controls**.** [17]

Dyslipidemia

Various epidemiologic studies have shown that raised levels of total cholesterol and low-density lipoprotein cholesterol (LDL-C) and reduced levels of high-density lipoprotein cholesterol (HDL-C) are associated with greater cardiovascular mortality.Independent risk factors for the development of PAD are total cholesterol, LDL-C, triglycerides, and lipoprotein (a). The Framingham study found that the ratio of total cholesterol to HDL-C was the best predictor of PAD. Treatment of hyperlipidemia has been shown to reduce the progression of PAD and the development of critical ischemia.[17]

Hyperhomocysteinemia

Alterations in the metabolism of homocysteine are an important risk for arteriosclerosis and, especially, for PAD. Up to 30% of young patients with PAD have hyperhomocysteinemia. The mechanism of action could be double: on one hand, it promotes the oxidization of LDL-C and, on the other hand, it inhibits the synthesis of nitric oxide.[17]

Inflammatory Markers

Endothelial dysfunction, Progressive micro-vascular degeneration are the major factor in progression of diabetic vascular complications.

Adrenomedullin (AM) and basic-Fibroblast growth factor (b-FGF) are strongly correlated with angiogenesis in vascular diseases.

The rise of AM in diabetic PVD may be a consecutive and compensatory vasculo-protective effect as its angiogenic and anti-inflammatory properties act to relief the endothelial insult .Down expression of b-FGF may be a predisposing factor for micro-vascular derangement.[30]

The soluble adhesion molecules: Intercellular adhesion molecule –1 (sICAM-1) and vascular cell adhesion molecule-1(sVCAM-1) lack specificity and are increased in inflammatory processes. Both markers are increased in vascular disease. sICAM-1 level predicts the risk for cardiovascular disease or diabetes mellitus in healthy individuals. sE-selectin is specific for the endothelium and is increased in arterial disease and diabetes mellitus. sE-selectin is also associated with diabetic risk. The endothelium-specific marker, soluble thrombomodulin, is associated with severity of coronary artery disease, stroke or peripheral occlusive arterial disease and is not increased in healthy or asymptomatic subjects. Interestingly, thrombomodulin decreases during treatment of hypercholesterolemia or hyperhomocysteinemia. In contrast, von Willebrand factor is the best endothelial biomarker and predicts risk for ischemic heart disease or stroke.[31]

High presurgical values of CRP,has proven to be associated with advanced PAD & risk of MI independently of the presence of the factors traditionally considered for cardiovascular risk or a clinical history of ischemic heart disease.The values for fibrinogen and alterations in the hemorrheologic properties of the blood have also been associated with a greater prevalence of PAD.High concentrations of fibrinogen cause an alteration of the microcirculation that is associated with more pronounced symptoms of intermittent claudication.[17]

Table 1.2 PARC Lesion and Vessel Characteristics and Definitions.[3]

PARC Lesion and Vessel Characteristics and Definitions		
Lesion or Vessel	**Term**	**Definition**
Significant peripheral artery stenosis*	Mild	<50%
	Moderate	50%–69%
	Severe	70%–99%
	Occluded	100%
Lesion length	Focal	≤1 cm
	Short	>1 and <5 cm
	Intermediate	≥5 and <15 cm
	Long	≥15 cm
Degree of lesion calcification	Focal	<180° (1 side of vessel) and less than one-half of the total lesion length
	Mild	<180° and greater than one-half of the total lesion length
	Moderate	≥180° (both sides of vessel at same location) and less than one-half of the total lesion length
	Severe	>180° (both sides of the vessel at the same location) and greater than one-half of the total lesion length
Anatomic level of LE-PAD	Aortoiliac	Aortoiliac (distal limit bottom of pelvic rim in the AP view by angiography or inguinal ligament)
	Femoropopliteal	Femoropopliteal (distal limit is origin of anterior tibial artery)
	Tibialpedal	Tibialpedal (anterior tibial and below including foot arteries)
	Aortoiliac segment	Infrarenal abdominal aorta Common iliac artery Internal iliac artery External iliac artery
	Femoropopliteal	Common femoral artery Profunda femoris artery Superficial femoral artery P1 segment (above knee popliteal artery): from Hunter's canal to proximal edge of patella P2 segment: from the proximal part of patella to center of knee joint space P3 segment (below knee popliteal artery): from the center of knee joint space to origin of anterior tibial artery
	Tibialpedal	Tibial-peroneal trunk (from the origin of the anterior tibial artery to the bifurcation of the posterior tibial and peroneal artery) Anterior tibial artery Posterior tibial artery Peroneal artery Plantar pedal loop pedal vessel PT, DP†‡
Target lesion	Any vascular segment treated or attempted to be treated during the trial procedure with the index device. The target lesion is the treated segment including **10 mm proximal** and **ending 10 mm distal** to the index device or therapy (stent, balloon, or atherectomy catheter).	
TLR	TLR is **any repeat** intervention of the target lesions (**plus** 10 mm proximal and distal to the index device) or surgical bypass of the target vessel performed for restenosis or other complication involving the target lesion. If the target vessel is occluded and bypass is done to another artery below the knee, this should be considered TLR. In the assessment of TLR, angiograms should be assessed by an angiographic core laboratory (if designated) and made available to the clinical endpoints committee for review.	
Target vessel	Any vessel (e.g., noncardiac or nonintracranial) that contains the target lesion treated with the study device. The target vessel includes the target lesion as well as the entire length of native vessel upstream and downstream from the target lesion, including side branches.	
Target limb	Any symptomatic limb that contains the target lesion and all vessels from aortic bifurcation to the foot.	

DP=dorsalis pedis artery,PT=posterior tibial artery,QCAquantitative coronary angiography,TLR=target lesion revascularization

1.6 Classification and Outcomes

In studies of outcome following lower limb revascularisation for critical limb threatening ischaemia (CLTI), patients with and without diabetes are typically reported as one group. The unique characteristics of PAD in diabetes, in its distribution and presentation, make it difficult to extrapolate clinical significance from data on unselected patients. Additionally, CLTI remains a problematic definition in patients with diabetes as symptoms of ischaemic pain (claudication, rest pain) may be masked by the presence of distal symmetric polyneuropathy, and ulceration may develop with very mild PAD of little haemodynamic significance. In contrast, patients without diabetes are unlikely to develop tissue loss in the absence of a severe perfusion deficit. A haemodynamic classification of PAD using ankle brachial index (ABI), toe pressures or transcutaneous oxygen tension is more useful in patients with diabetes with the caveat that ABIs may be falsely elevated due to arterial calcification and have a poor predictive value. Patients with diabetes need to be identified as an important subgroup in the PAD literature to allow pooling of results for systematic review and meta-analysis.[16] Several angiographic classification schemes exist to describe the anatomical distribution of disease in patients with PAD.The limitations of the currently available schemes may, inpart, explain the poor reporting of PAD distribution in the literature. TheTrans-Atlantic Inter-Society Consensus (TASC) guidelines classify femoral popliteal lesions based on their anatomical distribution,(32) however,the classification of infrapopliteal lesions is not specifically addressed.This is significant given that the patency of the outflow artery is critical in determining the success of arterial bypass, and this is especially true in diabetes where run-off is more likely to be poor. The Bollinger score,[16] albeit more cumbersome clinically, describes the infrapopliteal arterial segments in some detail and is advantageous in this respect.In the

BASIL trial, below knee Bollinger scores were significantly greater in patients pesenting with tissue loss; however the same difference in above knee scores was not significant.Interestingly there was a negative correlation between mean above and below knee Bollinger scores, suggesting that the TASC score, in its current form, may underestimate disease severity in a cohort of patients with diabetes and relative sparing of the above knee arterial segments. Several validated scoring systems have been developed for use in diabetic foot ulcers. These include the University of Texas Wound Classification system and the Size (Area and Depth), Sepsis,Arteriopathy, and Denervation (SAD) score.[16] The latter of which has been prospectively validated in different ethnic groups and is a reliable predictor of healing. [16,33] The PEDIS score of the International Working Group on the Diabetic Foot (IWDGF) was developed for research purposes,[16] but the grading of infection in this system according to its severity is also advocated for clinical use as it predicts outcome.[16]A universal classification system of diabetic foot ulcers would enable consistent reporting among studies in DFU to guide the development of novel therapies while increasing the external validity of research in this field and allowing fair comparison between centres.[16,34] To this end the European Wound Management Association (EMWA) has produced a set of recommendations for standardized reporting of outcomes in studies of wound management.[35] Clearly there will be some overlap with the Society for Vascular Surgery standard reporting criteria for the lower limb ischaemia.The balance of risk and benefit for interventions in diabetic foot disease is probably best assessed through a combination of defined clinical endpoints including mortality, amputation-free survival, healing and re-ulceration with patient-reported outcome measure. [16]

Overview of Classification Systems in Peripheral Artery Disease

To refocus the approach to the patient with a threatened limb and a component of chronic ischemia according to disease severity rather than arterial lesion characteristics. There are two major problems with current classification systems:

(1) The validity and natural history of the concept of CLTI, and

(2) The failure of most existing systems to assess and grade the major factors that influence both risk of limb loss and clinical management.As presently defined, CLTI is associated with decreased quality of life, increased risk for amputation, and increased mortality.[36]

1.6.1 Fontaine Classification

The first classification system emerged from the European Society of Cardiovascular Surgery in 1952 and was published in 1954 by Fontaine et al.[37]

The system is solely based on clinical symptoms, without other diagnostic tests, and is typically used for clinical research and not routinely used in patient. [38]

Table 1.3 Fontaine classification [38]

Grade	Symptoms
Stage I	Asymptomatic, incomplete blood vessel obstruction
Stage II	Mild claudication pain in limb
Stage IIA	Claudication at a distance > 200 m
Stage IIB	Claudication at a distance < 200 m
Stage III	Rest pain, mostly in the feet
Stage IV	Necrosis and/or gangrene of the limb

1.6.2 Rutherford Classification

The symptomatic classification was adapted by Rutherford in 1986,[39] with revision in 1997. Rutherford classified PAD into acute and chronic limb ischemia, emphasizing that each presentation requires different treatment algorithms.

Acute versus chronic presentation implies timing of symptom onset;

Rutherford's chronic limb ischemia classification most resembles Fontaine's classification, with the addition of objective noninvasive data.[40]

The character of the patients' pain and onset should be evaluated. Claudication onset should be determined,and reliably verified by walking/treadmill tests in the noninvasive vascular diagnostic laboratory.[38,40]

Table 1.4 Rutherford classification for chronic limb ischemia.[38]

Grade	Category	Clinical description	Objective criteria
0	0	Asymptomatic–no hemodynamically significant occlusive disease	Normal treadmill or reactive hyperemia test
	1	Mild claudication	Completes treadmill exercise; AP after exercise > 50 mm Hg but at least 20 mm Hg lower than resting value
I	2	Moderate claudication	Between categories 1 and 3
	3	Severe claudication	Cannot complete standard treadmill exercise, and AP after exercise < 50 mm Hg
II	4	Ischemic rest pain	Resting AP < 40 mm Hg, flat or barely pulsatile ankle or metatarsal PVR; TP < 30 mm Hg
III	5	Minor tissue loss–nonhealing ulcer, focal gangrene with diffuse pedal ischemia	Resting AP < 60 mm Hg, ankle or metatarsal PVR flat or barely pulsatile; TP < 40 mm Hg
	6	Major tissue loss–extending above TM level, functional foot no longer salvageable	Same as category 5

Abbreviations: AP, ankle pressure; PVR, pulse volume recording; TM, transmetatarsal; TP, toe pressure.

Rutherford's ALI classification divides an extremity into viable, threatened, or irreversibly damaged categories. All patients with ALI are initially managed with intravenous heparin unless there is a contraindication. Patients with category I and IIa ischemia with onset within 14 days and low risk of myonecrosis or ischemic nerve damage are often treatedwith endovascular methods including catheter-directed thrombolysis. Category IIb patients require more immediate revascularization due to higher risks of permanent nerve/tissue injury and muscle necrosis;this is often accomplished with

operative thrombectomy and fasciotomy when clinically indicated. Patients with category III ischemia are nonviable and are treated with amputation.[38]

Table 1.5 Rutherford classification for acute limb ischemia.[39,40]

Category	Description/Prognosis	Findings		Doppler signal	
		Sensory loss	Muscle weakness	Arterial	Venous
I. Viable	Not immediately threatened	None	None	Audible	Audible
II. Threatened					
a. Marginally	Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
b. Immediately	Salvageable with immediate revascularization	More than toes, associated rest pain	Mild, moderate	Inaudible	Audible
III. Irreversible	Major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Profound, paralysis	Inaudible	Inaudible

1.6.3 Bollinger Angiographic Classification

Fontaine and Rutherford's classifications are based on clinical symptomatology. Incontrast, other systems have been developed based on location and severity of atherosclerotic lesions. Anatomic classification systems have usually been based on catheter-directed angiography. The first angiographic-based system was proposed by Vogelberg in 1975. This system divides the peripheral circulation into pelvic, thigh, and calf vessels. Each segment is given a score of 1 to 9 depending on atherosclerotic disease burden. Each leg can be given a score of 1 to 27, with a bilateral total score up to 54. Bollinger et al proposed a similar angiographic methodology for classification, but differentiates the lower extremity arteries into smaller defined segments .Each segment is given an additive score of four categories of severity:

Occlusion, luminal stenosis greater than 50% of the lumen,

Stenosis 25 to 49% of the lumen, and

Plaques <25% of the lumen

The angiogram is also graded by the number of lesions:

-Single lesion,

-Multiple lesions: encompassing less than half of the diseased segment, and --multiple lesions encompassing more than half of the diseased segment.

In the presence of an occlusion, the stenosis and plaques are not considered. If there are stenosis and plaques, an additive score is given.For example, an occlusion less than half of the segment receives a score of 13. If a segment has multiple stenoses over the length of the vessel causing 25 to 49% stenosis and if there is an additional single 75% stenosis, the total score would be 8 (4 + 4). On repeat angiograms, changes in occlusion are considered. For occlusion length increases over 2cm, one point is added to the score.Conversely, for decreases in length over 2cm, one point is subtracted from the score. Bollinger et al also described a vector method of scoring angiograms,listing each subcategory of PAD in each column of subcategory.[(41)]

Bollinger methods of classification of PAD were used in the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial to characterize and follow patients. The classification system is used for chronic limb ischemia, and has not been validated for ALI. The classification system might be useful in computed tomographic angiography or magnetic resonance angiography; however, no validation for these imaging modalities has been published.This system is not used clinically.[(38)]

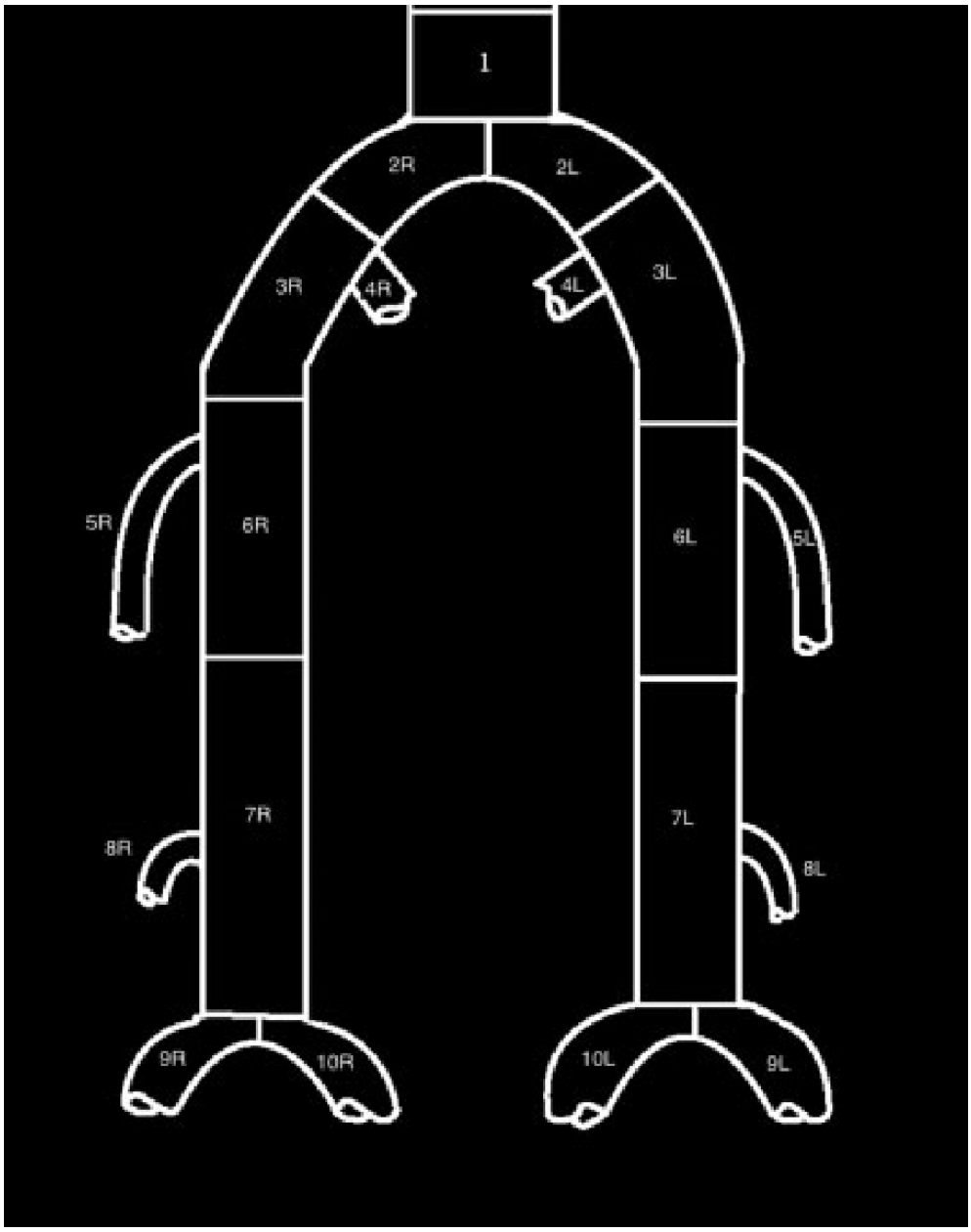


Figure 1.2 Bollinger classification. 1—abdominal aorta; 2—common iliac; 3—external iliac; 4—internal iliac; 5—profunda; 6—superficial femoral; 7—popliteal; 8—anterior tibial; 9—peroneal; 10—posterior tibial; R—right; L—left.[(38)]

Table1.6 Bollinger scoring system.[41]

Bollinger classification card			
Location	Occlusive pattern		
	Plaque < 25%	Stenosis ≤ 50%	Stenosis > 50%
Single	1	2	4
Multiple ≤ 50% segment	2	3	5
Multiple > 50% segment	3	4	6
Occlusions		< 50% = 13	
		≥ 50% = 15	
Follow-up: 2+ cm decrease = − 1; 2+ cm increase = +1			

Notes:Evaluate each Bollinger segment and score based on occlusions and stenoses.In the presence of occlusions,plaques and stenosis are not considered.On follow-up examinations,if occlusion segment length increases over 2cm,it adds a point(e.g.,occlusion initially receiving score of 13 would be graded as 14). Occlusion segment decrease of 2 cm would subtract one point.

1.6.4 Graziani's Morphologic Categorization

PAD in patients with diabetes has a different presentation than critical limb ischemia related purely to atherosclerotic disease.Critical limb ischemia was first defined solely in patients without diabetes as it, "…was generally agreed that diabetic patients who have a varied clinical picture of neuropathy, ischemia and sepsis make definition even more difficult and it is desirable that these patient be excluded…or should be clearly defined as a separate category."[(42)] Jude et al

Demonstrated that in diabetic patients, foot ulcers and gangrene were more prevalent than rest pain in patients with PAD without diabetes.In addition, the distribution of occlusive disease in diabetics was different from that in nondiabetics.Given the differences in PAD patients with and without diabetes, separate classification systems have been proposed that address these differences.The categorization by Graziani is based on an anatomic distribution.[(43)] This classification system places greater emphasis on the below the knee vessels than previous anatomic classifications. Classification is also graded on the basis of catheter directed angiography.The initial cohort of patient for Graziani's classification included 417 patients, all with ulcers or gangrene.In the population studied by Graziani,the majority of patients with diabetes had two or three of the tibial/peroneal arteries occluded with femoral and popliteal stenosis and/or occlusions.[(38)]

Limitation of the classification system by Graziani is that the system was not validated in aseparate population of diabetics for predicting symptom severity. In addition, diabetics without tissue loss were not studied.Most importantly; anatomic distribution of occlusions and stenosis may be present in asymptomatic diabetics, the significance of which is not addressed by Graziani's morphologic categorization of disease severity.[(38)]

Table 1.7 Graziani's morphologic categorization of disease severity[43]

Class	Angiographic finding
1	Isolated, one vessel tibial or peroneal artery obstruction
2a	Isolated femoral/popliteal artery or two below knee arteries obstructed but with patency of one of the two tibial arteries
2b	Isolated femoral/popliteal artery or two below knee tibial arteries obstructed but with patency of the peroneal artery
3	Isolated, one artery occluded and multiple stenosis of tibial/peroneal and/or femoral/popliteal arteries
4	Two arteries occluded and multiple stenoses of tibial/peroneal and/or femoral/popliteal vessels
5	Occlusion of all tibial and peroneal arteries (below knee cross-sectional occlusion)
6	Three arteries occluded and multiple stenosis of tibial/peroneal and/or femoral/popliteal arteries
7	Multiple femoropopliteal obstructions with no visible below the knee arterial segments

Notes: Anatomic classification of patients with diabetes with foot ulcers or gangrene. Increasing class is associated with increasing disease severity.

1.6.5 Trans-Atlantic Inter-Society Consensus Document II

Fourteen societies representing guidelines in medicine,vascular surgery, interventional radiology, and cardiology from Europe and North America came together in 2000 to form a consensus in the classification and treatment of patients with PAD.The focus was to provide recommendations in the epidemiology of PAD, clinical evaluation, diagnosis, treatment, and follow-up of patients with intermittent claudication, ALI, and chronic limb ischemia. The resulting document was referred to as the Trans-Atlantic Inter-Society Consensus Document (TASC). In 2007, the consensus was updated and involved additional representatives from Australia, South Africa, and Japan and is referred to asTASCII. TASCII is comprehensive in reviewing the literature relating to PAD up to 2007.[38]

While TASC II addresses all aspects of PAD, the anatomic classification detailed in TASC II has received the significant focus of the review as well as considerable criticism of the recommendations. Specific categories are assigned treatment algorithms (surgical vs.endovascular) based on lesion classification. TASC II divides anatomic distribution of lesions into aorto-iliac and femoral popliteal. Lesion patterns are grouped into A–D lesions. Based on this group recommendation, TASC A lesions are those that should have excellent results from endovascular management alone.TASC B lesions are those that should have good results from endovascular management, and endoluminal interventions should be the first treatment approach. TASC C lesions are those for which surgical management provides superior long-term results and endovascular techniques should be reserved for patients who are surgically high risk. TASC D lesions should be treated by open surgery. While TASC II provides a framework to compare therapeutic techniques, advancement of endovascular techniques have led to many trials suggesting that endovascular management of TASC II C and D lesions is a potential alternative treatment to open strategies. [44–49]

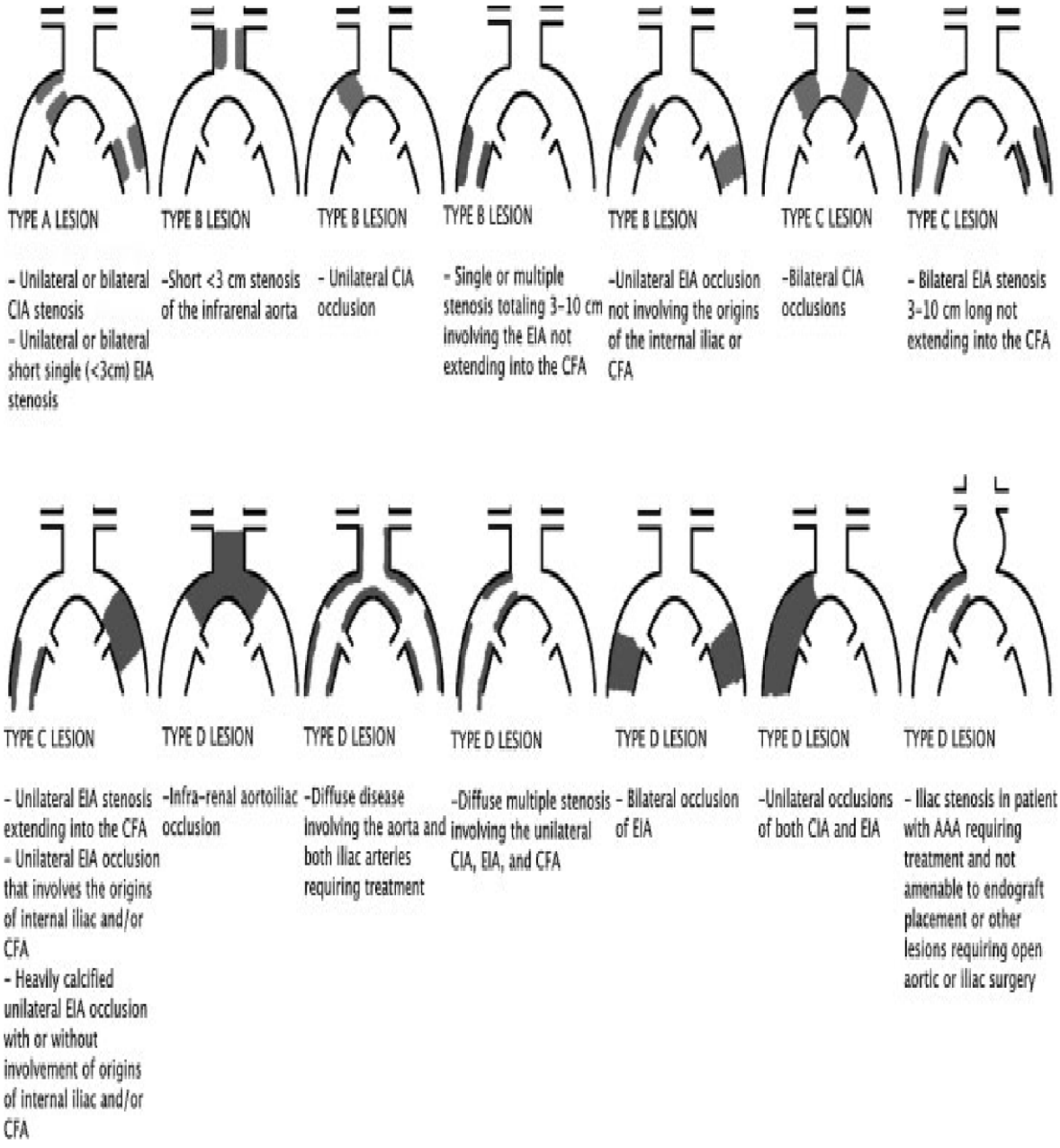


Figure1.3 Trans Atlantic Inter Society Consensus Document classification of aortoiliaclesions. CIA, common iliac artery; EIA, external iliac artery; CFA, common femoral artery; AAA, abdominal aortic aneurysm.[(38)]

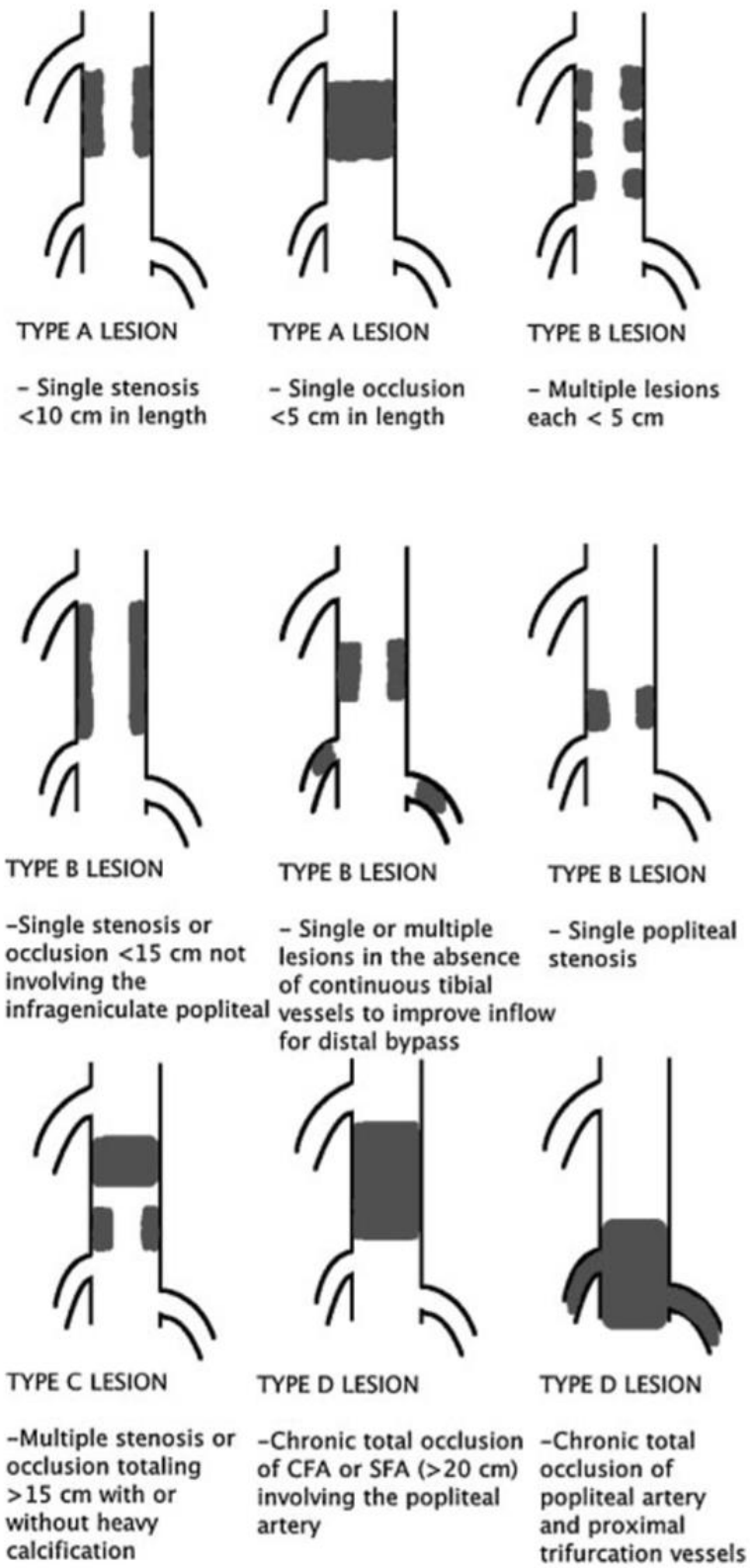


Figure 1.4 Trans-Atlantic Inter-Society Consensus Document classification of femoral popliteal lesions. CFA, common femoral artery; SFA, superficial femoral artery.[38]

1.6.6 University of Texas Diabetic Wound Classification

Table1.8 University of Texas Diabetic Wound Classification. [50]

.... Classification System

A. Stages
    1. Stage A: No infection or ischemia
    2. Stage B: Infection present
    3. Stage C: Ischemia present
    4. Stage D: Infection and ischemia present

B. Grading
    1. Grade 0: Epithelialized wound
    2. Grade 1: Superficial wound
    3. Grade 2: Wound penetrates to tendon or capsule
    4. Grade 3: Wound penetrates to bone or joint

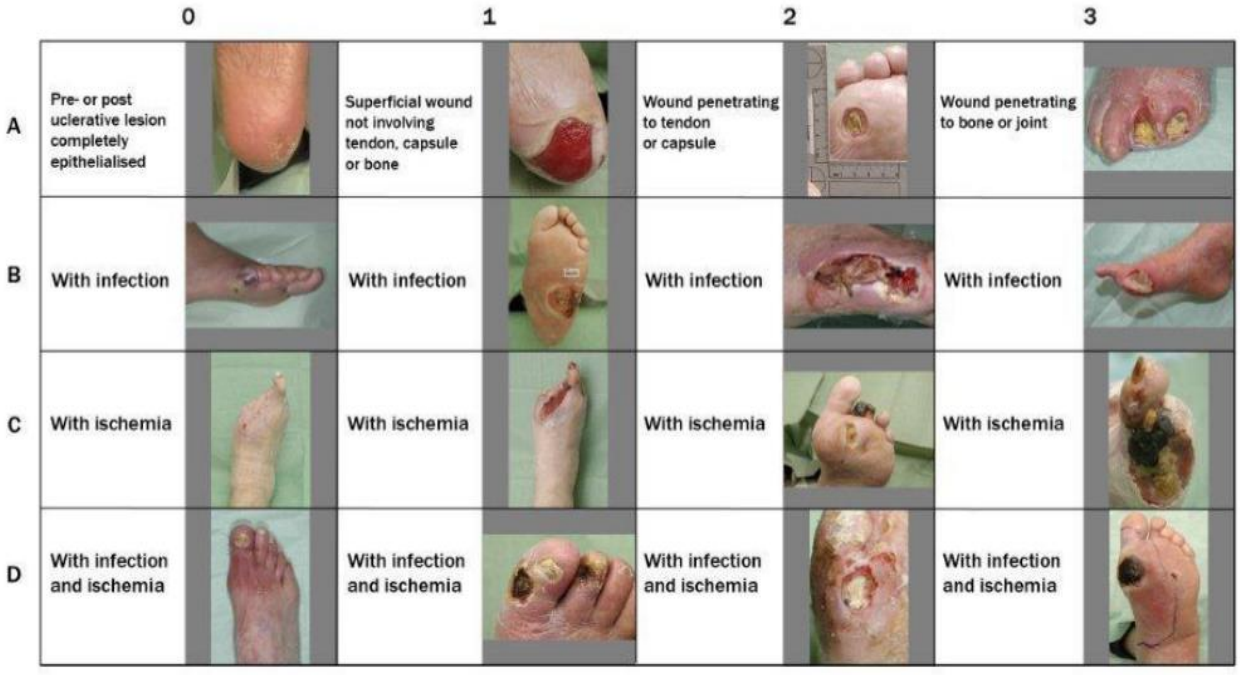
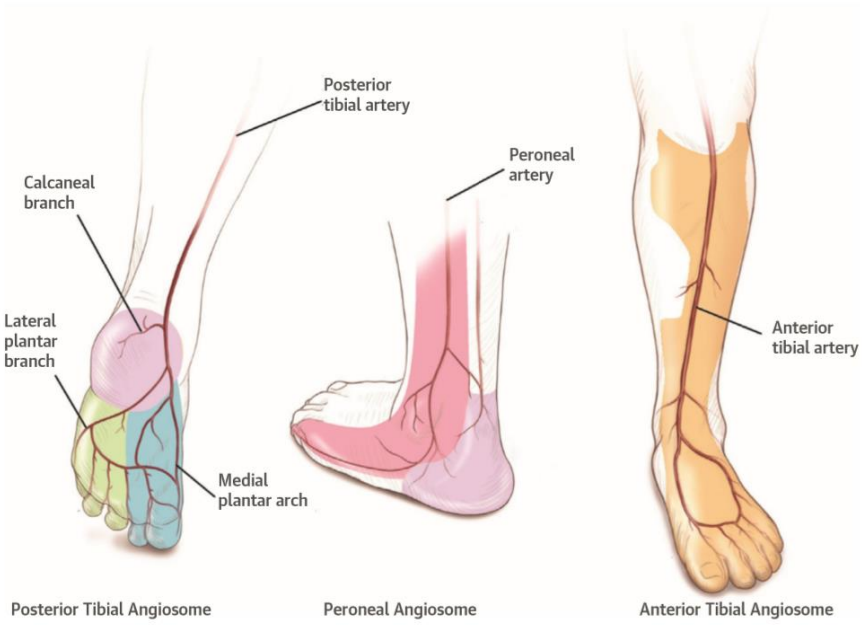


Figure1.5 University of Texas Diabetic Wound Classification

1.6.7 Angiosomes

One classification system that has been described in the plastic surgery literature and has gained acceptance in PAD is the concept of arterial perfusion via angiosomes.The concept was first described by Taylor and palmer. the territories correlate strongly with neurologic dermatomes in the torso and head, but deviate from dermatomes in the extremities.Each angiosome comprises the muscle and overlying subcutaneous tissue and dermis; six angiosomes define the lower extremities.The posterior tibial artery feeds three angiosomes: the medial calcaneal artery angiosome, the medial plantar artery angiosome, and the lateral plantar artery angiosome.the anterior tibial artery has one angiosome: the anterior tibial artery–dorsalis pedis artery angiosome.the peroneal artery feeds two angiosomes: the lateral calcaneal artery angiosome and anterior perforator artery angiosome. the adjacent angiosomes can be feed by collateral vessels in the presence of necrosis, termed by taylor as “choke vessels.” the conventional endovascular plan to heal foot ulcers and gangrene is to improve whichever vessel is easiest to recanalize and allow collateral flow to heal an ulcer.several groups have looked at whether recanalizing the direct vessel to the affected angiosome has improved efficacy over “indirect” or nonselective revascularization.[38,51]



The below-the-knee skin and tissue are supplied by 3 main arteries and 6 angiosomes. The anterior tibial artery supplies the anterior shin and dorsum of the foot, the posterior tibial artery supplies the medial heel and the medial and lateral plantar angiosomes, and the peroneal artery supplies the lateral aspect of the heel and the lateral border of the foot.

Figure1.6 Six Angiosomes of the Below-the-Knee Lower Extremity.[(52)]

1.6.8 WIFI classification

Wound, Ischemia, and Foot Infection In response to the increasing number of diabetics comprising patients with critical limb ischemia, the Society for Vascular Surgery proposed a new classification scheme that combines the classification schemes based on PAD perfusion patterns with foot ulcer schemes. Several grading systems exist to characterize foot ulcers including PEDIS (perfusion, extent/ size, depth/tissue low, infection, sensation), UT (University of Texas), Wagner, SAD (sepsis, arteriopathy, denervation), and Saint Elian. Diabetic foot ulcer schemas are based on size and depth of ulcers as well as foot gangrene. The new classification system takes into account foot wounds , infection and limb perfusion and is titled WIfI (wound, ischemia, and foot infection).The Society of Vascular Surgery document addresses the importance of all three components of ulcer, concomitant

infection, and limb vascularity in the treatment and outcomes of critical limb ischemia. A separate grade is given to the wound (the presence and depth of ulcer), ischemia (based on ABI, toe pressure, or transcutaneous oximetry (TcPO2), and infection (local to systemic).[38]

Table1.9 Assessment of the risk of amputation:the WIFI classification.[19]

Component	Score	Description		
W (Wound)	0	No ulcer (ischaemic rest pain)		
	1	Small, shallow ulcer on distal leg or foot without gangrene		
	2	Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes		
	3	Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene		
I (Ischaemia)		ABI	Ankle pressure (mmHg)	Toe pressure or $TcPO_2$
	0	≥0.80	> 100	≥60
	1	0.60–0.79	70–100	40–59
	2	0.40–0.59	50–70	30–39
	3	<0.40	<50	<30
fI (foot Infection)	0	No symptoms/signs of infection		
	1	Local infection involving only skin and subcutaneous tissue		
	2	Local infection involving deeper than skin/subcutaneous tissue		
	3	Systemic inflammatory response syndrome		

Table1.10 Society for Vascular Surgery WIfI (wound, ischemia, foot infection) classification. [36,53]

Wound

Grade	Ulcer	Gangrene
0	No ulcer	No gangrene
1	Small, shallow ulcer on distal leg or foot; no exposed bone, unless limited to distal phalanx	No gangrene
2	Deeper ulcer with exposed bone, joint, or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement	Gangrenous changes limited to digits
3	Extensive, deep ulcer involving forefoot and/or midfoot; deep, full-thickness heel ulcer ± calcaneal involvement	Extensive gangrene involving the forefoot/ midfoot; full-thickness heel necrosis ± calcaneal involvement

I: Ischemia

Hemodynamics/perfusion: Measure TP or $TcPO_2$ if ABI incompressible (>1.3)

SVS grades 0 (none), 1 (mild), 2 (moderate), and 3 (severe).

Grade	*ABI*	*Ankle systolic pressure*	*TP, $TcPO_2$*
0	≥0.80	>100 mm Hg	≥60 mm Hg
1	0.6-0.79	70-100 mm Hg	40-59 mm Hg
2	0.4-0.59	50-70 mm Hg	30-39 mm Hg
3	≤0.39	<50 mm Hg	<30 mm Hg

fI: foot Infection:

SVS grades 0 (none), 1 (mild), 2 (moderate), and 3 (severe: limb and/or life-threatening)

SVS adaptation of Infectious Diseases Society of America (*IDSA*) and International Working Group on the Diabetic Foot (IWGDF) perfusion, extent/size, depth/tissue loss, infection, sensation (*PEDIS*) classifications of diabetic foot infection

Table1.11 Clinical manifestation of infection. [(36)]

Clinical manifestation of infection	*SVS*	*IDSA/PEDIS infection severity*
No symptoms or signs of infection	0	Uninfected
Infection present, as defined by the presence of at least 2 of the following items: • Local swelling or induration • Erythema >0.5 to ≤2 cm around the ulcer • Local tenderness or pain • Local warmth • Purulent discharge (thick, opaque to white, or sanguineous secretion)	1	Mild
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). Exclude other causes of an inflammatory response of the skin (eg, trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)		
Local infection (as described above) with erythema >2 cm, or involving structures deeper than skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, fasciitis), and No systemic inflammatory response signs (as described below)	2	Moderate
Local infection (as described above) with the signs of SIRS, as manifested by two or more of the following: • Temperature >38° or <36°C • Heart rate >90 beats/min • Respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg • White blood cell count >12,000 or <4000 cu/mm or 10% immature (band) forms	3	Severe[a]

$PACO_2$, Partial pressure of arterial carbon dioxide; *SIRS*, systemic inflammatory response syndrome.

[a]Ischemia may complicate and increase the severity of any infection. Systemic infection may sometimes manifest with other clinical findings, such as hypotension, confusion, vomiting, or evidence of metabolic disturbances, such as acidosis, severe hyperglycemia, new-onset azotemia.

From Lipsky et al.[42]

Table 1.12. a and b, Risk/benefit: Clinical stages by expert consensus.[(36)]

a, Estimate risk of amputation at 1 year for each combination

	Ischemia – 0				Ischemia – 1				Ischemia – 2				Ischemia – 3			
W-0	VL	VL	L	M	VL	L	M	H	L	L	M	H	L	M	M	H
W-1	VL	VL	L	M	VL	L	M	H	L	M	H	H	M	M	H	H
W-2	L	L	M	H	M	M	H	H	M	H	H	H	H	H	H	H
W-3	M	M	H	H	H	H	H	H	H	H	H	H	H	H	H	H
	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3

b, Estimate likelihood of benefit of/requirement for revascularization (assuming infection can be controlled first)

	Ischemia – 0				Ischemia – 1				Ischemia – 2				Ischemia – 3			
W-0	VL	VL	VL	VL	VL	L	L	M	L	L	M	M	M	H	H	H
W-1	VL	VL	VL	VL	L	M	M	M	M	H	H	H	H	H	H	H
W-2	VL	VL	VL	VL	M	M	H	H	H	H	H	H	H	H	H	H
W-3	VL	VL	VL	VL	M	M	M	H	H	H	H	H	H	H	H	H
	f-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3

fI, foot Infection; I, Ischemia; W, Wound.

Premises:

1. Increase in wound class increases risk of amputation (based on PEDIS, UT, and other wound classification systems)
2. PAD and infection are synergistic (Eurodiale); infected wound + PAD increases likelihood revascularization will be needed to heal wound
3. Infection 3 category (systemic/metabolic instability): moderate to high-risk of amputation regardless of other factors (validated IDSA guidelines)

Four classes: for each box, group combination into one of these four classes

Very low = VL = clinical stage 1
Low = L = clinical stage 2
Moderate = M = clinical stage 3
High = H = clinical stage 4
Clinical stage 5 would signify an unsalvageable foot

The 16 possible combinations in ischemia 0 are unlikely to require revascularization. The spectrum of ischemia requiring vascular intervention is, thus, reduced to 48 possibilities. Most of the patients in the ischemia 1 and

2 blocks of 16 combinations suffer from “situational ischemia.” As wound complexity and infection severity increase (a shift down and to the right in each box of 16), the likelihood that revascularization will be required increases. In the ischemia 3 category, small wounds without infection may not always require vascular intervention, but such an intervention may speed healing. Again, shifts down and to the right within this box increase the odds that vascular intervention will be required; it likely will be mandatory for W 2 and W 3 patients, especially in the presence of infection.[36]

1.6.9 AMA Criteria for Lower Extremity Impairment

One final categorization that can be of interest to the interventional radiologist is the classification of PAD by the American Medical Association (AMA).The purpose of the AMA classification is to determine an individual’s health impairment due to the disease. The AMA classification combines disease due to PAD and venous insufficiency. Questionnaires are available to narrow the patients’ symptoms and classify their improvement.Other systems that have similar categories include workers’ compensation, United States Social Security Administration classification, and private insurers.[38]

Table 1.13 American Medical Association Whole Person Impairment Classification.[38]

Class	WPI	Signs and symptoms
0	0%	Patient does not have claudication or pain at rest Patient experiences transient edema and one of the following is present: • Loss of pulses • Minimal loss of subcutaneous tissue • Calcification of arteries detected on radiographic examination • Asymptomatic dilation of arteries or veins not requiring surgery and not resulting in curtailment of activities
1	2–10%	Patient has at least one of the following: • Intermittent claudication walking at least 100 yards at average pace • Moderate edema persists and is incompletely controlled by elastic supports • Evidence of tissue damage such as healed amputation (single digit) or healed ulceration
2	11–24%	Patient has at least one of the following: • Intermittent claudication on walking 25–100 yards at average pace • Marked edema present that is only partially controlled by elastic supports • Evidence of tissue damage such as healed amputations (2+ digits single extremity) or healed ulceration
3	25–44%	Patient has at least one of the following: • Intermittent claudication walking <25 yards • Intermittent pain at rest • Marked edema that cannot be controlled by elastic supports • Amputation at or above an ankle of one extremity, or amputation of 2+ digits of two extremities with persistent vascular disease with persistent widespread or deep ulceration involving one extremity
4	45–65%	Patient has at least one of the following: • Severe and constant pain at rest • Tissue damage such as amputation at or above the ankles of both extremities, or amputation of all digits of two or more extremities and evidence of widespread or deep ulceration involving two or more extremities

Abbreviation: WPI, Whole Person Impairment.

Table 1.14 Comparison of classification systems.[38]

Classification	Symptom based	Anatomic	Direct treatment	Apply to acute limb ischemia	Specifically for diabetes	Pros	Cons
Fontaine	Yes	No	Yes	Not classically	No	Historically proven; easy to apply to patient	No objective criteria
Rutherford	Yes	No	Yes	Yes	No	Historically proven, quickly apply to patient, objective	Classically should not be applied in diabetes, no consideration for wounds
Bollinger	No	Yes	No	No	No	Categorical variable can be used in research, allows for documentation of change in follow-up	No basis on symptoms, applied poorly to diabetes
Graziani	No	Yes	No	No	Yes	Application in diabetes	Does not address aortoileal disease, does not direct therapy
WIfI	Yes	No	Yes	No	Yes	Robust to account for several factors in PAD	New and not validated in many research studies
TASC II	No	Yes	Yes	Yes	No	Defined disease process, used in several research studies	Treatment recommendations not widely accepted and may need updating
Angiosome	No	Yes	Yes	Not described	No	May help optimize revascularization strategy	Needs further validation
AMA	Yes	No	No	Yes	No	Good for use in disability, reflects state of the patients global health	Not intended to direct treatment, mixed arterial and venous categories

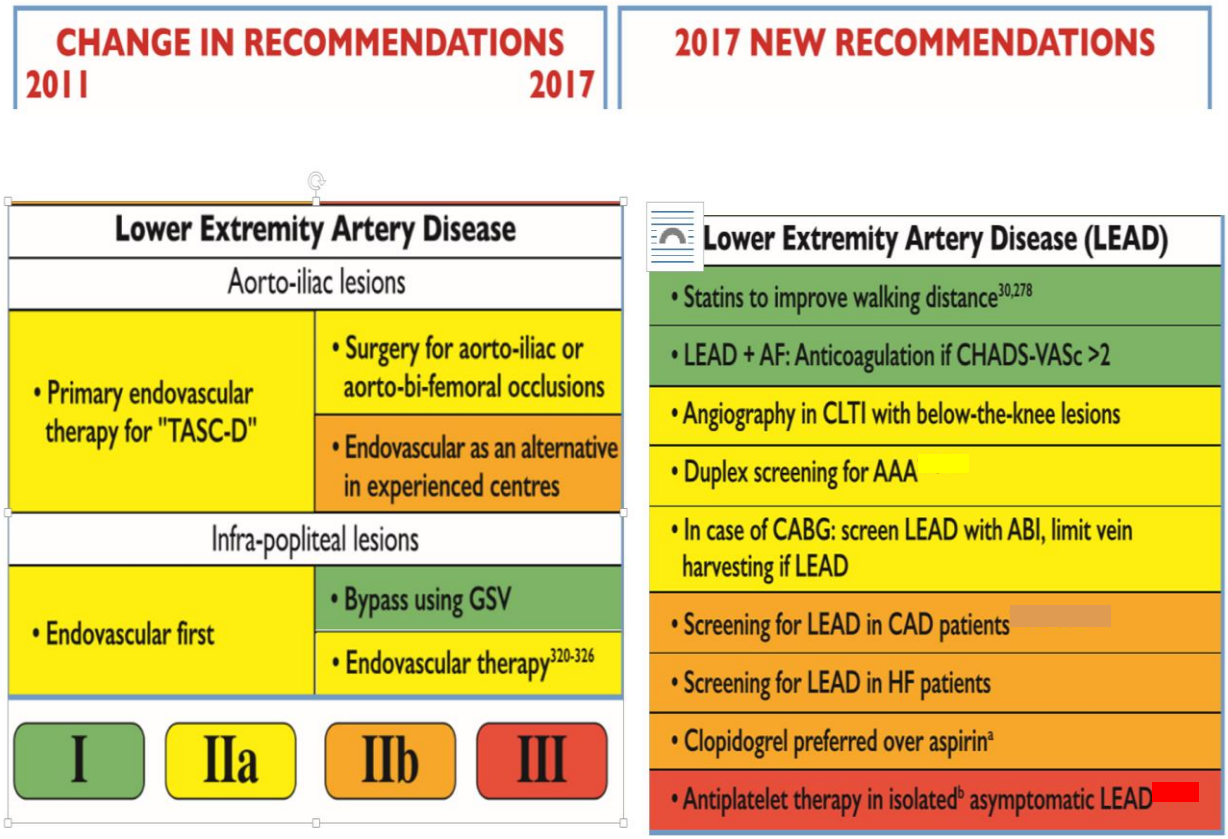
Abbreviations: AMA, American Medical Association; PAD, peripheral artery disease; TASC II, Trans-Atlantic Inter-Society Consensus Document; WIfI, wound, ischemia, foot infection.

The concept of a single dichotomous hemodynamic cutoff point for CLI no longer applies to the majority of patients encountered in current clinical practice; various degrees of ischemia may prove “critical” depending on the overall status of the limb. It has become clear that limb ischemia does not have sharp cutoff points but consists of a gradual spectrum in the pattern of a sigmoidal curve. Wound healing, thus, depends not only on the degree of ischemia, but also on the extent and depth of the wound and the presence and severity of infection. Thus, some patients with moderate ischemia may heal faster with revascularization or even require it to heal large wounds, although

they do not meet current “CLTI” criteria. Other patients with “CLTI” may heal with wound care alone, without revascularization, or may be managed with analgesics for long periods of time while retaining a functional limb.[36]

The ESC and ESVS also join their efforts to provide increased medical and public awareness about PADs. Indeed, while stroke is acknowledged as a serious condition with significant burden throughout Europe, other PADs can be as lethal and disabling. Major efforts are still necessary to sensitize healthcare providers, decision makers and the general population about the need for earlier and more efficient prevention and management strategies for the 40 million individuals of our continent affected by PADs.[19]

Table1.15 2017 ESC guidelines of PAD(new changes).[19]



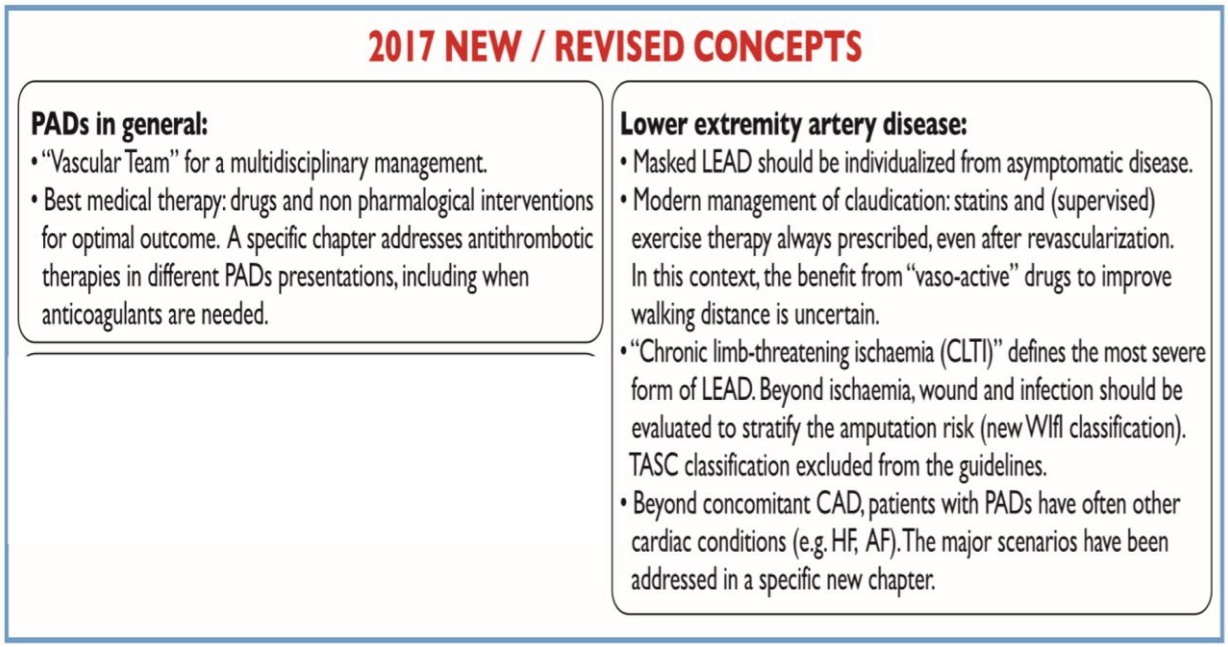


Figure 1.7 2017 New revised concepts.[19]

1.7 Treatment approach

Although revascularization is the primary therapy for CLTI, medical therapy serves as an essential therapeutic adjunct. The primary goal of medical therapy is to prevent myocardial infarction, stroke, and death, but it further helps to accelerate wound healing prevent amputation, and improve quality of life.[52]

Best medical therapy (BMT) includes CV risk factor management, including: 1.best pharmacological therapy includes antihypertensive, lipid-lowering and antithrombotic drugs. In diabetic patients, optimal glucose level control should be obtained as recommended. Treatment of concomitant infection and pain control as well as, 2.non pharmacological measures such as smoking cessation, healthy diet, weight loss and regular physical exercise, use of adapted footwear .[19,54–56]

1.7.1 Best Medical Therapy (BMT)

1. Vasodilators Prostanoid treatment (i.e., the intravenous infusion of a stable prostacyclin (PGI2) analogue such as iloprost/ Alprostar for 3-4weeks) is not an alternative to peripheral revascularisation in diabetic patients with PAD For ethical reasons, no randomised clinical trials have been carried out in order to compare the efficacy of prostanoid treatment with that of surgery in patients with critical ischaemia. However, it is important for relieving pain while awaiting surgical revascularisation, improving post revascularisation perfusion and improving the patients' quality of life.[57]

2. Lipid-lowering drugs All patients with PADs should have their serum low-density lipoprotein cholesterol (LDL-C) reduced to<1.8mmol/L (<70mg/dL) or decreased by≥50% if the initial LDL-C level is between 1.8 and 3.5mmol/L (70 and 135mg/dL). In the Reduction of Atherothrombosis for Continued Health (REACH) registry, among patients with LEAD, statin

use was associated with a 17% decrease in adverse CV events rates, even in the most advanced stages of disease, statin therapy is associated with lower 1-year rates of mortality and major CV adverse events. Combination treatment with ezetimibe in selected patients is also beneficial.[19]

3. Antithrombotic drugs Antiplatelet agents are used for secondary prevention of CV events in patients with symptomatic PADs. The evidence is mostly available in patients with LEAD and cerebrovascular disease.[19]

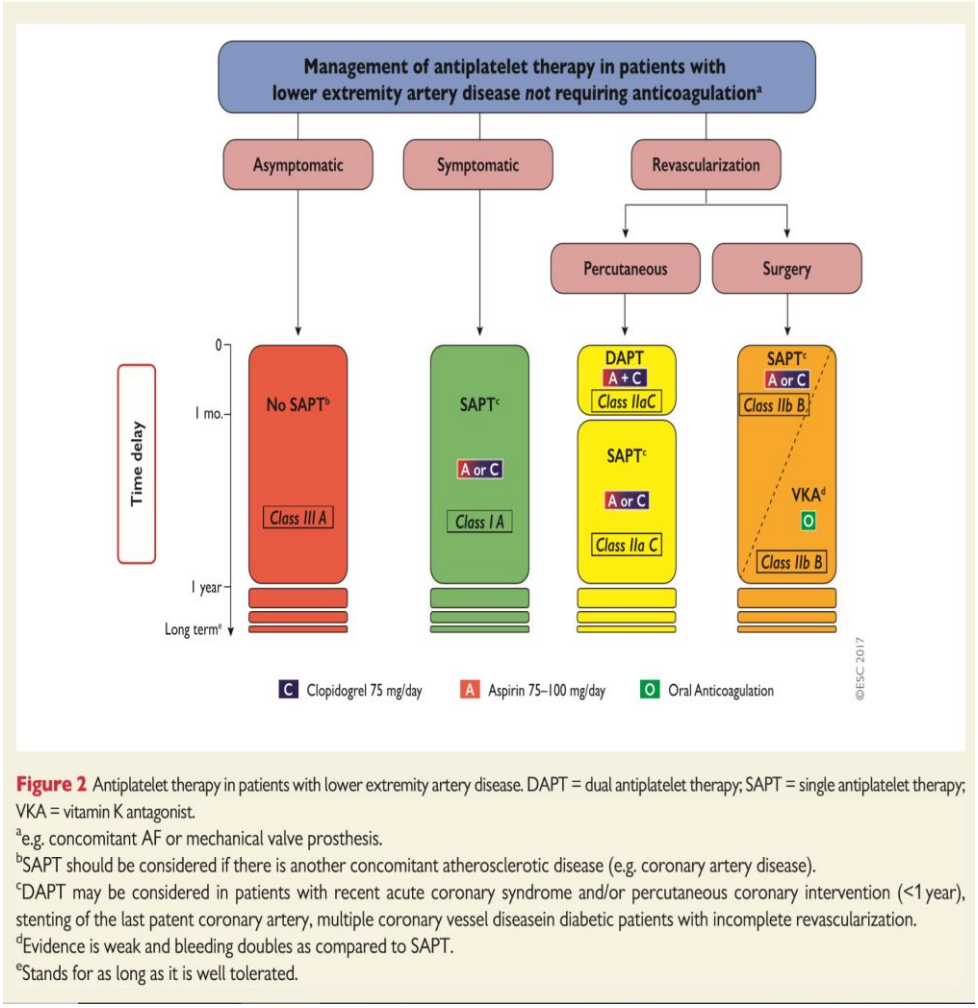


Figure 2 Antiplatelet therapy in patients with lower extremity artery disease. DAPT = dual antiplatelet therapy; SAPT = single antiplatelet therapy; VKA = vitamin K antagonist.
[a]e.g. concomitant AF or mechanical valve prosthesis.
[b]SAPT should be considered if there is another concomitant atherosclerotic disease (e.g. coronary artery disease).
[c]DAPT may be considered in patients with recent acute coronary syndrome and/or percutaneous coronary intervention (<1 year), stenting of the last patent coronary artery, multiple coronary vessel diseasein diabetic patients with incomplete revascularization.
[d]Evidence is weak and bleeding doubles as compared to SAPT.
[e]Stands for as long as it is well tolerated.

Figure1.8 Antiplatelet therapy in patient with LEAD not requiring anticoagulant.[19]

Table 1.16 Recommendations on antithrombotic therapy in patients with peripheral arterial diseases. [19]

Lower extremities artery disease		
Long-term SAPT is recommended in symptomatic patients.	I	A
Long-term SAPT is recommended in all patients who have undergone revascularization.	I	C
SAPT is recommended after infra-inguinal bypass surgery.	I	A
In patients requiring antiplatelet therapy, clopidogrel may be preferred over aspirin.	IIb	B
Vitamin K antagonists may be considered after autologous vein infra-inguinal bypass.	IIb	B
DAPT with aspirin and clopidogrel for at least 1 month should be considered after infra-inguinal stent implantation.	IIa	C
DAPT with aspirin and clopidogrel may be considered in below-the-knee bypass with a prosthetic graft.	IIb	B
Because of a lack of proven benefit, antiplatelet therapy is not routinely indicated in patients with isolated[d] asymptomatic LEAD.	III	A

4. Glycemic control

No direct evidence supports a role for tight glycaemic control in preventing ulceration, although epidemiological data suggests that optimizing blood glucose levels can prevent peripheral neuropathy and PAD in patients with diabetes. In the UK Prospective Diabetes Study, a reduction in HbA1C of 1% was associated with a reduction in risk of 43% for amputation or death from PAD.[19]

5. Antihypertensive drugs

Lowering systolic blood pressure (SBP) reduces CV events. According to the current ESC/European Society of Hypertension guidelines, a target BP<140/90mmHg is recommended except in patients with diabetes, for whom a diastolic blood pressure ≤85mmHg is considered safe.[19]

In subjects with hypertension, calcium antagonists or ACEIs/ARBs should be preferred because of their potential in peripheral arterial dilatation however they may create a steal phenomenon by dilating vessels in normally perfused tissues thus shifting the distribution of blood flow away from muscles supplied by obstructed arteries. [16]

Table1.17 Recommendations in patients with peripheral arterial disease:Best MedicalTherapy.[(19)]

Recommendations	Class[a]	Level[b]
Smoking cessation is recommended in all patients with PADs.	I	B
Healthy diet and physical activity are recommended for all patients with PADs.	I	C
Statins are recommended in all patients with PADs.	I	A
In patients with PADs, it is recommended to reduce LDL-C to < 1.8 mmol/L (70 mg/dL) or decrease it by ≥ 50% if baseline values are 1.8–3.5 mmol/L (70–135 mg/dL).	I	C
In diabetic patients with PADs, strict glycaemic control is recommended.	I	C
Antiplatelet therapy is recommended in patients with symptomatic PADs. [1]	I	C[d]
In patients with PADs and hypertension, it is recommended to control blood pressure at < 140/90 mmHg.	I	A
ACEIs or ARBs should be considered as first-line therapy[c] in patients with PADs and hypertension.	IIa	B

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin-receptor blockers; LDL-C = low-density lipoprotein cholesterol; PADs = peripheral arterial diseases.
[a]Class of recommendation.
[b]Level of evidence.
[c]Calcium channel blockers should be proposed in black individuals.
[d]Evidence is not available for all sites. When evidence is available, recommendations specific for the vascular site are presented in corresponding sections.

Table 1.18 ESC. Recommendations for the diagnosis and mangment of peripheral arterial disease in patients with diabetes.[58]

LEAD management		
In patients with DM and symptomatic LEAD, antiplatelet therapy is recommended.	I	A
As patients with DM and LEAD are at very high CV risk,[d] an LDL-C target of <1.4 mmol/L (<55 mg/dL), or an LDL-C reduction of al least 50% is recommended.	I	B
In patients with DM with CLTI, the assessment of the risk of amputation is recommended; the WIfI score[e] is useful for this purpose.	I	B
In case of CLTI, revascularization is indicated whenever feasible for limb salvage.	I	C
In patients with DM with CLTI, optimal glycaemic control should be considered to improve foot outcome.	IIa	C
In patients with DM and chronic symptomatic LEAD without high bleeding risk, a combination of low-dose rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered.	IIa	B

Table 1.19 ESC.Recommendations on the mangment of chronic limb-threatening ischemia.[(19)]

Recommendations	Class[a]	Level[b]
Early recognition of tissue loss and/or infection and referral to the vascular team is mandatory to improve limb salvage.	I	C
In patients with CLTI, assessment of the risk of amputation is indicated.	I	C
In patients with CLTI and diabetes, optimal glycaemic control is recommended.	I	C
For limb salvage, revascularization is indicated whenever feasible.	I	B
In CLTI patients with below-the-knee lesions, angiography including foot runoff should be considered prior to revascularization.	IIa	C
In patients with CLTI, stem cell/gene therapy is not indicated.	III	B

CLTI = chronic limb threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

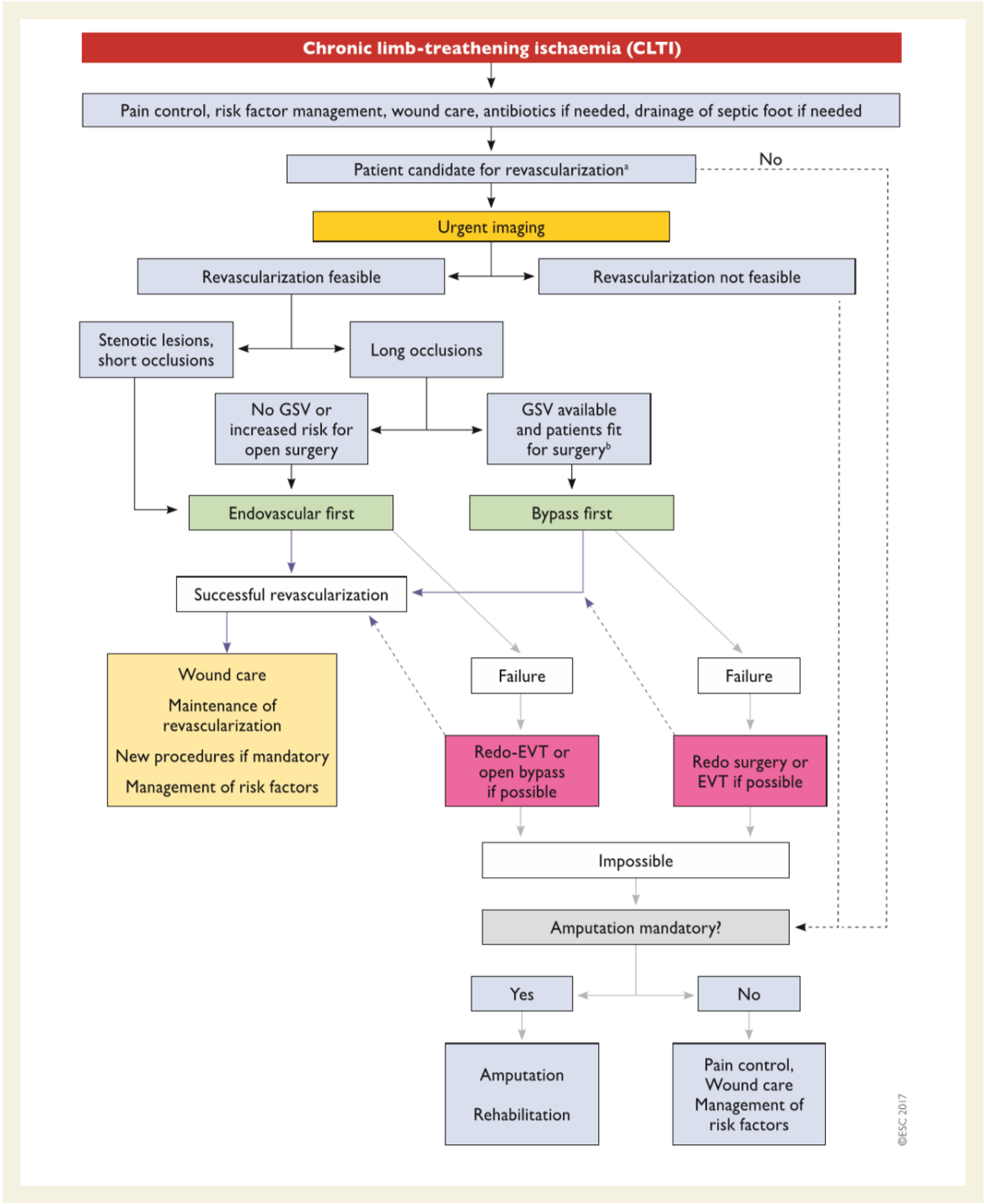


Figure 1.9 Mangment of patient with chronic limb-threatening ischemia.[(19)]

EVT=endovascular therapy; GSV=great saphenous vein.

A. In bedridden, dementedand/orfrail patients, primary amoutation should be considered.

B. In the absence of contra-indications for surgery and in the absence of adequate targetfor anstamossi /runoff.

Table 1.20 Recommendations on revascularization of infra-popliteal occlusive lesions.[19]

Recommendations	Class[a]	Level[b]
In the case of CLTI, infra-popliteal revascularization is indicated for limb salvage.	I	C
For revascularization of infra-popliteal arteries:		
• bypass using the great saphenous vein is indicated	I	A
• endovascular therapy should be considered.	IIa	B

CLTI = chronic limb threatening ischaemia.
[a]Class of recommendation.
[b]Level of evidence.

1.7.2 Ulcer /Wound Management and Dressings

A: Ulcer

The evidence to support the use of a particular dressing or topical therapy for the ulcer bed is thin. Providing a comprehensive environment to improve healing with antibiotics, debridement and offloading is superior to the use of a novel, and often expensive, dressing. It is what you take off the wound and not what you put on it that counts.[16]

B: Wound Care

Wound care principles include improving perfusion into the limb, treating infection, avoiding pressure on a wound, debridement, and adequate nutrition. Debridement of devitalized or infected tissue by scalpel, collagenases, or even maggots promotes wound healing. Antibiotics may be required to treat infection to prevent osteomyelitis. Avoiding pressure on the wound (eg, off-loading the foot) also assists wound healing. The local temperature of the limb can be increased using sheepskin (Rooke) boots and may improve superficial collateral flow to help perfuse a limb. Negative pressure dressings (eg, vacuum-assisted) increase capillary flow and help drain wounds. Hyperbaric oxygen therapy offers no advantages for amputation prevention, but may improve the more subjective end point of wound healing in diabetes mellitus. In patients where there are no revascularization options, intermittent pneumatic compression (arterial flow Pump) may assist wound healing and prevent major amputation. [(59)]

1.7.3 Infection/Antibiotics

Infection of a foot ulcer can be a major threat to limb and life and should be treated promptly. The IWGDF has produced guidelines for the treatment of diabetic foot infections based on the severity of infection, which predicts amputation. Ulcers with superficial infection should be treated with debridement and oral antibiotics aimed at Staphylococcus aureus and streptococci. Targeted therapy against gram positive cocci has been shown to be equally effective as broader spectrum regimens (level I evidence), even in the presence of osteomyelitis which will respond to antimicrobial therapy in most cases. Deep infection, characterized by purulent discharge or fullness in the plantar space, necessitates urgent debridement of necrotic tissue including infected bone, and revascularisation if indicated. Intravenous broad-spectrum

antibiotics should target Grampositive and negative micro-organisms, including anaerobes. Signs of life and limb threatening infection include bullae, ecchymoses, soft tissue crepitus and rapid spread of infection.[16]

1.7.4 Revascularization

Revascularization is the cornerstone of therapy for CLTI and has a Class I recommendation by all professional guidelines. Without revascularization up to 40% of patients with CLTI will require lower limb amputation by 1 year. Furthermore, after an index amputation, a significant number of patients will require contralateral amputation (5.7% and 11.5% at 1 and 5 years, respectively), have recurrent ulcers on the ipsilateral leg, or die.[52]

Revascularisation is indicated in patients with chronic obstructive arterial disease and: disabling claudication and/or pain at rest and atrophic lesion and foot TcPO2 of <30 mm Hg or atrophic lesion that shows no sign of healing after being adequately treated for 1 month.

Revascularization options for patients with CLI include endovascular, surgical, or the combination of both (hybrid procedure).[52]

Although long-term patency is better after bypass surgery than after angioplasty, which is burdened by a high restenosis rate,angioplasty can also be proposed for patients who cannot be candidates for a bypass because of significant co-morbidities, a reduced life expectancy, infection or gangrene in the possible sites of distal anastomoses, the unavailability of suitable veins or the absence of an adequate ‘landing zone’ for the distal part of the bypass.[57]

Short history of endovascular treatment invention
Charles Theodore Dotter The Father of Intervention

The 1st percutaneous transluminal angioplasty marked a new era in the treatment of peripheral atherosclerotic lesions. The early techniques used in peripheral percutaneous transluminal angioplasty form the basis for subsequent percutaneous intervention both in the peripheral and coronary arteries and are largely the contribution of Charles Dotter. Dotter was the 1st to describe flow-directed balloon catheterization, the double-lumen balloon catheter, the safety guidewire and the"J" tipped guidewire, percutaneous arterial stenting,and stent grafting by placing the 1st percutaneous "coilspring graft" in the femoral artery of a dog. This practical genius contributions to clinical medicine, research, and teaching have saved millions of limbs and lives all over the world.[(60)]

Charles Theodore Dotter is generally credited with developing a new medical specialty, interventional radiology. His contributions to vascular and interventional radiology are fundamental and broad in scope.He was a leading force in Machlett's development of an x-ray tube capable of obtaining millisecond exposures. Percutaneous transluminal angioplasty was his landmark Contribution. He pioneered the techniques of low-dose fibrinolysis with injection of streptokinase directly into an occluding thrombus. Dotter (along with Marcia K. Bilbao) invented the "loop-snare catheter" for retrieving intravascular foreign bodies. He developed tissue adhesives for vascular occlusion and organ ablation.[(60)]

The main theme of Dotter's work was the use of catheters for diagnosis and treatment in an attempt to replace the scalpel. His technique was even affectionately referred to as "Dottering an arterial stenosis."*[(60)]

Dotter was born in Boston on 14 June 1920.He derived great satisfaction fromWorking with tools and rarely encountered a machine in adulthood, Dotter designed his own "conceptual trademark" in the form of a crossed pipe

and Wrench, both because he loved mechanical things and because this emblem meant “that if a plumber can do it to pipes, we can do it to blood vessels.”

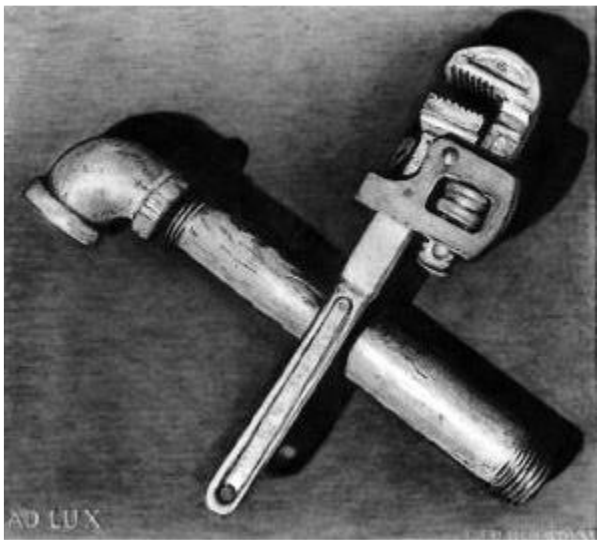


Figure 1.10 Dotter’s crossed pipe and wrench.

My favorite conceptual trademark is a sketch that I did years ago of a crossed pipe and wrench. It’s a gross over simplification, of course, but what it means to me is that if a plumber can do it to pipes, we can do it to blood vessels.” (Courtesy of the Dotter Interventional Institute) [60]

Unique aspects and challenges

Diabetic-associated PAD presents several unique characteristics on contrast to traditional PAD, The most evident is the presence of significant medial calcinosis. Large calcium burden is known to increase the risk of embolization with intervention, increase difficulty of crossing total occlusions, and increase the incidence of restenosis in treated segments. In addition, severe medial calcinosis makes standard measures of severity of disease unreliable and complicates the follow-up of lesions. Lack of progress of a wound should mandate re-evaluation. In general, wound healing, on average, after endovascular therapy requires 7 months, whereas it requires only 4 months after open-revascularization, although the overall rate of wound healing may be equal 3-5 month. Revascularisation in patients with diabetes can be technically difficult by also due to the distal distribution of the disease, impaired collateral formation.[(61)]

Indications for revascularization

The concept of 'time is tissue' also applies to the foot, and so delayed or inadequate treatment leads to the irreversible loss of portions of foot tissue In the case of a foot ulcer in a diabetic patient with PAD, it is first necessary to evaluate the usefulness of revascularisation and then choose the method of revascularisation on the basis of the following clinical criteria: the healing potential of the ulcer;the local condition of the foot and its residual function after the healing process; the condition of the vascular tree; and finally the general condition of the patient. The (absolute or relative) exclusion criteria are a life expectancy of <6 months, psychiatric disorders, untreatable antalgic flexion of the leg on the thigh, chronic bed confinement and the absence of deambulation. [(57)]

It is probably better not to generalise but to evaluate the situation from time to time, also considering the improved quality of life that comes from pain

control when the ischaemia is removed. Once a perfusion deficit has been diagnosed, revascularisation should always be considered. endovascular treatment of any coronary and/or carotid perfusion deficit has priority over peripheral revascularisation.

Advantageous aspects of endovascular interventions in the diabetic patient; there is no question that endovascular techniques have afforded the ability to treat many patients who have no open surgical options. This may be the case because of poor target and run-off, which would not sustain a bypass, absence of adequate saphenous vein conduit, poor medical condition, or a failed prior open revascularization. Furthermore, endovascular techniques often give us the ability to treat a multitude of tibial vessels, as opposed to open bypass where usually just one vessel is targeted. Multiple revascularizations may provide better flow as well as angiosome-specific revascularization. Furthermore, endovascular interventions are relatively non-invasive and not associated with the potential wound morbidity of open bypasses. No extensive preoperative cardiac work up is necessary, and interventions can be easily repeated.[61]

Revascularization should be attempted as much as possible.[62] So far, only one randomized trial, the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial, has directly compared endovasculartherapy to open surgery in CLTI patients.At 2years there was no significant difference between endovascular therapy and surgery regarding amputation-free survival. In survivors after 2years, bypass surgery was associated with improved survival (on average 7months, P = 0.02) and amputation-free survival (6months, P= 0.06).[63] These data are challenged by more recent endovascular therapy techniques. So far, drug-eluting balloons in below-the-knee disease have shown no superiority over plain balloon angioplasty. The

results of two ongoing RCTs,BASIL-2 and Best Endovascular vs. Best Surgical Therapy in Patients with Critical Limb Ischaemia(BESTCLI), are awaited.Meanwhile, in each anatomical region, both revascularization options should be individually discussed.[19,64]

Aorto-iliac disease. CLTI is almost never related to isolated aorto-iliac disease,and downstream lesions are often concomitant.In addition to CTA and/or MRA, complete DSA down to the plantar arches is required for proper arterial network assessment and procedure planning.Hybrid procedures(e.g.aorto-iliac stenting and distal bypass) should be encouraged in a one-step modality when necessary.[65]

Femoro-popliteal disease. CLTI is unlikely to be related to isolated SFA lesions; usually femoro-popliteal involvement combined with aorto-iliac or below-the-knee disease is found. In up to 40% of cases, inflow treatment is needed.The revascularization strategy should be judged on lesion complexity. If endovascular therapy is chosen first, landing zones for potential bypass grafts should be preserved. When bypass surgery is decided, the bypass should be as short as possible,using the saphenous vein.[19]

Infra-popliteal disease. Extended infra-popliteal artery disease is mainly seen in diabetic patients, often associated with SFA lesions (inflow disease). Full-leg DSA down to the plantar arches is mandatory to explore all revascularization options.In stenotic lesions and short occlusions, endovascular therapy can be the first choice. In long occlusions of crural arteries, bypass with an autologous vein gives superior long-term patency and leg survival. If the patient has increased risk for surgery or does not have an autologous vein, endovascular therapy can be attempted. The decision of revascularization should also consider the angiosome concept, targeting the ischaemic tissues. [19,65]

New Techniqes of Infrapopliteal Revascularization

The considerable industrial effort that has been made to create new instruments (very long, low-profile balloons, drug-eluting balloons, Drug-eluting or non drug eluting self-expandable stents, drugeluting bioabsorbable scaffolds,atherotomes, etc.) means that angioplasty can be increasingly proposed even in extreme situations and assures the better long-term patency of the treated vessels.[57]

The pedaleplantar loop technique can often restore a direct arterial inflow from both tibial arteries achieving a complete below-the-knee and below-the-ankle revascularisation and providing a high rate of acute success, intended as the ability to cross the lesions and inflate the balloon, achieving adequate angiographic results, without periprocedural complications.[57,66]

Subintimal angioplasty is another useful technique in the management of diabetic patients with occlusive disease. Finally, stenting may also have a role in the infrapopliteal level. Fine guidewires (0.014) and rapid exchange catheters, balloons and stents may improve the management of such difficult lesions and patients.[67,68]

Retrograde tibiopedal access has gained significant momentum worldwide .This approach improves lesion traversal rates. The retrograde approach can potentially lower costs by reducing the need for chronic total occlusion devices, decrease lesion crossing time, favor intraluminal crossing, and improve procedure success rates. Pedal access can be and is frequently obtained with ultrasound guidance, although many operators also prefer the fluoroscopic approach.Tibial access can lead to bleeding with resultant compartment syndrome; meticulous attention to hemostasis at the tibial access site can minimize this risk. In general, the operator should minimize

sheath size and manipulation of these vessels to reduce spasm, trauma, and occlusion.[52,66]

Ostial lesions in the proximity of the popliteal trifurcation may also require "*kissing" techniques* to ensure patency of all neighbouring arteries particularly long lesions.

Finally, other endovascular adjuncts include cutting balloon or laser-assisted angioplasty, cryoplasty, brachytherapy, atherectomy techniques and remote endarterectomy.[67]

Follow up after revascularization

should be clinical, oximetric and/or ultrasonographic, and the examinations should take place 1, 3, 6 and 12 months after treatment, and every 12 months thereafter. However, just as the treatmentof DF needing a multidisciplinary approach.[57]

In the case of percutaneous revascularisation, the follow-up criteria are uncertain. Given that extreme revascularization of the infra-popliteal arteries is burdened by early restenoses (70% after 3 months), an exclusively vascular follow-up aimed at identifying and treating such restenoses could lead to an incessant re-treatment without reflecting the clinical reality.The occurrence of restenosis is not always an indication for re-treatment per se, but re-treatment should be considered in patients with recurrent clinical symptoms or patients in whom the process of wound healing has been interrupted.[57]

Clinical follow-up criteria

These criteria include limb salvage (the avoidance of major amputation of the leg or thigh), wound healing (the complete closure of skin lesions) and healing after 'minor amputation' of the toes, rays or tarsal region. Clinical criteria such as the healing time of foot lesions, the restoration of walking

capacity and the time needed for this restoration (time to walking) are currently underestimated in the literature and should be reconsidered as primary criteria.[57]

1.7.5 Amputation

Primary amputation is a demolitive operation that is not preceded by any attempt at revascularisation, and it is considered primary therapy only in some cases of DF.Major amputations (above the ankle) are necessary when there is a life-threatening infection & gangrene that cannot be controlled by antibiotics.And those who are non-ambulatory with severe comorbidities may be best In this context, amputation is indicated on the basis of the patient's general condition and the fact that any delay could affect patient survival.[57]

Secondary amputation should be performed when revascularization has failed and re-intervention is no longer possible or when the limb continues to deteriorate because of infection or necrosis despite patent graft and optimal management. In any case, infragenicular amputation should be preferred, because the knee joint allows better mobility with a prosthesis. For bedridden patients, femoral amputation may be the best option.[19,69]

As summarized in *Journal of Diabetes and its Complications*, major amputation rates were 17% after endovascular surgery and 16.8% after open vascular surgery ($P = .97$) at 3 years. Mortality was 43.1% after endovascular surgery and 46.5% after open vascular surgery ($P = .55$).

In the propensity score–adjusted analysis, patients undergoing endovascular surgery first had similar outcomes in terms of major amputation, mortality, and combined major amputation/mortality compared with those undergoing open vascular surgery. A longer time to intervention ($P = .003$) was

associated with an increased major amputation rate in the multivariable Cox regression analysis. [(70)]

FUTURE PERSPECTIVES

There are encouraging developments in other treatment modalities, including stem cell and progenitor cell therapy.As discussed previously, PAD is present in around half of patients with DFU. The impact of PAD on wound healing is compounded by impaired formation of new capillaries (angiogenesis) and proliferation of pre-existing micro-vessels into collateral arteries (arteriogenesis) in patients with diabetes. Stimulation of angiogenesis and arteriogenesis represent attractive approaches in DFU and there is accumulating evidence to confirm their efficacy in the treatment of critical limb ischaemia. Pooled data from studies of autologous bone marrow mononuclear cell (BMMNC) therapy in patients with PAD show increases in ABI values between 0.1 and 0.2 points, TcPO2 increases between 10 and 20 mmHg O2 and improvements in walking distances. Although data in selected populations with DFU are limited, one study in China demonstrated improved ulcer healing rates with BMMNCs and bone marrow mesenchymal stem cells compared with controls. Further research should clarify the role of cell therapies in DFU.[(16)]

CHAPTER TWO

PATIENTS &METHODS

Patients & Methods

2.1 Patients & Methods

The study is a interventional single center study in Sulaimanyah a city of Iraq, showing the short term effectiveness of endovascular revascularization (PTA) regarding wound healing and saving the limb from amputation in patients with ischemic diabetic foot, Approval had been obtained from medical ethics committee of the Collage of Medicine /University of Sulaymaniyah & written informed consents from the patients following the explanation of the procedure & its possible complications to the patients.

This study started from Jan.2018-March.2020; (26 monthes), took two years & two monthes.

suspected cases were referred from Sulaimaniyah diabetic centre that were:

(1) A known cases of diabetes mellitus diagnosed on the basis of the American Diabetes Association criteria

(2) An ischaemic foot lesion (started from Fontaine stage III, IV; Rutherford category4, 5 and 6);

(3) The presence of critical -BTK (below the knee) artery lesions, defined as >70% stenosis or occlusion involving either three leg vessels (anterior tibial, posterior tibial and peroneal arteries), with or without foot-vessel involvement (pedal or plantar).

(4) Cases with femoropopliteal critical lesion (>70% diameter stenosis or occlusion) underwent first step revascularization as inflow correction procedure.

The cases under went complete examination for peripheral pulses latter every case(155 cases) underwent Doppler ultrasound study(DUS), which allowed localization , visualisation and haemodynamic assessment of the arteries

using grey-scale, also known as B-mode imaging, color-flow Doppler mapping, power Doppler and pulsed-wave Doppler interrogation of blood flow a two fold increase in the peak systolic velocity generally indicates a 50% narrowing of the artery, while a 2.5-fold increase indicates a narrowing of greater than 50%.

Distal to a stenosis, the Doppler waveform changes shape due to damping with reduction in peak systolic velocity and a slower acceleration time (time from end diastole to peak systole;

- **Duplex ultrasound done** by using Affiniti 70 from Philips &Voluson E6 from GE ultrasound machines (from the 155 cases 145 cases continue the study as they had vascular abnormality , those who have normal Doppler are excluded from the study (10 patients) .then patient with Doppler signs of ischemia processed to ;
- **Lower limb computed tomo-angiography (CTA)** for 129 patients Using SOMATOM Definition AS OPEN 64 sclice from SIEMENS. CT angiography provides detailed assessment of vascular anatomy, disease burden and location, and lesion character helps localize the lesions targeted for revascularization, the selection of appropriate equipment or adjunctive devices, and the choice of arterial access site (ie, antegrade versus retrograde common femoral access, retrograde pedal access). These considerations will determine the patient position on the procedure table, room preparation, and can help minimize procedure duration, contrast use, and radiation exposure.These imaging procedures are conducted in X-ray Centre & Cardiac centers in Slemani teaching hospital. (16) Patient with renal impairment were excluded from CT angiography 4 of them just do DUS did not underwent CTA nor DSA.

- **Conventional angiography; 53** patients under went conventional angiography 12 of them directly underwent angiography because of renal impairment .13 of the cases excluded from the outcome (3 of them had SFA lesions only, 10 had variations (3 radumentary Anterior tibial artery, others non-significant lesions).

Eighty-eight (88) cases had signs of ischemia clinically & radiologically but cannot undergo intervention, some of them were toxic, presented late and his general conditions did not allow to undergo intervention, some patients were not convence to do such an intervention for already diblitated bed riddin patient, some times we faced shortage of material, as far as patients are not covered by insurance some of them faced finential problemes.

The comparison in outcome will be between those underwent intervention & those did not

2.2 Treatmnet protocol

All of the patients were treated in a sulaimanyah diabetic-foot clinic which is specialized clinit for dieabetes and underwent a three-step treatment protocol:

1.*Pre-PTA*: Surgical treatment to remove necrotic tissue and drain the abscess and phlegmon; broad-spectrum antibiotic therapy (Teicoplanin or Meropenem or ciprofloxacine + metronidazole) until a more specific indication emerged from the microbiological specimens; glycaemic control; and double antiplatelet therapy with aspirin (100 mg per day) and clopidogrel (a 300-mg loading dose followed by 75 mg per day).

A renal-protection protocol was used in all patients with creatinine levels of >1.1 mg dl^{-1}: a 1.0 ml kg^{-1} h^{-1} saline infusion (0.5 ml kg^{-1} h^{-1} in patients with a history of heart failure) 12 h before and 24 h after the procedure respectively and oral *N*-acetyl-cysteine 1200 mg twice daily on the day

before and the day of the procedure. Metformine was stopped 2 days before angiography & restarted when necessary after 2 days.
& post procedural preparation under taken for renal dialysis just in case if the patient proceed to renal failure or for cases that already had dialysis.

2. *Angiography and PTA*: cases are checked for blood urea & serum creatinine and viral markers as routine pre-procedural investigations.The procedures were performed under local anesthesia. An anterograde puncture of the ipsilateral or retrograde puncture of contralateral side of common femoral artery were systematically used, as was a 6/F introducer sheath. Optimal imaging of the vessel tree was obtained by using the non-ionic contrast medium iohexol (Omnipaque 350mg/ml), (GE Healthcare, USA) digital subtraction angiography, multiple oblique views and a lateral foot projection. A 0.014″ wire (Boston Scientific, and USA) was used to cross the lesions. Total occlusions were preferably re-canalized through the true arterial lumen using dedicated 0.014″ coronary wires such as Cruiser-18(BIOTRONIK) or Confianza (Asahi, Japan), but a sub-intimal approach was used in three cases after the failure of the endoluminal approach.Monorail PTCA dilatation catheter such as Mavrick (Boston Scientific ,USA) or NC Quantum Apex (Boston Scientific ,USA) wer used as predilatation step,then RapidCross(ev3 ,USA)or drugeluting balloon such as Passeo-18 LUX(BIOTRONIK)were inflated to 12–15 atm for 2-3 min. The balloon dimensions were chosen on the basis of the size of the artery 1:1 and the length of the lesion. We did not need Stenting as we hadnot faced flow-limiting dissection only 1 case had discsection that was resolved by prolonged (5–10-min) balloon inflations. Just with insertion of guide wire 70IU/kg intravenous heparin admenstred. If vessel spasm occurred, 0.1–0.2 mg of nitroglycerine was infused as an intra-arterial bolus. At the end of the procedure, haemostasis was obtained by means of local compression.

3. *Post-PTA treatment*: Some of the patients were reffered again to orthopedic surgeon again for the remavale of remnant necrotic tissue &further debridmnet. All of the patients received double antiplatelet therapy for a minimum of 1 month (aspirin 100 mg and clopidogrel 75 mg per day); the treatment was not interrupted when surgical procedures were undertaken. Glycemic control, antibiotics. After discharge, the patients were seen in the out-patient clinic every 3 months for minimum 9 monthes . All of the patients received optimal medical treatment for vascular risk factors.

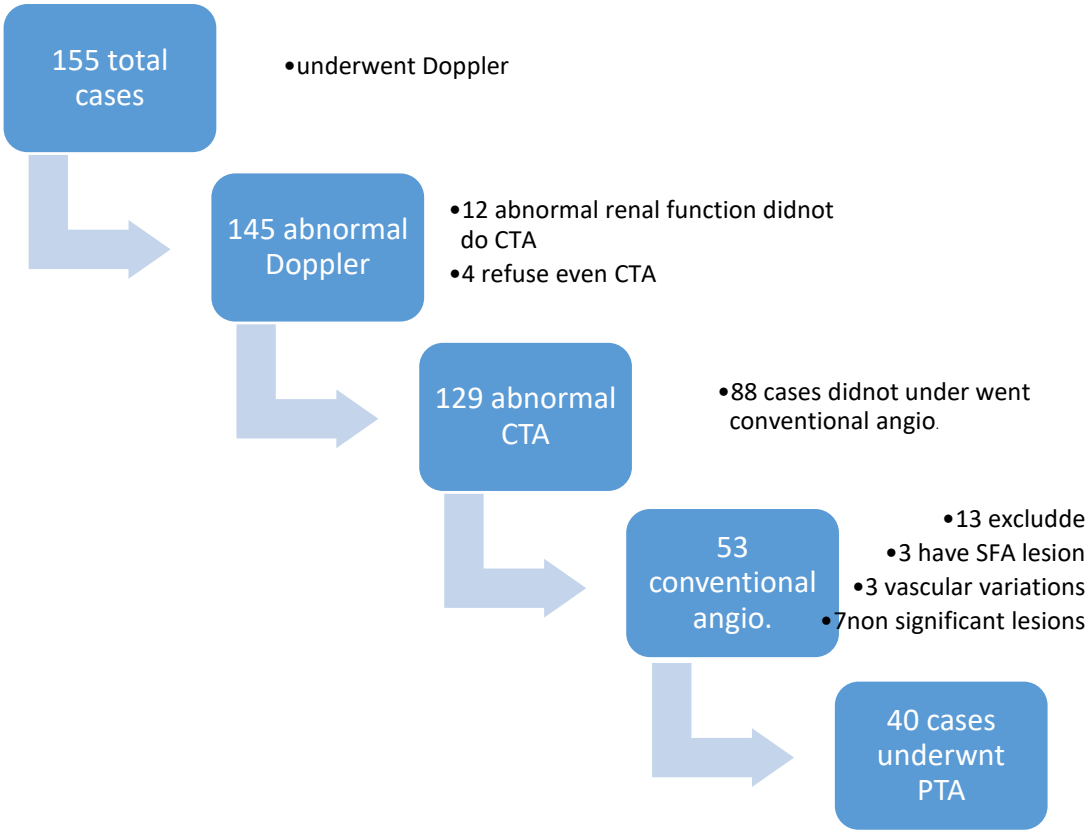


Figure 2.1 Diagram of the study particiants

CHAPTER THREE

RESULTS

Results

3.1 Results

A total of 155 patient were screened as suspected cases with limb ischemia ,145 of them has Doppler signs of ischemia the others were exclude ,129 of them under-went CTA (16 of them had abnormal renal function tests or refuse to do CTA),

53 of patients did conventional angiography & 40 of these underwent the definitive treatment by conventional PTA. 8 of the patients under went inflow lesions treatment (all of them had SFA lesions).

Those who did the Doppler study & CTA or only Doppler but not the angioplasty are (control group) were comparable with those who underwent angioplasty, both groups showed no significant difference in socio-demographic data such as: age, sex, smoking, renal impairment, presentation.

Table 3.1 Relevant patient`s characteristics

Patient characteristics / catheterization	Catheterization		Total	P value
	Yes	No		
Age				
Mean ± SD	64.0 ± 9.7	61.3 ± 10.1	62.2 ± 10.0	0.17
36 - 50 years	3 (7.5%)	11 (14.1%)	14 (11.9%)	0.43
51 - 65 years	21 (52.5%)	43 (55.1%)	64 (54.2%)	
> 65 Years	16 (40%)	24 (30.8)	40(33.9%)	
Sex				
Male	28 (70%)	45 (57.7%)	73 (61.9%)	0.19
Female	12 (30 %)	33 (42.3%)	45 (38.1%)	
Smoking				
Yes	7 (17.5%)	7 (9.0%)	14 (11.9%)	0.18
No	33 (82.5%)	71(91.0%)	104 (88.1%)	
Renal impairment				
Yes	11 (27.5%)	9 (11.5%)	20 (16.9%)	0.03
No	29 (72.5%)	69(88.5%)	98 (83.1%)	
Fontaine				
III	1 (2.5%)	1 (1.3%)	2 (1.7%)	0.24
IV	39 (97.5%)	72 (92.3%)	111 (94.1%)	
Both IV	0 (0%)	5 (6.4%)	5 (4.2%)	
Rutherford				
4	1 (2.5%)	1 (1.3%)	2 (1.7%)	0.12
5	28 (70.0%)	67 (85.9%)	95 (80.5%)	
6	11 (27.5%)	10 (12.8%)	21 (17.8%)	
Presentations				
Unilateral ulcer	38 (95.0%)	69 (88.46%)	107 (90.7%)	0.30
Bilateral ulcers	1 (2.5%)	8 (10.26%)	9 (7.6%)	
Rest pain	1 (2.5%)	1 (1.28%)	2 (1.7%)	

22.5% of the lesions were subtotal calcified (>90% stenosis +calcification),

65% were chronic total obstruction (CTO),

12.5% were critical stenosis (>70%stenosis).

30% of the lesions were short segment while 70 % were multifocal long segment.

Unilateral & bilateral limbs lesions were equal 50% for each.

According to Graziani`s classification of the lesions 75 % of the lesions angiographically were class 4, 5&6.

35% of the lesion were TASC C & 65% TASC D lesions.

This explain the late presentation & the severity of type of the lesion in diabetics.

Table 3.2 Angiographic features of the lesions

	Frequency	%
Type of BTK the lesion according to PARC classification.		
Subtotal calcified	9	22.5%
CTO	26	65.0%
Critical stenosis	5	12.5%
Length of BTK lesion according to PARC classification		
Short segment	12	30%
Long segment	28	70%
Unilateral or bilateral BTK lesion		
Unilateral	20	50%
Bilateral	20	50%
TASC C lesion *	14	35.0%
TASC D lesion *	26	65.0%
Graziani`s morphological classification		
Class 1	1	2.5%
Class2a	1	2.5%
Class 3	8	20%
Class 4	25	62.5%
Class 5	4	10%
Class 6	1	2.5%

TASC C: multiple stenosis or occlusions with or with out calcification

TASC D: chronic total occlusion of the proximal leg arteries

During angiography 1 patient had distal Post tibial A. perforation of long segment CTO lesion as a complication which is sealed conservatively & need no specific intervention and one patient had failure of revascularization.

As the main purpose result of the study 67.5% (27patient)of those underwent PTA got healing despite their lesions were critical or left for long time without treatment in comparison to those who did not got intervention 34.6%(27patients) got healing.

The minor amputation rate was 7.5 %(3patients) in whom underwent successful procedure & they protected from major amputation or septicemia by effect of the PTA and had stump healing & complete coverage of the bones, they get rid of infection & gangrenous tissue. While 2.6 %(2 apteints) had minor amputation in the control group who did not get intervention because they get major amputation more.

5 %(2 patients) had major amputation in those underwent PTA 1 above the ankle, 2 below the knee as had extensive tissue loss & wound infection. While control group had 10.3 %(8patients) underwent major (BTK) amputation as life protective measure.

From those who underwent PTA, 20 %(8patients) had no healing or experience recurrence (2 restenosis, 2 had associated uncontrollable infection, the other 4 although they still they have ulcer but it is smaller in size & dry).

While 47.4 %(37patients) their ulcers did not heal in those who did not get intervention.They followed clinically & by Doppler study.

Finally, in those who did not get PTA 5.1 %(4pt) passed away (2 by septicemia, 2 by stroke within 3 months from diagnosis of limb ischemia while no mortality in those who underwent PTA.

Table 3.3 comparison of the outcomes between those who underwent PTA (percutaneous transluminal angioplasty) & those who did not.

Outcome / Catheterization		**PTA**		**Total**	**P value**
		Yes	**No**		
Outcome	Healing	27 (67.5%)	27 (34.6%)	54 (45.8%)	0.003
	No healing or recurrence	8 (20%)	37 (47.4%)	45 (38.1%)	
	Major amputation	2 (5%)	8 (10.3%)	10 (8.5%)	
	Minor amputation	3 (7.5%)	2 (2.6%)	5 (4.2%)	
	Death	0 (0%)	4 (5.1%)	4 (3.4%)	
Total		40 (100%)	78 (100%)	118 (100%)	

Before **After**

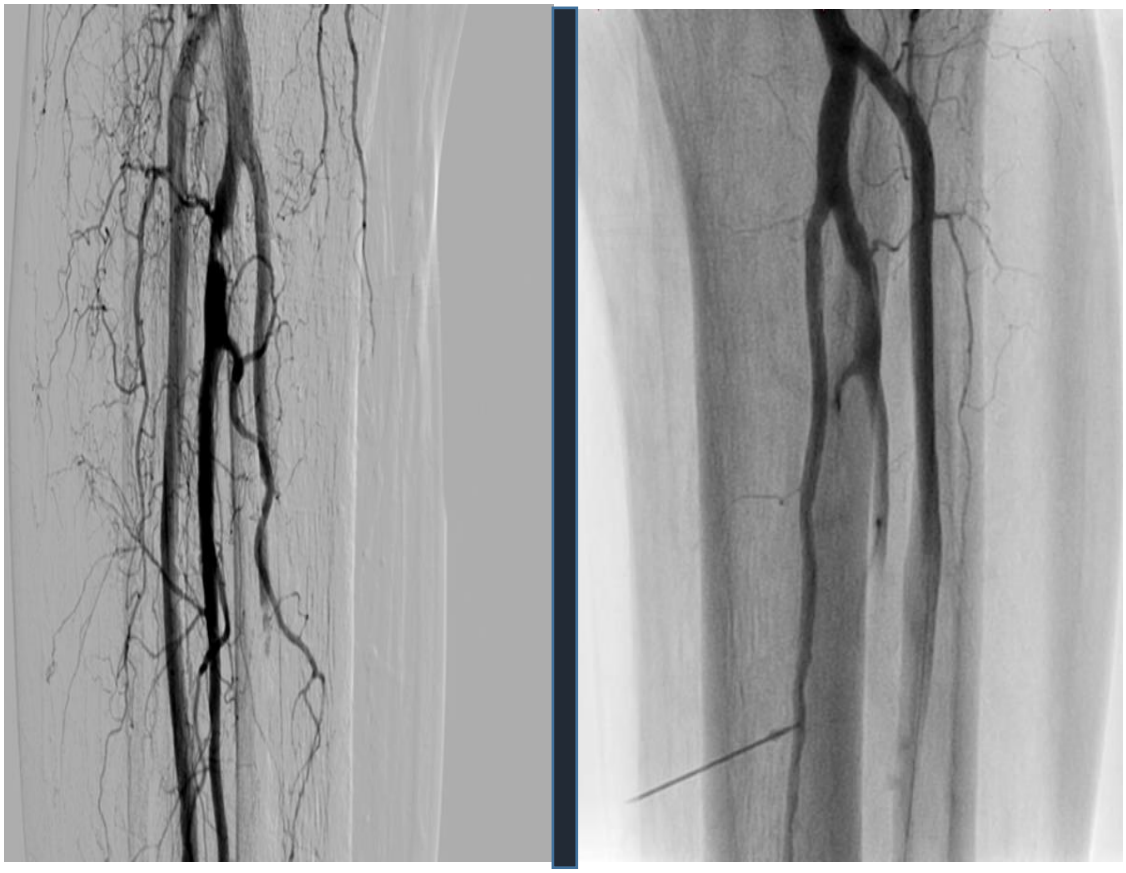


Figure 3.1 Angiographic images of posterior tibial artery before & after balloon dilatation

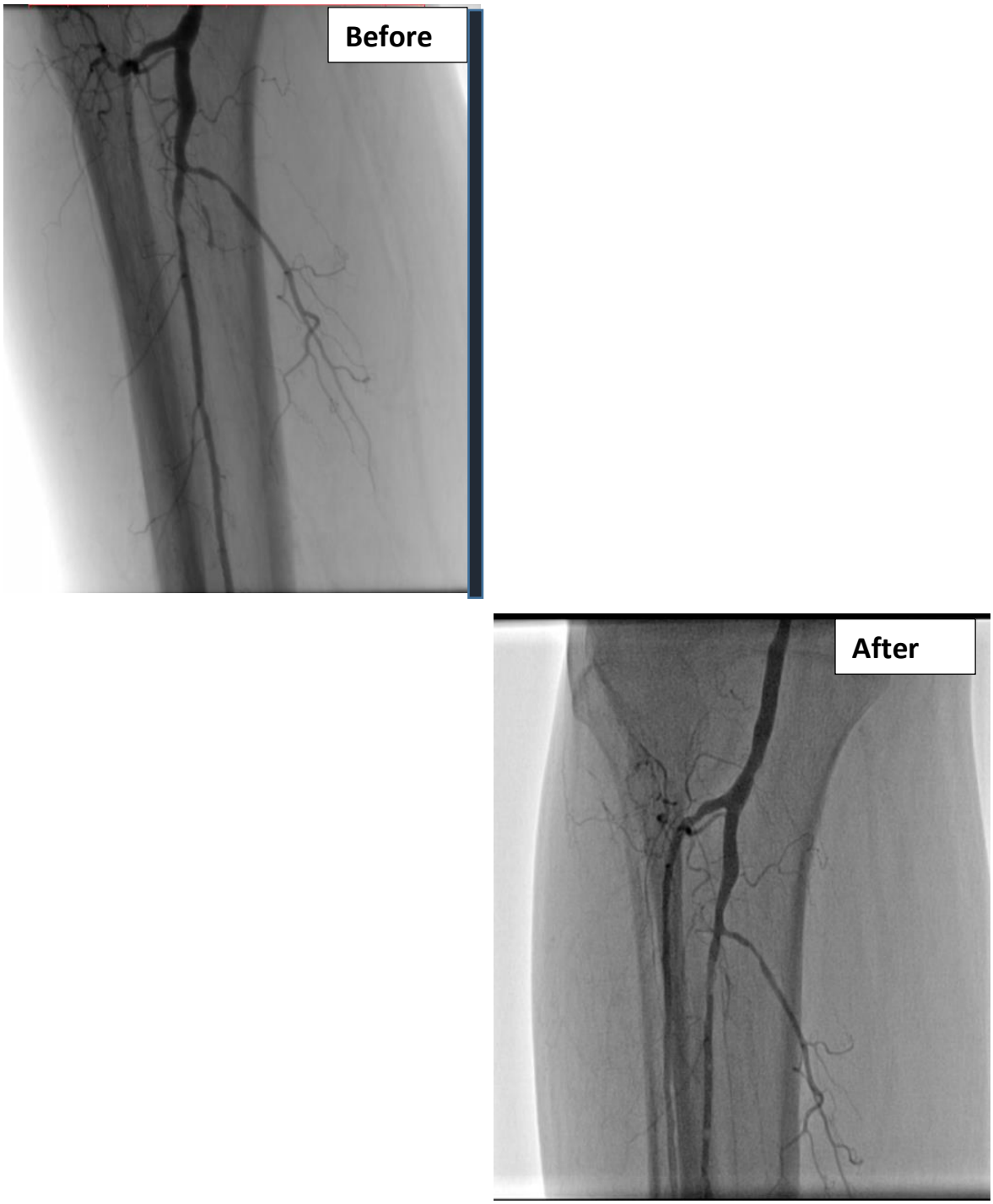


Figure 3.2 successful balloon dilatation of anterior tibial artery

Figure 3.3 posterior tibial artery ballooning

CHAPTER FOUR

DISCUSSION

4.1 Discussion

The main finding of our study is that a successful endovascular procedure decreased amputation rates(87.5%) ,decreased death rates(0%),as observed by other authors such as Fagilla et al&Ferrares et al.[71,72]

CLI is modifibele disease, treatable with medical& advanced surgical &/or endovascular techniques. The systemic atherosclerotic changes associated with CLI have high mortality rates exceeding those for every other form of occlusive cardiovascular disease, including symptomatic coronary artery disease (CAD). In association to the poor survival rates, prognosis with respect to limb preservation in CLI patients is poor.[73]

Revascularisation Data from the EURODIALE Study (a prospective study of newly presenting patients with DFU to 14 experienced European diabetic foot centres) would seem to suggest that many patients are not having vascular imaging nor being considered for revascularisation.[74]

Bypass surgery using outflow vessels in the distal ankle and foot should be considered the standard of care in patients with CLI due to BTK-vessel disease. However, it needs good vein conduit and at least one open foot artery and is associated with 0.9% perioperative mortality, 3.0% myocardial infarction or acute congestive heart failure and 6.6% early re-operation for graft thrombosis, postoperative bleeding or infection.[75] Studies showed a trend toward more endovascular as compared to surgical revascularization procedures and suggested a potential causal relationship between the increased number of endovascular procedures, especially in the high surgical risk patients, and reduced amputation rates.[57,73]

But, although many published papers have described interesting findings concerning the efficacy of the endovascular treatment of peripheral artery disease in such patients, there are discrepancies between the short- and long-

term results because the studies have not involved carefully selected patient populations or appropriately stratified the vessels on the basis of the degree and localization of atherosclerosis. In particular, the use of PTA to treat BTK arteries is criticized because of the small diameter and length of the treated vessel both of which tend to lead to a high restenosis rate; furthermore, it is not clear whether the clinical success of BTK-artery PTA is authentic or simply the result of improved outflow due to concomitant ATK procedures.[71]

70% of the patients had long BTK lesions & all of the lesions were either calcified critical or CTO lesions (table3.2) this represents the severity of the cases referred for CLI treatment, they are technically challenging, and our results support the role of PTA as the therapeutic option for CLI patients with BTK-artery disease.
Healing of ulcers occurred in about 67.5% of the cases & 20 % of the cases experience no healing or recurrence(still they have small dry ulcer) but did not need any amputation (in total limb salvage =87.5%)(table3.3) which is near the result study done by R. Ferraresi et al. [57,71,73]

27.5% from PTA group had renal imapirmnet &11.5% from control grup (who stayed on medical treatment)(table 3.1).Data pooled by the IWGDF from 19 studies of patients with DFU and PAD showed a median limb salvage rate of 85% at 1year. Half of patients with DFU and PAD can expect to be alive at 5-years and mortality rises to 50% in 2-years following a major amputation. Patients with co-existing chronic kidney disease (CKD) fare worse and the severity of CKD has been shown to correspond with poor outcomes and mortality following revascularisation.[16]

The effectiveness of PTA was demonstrated clinically & by the US wave-form changes which may explain the low rate of major amputations, 2 patient out of our 40 patients(5%) in comparison to those who did not underwent PTA which was 8 patients out of 78 (10%) (table 3.3), as reported by Faglia et al.[76] Who looked specifically at the prognostic value of this index.
As summarized in *Journal of Diabetes and its Complications*, major amputation rates were 17% after endovascular surgery and 16.8% after open vascular surgery ($P = .97$) at 3 years. Mortality at 3 years were 43.1% after endovascular surgery and 46.5% after open vascular surgery ($P = .55$).
In the propensity score–adjusted analysis, patients undergoing endovascular surgery first had similar outcomes in terms of major amputation, mortality, and combined major amputation/mortality compared with those undergoing open vascular surgery. A longer time to intervention ($P = .003$) was associated with an increased major amputation rate in the multivariable Cox regression analysis, reported by the investigators in *Journal of Diabetes and its Complications*. [77]

Finally, the incidence of follow-up mortality was 0% in PTA group (table 3.3), which is lower than the annual 20% death rate for patients with CLI reported in the 'TASC 2007' document , probably this related to the higher number of patients included in their study &nonhomogenous patient selection .while 4 cases (5.1%) deaths occurred in those patients who had not undergone PTA and showed diffuse and heavy calcification of the limb and foot arteries, a marker that has been previously identified as a strong predictor of a poor prognosis.[32] In which two of the patients died because of septicemia & wound infection.
Comparison of patients with PAD versus age-matched controls shows an incidence of cardiovascular death of 0.5% in controls and 2.5% in the patients with PAD. Additionally, in persons with known coronary artery disease, the

presence of PAD raises the risk of death by 25% in comparison with controls. It is thus important to examine for PAD, even in asymptomatic patients, in order to control the risk factors as soon as possible and reduce mortality.[32]

We achieved techniqul success in 39 patients out of 40 patients, as reported by Faglia et al; the restoration of straight-line flow down to the foot in at least one crural artery is of paramount importance for short- and long-term clinical success. Another explanation for successful procedure may be the combination of PTA and a good surgical approach to foot lesions (before and after the procedure), together with a strict clinical follow-up. Follow-up re-stenosis in the surviving limbs was only ascertained by US. It is well known that angiography is the gold standard for evaluating infrapopliteal arteries, but US can be used to assess infrapopliteal artery patency if appropriate criteria are adopted.[71]

A review of the literature on this subject suggests a 50% recurrence rate at less than 1 year and roughly a 25% limb loss rate annually. A review published in the Annals of Vascular Surgery in 2009 examined 45 patients undergoing tibial intervention for CLI. A total of 90% of patients were diabetic and 45% were on dialysis. Nearly half required concomitant superficial femoral angioplasty. Symptoms recurred in 43% at 8 months. There was also a 25% major amputation rate in that time period. Another review of 176 cases was published in the Journal of Vascular Surgery in 2008. At 1 year, there was a 46% primary patency and 84% limb salvage rate. A total of 15% of patients required surgical bypass. Those unsuitable for bypass had a higher rate of restenosis and limb loss.There is some data to suggest that atherectomy may be of benefit in the diabetic patients with PAD. In a comparison of diabetic versus non-diabetic patients, Sixt et al. demonstrated equivalent outcomes with respect to major adverse events and improvement in ischemia measures in a comparison of 80 diabetic patients

Versus 92 non-diabetics. Empirically, debulking of the heavy plaque burden in the calcified vessels may lead to an improvement of overall endovascular therapy. In our practice, balloon expandable drug eluting stents for focal tibial lesions have been performed with good results, but this has not been validated in any trial to date.None are available in long lengths for extensive chronic total occlusions (CTO). Drug eluting balloons appear to be of benefit over regular balloons in infrapopliteal lesions but are not available in the US. [(61)]

There are no randomized trial data comparing surgical bypass and endovascular interventions in selected patients with diabetes or infrageniculate disease, however, in patients with diabetes and an ischaemic foot ulcer, these techniques appear to offer equivalent outcomes where revascularisation is successful.The BASIL trial,43 which randomized patients with severe limb ischaemia (rest pain or tissue loss for >2 weeks) to bypass or balloonangioplasty, demonstrated similar outcomes in terms of health-related quality of life and amputation-free survival, although less than half of randomized patients had diabetes and no sub-group analyses were performed. Endovascular techniques performed under local anaesthesia are lower-risk than bypass surgery and cost considerably less; however, an increased re-intervention rate following angioplasty in the BASIL trial reduced any overall cost difference. Data from the BASIL trial suggest they are also associated with lower short-term morbidity and, as such, endovascular therapy is probably justified as the initial approach to restoring perfusion. Surgical bypass has the advantage of increased durability when autologous vein is used but patients with multiple comorbidities and a short life expectancy (6-12 months) are unlikely to realize this benefit. The distal distribution of PAD in diabetes has brought about innovation and development in both endovascular techniques and open bypass surgery.

Some authors advocate revascularisation based on the angiosome model of perfusion, where the target artery corresponds to the area of tissue loss. It is important to note that angiosomes are a representation of normal anatomy and changes to the collateral circulation that result from PAD mean the success of this technique in reconstructive surgery will not necessarily extrapolate to revascularization in cases of DFU.[16]

A Swiss prospective study evaluated 426 limbs with CLI, 46% of which were diabetic. The study was not randomized; 207 limbs were treated with angioplasty, 85 with surgery, and 108 were observed. The initial clinical success was better in non-diabetics versus diabetics, but more frequent re-interventions in diabetics made the results equivalent to the non-diabetic patients. The limb salvage rate was the same in endovascular and open surgery in the diabetic group. Romiti et al. published a meta-analysis of 30 studies. At 3 years, primary patency was much better for bypass (72%) than angioplasty (49%) but limb salvage remained the same. It is unclear as to whether the addition of newer technology, such as atherectomy, covered stenting, or drug elution, will change the balance in favor of endovascular therapy. In a more contemporary analysis of vein bypass, amputation-free survival continues to be 80%, even in high-risk patients. [61,78]

4.2 Study limitation

Only 53 patient out of 155 ptients underwent catheterization & the other did not!

In our country Iraq as general & Kurdistan region of Iraq specially ; this is the 1st time to establish such a work by radiologist ,till the time peripheral endovascular intervention is the job of our cardiologist colleagues and because it is time consuming procedure for the cardiologists & the lack of the distal run off of the arteries makes a great obstacle for vascular surgeons

On the other hand CLI generally & diabetic foot specially is not well-known disease in the community most of the patients are elderly debilitated & already have a lot of co-morbidities & not active in the community so we try to introduce this spectrum in other way to the public awareness & as well to the other specialty doctors in our region.

At the most bigning; dedicated peripheral instruments for the peripheral interventions was not well-konwn. Over the last 3 years we try to introduce these instruments to the health care sector in the government in order to reduce the financial load for the patients as far as we are in a region not covered by health insurance and we faced the shortage of instrument in public sector the patients some times has to do these procedures in private sector which is coasty for a patient who is already not employee & not active any more.

In other way we try to orient community about this spectrum of disease as its symptom intermingle with other symptoms for example intermittent claudication with symptoms of disc prolapse & neurological diseases or impotence as symptom of ischemia.

We as a team faced a lot of difficulties to convene the patient to do peripheral catheterization because a lot of them did not hear other than cardiac cauterization.

In the study period the sample size was limited because our cases are diabetic with critical limb ischemia many of them experience associated renal impairment which precluded CTA &PTA

CHAPTER FIVE

CONCLUSION & RECOMMENDATIONS

5.1 Conclusion

Endovascular intervention has been minimized the death rate & other consequences of PAD.

Endovascular intervention helped in increasing limb salvage rate.thus improves quality of life.

Most of the people in the community are not oriented about this condition that is why they present late which makes any intervention difficult.

5.2 Recommendations

Based on the current study conclusions this study recommend

1. We recommend further support from directorate of governmental health sector in providing dedicated peripheral cathlab.involving DSA machine, dedicated peripheral instruments for intervention.
2. Peripheral arterial disease is a grave systemic disease, we encourage DUS as it is available, useful tool for screening of Diabetic patient.
3. Endovascular & vascular surgeons working as a team with further collaboration with other specialities.

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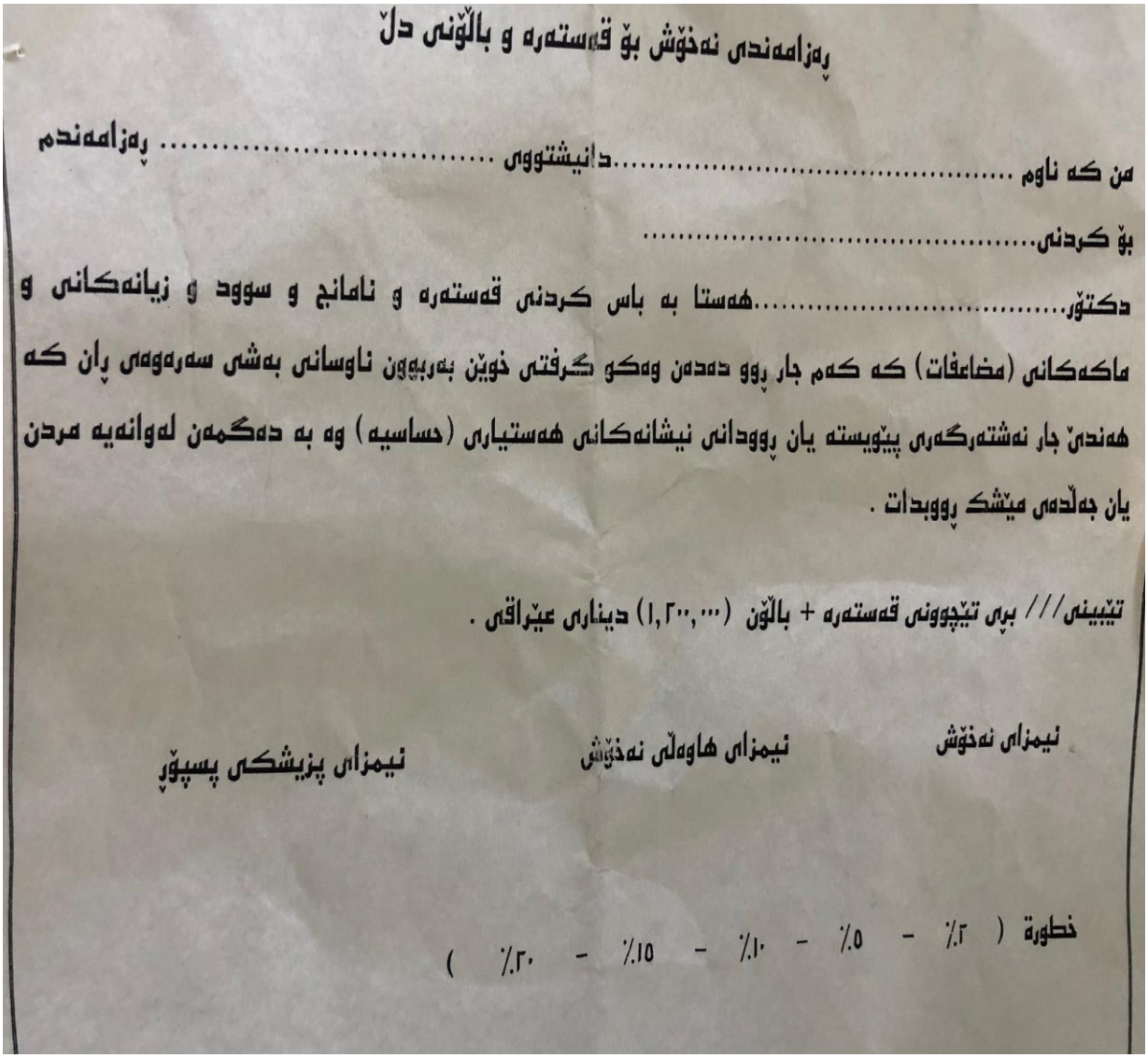
Inform consent for the patients



ڕەزامەندی نەخۆش بۆ قەستەرە و باڵۆنی دڵ

من کە ناوم .....دانیشتووی ..... ڕەزامەندم

بۆ کردنی.....

دکتۆر.....هەستا بە باس کردنی قەستەرە و نامانج و سوود و زیانەکانی و

ماکەکانی (مضاعفات) کە کەم جار ڕوو دەدەن وەکو گرفتی خوێن بەربوون ناوسانی بەشی سەرەوەی ڕان کە

هەندێ جار نەشتەرگەری پێویستە یان ڕوودانی نیشانەکانی هەستیاری (حساسیە) وە بە دەگمەن لەوانەیە مردن

یان جەڵدەی میشک ڕووبدات .

تێبینی/// بڕی تێچوونی قەستەرە + باڵۆن (١,٢٠٠,٠٠٠) دیناری عێراقی .

نیمزای نەخۆش نیمزای هاوەڵی نەخۆش نیمزای پزیشکی پسپۆڕ

خطورة (٢٪ - ٥٪ - ١٠٪ - ١٥٪ - ٢٠٪)

Log in

CLINICAL RESEARCH

Below-the-Knee Intervention for Ischemic Diabetic Foot in Kurdistan, Iraq: A Case-Control Study

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PlumX Metrics

Highlights

- Management of infrapopliteal arterial disease in diabetics is challenging.
- Healing ulcers in diabetic feet is crucial for improving patients' quality of life.
- No single revascularization procedure is currently outstanding for ulcer healing.
- Surgical bypass, catheter intervention, and hybrid procedures are 3 available options.
- Intervention healed more diabetic foot ulcers than medical therapy in this study.

Background

Management of the ischemic diabetic foot (DF) due to infrapopliteal arterial disease is challenging and controversial. Observation, bypass surgery, and endovascular intervention are the 3 available options. Outcome of percutaneous transluminal angioplasty (PTA) versus conservative therapy is evaluated in this prospective study from Sulaymaniyah, Iraq.

وزارة التعليم العالى

و البحث العلمى

جامعة السليمانية

اِجرء التداخلات القسطرية عند مرضى القدم السكري بسبب اِنسداد شرايين تحت الركبة

أطروحة مقدمة الى مجلس كلية الطب/ جامعة السليمانية، كجزء من متطلبات نيل شهادة الدكتورا في قسم الأشعة والتدخلات القسطارية.

من قبل

نارين نوزاد محمود

دبلوم عالي في الأشعة التشخيصية

بِاشراف

د. ناصر عبدالله محمد

أستاذ مساعد في الأشعة التشخيصية

د.ئارام جمال ميرزا

أخصائي القلب والتداخلات القسطارية

جماد الثاني 1442

كانون الثاني 2021

الخلاصة:

الخلفية العلمية:

علاج القدم السكري بسبب انسداد الشرايين تحت الركبة يتحمل المزيد من التحديات.

علاج بالأدوية أو العمليات الجراحية المتنوعة أو التداخلات القسطرية هي الأحتمالات العلاجية المتوفرة.

الهدف:

نتيجة العلاج بالتداخلات القسطارية تمت مقارنتها مع نتيجة المرضى اللتي لم تجرى لهم أي تداخلات و تمت معالجتهم بالأدوية فقط (كونترول).

الطريقة:

على مدى أكثر من سنتين ابتداءاً من الكانون الثاني 2018، 40 مصابا بالقدم السكري تم علاجهم باقسطرة والبالون و تمت مقارنتهم مع 88 مريض لم تجرى لهم القسطرة، بعد الفحص السريري جميعهم أجريت لهم دوبلر أو سونار ملون لشرايين الأطراف السفلية بينما اجراء الأشعة الملونة التقليدية أُجريت في المرحلة الأخيرة للمرشحين للعلاج بالقسطرة والبالون، واللذين تمت مقارنة نتائجهم بالمرضى اللذين تم معالجتهم بالأدوية فقط.

النتائج:

متوسط العمر كان 64 سنة، 28 مريضا منهم كانوا ذكوراً (70٪) ونسبة الذكور:الأناث كان 1:203. المصابين بأعتلال الكلية كانوا 11 مريضا (27.5٪) و 7 من المرضى كانوا من المدخنين (17.5٪). من أكثر الأعراض شيوعا هو عدم شفاء القدم السكري (39 مريضا 97.5٪) وبعضهم حذفوا كفونتاين 4 ورذرفورد 5 و 6 ومنهم الأنسدادات كانت معقدة من الناحية التشريحية. و منهم كانوا (TASC) C و D و كرازياني 4 (75٪) أنسداد طويل 28 مريض (70٪) أنسداد كامل (26 مريض 65٪)، نسبة النجاح كانت عند 38 مريض 95٪ وعدم وجود حالات الوفاة، شفاء تقرح القدم السكري كان أعلى في المرضى اللذين أجريت لهم القسطرة والبالون مقارنة مع المرضآ اللذين لم يجرى لهم (67.5٪ مقابل 34.6٪) ونسبة عودة التقرح 20٪ مقابل 47.5٪ ولكن نسبة البتر لم تكن نسبة مختلفة من الناحية الأحصائية (12.5٪ مقابل 12.8٪).

الأستنتاج:

مع أن نسبة البتر والوفاة لم تكن عالية إلا إن إجراء القسطرة والبالون للمريض ساعد على شفاء التقرح مقارنة مع اللذين لم تجرى لهم القسطرة والبالون.

وەزارەتی خوێندنی باڵا و

تـوێژینەوەی زانستی

زانکۆی سلێمانی

قەستەرەی دەمارەکانی ژێر ئەژنۆ لە بریتی پێی تـوشبووان بە نەخۆشی شەکرە لە کوردستانی عیراق

لێکۆڵینەوەیەکە، پێشکەش بە ئەنجوومەنی کۆلێژی پزیشکی زانکۆی سلێمانی کراوە، وەک بەشێک لە پێداویستییەکانی پلەی دکتۆرا لە زانستی رادیۆلۆژی.

لەلایەن

نارین نوزاد محمود

دبلۆمی باڵا لە رادیۆلۆژی

بە سەرپەرشتی

د. ناصر عبدالله محمد

پرۆفیسۆری یاریدەدەر لە رادیۆلۆژی

د. ئارام جمال میرزا

دکتۆرا لە نەخۆشییەکانی دڵ و دەمارەکان

بەفرانبار ٢٧٢٠

کانونی دووەم ٢٠٢١

سەرەتا:

چارەسەرکردنی بڕینی پێی تۆشبووان بە نەخۆشی شەکرە بە هۆی گیرانی دەمارە خوێنبەرەکانی لە خوار ئەژنۆوە کارێکی گفتوگۆ هەڵگرە. چارەسەر بە دەرمان یان نەشتەرگەری یان ئەنجامدانی قەستەرە، سێ جۆری ڕێگای چارەسەرکردنن.

ئامانج:

ئەنجامەکانی چارەسەر لە ڕێگەی قەستەرە بۆ دەمارە خوێنبەرەکانی خوار ئەژنۆ، لەگەڵ چارەسەرکردن لە ڕێگەی دەرمانەوە بەراورد کراون لەم تۆێژینەوەدا لەسلێمانی/ عیراق.

ڕێگای کارکردن:

لەماوەی دووساڵ لەکانونی دووەمی (٢٠١٨) هوە (٤٠) نەخۆشی تۆشبوو بە بڕینی پێی نەخۆشی شەکرە، قەستەرە و باڵۆنیان بۆ ئەنجام دراوە بەرامبەر بە (٨٧) نەخۆش کە تەنها لە ڕێگەی بەکارهێنانی دەرمان چارەسەر کراون وەکو کۆنترۆڵ گروپ پاش هەڵسەنگاندنی کلینیکی نەخۆشەکان، هەموو نەخۆشەکان دۆپلەری دەمارەکانی قاچیان بۆ کراوە لە ڕێگەی ئەنجامدانی تیشکی سیتی سکانی ڕەنگاوڕەنگ بۆ دەمارەکان، و لە کۆتاییدا ئەنجامدانی قەستەرە دەستنیشان کردنی کۆتایی. ئەو نەخۆشانەی قەستەرە و باڵۆنیان بۆ ئەنجام دراوە بەراورد کراون بە گروپی کۆنترۆڵ.

ئەنجامەکان:

ناوەندی تەمەنی نەخۆشەکان (٦٤) ساڵ بووە: لە ٧٠٪ (٢٨ نێر) ڕێژەی نێر:مێ ١/٢٠٣. سستی گورچیلەکان لە ١١ نەخۆشدا هەبووە (٢٧.٥٪) وە ٧ نەخۆش (١٧.٥٪) جگەرەکێش بوون، باوترین نیشانەی نەخۆشەکان سارێژ نەبوونی بڕینەکانی پێیە (٣٩ نەخۆش) لەوانەبوون کە پلەی ٤ فۆنتاین وە ٦ رزەرفۆرد بوون یان (TASC) C وD بوون دەیان گرازیانی پلەی ٤ بوون ڕێژەی کردنەوەی دەمارەکان بە سەرکەوتویی لە ٩٥٪ واتە ٣٨ نەخۆش و هیچ نەخۆشێک گیانی لەدەست نەداوە.ڕێژەی سارێژبوونی بڕینەکان بێ بەرزترە بە ڕێژەی(٦٧.٥٪) بەرامبەر (٣٤.٦٪) ، ڕێژەی سەرهەڵدانەوەی بڕینەکان کەمتر بوو (٢٠٪) بەرامبەر بە (٤٧.٤٪) بەڵام ڕێژەی قاچ بڕینەوە جیاوازیەکی بەرچاوی نەبووە (١٢.٥٪) بەرامبەر (١٢.٨٪)