abstract

Arterial occlusive disease of the lower extremities is an important cause of disability in older adults and those with risk factors for atherosclerosis. The process may be asymptomatic or manifest as a progression from claudication to ulceration. Identification of patients at risk is vital to careful surveillance and early intervention. Revascularization remains the mainstay of therapy for critically ischemic limbs. Catheter-based techniques such as angioplasty are useful for focal disease. Conventional bypass surgery remains the mainstay of therapy for more extensive disease with ulceration and may be supplemented by adjunctive plastic surgery procedures for soft tissue coverage and limb salvage. Amputation is performed when reconstruction is not feasible or in the setting of severe progressive infection. The current article provides a more detailed review of lower extremity ischemia.

Key words: Peripheral arterial occlusive disease (PAOD), atherosclerosis risk factors, bypass, angioplasty, patency rates.

Lower Limbs Critical Ischemia

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Background

Peripheral arterial occlusive disease (PAOD) represents an arteriosclerotic process of lower extremity's tree and may involve the aortoiliac and/or femoropopliteal tibial arteries. Clinical manifestations of this condition typically begin with intermittent claudication and may progress to disabling pain at rest, infectious complications and, ultimately, gangrene and limb loss.

The risk factors for PAOD are those for atherosclerosis in general and include male sex, advanced age, cigarette smoking, hypertension, diabetes, and hyperlipidaemia.

Treatment of PAOD depends on the stage of the disease. It includes risk factors modification, meticulous foot care, antibiotics use for associated infections, and selective revascularization procedures. Interventions should aim to relieve ischemic symptoms and associated disability with a broad view toward improving functional capacity and preventing progression toward gangrene and limb loss. Prevention of associated cardiovascular and cerebrovascular events is crucial as well.

Pathophysiology

Atherosclerosis is a degenerative systemic arterial disease that begins early in life.[1] It is characterized by the thickening and hardening of medium-size and larger arteries, with narrowing of the arterial lumen by atherosclerotic plaques. The basic lesion is a raised focal plaque that develops within the intimal layer of the arterial wall.[2-4] Plaque disruption results in alteration of endothelial integrity that lead to thrombus formation. Once the thrombus forms, further clot deposition occurs and leads to narrowing of the arteries.

It is generally accepted that the atherosclerotic plaque is the precursor of occlusive lesions leading to the expression of clinical symptoms in PAOD.[5] Plaques are distributed in a segmental pattern throughout the body. Lesions are commonly found in the terminal aorta, the aortic bifurcation, the common iliac bifurcation, the common femoral, and the popliteal and proximal portions of the tibial arteries.

As stenosis develops slowly over time in the larger arteries, blood flow is diverted through the smaller arterial braches (collateral circulation) proximal to the stenotic areas.[6] The ability to develop such collateral vessels may delay or even prevent extremity symptoms, even in the setting of total occlusion of a major artery. This compensating mechanism, however, is often unable to meet the increased metabolic demand imposed by exercise and ischemic pain occurs.

When the atherosclerotic process becomes more diffuse, longer segments are affected and vessels become occluded. Perfusion is therefore further compromised, and pain may be exacerbated, occurring even at rest. The leg may feel cold, pulses may become weak or absent, and the skin is often pale. Capillary refill is often delayed and nail loss may be noted. Superficial skin ulcers may occur either spontaneously or following even minor trauma. Ultimately, gangrene may develop.

Gradual evolution of atherosclerosis may be punctuated by acute deterioration. Rapid progression in the absence of an adequate compensatory mechanism results in critical limb ischemia.

Collateral development is often viewed as the compensatory mechanism when stenosis occurs in the larger, more

proximal arteries. However, there are fewer collateral vessels in the lower leg. Thus, stenotic and occlusive disease in the distal popliteal and proximal tibial arteries causes severe resting pain and ischemia.

Risk Factors

The risk factors for developing PAOD are similar to those for other atherosclerotic lesions and include the following:

1. Age: The prevalence of PAOD increases with age in both sexes.[7-14] In addition, there is a general pattern of a gradually increasing prevalence up to age 70.[12,14-16] Age has also been associated with an increased risk of local disease progression.

2. Sex: The prevalence of PAOD is greater in men than in women of all age groups. The overall male/female prevalence ratio is 1.2 to 2.9.[17-19] In addition, male gender has been associated with an increased risk of local disease progression.

3. Smoking: Most of the epidemiological studies of PAOD have confirmed that the cigarette smoking is a strong risk factor for the development of PAOD.[7,8,12,18,20-25] The relative risk for developing PAOD in smokers varies from 1.7 to as high as 7.5. In addition, PAOD is diagnosed up to a decade earlier in smokers than in nonsmokers.[26] Furthermore, the evidence suggests that smoking may in fact be a more important risk factor for the development and progression of PAOD than for coronary artery disease (CAD).[22,24]

4. Diabetes mellitus: Many studies have shown an association between diabetes and the development of PAOD.[20-24,27,28] Overall, intermittent claudication seems to be about twice as common among diabetic patients as among non-diabetic patients. PAOD in patients with diabetes is more aggressive, with early large vessel involvement coupled with microangiopathy. In patients with PAOD and diabetes, the progression of the local disease and the risk of major amputation are much higher when compared with nondiabetic patients.[29,30]

5. Hypertension: In most studies, systolic blood pressure is positively correlated with the development of PAOD.[8,18,20,21,23,25,31] The relative risk for developing PAOD in hypertensive individuals is 2.5 in men and 3.9 in women. However, some studies failed to show this association.[13,32] The role of hypertension in the clinical progression of the local disease is not clear. Although Jelnes *et al*[30] noted that the risk of deterioration was related to hypertension, Dormandy and Murray[33] found that hypertension did not influence the local progression of PAOD.

6. Hyperlipidemia: There is conflicting evidence regarding the relationship between hyperlipidemia and PAOD. Although some studies have showed strong association between cholesterol level and PAOD,[18,34] others have failed to confirm this association.[12,25,35] However, there is evidence that treatment of hyperlipidaemia reduces both the progression and incidence of PAOD.[36,37]

7. Other risk factors: A number of other potential risk factors have been investigated. Serum fibrinogen,[12,38,39] hematocrit1[8,38,39] and blood viscosity[38,39] are consistently higher in PAOD patients.

Critical Limb Ischemia (CLI)

CLI is the term used to delineate those patients whose arterial disease resulted in a breakdown of the skin (ulcer or gangrene) or pain in the foot at rest.[17]

Symptoms

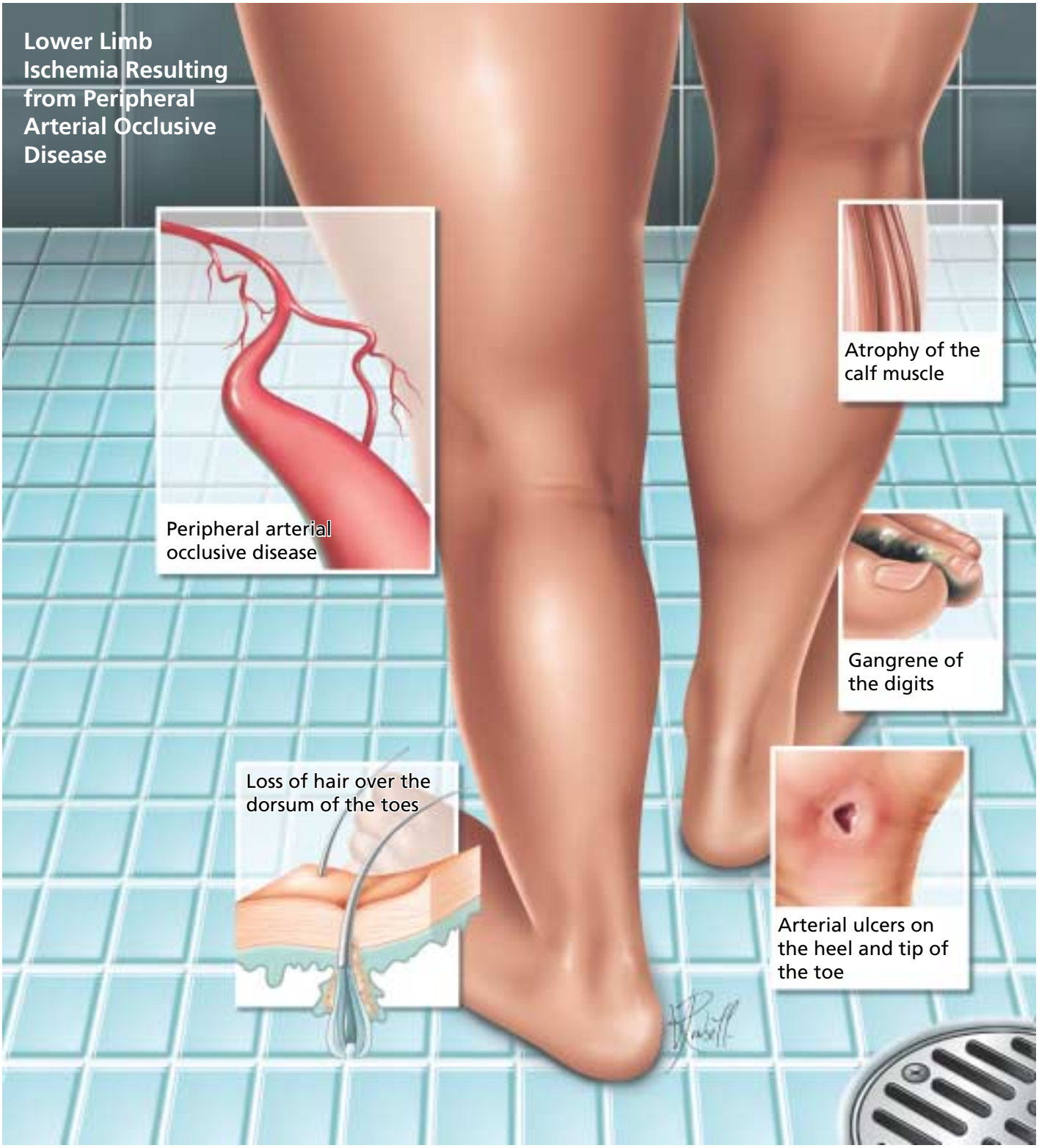
The history is dominated by pain; in most cases, the pain is described as severe, unrelenting, and intolerable. It may cause the patient to awaken at night, and it responds variably to strong analgesics or opiates. The pain is localized in the distal part of the foot or in the vicinity of an ischemic ulcer or gangrenous toe. Pain is exacerbated by elevating the foot and may be relieved by keeping the foot in a dependent position. Severe ischemia is often associated with atrophy of calf muscles and loss of hair growth over the dorsum of the toes and foot. Arterial ulcers usually involve the tips of the toes, the heel of the foot, or wherever local pressure has caused further decrease of perfusion. Gangrene usually affects the digits; in severe cases, it may involve the distal parts of the forefoot. Pulses are usually absent or diminished. Diabetics with neuropathy pose may be delayed in their presentation due to the absence of pain and late recognition of these changes.

Prevalence

There is little direct information on the incidence and prevalence of CLI. The yearly incidence of CLI has been estimated to be 30–50 per 100,000.[17]

Seeking Consultation with a Vascular Specialist

Obtaining additional input regarding additional evaluation, treatment options, or possible interventions is, to a great extent, dependent on the primary practitioner's experience with vascular disease. The patient with typical claudication may be managed conservatively and followed, or referred for additional evaluation. Similarly, screening lower extremity vascular studies may be appropriate for any patient with risk factors for vascular disease who does not have palpable pedal pulses to facilitate appropriate surveillance. Those patients with rest pain, pain at night, impending soft tissue compromise, or frank ulceration should be assessed by a vascular surgeon as soon as possible. While not all legs are compromised due to ischemia, vascular insufficiency remains the most prevalent, manageable cause of limb loss in patients with risk factors for atherosclerosis. Even those patients with significant cardiopulmonary disease ought to be assessed, as rehabilitation after amputation is particularly challenging, and preservation of a weight-bearing surface is critical to maintaining quality of life.



Treatment

All patients with ulcers, gangrene, or pain in the foot attributable to PAOD should be considered urgent cases. The basic treatment should include pain control, foot care, topical therapy for ulcers and gangrene, the use of systemic antibiotics in patients with cellulitis, and risk factor modifications.[17] Glycemic management is vital. Most patients with CLI require revascularization to avoid major amputation.[17] Patients with focal disease and restorable run-off will generally benefit from PTA. However, most patients with CLI have diffuse disease and poor run-off, which requires surgical revascularization.

Role of Revascularization Procedures

Many classification systems have been developed to address the best intervention procedures for patients with PAOD. Generally, percutanous transluminal angioplasty (PTA), with or without stenting, is preferred for patients with focal disease and restorable run-off, and surgery is preferred for patients with diffuse disease and poor run-off.[17] Most patients with intermittent claudication (IC) have focal disease and can benefit from PTA; conversely, most critical leg ischemia (CLI) patients have diffuse disease that requires surgical intervention. The indications for intervention include:

1. Severe claudication not responding to conservative management, including exercise programs
2. Rest pain
3. Tissue loss

Aortoiliac Occlusive Disease

PTA is generally applied to more focal disease of the distal abdominal aorta, common iliac arteries and external iliac arteries. For diffuse, extensive, complex, multilevel, multifocal or totally occluded atherosclerotic segments of the infrarenal abdominal aorta and iliac arteries, the procedure of choice is surgery.[17]

Surgical procedures

1. Aortobifemoral bypass (ABF): ABF is one of the most commonly performed procedures. The distal anastomosis is usually performed on the common femoral artery, and proximal anastomosis is performed on the infrarenal aorta near the renal arteries. The procedure is associated with 1–5% operative mortality.[40-45] The cumulative survival rates are 68–80% and 38–52% at five and 10 years, respectively.[43,45-47] The cumulative limb salvage rates are 76–95% and 82–91% at five and 10 years, respectively.[41-43,45] The cumulative graft patency rates are 80–94% and 62–83% at five and 10 years respectively.[41-45,47]
2. Unilateral aorto or iliac to femoral bypass: When a single iliac is involved in the ischemic process, it may be desirable to conduct a unilateral procedure. The procedure is associated with a 0–5% operative mortality.[48-53] The cumulative graft patency rate is 83–92% at three years.[49-54] The cumulative survival rates are 78–90% and 55% at three and five years, respectively.[48,49,54,55] The cumulative limb salvage rate is 77–88% at three years.[49,54]

Extra-anatomic bypass:

1. Femoral-femoral bypass: This may be used for patients with unilateral iliac disease if the remaining artery does not have a significant disease. The procedure is associated with a zero to 6% operative mortality.[55-59] The cumulative graft patency rate is 57–92% at five years.[55-59] The cumulative survival rate is 70–80% at six years.[48,55,59,60] The limb salvage rates are 85% and 83% at three and six years, respectively.[59-61]

2. Axillobifemoral bypass: This procedure is used for high-risk patients who require vascularization but cannot tolerate ABF. The procedure is associated with 3–11% operative mortality.[62-68] The cumulative graft patency rate is 59–76 % at five years.[62-67] The cumulative limb salvage rate is 75–89% at five years.[62,64,65,67] The cumulative survival rates are 39–45% and 23 % at five and 10 years, respectively.[62,65-67]

PTA and Stenting Procedures

These procedures are predominantly performed for claudication; 77–82% of iliac PTA and 78–86% of iliac stenting are performed for patients with IC.[17] PTA and stent placement have the advantages of lower morbidity and mortality risk compared with open surgical revascularization.[69,70] However, PTA and stents offer less durable results when compared with surgery.[17] The 30-day mortality rate averaged 0.8% for PTA and 1% for stent procedures.[17] The mean systemic complication rate is 1.3%, the local complications rate, 9.6%, and the mean rate of major complications necessitating treatment is 4.3% for PTA and 5.2% for stents.[70] Four-year primary patency rates are 65% for stenoses versus 54% for occlusions after PTA to treat claudication, and are 53% for stenoses versus 44% for occlusions after PTA to treat critical ischemia.[70] Four-year primary patency rates are 77% for stenoses versus 61% for occlusions after stent placement to treat claudication, and 67% for stenoses versus 53% for occlusions after stent placement to treat critical ischemia.[70]

Infrainguinal Occlusive Disease

This includes occlusive disease of the common femoral, superficial, deep femoral, popliteal, and tibial arteries.

Surgical procedures

The overall perioperative mortality rate for all patients undergoing infrainguinal arterial reconstruction ranges from 2–6%,[71] and the five-year cumulative survival rate ranges from 38–59%.[71-73] The long-term graft patency and limb salvage rates depend on the graft material used, type of PAOD, and the presence of comorbidities.

1. Femoropopliteal bypass: This procedure is required in patients with occlusive disease in the femoral vessels. The five-year graft patency rate is 33–88%.[74] The cumulative limb salvage rate at five years is 60–98%.[72,75-81]

2. Femorotibial bypass: This procedure is required in patients with occlusive disease in the popliteal and tibial vessels. The five-year primary patency rate of vein bypass is 56–69%, with five-year limb salvage rates of 47–92%.[75,82-87]

PTA and Stenting Procedures

The efficacy of these procedures depends on the anatomic selection of the lesions and the patient selection.[17] Patients with focal disease and restorable run-off will generally benefit; conversely, patients with diffuse disease and poor run-off will

not.[17] For femoropopliteal PTA, 50–70 % of anatomically selected patients will show clinical benefit at two years. Tibial PTA has generally been reserved for limb salvage patients, and with appropriate patient selection, two-year limb salvage rates of 80% can be expected.[17]

Role of Amputation

Primary amputation, defined as an amputation of the ischemic lower extremity without antecedent attempt at revascularization,[17] is indicated in patients with CLI in which the following conditions hold:

1. There is unreconstructible arterial occlusive disease
2. The PAOD patient is terminally ill or has a very limited life expectancy because of comorbid conditions
3. There is necrosis of significant areas with persistent infection that may lead to systemic sepsis
4. The patient lacks potential for ambulation or weight-bearing capacity even after successful revascularization, as in patients with fixed, unremediable flexion contracture of the leg

Secondary amputation, defined as amputation for the ischemic lower extremity with a previous attempt for revascularization,[17] is indicated in patient with CLI in which the following pertain:

1. Unreconstructible arterial occlusive disease remains after revascularization has been attempted and vascular intervention is no longer possible
2. Infection persists despite aggressive vascular reconstruction
3. The limb continues to deteriorate despite the presence of a patent graft

Prognosis

The prognosis of patients with CLI is considered limited, predominantly due to associated comorbidities. The initial overall treatment of all patients presenting with CLI results in a 20% mortality rate. Survival after amputation stands at 35%, and 45% will be alive without it.[17] In an older report, De Weese and Rob [88] found that virtually all (95%) patients who presented with ischemic gangrene and 80% of those presenting with rest pain were dead within 10 years. Clearly, early recognition of CLI and management of the associated risk factors has allowed for progress both in limb salvage and overall survival. ◆

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Note: Due to space limitations, the following represents a partial list of this article's references. For full references, consult the online edition of this article at *www.geriatricsandaging.ca.*

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