CHAPTER 114

Digital Gangrene - How and How Much to Investigate?

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Introduction

Peripheral vascular disease affects nearly 10 million of the Indian population.[1] It is also associated with decrease in functional capacity and quality of life and an increased risk of amputations.

The underlying clinical conditions which present with features of peripheral limb ischemia are numerous. Since the differential diagnosis of the peripheral ischemia is vast, there are a multitude of clinical and lab tests available for diagnosis of the condition. This is further complicated by the numerous invasive and non invasive imaging modalities available at the clinician's disposal. The choice of the best modality of investigation or treatment needs to be individualized in each clinical scenario for optimal management of the patient.

Mechanisms of Vascular compromise leading to Peripheral limb ischemia

Embolic Occlusion

80% of the emboli originate from cardiac source – vegetation on valves, mural thrombi dislodged during episodes of atrial fibrillation or other arrthymias.[3] 20% are from non-cardiac source - thrombosed aneurysm, ulcerated atherosclerotic plaque

In India there is increased incidence of embolic occlusion due to widespread prevalence of rheumatic heart disease.

Most commonly emboli lodge in the femoral artery bifurcation, aortoiliac arterial system, brachial artery.

Thrombotic Occlusion

- Atherosclerotic thrombus formation especially in diseased arteries e.g. popliteal artery
- Secondary thrombi in pre existing vascular grafts are common.
- Accelerated atherosclerosis occurs in autoimmune conditions like SLE.

Extrinsic compression of arterial lumen

- Aortic or vascular dissection, creating pseudo lumen which compromises true lumen
- Compartment syndrome in trauma or burns.
- Thoracic outlet syndrome: Condition with scalene muscle scarring and/or a cervical rib causing neurovascular compression in the superior thoracic cavity, leading to arm pain and paresthesias.

Vasospasm

Raynaud's phenomenon: A vasospastic condition causing well-demarcated ischemia to fingers and toes. Three stages: Pallor (hypoperfusion),

then cyanotic (hypoxemia), then hyperaemia (reperfusion), usually bilateral limb involvement.

It can be primary Raynaud's Disease or Secondary to autoimmune diseases like SLE, Scleroderma, etc.

Causes of peripheral limb ischemia

There are a wide variety of conditions causing peripheral limb ischemia other than the traditional causes like atherosclerosis. Though rare these conditions should be kept in mind whenever evaluating a patient with either acute or chronic ischemia. The following table enlists the variety of etiological conditions which may present with limb ischemia or peripheral vascular disease. Two major contributors of limb ischemia i.e. atherosclerosis and autoimmune diseases are discussed in brief in the following text.

Atherosclerosis

Atherosclerosis is a major cause of peripheral artery disease and limb ischemia. Atherosclerosis affects up to 10% of the Western population older than 65 years. With the elderly population expected to increase 22% by the year 2040, atherosclerosis is expected to have a huge financial impact on medicine. When claudication is used as an indicator, estimates are that 2% of the population aged 40-60 years and 6% older than 70 years are affected [4]. 40 % of patients with atherosclerotic coronary artery disease also have peripheral vascular disease. Most of the autoimmune disorders like systemic lupus erythematosus also cause arterial disease by the process of accelerating atherosclerosis.

Rheumatological conditions

Rheumatological conditions presenting as peripheral limb ischemia or gangrene are numerous, but generally underdiagnosed. A variety of conditions causing accelerated atherosclerosis get overlooked during evaluation and only the atherosclerotic nature of the illness treated. The tables 2 shows the prevalence of peripheral limb disease in a cohort of patients attending the rheumatology clinic in K.E.M Hospital Mumbai.

As seen in the above results a significant amount of peripheral limb ischemia can be attributed to autoimmune rheumatological diseases apart from the traditional causes like atherosclerosis.

Need for early diagnosis and treatment

- Coronary artery disease is frequently seen in association with peripheral arterial occlusive disease especially when the cause is accelerated atherosclerosis.

- Coronary artery disease with a subsequent myocardial event is the major contributor to outcome to the mortality in patients with peripheral vascular disease.

- The morbidity of arterial occlusion is related to the development of critical limb ischemia and subsequent need for amputations.

- Predicted mortality rates for patients with claudication at 5, 10, and 15 years of follow-up are approximately 30%, 50%, and 70%, respectively.

- "Time is limb and life"

  Golden Time Window = 6 hours (before irreversible neuromuscular damage)

  Amputation rate = 6-20%

  - 6% if revascularization performed within 12 hrs of symptom onset.

  - 12% if revascularization performed during 12-24 hours.

  - 20% if revascularization performed after 24 hrs.

Hence the earlier the diagnosis and early specific pathology directed treatment would reduce both the morbidity and mortality of peripheral limb ischemia [7].

Clinical Features of Peripheral Vascular Disease

The classic historical description of peripheral vascular disease is the six classic "P"s

Table I

Sr no	Etiology	Important Points to be Noted
1	**Atherosclerosis**	Atherosclerosis affects the arteries in segments with areas of minimal to critical narrowing. The initial lesion is a fatty streak followed by plaque formation. The rupture of such plaques with subsequent thrombus formation leads to vascular lumen compromise.
2	**Autoimmune**	
	SLE	Vascular involvement in SLE may be due to accelerated atherosclerosis, hyperlipedemia, associated Anti Phospholipid antibodies or associated vasculitis [4].
	Scleroderma	Characterised by arterial vasospasm, smooth muscle proliferation and eventual vascular occlusion. Nailfold capillary changes, telangectasia, Raynaud's phenomenon and claudication are the clinical manifestataions in scleroderma. Severe cases manifest as digital ulcers and gangrene.
	APLA Syndrome	Arterial and/or venous thrombosis, recurrent pregnancy loss, thrombocytopenia and the presence of Anti Phospholipid antibodies.
3	**Vasculitis**	
	Buerger's disease	Segmental, inflammatory vaso-occlusive disease of small and medium arteries. Heavy tobacco use is a significant risk factor. Common in young males.
	Temporal arteritis	Inflammatory condition of medium and large arteries
	Takayasu's arteritis	Chronic, inflammatory, large-vessel disease of aorta and its large branches, found in young women (age 20-30), clinically a pulseless upper extremity.
4	**Shock**	
	CHF, dehydration, sepsis	
5	**Thrombophilias**	
	Factor V mutation	
	Hyperhomocystenemia	
	Antithrobmin III def.	
	Protein C, S deficiency	
6	**Trauma**	
	Crush injuries,burns, compartment syndrome.	
7	**Infections**	
	Chlamydia, salmonella, syphilis.	
8	**Drugs**	
	Ergot abuse	
9	**Insect bites**	
	Brown Recluse Spider	
10	**Parasites**	
	Filariasis	
11	**Others**	
	Radiculopathies and spinal stenosis	Patients experience "pseudo claudication", which is leg pain which is exacerbated by walking and relieved with rest and, uniquely, leaning forward. Spine flexion actually increases the diameter of the neural canal and there is less impingement of the spinal cord and peripheral nerve roots. Patients are often misdiagnosed with mild claudication from peripheral vascular disease instead [6].

Table 2 : Prevalence of gangrenous episodes involving the limbs in rheumatologic diseases (KEM Hospital, Mumbai from May 2004 to August 2006)

Disease	Total patients	Patients with gangrene	%
SLE	137	10	7.29
Scleroderma	52	14	26.92
MCTD	6	2	33.3
Rheumatoid arthritis	47	1	2.12
APLA syndrome	5	3	60
Systemic vasculitis	20	9	45

Pain, **P**allor, **P**oikilothermia, **P**ulselessness, **P**aresthesia, and **P**aralysis.

The various **clinical stages** in the clinical spectrum of peripheral limb ischemia includes

- Asymptomatic stage
- Intermittent Claudication
- Rest Pain
- Ischemic Ulceration
- Critical Limb Ischemia

Evaluation in the Emergency Medical Department

Whenever a patient with either of the symptoms suggestive of peripheral arterial disease presents to the emergency department a full detail history, examination, and bedside tests should be performed along with non invasive tests [10].

Early risk stratification of the patient should be done for availing conventional angiography and revascularization.

Clinical history

- Intermittent claudication and claudication distance.
- Rest pain
- Ulceration and gangrene.
- Cardiac complaints including palpiatations
- History of smoking or drug abuse.
- Associated co morbid illnesses like diabetes.
- Recent surgery, trauma or immobilization.

- Rash, photosensitivity, hair loss, oral ulcers, Raynaud's phenomenon, fever.

Use of Clinical Questionnaires: eg Edinburgh Questionnaire

1. Do you get a pain or discomfort in your leg(s) when you walk?

   If the answer is no, the person does not have intermittent claudication, and no further questions are asked. If the answer is yes, then the following five questions are asked:

2. Does this pain even begin when you are standing still or sitting?

3. Do you get it when you walk uphill or hurry?

4. Do you get it when you walk at an ordinary pace on the level?

5. What happens to it if you stand still? (Options: Usually continues more than 10 minutes, or Usually disappears in 10 minutes or less).

6. Where do you get the pain or discomfort? For the latter question, a drawing of the legs from front and back allows the patient to draw the affected area.

*Scoring is based on the pattern of response, with a diagnosis of claudication requiring "Yes" to questions 1 and 3 "No" to question 2, and "Usually disappears in 10 minutes or less" to question 5. Question 4 distinguishes grades of severity. Question 6 distinguishes "definite"claudication (if the calf is involved) from atypical claudication (thigh or buttocks pain in the absence of calf pain).

Other patterns are not considered indicative of claudication.

Clinical Signs of Peripheral Vascular Disease

Classic appearance of extremity

- Pale and cool
- Mottled cyanosis
- Dependent rubor
- Muscle rigidity and limb woodiness are signs of an unsalvageable limb

Physical Examination: Best tests

- Palpate for decreased or absent pulses.
- Patterns of pulse abnormality may indicate sites of stenosis.
- Auscultate for bruits, which may indicate arterial stenosis.
    - Sites of Bruits: Abdomen, Pelvis, and Inguinal areas.
- Check for foot pallor
    - At rest, with leg elevation, and after exercise of the calf muscles.
- Signs of chronic limb ischemia
    - Subcutaneous atrophy
    - Hair loss
    - Coolness
    - Pallor
    - Cyanosis, dependent rubor, or both
    - Petechiae, fissures, ulceration, and gangrene with critical limb ischemia.
- Capillary Refill Time
    - A prolonged capillary refill time (>5 sec) has a likelihood ratio (LR) 1.9 for mod-severe peripheral arterial disease. A caveat being that CR time is non-diagnostic in diabetic patients [9].

Bedside non invasive testing

Ankle Brachial Pressure Index

This is the most useful initial screening method especially in the lower extremity. It is determined either by ausculatatory method or by using continuous wave Doppler recording of the lower limb pulses. It is checked in the arm for the brachial artery and the ankle for the dorsalis pedis or posterior tibial artery [10].

ABPI = ankle systolic pressure / brachial systolic pressure.

ABPI < 1.0 implies that peripheral arterial disease may be present.

ABPI < 0.9 implies definite evidence of arterial disease with 95 % sensitivity and 100% sensitivity.

ABPI < 0.8 implies a definite high risk of cardiovascular morbidity irrespective of peripheral arterial symptoms.

Caveats include occult upper limb arterial disease and diabetes. In such cases a toe systolic pressure index (> 0.6) can be used.

The choice between auscultatory and Doppler methods of ABPI measurement is governed by the likelihood ratios. Recent studies have shown that Doppler is superior to auscultatory method.

The auscultatory method has a good negative predictive value when the measured ABPI is > 0.9 by the auscultatory method [11].

Duplex Ultrasonography and Doppler colour flow imaging:

The ultrasound diagnostic criteria include gray scale imaging; Doppler pulse continous wave spectral imaging and Doppler colour flow imaging.

Gray scale imaging is used to characterize the morphology of the vessel and denote the presence of arterial plaques.

Colour flow imaging is used to identify subtotal occlusion of arteries with collateral formation and direction of blood flow [12].

On continuous wave spectral imaging, the peak systolic velocity is the most reliable form of measurement with the minimal interobserver variability.

Electro Cardio Gram

To assess for underlying coronary artery disease or cardiomyopathy and especially to check for atrial fibrillation a baseline ECG is a must.

It provides information regarding potential cardiac conditions which may affect the treatment of a patient e.g during anaesthesia for vascular bypass surgery. It may also highlight some potential cardiac conditions which may predispose to formation of a mural thrombus or vegetations.

Acute Limb Ischemia Categorization (Table 3)

After an initial assessment of the patient by clinical tests and bedside non invasive tests, the patient should be categorised into various Rutherford classes as given below and the further line of management decided accordingly.

- Usually thrombotic occlusions are class I or IIA.

- Usually embolic occlusions are class IIB or III.

Class I and IIA patients can be worked up for definite cause of ischemia and treated accordingly.

Class IIB and III patients require an urgent angiogram and revascularization procedure.

Class I and IIA patients can be subjected to further evaluation for the aetiology of the peripheral vascular disease and also the extent of peripheral vascular disease.

Assessment of patient triaged to Critical Limb Ischemia

The general management principles include urgent imaging procedures and urgent revascularization.[13]

- A patient with class III limb ischemia with sensory loss of the affected extremity is generally taken up for emergency revascularization procedure rather than waiting for an angiogram. Revascularization includes catheter embolectomy with intra operative intra arterial thrombolysis if required.

- Occasionally class II B patients may be referred for an angiogram which is the gold standard for imaging. The choice is between a Digital Subtraction Angiogram versus a MR angiogram versus a CT angiogram.

- DSA is the preferred choice because if required intra arterial thrombolysis can be initiated during the procedure. Considerable time is lost in CT and MR angiogram.

Current Imaging Recommendation

Continue with angiography as first-choice imaging approach for ACUTE limb ischemia, because of the benefit of concurrently diagnosing and treating the arterial occlusion. Sending a patient to ultrasound, CT, or MRI with active limb ischemia will often delay treatment.

Table 3 : Assessment of Peripheral Limb Ischemia Adapted from Society of Vascular surgery/ International Society for Cardiovascular Surgery

Class	Category	Prognosis	Sensory Loss	Muscle Weakness	Arterial Doppler Signal	Venous Doppler Signal
I	Viable	No immediate limb threat	None	None	Audible	Audible
II A	Threatened : Marginal	Salvageable if treated promptly	Minimal – none	None	Audible	Audible
II B	Threatened : immediate	Salvageable if treated immediately	More than just toes	Mild- Moderate	Rare audible	Audible
III	Irreversible	Limb loss or Permanent damage	Profound	Profound	None	None

Table 4 : Likelihood ratios for symptoms, signs and tests for limb ischemia

Asymptomatic patient		Symptomatic patient	
Parameter	**Likelihood Ratio**	**Parameter**	**Likelihood Ratio**
IC Present	3.30 (95 % CI)	**Cool Skin**	5.90 (95 % CI)
IC absent	0.57 (95 % CI)	**Skin Discoloration**	2.80 (95 % CI)
Femoral Bruit	4.80 (95 % CI)	**Ischemic Sores**	5.90 (95 % CI)
Abnormal pulses	3.10 (95 % CI)	**Bruit Present**	5.60 (95 % CI)
Normal Pulses	0.86 (95 % CI)	**Bruit Absent**	0.39 (95 % CI)
		Pulse Abnormality	4.70 (95 % CI)
		Pulse Normal	0.38 (95 % CI)
		Edinburg Questionnaire	
		Positive	**90.0** (95 % CI)
		Negative	0.1 (95 % CI)
		ABPI < 1.0	8.6 (95 % CI)
		ABPI > 1.0	0.03 (95 % CI)

Figure 1: Algorithm for Evaluation of Peripheral Ischemia*

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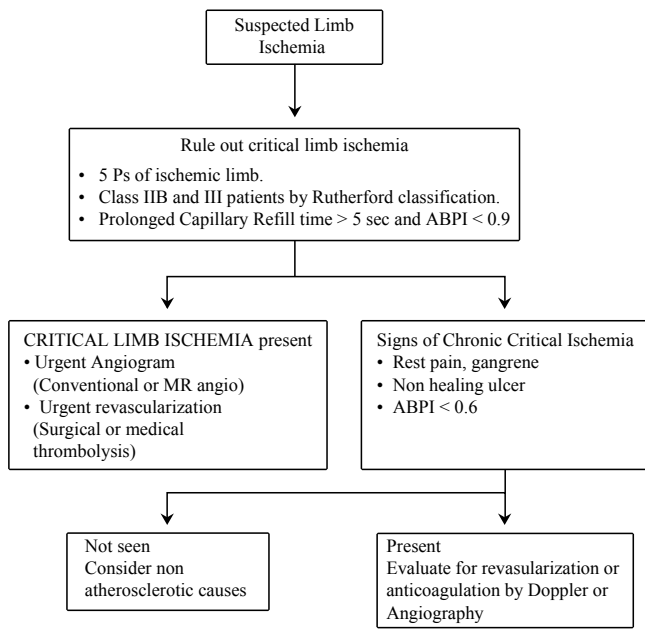
***Exceptions**

- Duplex ultrasonography if: Infrainguinal arterial disease, severe contrast allergy, high risk for contrast-induced nephropathy, or equivocal exam for ALI.

- CT angiography or MR angiography if: Equivocal exam for ALI and no immediate intervention needed.

- Perform amputation without imaging for hemodynamically unstable patient – Reduces risk for further multiorgan failure and cardiovascular collapse. "Save life over limb."

Assessment of a patient triaged to chronic limb ischemia: Likelihood ratios.

The assessment of chronic ischemia can be done in details guided by the principles of pre test probability and likelihood ratios. These have been established for clinical symptoms, signs and investigations available for better treatment of the patient. Table 4 shows the likelihood ratios for both symptomatic and asymptomatic patients.

According to the above ratios the Edinburg questionnaire was the best tool in symptomatic patients to predict underlying chronic limb ischemia.

In asymptomatic patients, the presence of symptoms of intermittent claudication or presence of femoral bruits or presence of abnormal pulses on palpation were good predictors for underlying arterial disease.

Emergency physicians should always look out for these parameters which have a good post test probability for predicting arterial ischemia [14, 15].

Figure 2: Chronic Limb Ischemia: Algorithmic approach to aetiology
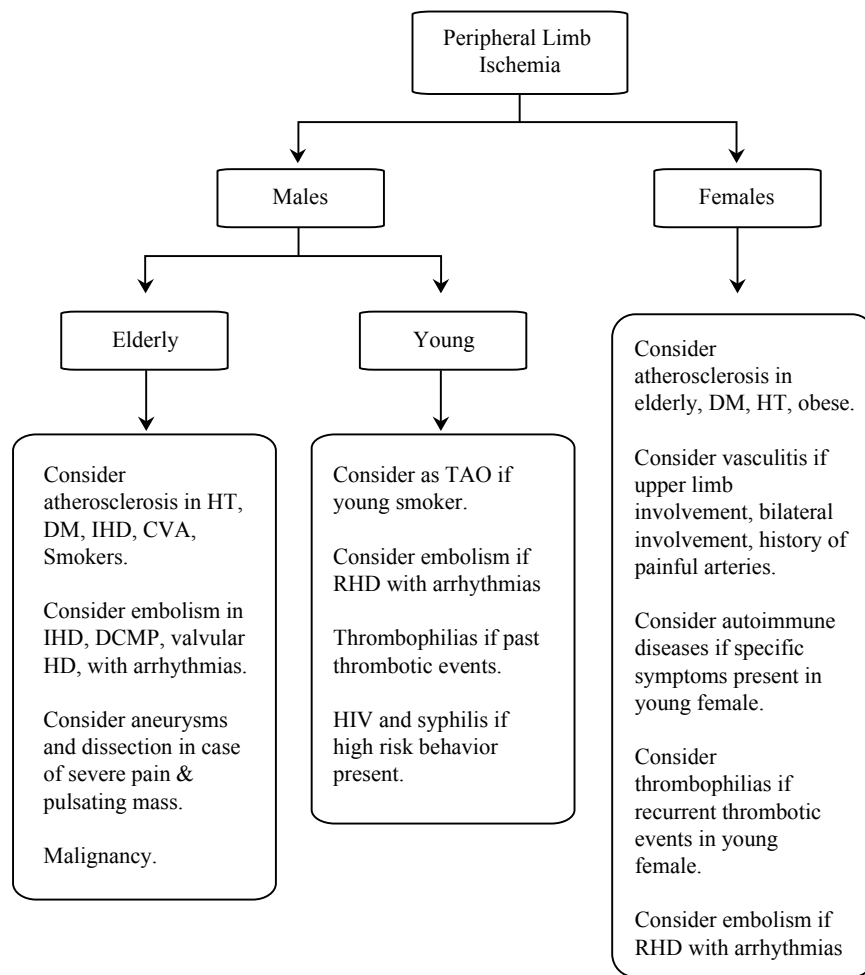
Peripheral Limb Ischemia and Digital Gangrene: How much to and how to investigate?

So out of a constellation of symptoms, signs and clinical conditions which may present as peripheral limb ischemia, how to decide on the most clinically relevant and specific investigation to arrive at a diagnosis?

Table 5 denotes the common clinical scenarios faced in daily practice with the most relevant diagnosis and the most specific investigation.

Conclusion

The vast majority of disorders that present with peripheral limb ischemia generally have limited therapeutic options in the form of antiplatelet therapy, anti coagulation, rheological agents, surgical bypass grafts and thrombectomy.

All modalities of therapy have reduced the mortality in this condition and have reduced the morbidity in the form of amputations.

The real expertise on the part of the treating physician, surgeon or a vascular surgeon depends on the accurate diagnosis of the underlying disease which manifests as peripheral limb ischemia.

The use of clinical history, likelihood ratios and appropriate investigations asked in the right clinical scenario greatly enhance the accuracy of diagnosis of the underlying disease entity.

Table 5 : Common Clinical Scenarios in Digital Gangrene

Symptoms n Signs	Possible Etiology	Diagnostic Evaluation
Elderly, HT, DM, obese, IHD Symptoms of chronic Ischemia Abnormal pulses, bruits, ulcerations, ABPI < 1.0	Atherosclerotic arterial disease	1. Doppler USG. 2. Angiography. 3. Lipid profile and Sugars.
Elderly, IHD or DCMP, on anticoagulants Palpitations, giddiness, syncope. Irregular pulses	Embolism from cardiac source	1. ECG 2. 2D ECHO cardiography 3. PT / INR
Young male or female, RHD with mitral or aortic valve disease. Palpitations, on anti arrthymics Cardiac murmurs.	Embolism from cardiac source. Fever – Infective endocarditis Atrial fibrillation – Mural thrombus	1. ECG 2. 2D ECHO 3. Blood cultures if IE suspected. 4. PT/INR
Elderly male or female, Pulsating mass, sudden severe excrutiating pain Unequal pulses	Aneurysm +/- Dissection	1. Doppler USG. 2. Angiography.
Young male, Heavy smoker,	Thromboangitis Obliterans	1. Angiography
Young female, Upper limb involvement, Bilateral involvement, Recurrent ischemic events Painful superficial arteries Systemic symptoms	Vasculitis New onset headache, jaw claudication, bead like tender temporal artery implies Giant cell arteritis Asymetrical pulses or totally absent upper limb pulses with bruits implies Takayasu's arteritis or aorto arteritis	1. ESR, CRP 2. ANCA, ANA 3. Angiography 4. Temporal artery biopsy
Females, Scleroderma Facies, CREST, Digital ulceration and gangrene, digit resorption, nail fold changes, telangectasia.	Scleroderma (Limited or diffuse)	1. Anti scl 70 Ab 2. Anticentromere Ab 3. ARA criteria (1980)
Young females Recurrent thrombosis Recurrent Pregnancy loss Arterial & Venous thrombosis Thrombocytopenia	APLA syndrome	1. Sapporo criteria 2. ACLA IgG IgM
Young patients, females > males, major vessels involved, cerebral venous sinus thrombosis, young stroke, deep venous thrombosis, increased incidence during pregnancy, recurrent thrombotic episodes, Strong family history of thrombosis	Congenital Thrombophilias • Factor V leiden mutation • Protein C and S deficiency • Pro thrombin gene mutation • Antithrombin III deficiency • Hyperhomocystenemia Acquired Thrombophilias • PNH, myeloproliferative disorders • Thrombocytosis, polycythemia	1. Thrombophilic workup 2. Hb, CBC, peripheral smear.

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