THE RELATIONSHIP BETWEEN THE LENGTH OF OCCLUSION IN INFRAINGUINAL VESSELS IN CRITICAL LOWER LIMB ISCHAEMIA AND THE OUTCOME AFTER ENDOVASCULAR INTERVENTION

Thesis

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ABSTRACT

Background: This study was done to assess the relationship between the length of occlusion in infrainguinal vessels in critical lower limb ischaemia and the outcome after endovascular intervention

Methods: The study was done on 40 patients presenting to the department of vascular and endovascular surgery, Kasr Al Ainy hospital, Cairo University along the period of 10/2012 to 4/2013. All patients presenting with chronic atherosclerotic critical lower limb ischemia. Endovascular intervention was our chosen approach dealing with all of the patients.

Conclusion: Amputation is not significantly related to the length of occlusion so the length of occlusion is not the only factor affecting the decision of major amputation. But it should be noted that length of occlusion is significant in primary and secondary patency

Key Words: Angioplasty, Critical Limb Ischemia, Clinical Outcome, Amputation, Patency.

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CRITICAL LIMB ISCHEMIA

Nomenclature and Definitions

Critical limb ischemia (CLI) is a manifestation of peripheral arterial disease (PAD) that describes patients with typical chronic ischemic rest pain or patients with ischemic skin lesions, either ulcers or gangrene. The term CLI should only be used in relation to patients with chronic ischemic disease, defined as the presence of symptoms for more than 2 weeks. The diagnosis of CLI should be confirmed by the ankle-brachial index (ABI), toe systolic pressure or transcutaneous oxygen tension. Ischemic rest pain most commonly occurs below an ankle pressure of 50 mmHg or a toe pressure less than 30 mmHg. Other causes of pain at rest should, therefore, be considered in a patient with an ankle pressure above 50 mmHg, although CLI could be the cause. (Norgren, et al., 2007)

Some ulcers are entirely ischemic in etiology; others initially have other causes (e.g. traumatic, venous, or neuropathic) but will not heal because of the severity of the underlying PAD. Healing requires an inflammatory response and additional perfusion above that required for supporting intact skin and underlying tissues. The ankle and toe pressure levels needed for healing are, therefore, higher than the pressures found in ischemic rest pain. (White, 2010)

Epidemiology and pathogenesis

The prevalence of symptomatic leg ischemia is increasing with figures quoted in the literature between 1.5 and 5% in men over 50 years. The incidence of CLI is estimated to be 50–100/100,000 per year in the European Consensus Document. Men are more frequently affected by CLI with a ratio of about 1.5:1. The pathological process resulting in critical limb ischaemia is almost invariably atherosclerosis.

Usually it requires the multilevel disease to progress to critical limb ischaemia but can also be the result of occlusion of collaterals. In diabetic patients, PVD develops at an earlier age, is more severe and more often affects distal vessels more than proximal vessels. Neuropathy or minor trauma may be the trigger for ulceration or gangrene. Poor healing and infection delays ulcer healing and promotes further ischaemic lesions and limb loss. In the diabetic, symptoms may be diminished or absent due to a peripheral neuropathy. About 2/3 of patients with CLI are first seen when rest pain is present, but in one-third of cases, they present with ischaemic ulcers or gangrene. (Pedrini, 2003) (McDermott, 2007)

It is important to diagnose CLI because it confers a prognosis of high risk for limb loss and for fatal and non-fatal vascular events, myocardial infarction and stroke. In general, the prognosis is much worse than that of patients with intermittent claudication. The diagnosis of CLI thus predicts a poor prognosis for life and limb. Patients should have aggressive modification of their cardiovascular risk factors and should be prescribed antiplatelet drugs. Ultimately, much of the care of CLI patients is palliative in nature, an issue that is very important when considering revascularization or amputation. (Norgren, et al., 2007)

Pathophysiology

CLI is usually caused by obstructive atherosclerotic disease; however, CLI can also be caused by atheroembolic or thromboembolic disease, vasculitis, in situ thrombosis related to hypercoagulable states, thromboangiitis obliterans, cystic adventitial disease, popliteal entrapment or trauma. Regardless of the etiology, the pathophysiology of CLI is a chronic and complex process that affects the macrovascular and microvascular systems, as well as surrounding tissues. Initially, the body response to ischemia is angiogenesis, or capillary sprouting, as well as arteriogenesis, thereby promoting the enlargement of pre-existing collaterals to aid in the increase of blood flow to the critically ischemic limb.

These responses fail to supply the necessary amount of blood flow and oxygen to the limb, causing arterioles in patients with CLI to become maximally vasodilated and insensitive to provasodilatory stimuli. This phenomenon, referred to as vasomotor paralysis, is thought to be the result of chronic exposure to vasorelaxing factors Together, these changes lead to edema, a major concern in these patients. In addition, patients with CLI often hold their limbs in a dependent position to alleviate ischemic rest pain; combined with impaired vasomotor control, this leads to further aggravation of the edema. Edema increases the hydrostatic pressure within the distal portion of the limb, compressing already compromised capillaries and impairing diffusion of nutrients to the tissue. (Varu, et al., 2010)

Etiology And Risk Factors

Atherosclerosis is the predominant cause for peripheral arterial disease. The risk factors that are responsible for developing atherosclerosis are implicated in the pathogenesis of peripheral arterial disease (PAD). Since atherosclerosis is a long-standing procedure, PAD is most commonly a disease of the elderly. Diabetes mellitus is strongly related to the development of PAD. Diabetes mellitus affects more the infrainguinal and infrageniculate vessels as well as the microcirculation of the extremities. PAD is more aggressive in patients with diabetes and several studies have showed the increased rates of acute ischemia and amputation in these patients when compared with non-diabetics. When diabetes is coupled with chronic renal insufficiency then morbidity and mortality rates are also increased. Smoking is another risk factor that seems to have a strong impact in development and progress of PAD. Almost 80% of patients with PAD are current or former smokers and there is a strong association between the number of cigarettes smoked daily and the severity of the symptoms.

Consequently, smoking cessation is strongly recommended and represents an integral part of the conservative treatment of PAD. (Kolnaris, et al., 2011)

Association of Peripheral Arterial Disease, Coronary Artery Disease, and Cerebrovascular Disease

Pooling evidence from available studies such as the Trans-Atlantic Intersociety Consensus (TASC) concluded that approximately 60% of patients with peripheral arterial disease have significant coronary artery disease, cerebrovascular disease, or both, whereas about 40% of those with coronary artery or cerebrovascular disease also have peripheral arterial disease. (AbuRahma, 2007)

Clinical Presentation of Critical Limb Ischemia

Critical limb ischemia (CLI) is a clinical definition involving a spectrum of clinical features to describe chronic and severe compromise in limb perfusion that results in failure to meet the basal metabolic needs. It is ordinarily manifested by the presence of rest pain, with or without trophic skin changes or tissue loss, including ischemic ulceration and/or ischemic gangrene with appropriate documentation of circulatory impairment. Typically, narcotic medications are required for analgesia. (White, 2010)

- **PAIN**

Ischemic rest pain, the main feature of patients with CLI, is typically described as burning pain, usually worse in the distal foot and in the toes and usually most severe at night. Rest pain is generally intolerably severe, aggravated by elevation, and relieved with dependency, presumably resulting from the increase in arterial pressure from gravity in a limb with a nonfunctioning venoarteriolar reflex due to ischemia.

The pain occurs or worsens with reduction of perfusion pressure: leg elevation with loss of the supplemental effects of gravity on blood flow. In diabetic patients the superficial pain sensation may be altered and they may experience only deep ischemic pain such as calf claudication and ischemic rest pain. In the most severe cases of CLI, rest pain is continuous, with episodes lasting minutes to hours but with constant diffuse pain remaining in between. Often the pain cannot be adequately relieved from foot dependency and responds only to opiates.

- **ULCERS AND GANGRENE**

Further progression of tissue hypoxia ultimately leads to tissue ulceration and gangrene. However, in many patients, particularly diabetic patients with diabetic neuropathy, CLI does not progress from rest pain to tissue loss but the initial presentation is with a neuroischemic ulcer or gangrene. On the basis of literature, there are significant differences at this stage of CLI between patients with or without diabetes. The former have been recognized and distinguished in a separate subcategory of CLI in the TASC "diabetic foot ulcers" Non diabetic gangrene and ulcers usually affect the digits or the pressure points (the heel in bedridden patients) and may extend to the distal parts of the foot. Gangrene is usually caused by a minor local trauma, local pressure (fitting shoes), or use of local heat. Gangrenous tissue can shrink and form a scar leading to mummification and spontaneous amputation. However, necrotic tissue may also be infected with spreading of tissue loss. (Cao, et al., 2009)

- **Diabetic Foot**

It has been estimated that about 15% of people with diabetes will develop foot ulcers during their lifetime and about 14% to 24% will require amputation.

Diabetic foot complications are the most common cause of non-traumatic lower extremity amputations in the world, but also the most preventable when detected early and treated appropriately. Early identification of the patient at risk and preventive foot care could prevent up to 85% of diabetic amputations. The most common pathway associated with the development of diabetic ulcers includes peripheral neuropathy; approximately 30% of diabetics have mild to severe forms of nerve damage. Loss of protective sensation leads to insensate foot more vulnerable to pressure points and repetitive activity .Motor nerve defects and limited joint mobility can cause structural foot deformities with pressure points further predisposing the patient to foot lesions. Because of autonomic neuropathy, loss of sweating, dry fissured skin, and increased arteriovenous shunting occur. Healing requires a greater increase in perfusion than needed to maintain intact skin. Although the majority of diabetic ulcers are neuropathic, the TASC classifies diabetic foot ulcerations in three broad categories, which are ischemic, neuroischemic, and neuropathic. (Cao, et al., 2009)

•SUBCRITICAL LIMB ISCHEMIA

It has been recently suggested that there is a subgroup of patients with CLI in whom severely reduced circulation to the foot does not manifest as rest pain, ischemic ulceration, or ischemic gangrene. Authors have defined “chronic subcritical limb ischemia (CSLI).” It has been recognized that patients with peripheral arterial disease do not usually go through gradual progression from claudication to advanced stages of CLI because many develop CLI without warning. At least part can be explained by this asymptomatic stage, CSLI, in. patients who do not ambulate for various reasons and therefore do not present with claudication or attribute their limited walking ability to other conditions such as arthritis or cardiopulmonary compromise.

At this stage foot skin is intact; however, they do not have sufficient perfusion to heal foot wounds, and should they receive minor trauma, the wound would result in non healing ischemic lesions and evident CLI with limb threat. These patients need to be discovered before these events precipitate in order to apply the following:

(i) preventive foot care to avoid foot infection,
(ii) risk factor control to improve mortality outlook,
(iii) regular follow-up, and
(iv) Attentive care.

However, there is currently no evidence to support that aggressive revascularization at early CSLI can be efficiently managed by medical treatment to prevent progressive disease. (Cao, et al., 2009)

Classification Systems for CLI

The main purpose of defining and grading chronic arterial limb ischemia is to predict outcome and to standardize reporting practices. Many classification systems for grading the severity of chronic arterial occlusive disease have been suggested. In the case of critical limb ischemia (CLI), attempts at a precise definition based on clinical grades of classification systems have been problematic. Current CLI definitions have been criticized for being arbitrary, unclear, and not able to predict outcome accurately. (Bosiers, et al., 2009)

Table 1. Classification of peripheral arterial disease: Fontaine's stages and Rutherford's categories.

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

Investigations of Critical Limb Ischemia

These investigations have a number of purposes:

1. To objectively confirm the diagnosis.

2. To localize the responsible arterial lesions and grade their relative severity.

3. To assess the need for intervention (by predicting the outcome of conservative management) and help in the choice of procedure should an operative intervention be necessary, additional diagnostic studies may be needed.

4. To assess operative risk and operative strategy. As with the patient presenting for the first time with claudication

5. Certain basic investigations, mainly uncovering atherosclerotic risk factors, are needed

6. The involvement of other systems with arteriosclerosis needs to be explored.

Hematologic Studies

At initial presentation, a patient with manifestations of PAD should undergo a battery of basic hematologic studies to characterize risk factors and identify end-organ involvement. Such as CBC, lipid profile, liver and kidney functions. (White, 2010)

- **Cardiac and Cerebrovascular Evaluation**

The importance of evaluating the extent of cardiac and cerebrovascular disease in patients with manifestations of PAD is being clarified. The systemic nature of atherosclerosis has a significant impact on all vascular beds to a greater or lesser extent. The presence of coronary artery and cerebrovascular disease must be assessed in all patients with a new onset of manifestations of PAD who have not undergone such studies. Indeed, the presence of any form of lower extremity arterial occlusive disease, even if asymptomatic, is associated with an elevated risk of MI and stroke. (White, 2010)

- **Cardiac Disease**

Patients undergoing peripheral vascular surgery are at high risk (>5% likelihood) of having a perioperative MI, and they frequently manifest more than one of the clinical predictors of MI, heart failure, or death. (White, 2010)

Vascular Imaging Studies

The decision to recommend surgical or percutaneous intervention for a patient with lower extremity arterial occlusive disease is based on many factors, including symptoms, co-morbid conditions, and location and severity of occlusive lesions. In addition, the anatomic pattern of the disease may have a significant impact on the type of procedure that can be used to improve distal perfusion. A clear understanding of the extent of PAD is required before a therapeutic plan can be established. (White, 2010)

- **COLOR DUPLEX IMAGING**

The improved resolution of duplex imaging has made this diagnostic modality a suitable alternative to contrast angiography in some patients. A significant advantage of this noninvasive modality is that it yields both anatomic and blood flow information, providing an assessment of the hemodynamic effect of arterial occlusive lesions without the use of nephrotoxic contrast agents. Current devices offer significantly improved image quality. Combined with an assessment of peak systolic velocity ratios, duplex imaging can characterize arterial anatomy and detect hemodynamically significant lesions with an accuracy similar to that of conventional contrast angiography. (White, 2010)

CDI is employed in the surveillance of arterial bypass grafts and is increasingly being used as a first-line investigation for patients presenting to vascular clinics. Arterial calcification can interfere with CDI. Medial sclerosis, frequently seen in the iliofemoral and infrageniculate arteries in diabetes, typically has a uniformly high signal on B-mode ultrasound, but generally permits flow analysis. However, waveform analysis proximal and distal to these areas can indicate whether significant disease is present.

Dampened waveforms with reduced peak velocity indicate the presence of significant stenotic disease proximal to the point of analysis. Further, there is the potential to fail to localize significant arterial disease proximally, particularly in obese individuals and to miss distal disease in small vessels so preventing accurate anatomical mapping. Obese individuals with type 2 diabetes are potentially a challenge for this modality. (Fig. 3) (Williams, 2009)

Ankle Pressure and Ankle-Brachial Pressure Index

This index is obtained by placing a pneumatic cuff around the leg above the malleolus and using the Doppler to obtain pressures at the DP and PT arteries. These pressures are then divided by the highest brachial artery pressure and the normal ratio is 1.0. Those with more severe ischemia may have an index 0.1 to 0.4, or it may even be undetectable). Patients with diabetes will often have calcified vessels; therefore, their ABI will be falsely elevated. (Singh, et al., 2009)

- ## Computed Tomographic Angiography

With improvements in computed tomography technology, CTA has become another frequently used imaging modality for viewing even the small distal tibial vessels. The studies are obtained quickly, requiring no more than a few minutes to scan from the proximal abdominal aorta to the feet, which minimizes issues related to patient noncompliance. (White, 2010)

Despite these excellent results, there are limitations to the widespread use of CTA for the evaluation of lower extremity ischemia. Of major concern is the requirement for an intravenous bolus of more than 100 mL of iodinated contrast in the average adult. This high contrast load limits the use of CTA to patients with normal renal function, unless medical necessity indicates otherwise.