Peripheral artery disease, shortly referred to as PAD, is a condition caused due to atherosclerosis. Estimated to be affecting around 200 million people in 2010, the intermittent claudication is a medical entity of rising impact, which every prospective physician should master. The underlying atherosclerosis is not only the most common arterial vascular disease but also the pathologic substrate for many other common and often life-threatening diseases. These include strokes, heart attacks or aneurysms—comorbidities and risks, which can first manifest as PAD. This article’s purpose is to illustrate how PAD is diagnosed and treated as well as to provide exam-oriented information.

Definition of PAD

Peripheral artery disease (PAD) is characterized by diminished blood flow in the arteries of the trunk, arms, and legs. 

PAD is of 2 types:
- **Occlusive**: Occlusive PAD is characterized by physical narrowing or blockage of arteries. Acute occlusive PAD involves complete blockage of an arterial vessel. It may occur suddenly, due to embolic incidents or as a complication of PAD.
- **Functional**: Functional PAD is characterized by decreased blood flow due to impaired function of the arteries, generally due to sudden muscle spasms in the walls of the arteries.

**Oclusive peripheral artery disease**

Occlusive PAD is a chronic disease involving arterial circulatory vessels in the extremities. It is the main cause of intermittent claudication. Most often, it also affects the arteries of the feet. The chronic atherosclerotic process leads to arterial stenosis and, at a later stage, to complete occlusion of the arteries. The resulting hypoperfusion leads to pain in the extremities—described as intermittent claudication with walking, which is also the primary disease symptom.

Many patients tend to stop while walking and are greatly limited by the distances they can manage. Clinically, as the disease progresses, hypoperfusion leads to paleness, cold, and paresthesia of the affected extremities. Trivial wounds heal much slower in these circumstances, and in the worst-case scenario, may lead to necrosis or even gangrene, following infection.

PAD is caused by atherosclerosis in 85–95% of the cases.

**Epidemiology of PAD**

**Prevalence of PAD**

The prevalence of PAD rises with age and affects 15–21% of the population above 70 years of age. Studies conducted in 2014 show that the prevalence of PAD in the age group under 40 is less than 1%. It is important to remember, however, that asymptomatic PAD is more common than the symptomatic disease, and is not age-related.
Etiology of PAD

Causes of PAD

In 85–95% of the cases, occlusive PAD is caused by atherosclerotic plaques, namely deposits consisting of lipids, connective tissue, thrombi or calcium on the arterial walls. Atherosclerosis involves, by definition, the entire arterial wall, but it is often referred to as atherosclerosis of the tunica intima. Clinically, both expressions are used interchangeably and are practically synonymous.

The primary risk factors for atherosclerosis are:

- Nicotine abuse
- Diabetes Mellitus
- Arterial Hypertension
- Dyslipidemia

In less than 5% of the cases, PAD occurs as a result of recurrent emboli, thrombotic aneurysms, and compartment syndrome or vascular injury.

Symptoms of PAD

The primary symptom of PAD is pain occurring with physical activity, typically localized distally to the stenotic vessel. Pain causes patients to often come to a halt while walking, and the symptom is referred to as intermittent claudication (Latin for the 'occasional limp').
Typically, claudication is relieved after a pause during walking. Also, ensuring that the feet remain at a lower level than the heart restores part of the circulation, which is defective and leads to tissue hypoxia and pain in the feet. As a result, the skin becomes cold and pale distal to the stenosis, often with no palpable pulse.

The body generally overcomes minor stenosis through collateral circulation. The full panel of symptoms does not manifest until stenosis is more than 90%, which actually explains the extremely high percentage of asymptomatic PAD patients. Diminished circulation constitutes fertile ground for ulcers, healing disorders, necrosis or gangrene in the affected areas.

### Classification based on stenosis location and symptoms

<table>
<thead>
<tr>
<th>Stenosis location</th>
<th>Symptoms</th>
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<tbody>
<tr>
<td>Aortoiliac</td>
<td>Aortic bifurcation syndrome, buttocks, thighs</td>
</tr>
<tr>
<td>Femoral</td>
<td>Cramps</td>
</tr>
</tbody>
</table>
Symptoms of acute arterial occlusion

The late-stage disease is characterized by a complete blockage of the artery. In acute peripheral arterial occlusion, also acute ischemia of the extremities, the affected extremity may show necrosis, which requires amputation and can be potentially life-threatening.

The massive hypoperfusion in the extremities causes symptoms (the 6 P’s according to Pratt):

1. Pain
2. Pulselessness
3. Pallor
4. Paresthesia
5. Paralysis
6. Poikilothermia

N.B. Aortic bifurcation syndrome or Leriche syndrome: Aortic occlusion distal to the renal arteries, at the level of aortic bifurcation, or complete occlusion of both iliac arteries, leads to erectile dysfunction/impotence in men.

Stages of PAD

Progressive disease

Based on the symptoms, PAD is classified into different stages for an appropriate treatment plan.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
<th>Therapy plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Symptom-free</td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>Pain during physical activity; IIa: distances walked without pain &gt; 200 m; IIb: distances walked without pain &lt; 200 m</td>
<td>Intermittent claudication without acute danger to the extremities</td>
</tr>
<tr>
<td>Stage III</td>
<td>Ischemic pain at rest</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>Necroses, gangrene, ulcers; IVa: dry necroses, trophic disorders; IVb: infected necroses, moist gangrene</td>
<td>Indication for systemic therapy, otherwise risk of losing the extremity (in part); 1-year mortality rate between 20% and 40%</td>
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</tbody>
</table>

Diagnosis of PAD

The diagnosis of PAD is based on a multi-level assessment of patient’s medical history, physical examination, and imaging. Medical history and physical examination can be used to determine the 1st indications of PAD and also classify the disease.
PAD medical records

The patient should describe the circumstances under which the symptom occurs: the duration, location, and nature of the pain, along with distances they are able to walk. Risk factors for underlying atherosclerosis and diseases such as coronary heart disease should also be reviewed. The most important risk factors include nicotine abuse, diabetes mellitus, hypercholesterolemia, arterial hypertension, and hyperlipidemia.

Physical examination in PAD

Decreased blood flow in the affected extremity can be detected early by inspection, depending on the quality of the skin. A pale color, lower temperature, and increased sweat production are indications of diminished perfusion. The physical examination should look for visible lesions or complications such as ulcers, necrosis, and moist gangrene. The possibility of auscultation of the suspected/affected artery should be determined. In severe stenosis, with an occlusion of over 60-70%, a systolic murmur can be heard.

N.B. The dorsalis pedis artery pulse can be readily palpated lateral to the extensor hallucis longus tendon.

Since many patients carry asymptomatic PAD, the clinical diagnosis is facilitated by palpation of the foot pulses (comparing the 2), or determination of the ankle-brachial index (ABI). A treadmill ergometer is also used to objectively evaluate the distances reported by the patient as ‘walkable’ and assess the severity of the disease.

The Ratschow’s positioning test is a non-invasive test, involving maneuvering the position of the feet, used to diagnose PAD. The patient lies in the supine position, and as the legs are lifted to a 90° angle and then returned to a sitting position, a physician can visually assess the blood circulation and venous filling, depending on the time required by the feet to regain their normal color.

Ankle-brachial index in PAD
The ABI is a measured with a Doppler probe and is expressed via the ratio of the blood pressure at the ankle to the blood pressure in the upper arm.

<table>
<thead>
<tr>
<th>Characterization</th>
<th>Value</th>
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<tbody>
<tr>
<td>Normal value</td>
<td>0.9–1.2</td>
</tr>
<tr>
<td>Mild PAD</td>
<td>0.75–0.9</td>
</tr>
<tr>
<td>Moderate PAD</td>
<td>0.5–0.75</td>
</tr>
<tr>
<td>Severe PAD</td>
<td>&lt; 0.5</td>
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</table>

**N.B.** Diabetic patients may be affected by Mönckeberg’s atherosclerosis, where the arterial walls are hardened due to calcification of the tunica media. The rigid arterial walls can mislead the ABI measurement, showing falsely elevated values > 1.3.

### Imaging in PAD

In order to confirm the diagnosis of PAD and locate the stenosis, various non-invasive imaging modalities are used as the 1st choice:

- **Color-flow Doppler sonography** facilitates reliable measurement of the extent and location of the stenosis.
- **Digital subtraction angiography (DSA)** is the gold standard test.
- **Magnetic resonance angiography (MRA)** is the gold standard of interventions. It allows a comprehensive evaluation of the vascular system, including difficult differential diagnoses and is mandatory before any operative procedure is performed.
- **CT-angiography with contrast material** is indicated in the case of an aortic aneurysm.
Differential Diagnoses of PAD

Conditions with clinical pictures similar to PAD

The differential diagnosis should primarily evaluate whether the patient's symptoms are triggered by an arterial factor, or an alternate event arising from physical activity. The differential diagnosis of PAD includes:

- Arteriopathies
- Venous disorders
- Neuralgias
- Neurologic conditions
- Degenerative/inflammatory joint diseases

Therapy of PAD

Treatment of PAD is aimed at:

1. Improvement of the functionality of the affected leg, i.e., the ability to walk longer distances without pain, so that the patient's quality of life is significantly enhanced.
2. Impeding the progression of atherosclerosis.
3. Lowering the secondary risk of cardiac and cerebral events, such as a myocardial infarction or stroke.
4. Preservation of the extremity, under all possible circumstances, and avoidance of amputation.

Therapeutic options for PAD include conservative, medicinal, interventional, and operative approaches. Important general measures include resting the feet at a lower level than that of the heart, taking good and regular care of the feet and avoiding cold temperatures, infections, and trauma, especially in the last stages of the condition.

One of the most important therapeutic measures is the treatment of risk factors for atherosclerosis. One of the first steps is to advise the patient to quit smoking, followed by control of blood sugar levels with medications, lowering LDL-cholesterol, and restoration of normal blood pressure.

<table>
<thead>
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<th>Stage</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Stage I</td>
<td>In asymptomatic patients, there is no indication for measures to boost circulation or implement invasive procedures. A daily gait training session of 1–2 hours as well as a prophylactic intervention with platelet aggregation inhibitors (acetylsalicylic acid—ASA 100–300 mg/day) is indicated to decrease cardiovascular risk.</td>
</tr>
<tr>
<td>Stage II</td>
<td>The affected extremity is in no acute danger, but patient symptoms should be treated. Therapeutic measures include daily gait training and ASA (similar to stage I) as well as vasoactive agents such as cilostazol or naftidrofuryl. Invasive procedures have a limited indication and are only used after careful risk-benefit analysis and when the patient's quality of life is severely diminished.</td>
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</table>
Stage III/IV

Patients are plagued by pain at rest, which may also be accompanied by necroses. In these stages, revascularizing medication is the top priority, in order to avoid the loss of an extremity. In these cases, patients strictly follow individualized therapy regimens under the supervision of multidisciplinary teams of physicians and health professionals. Vasoactive prostaglandin E1 can be introduced into the regimen or as an alternative when operative revascularization is not feasible. Therapies for adequate pain relief involve metamizole, paracetamol, ASA or clopidogrel as basic treatment options, whereas severe pain is an indication for opioid medications, wherever legally permitted. Invasive measures include, depending on the circumstances, percutaneous transluminal angioplasty (PTA), bypass operation, thromboendarterectomy (PTE).

Invasive measures are indicated for stages III/IV to avoid the amputation of an extremity: PTA with/without stent insertion can dilate the affected vessel through a balloon catheter. Operative procedures include local PTE, during which the thrombus is extracted alongside a part of the vascular wall, as well as bypass implantation.

Here, an autologous vein, usually the great saphenous vein, is used as a substitute vessel. Surgery and PTA are commonly used as a combined treatment modality. In general, the success rate rises with the increase in vessel size.

N.B. 1) For stages I and II, an hour- to 2-hour-long daily gait training program is sufficient, and 2) in bypass operation, the autologous vessel used is the great saphenous vein.

Complications of PAD

Possible dangers in PAD

If left untreated, and in progressive stages, PAD can cause severe complications due to hypoperfusion of the tissues. The complications include healing disorders, wound infections and even sepsis. Acute arterial occlusion of an extremity can lead to necrosis and amputation as a worst-case scenario. Furthermore, PAD patients carry an increased risk of atherosclerotic secondary diseases, such as myocardial infarction and stroke.

References


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