Recommendations for the detection and treatment of peripheral arterial disease

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Abstract

The article presents recommendations for the management of patients with peripheral arterial disease from diagnosis and acute intervention to long-term follow up.

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1. Introduction

Peripheral arterial diseases include conditions in which blood supply to the limbs is impaired due to changes in the arteries. In clinical work, the distribution of ischaemic changes into acute and chronic proves helpful.

2. Acute ischaemia of the limb

2.1. Definition

Acute limb ischaemia is a condition in which sudden decrease in arterial blood flow poses a risk for survival of the affected limb (1,2). Acute limb ischaemia may occur in persons without any previous symptoms, although the majority of them have relevant concomitant diseases. Acute ischaemia is the term that applies to the condition within first 14 days from the onset of the event (1).

Acute limb ischaemia is most frequently caused by embolism or thromboembolism of a major artery. As rheumatic fever related diseases of the cardiac valves have become increasingly rare and patients with atrial fibrillation generally receive adequate treatment with anticoagulants, acute limb ischaemia is caused more frequently by arterial thrombosis than by embolism (1,3). The most relevant causes of acute limb ischaemia are presented in Table 1.

2.2. Epidemiology

The data on the incidence of acute limb ischaemia are relatively scarce. According to the English and Swedish reports, the annual incidence of acute limb ischaemia is 13–14/100,000 population (4,5). If we also add the cases of acute thromboses of surgical arterial by-

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Table 1: Causes of acute limb ischaemia.

Frequent causes:
• thrombosis of the artery due to atherosclerotic plaque detachment;
• thrombosis of a surgical arterial bypass;
• embolism (arising from cardiac chambers, aneurysms or atherosclerotic plaques);
• thrombosis of an arterial aneurysm (particularly popliteal).
Rare causes:
• injury of artery (incl. iatrogenic);
• dissection of aorta
• paradoxical embolism (generally coupled with pulmonary embolism);
• thrombosis associated with arteritis of large vessels;
• thrombosis associated with arteritis of large vessels;
• thrombosis of the popliteal artery due to pressure from abnormally positioned fibular biceps muscle;
• thrombosis of the popliteal artery due to adventitial cysts;
• thrombosis associated with a protracted vasospasm (e.g., at intoxication with ergot preparations)

passes, the annual incidence increases to approximately 17 cases per 100,000 population (5). The lower limbs are affected more frequently than the upper ones, so that the acute upper limb ischaemia represents only between 15–25 % of all acute limb ischaemia cases (6,7).

2.3. Diagnostic procedures

Acute limb ischaemia is an emergency that the physician should recognise on the first contact with the patient following targeted history and clinical examination in order to be able to take appropriate action. The Anglo-Saxon term for full-blown clinical picture of acute limb ischaemia is "5 P syndrome": the limb is *painful, pale, pulseless, paresthetic* and *paralytic*.

Recommendation 1 **I C**

When acute limb ischaemia is suspected at the level of primary health care, rather than advising any additional investigation we recommend an immediate telephone consultation with a vascular specialist (surgeon or spec. in internal medicine) at the referral hospital and emergency transport of the patient to the hospital.

2.3.1. Blood-flow examination with a Doppler detector

Doppler measuring of perfusion pressure in acute limb ischaemia often fails, because it is not possible to detect arterial signals in the affected limb at the level of the ankle. Arterial and venous Doppler signal detection in the ischaemic limb, however, has a predictive value for the outcome (1). When the arterial signals are detectable, this is a good prognostic sign that the limb is not acutely threatened. An absence of arterial and venous signal is a bad prognostic sign, which is most often indicative of an irreversible ischaemia of the limb (1). Clinical examination, together with the evaluation of arterial and venous blood flow by means of a Doppler detector, enables a specialist in surgery or internal medicine to obtain a quick clinical classification of acute limb ischaemia, which has a prognostic value (Table 2).

2.3.2. Emergency vascular imaging

Emergency vascular imaging, particularly computed-tomography angiography (CTA), is essential for confirming

the diagnosis, imaging the site and extent of vascular occlusion and for treatment planning. An advantage of CTA is its speedy performance while its disadvantage is the entailed exposure to ionising radiation and contrast medium, which may adversely affect renal function. The assessment and monitoring of renal function is particularly important in patients with pre-existing nephropathy, who are planned to be treated by transcutaneous catheter procedure and thereby exposed to additional doses of contrast medium (1). In patients with advanced renal disease, vascular ultrasonography may be used for the needs of treatment planning (2).

Recommendation 2 **I C**

In acute limb ischaemia, appropriate vascular imaging – most frequently CTA – should be performed prior to any therapeutic procedure, however, this should by no means cause a considerable delay to the beginning of treatment.

Prior to an emergency endovascular or surgical intervention, the patient undergoes blood pressure measuring and ECG monitoring, and has a blood sample taken for basic haematological, biochemical and coagulation investigations.

2.4. Treatment

Intervention measures in acute limb ischaemia are schematically presented in Figure 1. Acute limb ischaemia is an emergency that requires of a general practitioner to organise immediate transport of the patient to the referential hospital where quality management of arterial occlusion can be provided as necessary. While waiting for the transport, the patient should receive analgesics. In the absence of contraindications, the patient immediately receives an intravenous application of standard heparin (5,000 U) to prevent further growth of the thrombus and recurrence of embolic events (1,2). Particular contraindications for heparin application is a concomitant major haemorrhage or a fresh brain stroke.

Revascularisation treatment modality is chosen on the basis of the clinical assessment of limb endangerment (Table 2) by a vascular specialist, and the findings of emergency vascular imaging of the arteries.

Any directly endangered limb (category IIb or unclear delineation between categories IIb and III in Table 2) should be immediately treated with one of the methods that ensure fast revascularisation (1,2). With respect to the extent of arterial occlusions and the availability of therapeutic methods in the referential hospital we decide between thrombectomy using thromboaspiration catheter, surgical thromboembolectomy and surgical bypass (2). In acute arterial occlusion due to embolism, embolectomy by means of Fogarty catheter may be considered (2).

In a limb that is not directly endangered (categories I and IIa in Table 2) it is possible to treat arterial occlusion – particularly in the fist 14 days of its occurrence – by intraarterial thrombolysis, whereby a thrombolytic agent is fed directly into the thrombus by means of a catheter (1,2,8,9).

After successful revascularisation of acute limb ischaemia reperfusion tissue damage may occur. Namely, reperfusion through the damaged microcirculation gives rise to a local oedema. If the oedema progresses within the rigid muscular fascia, the pressure in the muscle may

rise to the point that it interrupts the very arterial inflow. The risk of muscular necrosis and acute renal failure requires immediate fasciotomy (1,5).

Patients with irreversible ischaemic limb (category III) with extensive tissue necrosis and nerve damage must undergo a life-saving limb amputation (1,2).

In all patients it is also necessary to treat their primary disease that led to acute limb ischaemia, e.g., appropriately address atrial fibrillation or atherosclerotic vascular disease. In the event of accompanying muscular damage, it is necessary to ensure adequate renal perfusion and alkalise urine to decrease tubular necrosis. Patients should be subject to regular follow up (1,5).

Recommendation 3 **I A**

In acute ischaemia that threatens the limb survival (category II), an emergency revascularisation intervention is indicated.

3. Chronic arterial perfusion disorders of the limbs

3.1. Definition

The term peripheral arterial disease (PAD) applies to chronic arterial perfusion disorders of the limbs. In the majority of cases they are caused by atherosclerosis (1,2). The lower limbs are affected most frequently. The disease develops slowly and can be for a long time without symptoms. The progressing stenosis of arterial lumen causes the symptoms of intermittent claudication with ischaemic pain that occurs at walking. In advanced stages of the disease, the ischaemic pain also occurs at rest and may be accompanied by tissue necrosis with gangrene. PAD is most frequently defined according to the clinical classification by Fontaine (10) or Rutherford (11) (Table 3). There are also various questionnaires available, which help us to evaluate the patient's mobility and quality of life (11). Chronic critical limb ischaemia is a con-

Table 2: Internationally recommended clinical classification of acute limb ischaemia. Adapted from Norgren L et al. (1) and The Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (2). Distinguishing between classes IIb and III can be difficult.

Category	Prognosis	Clinical signs:		Audible Doppler signal:	
		loss sensitivity	loss muscular strength	arterial	venous
I. Viable limb	non-acute at risk	no	no	yes	yes
II. Endangered limb					
a: Moderately	salvageable limb by revascularisation	yes (minimal, only in the fingers/toes)	no	no	yes
b. Directly	salvageable limb by immediate revascularisation	yes (more than just fingers/toes, accompanying pain)	yes (mild/moderate)	no	yes
III. Irreversible ischaemia	unavoidable loss of the tissue or permanent nerve damage	yes (anaesthetic limb)	yes (paralytic limb)	no	no

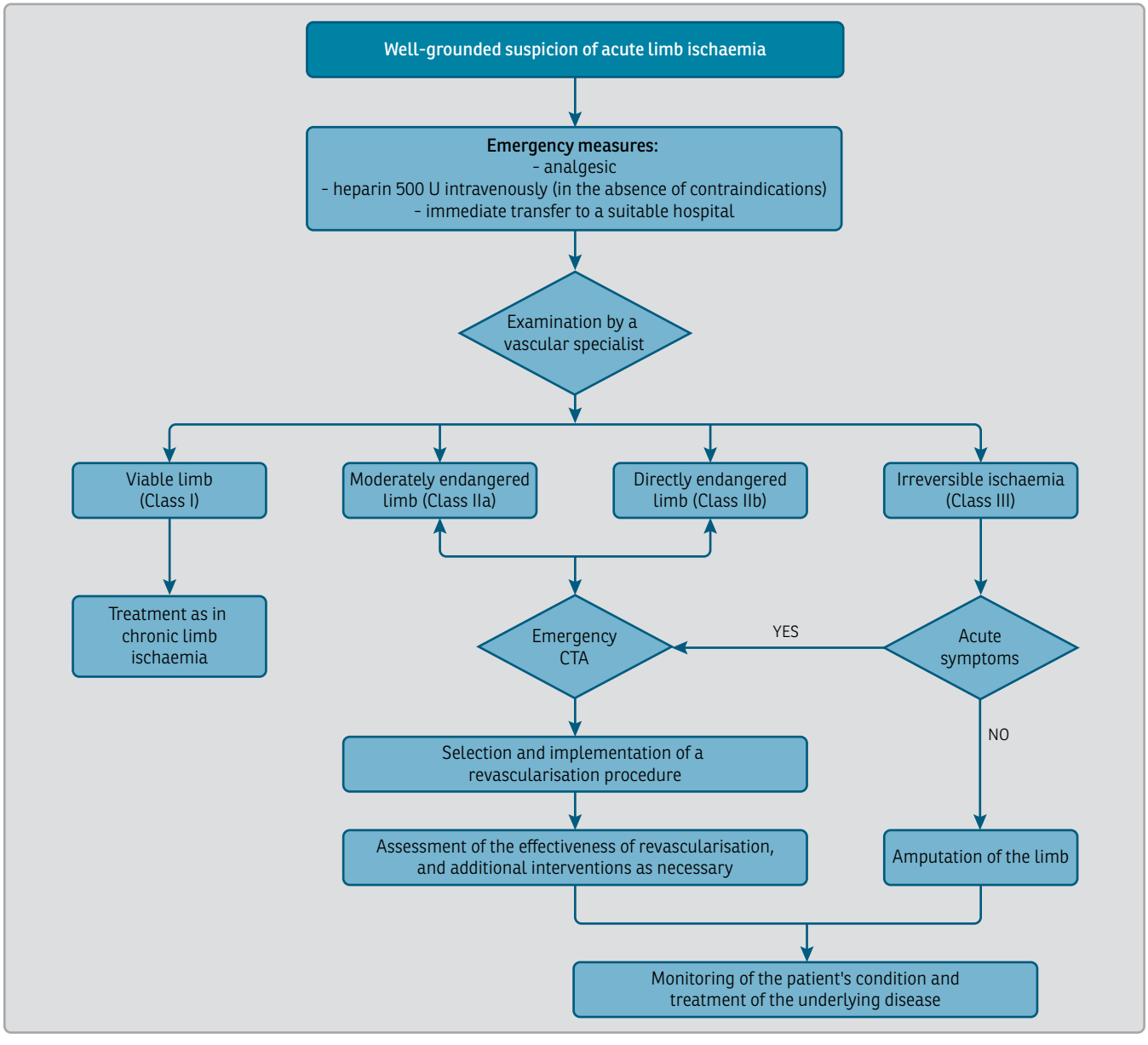

Figure 1: Algorithm of acute limb ischaemia management. CTA computed-tomography angiography. Adapted from 1.

dition where the patient presents with at least two-week lasting ischaemic pain at rest, which can be accompanied by ulcer or gangrene (1,2).

3.2. Epidemiology

In the developed world, asymptomatic PAB proven with a decreased ankle index value below 0.91 is found in 15–20 % of people older than 55 or 60 years (1). Approximately 5 % of the elderly population has intermittent claudication, the frequency of which increases with age, while 0.1 % has critical ischaemia with resting pain or gangrene (1,2,12). The incidence of PAB is higher among patients with diabetes (1,13) and those with advanced renal disease (1,14,15). The progression of PAB from the stages of intermittent claudication to the stage of chronic critical ischaemia affects annu-

ally only about 1 % of patients with intermittent claudication who do not have associated diabetes or end-stage renal failure (1).

3.3. Diagnostic procedures

3.3.1. History and clinical examination

Diagnostic procedures in the case of a reasoned suspicion of PAB are shown in Figure 2. Patients with PAB in asymptomatic phase do not have subjective complaints, however, they often cannot walk fast. In symptomatic patients, intermittent claudication is often a sufficiently characteristic symptom that allows the diagnosis of PAB to be established on the basis of history. At stenosis or occlusion of the abdominal aorta or pelvic arteries, claudication pain occurs not only in the calves but also in the buttocks and thighs. In isolated impairment of lower-leg arteries, the claudication pain is limited to the foot. It is characteristic of chronic critical ischaemia that pain is worst at night during lying and that it affects mainly the foot and toes. With lowering the legs from the bed, pain is temporarily relieved as the arterial pressure in the foot increases owing to the hydrostatic component.

In all patients with PAD we have to determine their mobility and risk factors for atherosclerotic cardiovascular events by means of anamnesis (smoking, arterial hypertension, hyperlipidemia, diabetes, nephropathy, premature atherosclerotic disease in close relatives), and ask them about possible symptoms of concomitant coronary or cerebrovascular disease (1,2).

In the clinical examination of a patient suspected of having arterial perfusion disorder of the lower limbs, the most important procedures include palpation of pulses on the lower limbs, the finding of trophic changes in the skin and skin adnexa as well as ulcers or gangrene. In order to determine the extent of vascular disease, it is necessary to palpate the pulses of the carotid and radial arteries and possible pulsations of the abdominal aorta, and detect by auscultation any murmur in the carotid, subclavicular and iliofemoral arteries. A full angiological investigation also includes a clinical examination of the heart (1,2).

In the differential diagnosis, the causes of pain or discomfort in the lower extremities that are not a consequence of

Table 3: Fontaine's and Rutherford's classification of limb ischaemia in peripheral arterial disease (10,11).

Categories by Fontaine	Categories byRutherford
Stage I asymptomatic	0 asymptomatic
Stage II ischaemic pain at walking	1 mild claudication
IIa long claudication distance (>200 m)	2 moderate claudication
IIb short claudication distance (<200 m)	3 severe claudication
Stage III ischaemic pain at rest	4 ischaemic pain at rest
Stage IV ulceration and gangrene	
IVa limited gangrene	5 small loss of tissue
IVb extensive gangrene	6 extensive loss of tissue

ischaemia should be considered, in particular: musculoskeletal pain, radicular pain (e.g., lumboischialgia or pain associated with spinal canal stenosis), neuropathic pain (e.g. in diabetic polyneuropathy) and restless leg syndrome (1,2).

3.3.2. Basic laboratory tests – the detection of risk factors for atherosclerosis

In patients with suspected PAD it is necessary – already at the initial stage of the diagnostic procedure – to identify and treat preventable risk factors for atherosclerosis and to identify possible anaemia or polycythaemia, which may impair limb perfusion. All patients must have blood pressure measured correctly, and possible arterial hypertension determined. The following basic laboratory tests should be performed: haemogram, lipidogram, serum levels of glucose and creatinine, and urinalysis for determining glycosuria and proteinuria (1,2).

3.3.3. Ankle-brachial index determination

Ankle-brachial index is a basic test for confirming the suspicion of PAD, and is generally performed already at the primary health care level. The sphygmomanometer's cuff is placed above the patient's ankle and the systolic pressure in the posterior and anterior tibial arteries measured by means of a Doppler detector; afterwards, the systolic pressure is also measured in both upper arms. The higher systolic pressure measured in each ankle is compared with the higher systolic pressure in the upper arm. Normally, the arterial pressure at the ankle is equal to or higher than the pressure in the upper arm. Scores of ankle-brachial index in the range between 0.91–1.40 are considered normal. An ankle-brachial index value of 0.9 or less proves the presence of PAD (1,2). The lower the ankle-brachial index, the more advanced the PAD. A score of ankle-brachial index under 0.4 is indicative of critical ischaemia, where the absolute values of systolic angle pressures are generally lower than 40–50 mmHg, however, in determining critical ischaemia clinical picture is of decisive importance (1,2).

Oscillometric measurement of the ankle index is simpler and faster than Doppler measurement, but it is useful mainly as a screening method, as it fails in advanced forms of PAD (16).

Recommendation 4 **I B**

The ankle-brachial index measurement is a basic objective, non-invasive investigation for the detection of PAD.

Due to the incompressibility of the lower-leg arteries, non-invasive ankle pressure measurement does not provide correct results in medial calcinosis, which is a frequent condition in patients with diabetes or chronic renal failure. Therefore, with the value of the ankle-brachial index above 1.40, further investigations are required to define PAD, which are carried out at the secondary healthcare level. Plethysmographic measurement of perfusion pressure on the big toe can be used, since medial calcinosis does not reach the arteries of the toes. The pressure in the arteries of the toes is approximately 10 mmHg lower than the arterial pressure at the ankle. Critical ischaemia is present when the pressure measured in the big toe is below 30 mmHg, while the values above 50 mmHg exclude the presence of critical ischaemia (1,2). Transcutaneous oximetry, which is a method for investigating microcirculation, is also useful in diagnosing critical limb ischaemia

with pronounced medial calcinosis of the lower-leg arteries with a falsely high ankle-brachial index. We can fairly reliably exclude critical limb ischaemia and predict ulcer healing if the partial pressure of oxygen in the subcutis exceeds 40 mmHG (1). Transcutaneous oximetry is also useful in the determination of the level of amputation in the case of distal gangrene of the limb with irreversibly damaged arteries.

When the clinical status and the ankle-brachial index are normal while the anamnesis is typical of intermittent claudication we use a walk test according to the PAD protocol, in which the subject is walking in a treadmill with a standardized speed and pitch. The initial and maximal claudication distance is recorded and perfusion pressure at the ankle measured before and after the physical stress. In relevant proximal stenoses of the limb arteries, immediately after the physical stress the perfusion pressure at the ankle decreases by 20 % in comparison with the pressure at rest (1,2).

3.3.4. Morphological investigations of arteries

Patients with a short claudication distance, who are hindered in daily activities, and especially those with critical ischaemia, require revascularisation. Prior to the procedure, we have to visualise the morphology of limb arteries and exactly define the site and form of stenoses or occlusions. The choice of an imaging method depends mainly on its availability in the individual healthcare institution.

Arterial ultrasonography (US) provides a fast non-invasive information on the pathoanatomy of arteries and perfusion, particularly in the femoropopliteal and low-leg segments, where the sensitivity of haemodinamically relevant stenosis detection is 85–90 %, with the sensitivity increasing to > 95 % if the imaging is performed by a skilled expert (2). Based on the arterial US, we can plan treatment and follow-up treatment success (2). Drawbacks of the UZ are its high dependency on the investigator's experience, the small anatomical area shown on an individual image, the difficulty in estimating highly calcined vascular sections, and the inability to examine veins in the area of ulcers or extensive scarring (2).

In the last years, computed-tomography angiography (CTA), where the contrast medium is injected intravenously, has become the leading diagnostic method for planning PAD surgery. In the aortoiliacal and femoropopliteal areas, the sensitivity and specificity of CTA do not differ from those of classical digital subtraction angiography (DSA); its yield is slightly worse only in the imaging of the lower-leg arteries (2). The advantage of CTA over DSA is in the imaging of atherosclerotic plaques, calcifications, vascular stents and bypasses. The drawback of CTA for the presentation of the abdominal, pelvic and lower leg vessels is in its high radiation exposure with an effective dose of 9 to 30 mSv (17,18). The contrast medium may cause a deterioration of the renal disease (1,2).

In terms of sensitivity and specificity, magnetic resonance angiography (MRA) using gadolinium contrast medium is comparable to DSA, but due to the use of different techniques, the results are fairly variable (2). In undergoing MRA, patients are not exposed to ionising radiation, but the investigation is not suitable for patients with a pacemaker or ferromagnetic implants and for patients with claustrophobia. MRA does not show calcifications. The use of gadolinium contrast medium is contraindicated in severe renal disease (estimated glomerular filtration rate

< 30 ml/min per 1.73 m^2) as it may cause nephrogenic systemic fibrosis (2). However, since 2013, the use of gadolinium contrast media with cyclically bound gadolinium (Gadovist – Bayer Schering) is again permitted in these patients. Nevertheless, enough information can often be obtained by MRA TOF technique, which does not use a contrast medium.

For many years, digital subtraction angiography has been a gold standard in angiographic diagnostics, but nowadays it is only indicated for the presentation of arteries immediately prior to a catheter revascularisation procedure (2). Ionising radiation exposure in DSA of the pelvic and peripheral arteries is lower than in CTA, provided that we do not use lateral projections (19), but otherwise it is comparable or higher than in CTA (19,20). Arterial puncture is associated with complications in approximately 1 % of patients (2).

Recommendation 5 **I A**

Morphological investigation of arteries is indicated in the case of a planned revascularisation procedure. It is reasonable to perform classical angiography when the diagnostic procedure is followed immediately by an endovascular catheterisation procedure.

3.4. Treatment

The treatment of PAD consists of two basic groups of interventions: systemic prevention of cardiovascular ischaemic events and locally targeted treatment of claudication symptoms or critical limb ischaemia. Treatment procedures for PAD are shown schematically in Figure 3.

3.4.1. The prevention of cardiovascular ischaemic events

PAD patients have a high risk of ischaemic complications also in the coronary and carotid vascular bed (1,2), therefore, they are treated according to common guidelines for the prevention of cardiovascular diseases, developed by a group of representatives of European associations for cardiology, hypertension, atherosclerosis, diabetes, behavioural medicine and family medicine (20). Patients with PAB are advised to maintain a healthy lifestyle without smoking, preferably everyday half an hour of physical activity, e.g. in the form of interval walking, maintenance of an appropriate body weight (body mass index ≤ 25 kg/m^2) and a Mediterranean type diet (2,21).

Cessation of smoking. Smoking is an important risk factor for PAD, limb amputation and death due to cardiovascular event (2). Therefore, all patients with PAD are advised to cease smoking. It is optimal that smokers join professionally controlled smoking cessation programs (2,21).

In patients with PAD, lipolytic treatment with statins decreases mortality rates from cardiovascular events as effectively as in other groups of high-risk patients (21). Although hypercholesterolaemia is more important risk factor for heart infarction than for PAD, statin therapy also inhibits the occurrence and aggravation of PAD (22). According to European recommendations, the LDL-cholesterol value in PAD patients should be decreased to ≤ 2.5 mmol/l, preferably to ≤ 1.8 mmol/l, or by at least 50 % with respect to the baseline value (2,21,22).

According to the meta-analysis of numerous studies, antiaggregation treatment in people with high cardiovascular risk, including PAD patients, reduces the incidence of heart attack, ischaemic stroke and sudden cardiac deaths by

20–30 % (23). In diabetic patients with asymptomatic PAD, antiaggregation therapy with acetylsalicylic acid failed to reduce the occurrence of cardiovascular events and mortality (24). In patients with PAD, mainly acetylsalicylic acid in a small, usually 100 mg dose is used as an anti-aggregation agent. In the CAPRIE study, Klopidogrel at a dose of 75 mg/day in PAD patients proved more protective against cardiovascular events and sudden cardiac death than acetylsalicylic acid (25). Less data are available on the effect of antiaggregation therapy on the progression of PAD, but a comprehensive primary prevention study from US doctors has shown that after 5 years the group taking acetylsalicylic acid required half as many revascularisation interventions on peripheral arteries as the placebo group (26).

In PAD patients blood pressure should be regulated following the joint recommendations of the European Association of Hypertension and the European Association for Cardiology (27). Their blood pressure should be maintained within the range of ≤ 140/90 mmHg, in diabetic patients within ≤ 140/85 mmHg. The angiotensin converting enzyme (ACE) inhibitors, which independently of the reduction in blood pressure further reduce the incidence of ischaemic cardiovascular events, are particularly useful (28,29). The ONTARGET study demonstrated the equivalence of ACE inhibitor ramipril and angiotensin receptor blocker telmisartan (30). In patients with critical ischaemia, intensive treatment of arterial hypertension should be pending till limb revascularisation (1). Beta blockers are not contraindicated in patients in the stage of intermittent claudication (1,2).

Regulation of serum glucose in diabetic patients reduces the incidence of diabetic micro-vascular and neuropathic complications, but less obvious are its positive effects on the macro-circulation. Nevertheless, serum glucose should be managed as best as possible. In subjects with diabetes, the desired value of glycated haemoglobin (HbA1c) <7 % is the preferred measure of glycaemic control (21).

Recommendation 6	**I B**
All patients with PAD are advised to cease smoking.	
Recommendation 7	**I C**
Antiaggregation therapy is indicated in all symptomatic PAD patients.	
Recommendation 8	**I C**
In PAD patients, we try to regulate LDL-cholesterol value with statins to ≤ 2.5 mmol/l, preferably to ≤ 1.8 mmol/l, or by at least 50 % with respect to the baseline value (2,21,22).	
Recommendation 9	**I A**
In PAD patients we try to regulate blood pressure to the level of ≤ 140/90 mmHg.	
Recommendation 10	**I C**
In PAD patients with diabetes, we try to regulate the level of glycated haemoglobin to ≤ 7 %.	

3.4.2. Non-invasive management of claudication symptoms

Interval walking is the basis of non-pharmacological treatment of patients with intermittent claudication (1,2). A meta-analysis of randomised stud-

ies has shown that interval training increases the ability to walk by 50–200 % (30). In order to achieve optimum performance, it is necessary to practice under expert supervision for 35–50 minutes 3–5 times a week for at least 6 months. Interval training consists of walking intervals with individually adjusted speed, so that walking after 3–5 minutes causes moderate pain in the calves, followed by rest, during which the pain completely vanishes. Successful interval training of walking requires good patient motivation and relatively well-preserved physical capacity (1,2,31). Since most patients can not be provided with a controlled exercise program, they are advised to walk in comfortable shoes until the onset of moderate pain in the calves, and then rest until the pain vanishes completely, which usually happens after a few minutes.

Pharmacological treatment of intermittent claudication is less effective than interval muscular training and is advised particularly in patients who cannot exercise effectively (1,2). In Slovenia, pentoxifylline (a methylxanthine derivative with haemorheological effects) is registered, which has statistically significant though modest effects on the extension of claudication distance (1,2).

Table 4: Morphological distribution of aortoiliacal segment damage according to TASC II (1). AIC – a. iliaca communis, AIE – a. iliaca externa, AII – a. iliaca interna, AFC – a. femoralis communis, AAA – an aneurysm of the abdominal aorta.

Type A:	• unilateral or bilateral AIC stenosis;
	• short (<3 cm) unilateral or bilateral AIC stenosis;
Type B:	• short (<3 cm) stenosis of the aorta distally to the bifurcation of the renal arteries;
	• unilateral AIC occlusion;
	• one or more stenoses in a total length of 3–10 cm, which involve AIC and do not extend into AFC;
	• unilateral AIC occlusion, which includes AII or AFC orifices.
Type C:	• bilateral AIC occlusion;
	• bilateral AIE stenoses in a total length of 3–10 cm, which do not extend into AFC;
	• unilateral AIE stenosis, which extends into AFC;
	• unilateral AIE stenosis, which includes AII and/or AFC orifice;
	• markedly calcined unilateral AIE occlusion, which does or does not include AII and/or AFC orifice;
Type D:	• aortoiliacal occlusion distally to the bifurcation of the renal arteries;
	• advanced aortopathy of both AIC, which requires revascularisation treatment;
	• advanced PAD with several unilateral AIC, AIE and AFC stenoses;
	• unilateral AIC and AIE occlusion;
	• bilateral AIE occlusion;
	• stenosis of the pelvic arteries in patients with AAA, in whom placement of closed vascular stent is not feasible, or in those with other vascular damage, which requires surgical treatme

Recommendation 11	I A
In order to relieve the symptoms of intermittent claudication, interval--walking training under expert supervision is advisable.	

Recommendation 12	I C
In order to relieve the symptoms of intermittent claudication, interval--waling training without expert supervision is advisable.	

3.4.3. Pharmacological treatment and care of ulcers in critical limb ischaemia

In chronic critical limb ischaemia analgesic therapy should be started immediately, which often requires a short-term use of opioid analgesics (1,2). A morphological examination of the vascular system and possibly revascularisation should be carried out as soon as possible, to preserve the functionality of the limb (1,2). When an ischaemic ulcer is present on the leg, it is treated according to the principles of wound care (1). If the ulcer is infected or the patient has a wet gangrene, systemic antibiotic treatment is indicated (1,2).

Pharmacological treatment of critical limb ischaemia is considered in the case when revascularisation interventions in the macro-circulation are not feasible, and the only remaining option is support to microcirculation in an attempt to prevent its final failure that leads to gangrene. For this purpose, prostanoids, in particular iloprost, which is a more stable prostacyclin analogue, can be used. (1,2)

Patients with critical limb ischaemia often present with severe concomitant pathologies, particularly cardiac and renal failure, which should be treated simultaneously.

Table 5: Morphological distribution of femoropopliteal arterial disorders according to TASC II (1). AF – a. femoralis, AFC – a. femoralis communis.

Type A:	• one stenosis, ≤ 10 cm long;
	• one occlusion, ≤ 5 cm long.
Type B:	• several stenoses or occlusions, each ≤ 5 cm long;
	• one stenosis or occlusion ≤ 15 cm long, which does not include the part of the popliteal artery, which is situated distally to the knee joint;
	• one or more stenoses or occlusions in the absence of adequately patent tibial artery, which could host a distal vascular bypass;
	• strongly calcined occlusion, ≤ 5 cm long;
	• one stenosis of the popliteal artery.
Type C:	• several stenoses or occlusions in a total length of > 15 cm, with or without severe calcinations;
	• recurrent stenoses or occlusions that require repeated treatment after two previous endovascular interventions.
Type D:	• total AFC occlusion or total AF occlusion, > 20 cm long, which includes the popliteal artery;
	• chronic total occlusion of the popliteal artery and the proximal lower-leg arteries.

3.4.4. Revascularisation procedures

In patients with PAD n the intermittent claudication stage, revascularisation interventions are considered mainly when a few months of interval training in walking fail to result in a satisfactory improvement (1,2), while in patients with critical limb ischaemia, the revascularisation procedure should be performed without delay (1,2).

Revascularisation interventions are divided into transcutaneous intravascular (endovascular) procedures that have undergone a great expansion in recent decades, and conventional surgical procedures, among which the most important is arterial bypass. The type of intervention is chosen with respect to the morphology and the length of arterial damage, and frequently also with respect to the physician's experience (1,2).

As a rule, the patient is maintained on a lifelong antiaggregation therapy (1,2). With stent placement into peripheral arteries, dual antiplatelet therapy with aspirin and clopidogrel in the duration of 1 to 3 months is recommended, based on the expert opinion and survey information on the antiplatelet therapy after coronary stent placement.

Recommendation 13	IIa C
Revascularisation interventions in PAD are indicated when the claudication distance is limitingly short.	

Recommendation 14	I A
Revascularisation interventions in PAD are indicated when the claudication distance is limitingly short.	

3.4.5. Revascularisation of the aortoiliacal segment

Morphological distribution of aortoiliacal arterial damage according to TASC II (TransAtlantic Inter-Society Consensus Working Group (1)) is presented in Table 4.

Recommendation 15	I C
According to the TASC II criteria, endovascular intervention is recommended for the treatment of aortoiliacal disorders of type A and B, and as the first intervention in type C disorders.	

Recommendation 16	IIb C
According to the TASC II criteria, aortoiliacal disorders of type D are generally treated surgically. In a patient with severe concomitant diseases, an endovascular intervention can be attempted, provided that it is performed by an experienced team of experts.	

Recommendation 17	IIb C
With endovascular revascularisation procedure in the aortoiliacal segment, primary vascular stent placement is recommended.	

3.4.6. Revascularisation of the femoropopliteal segment

Morphological distribution of femoropopliteal arterial disorders according to TASC II is presented in Table 5.

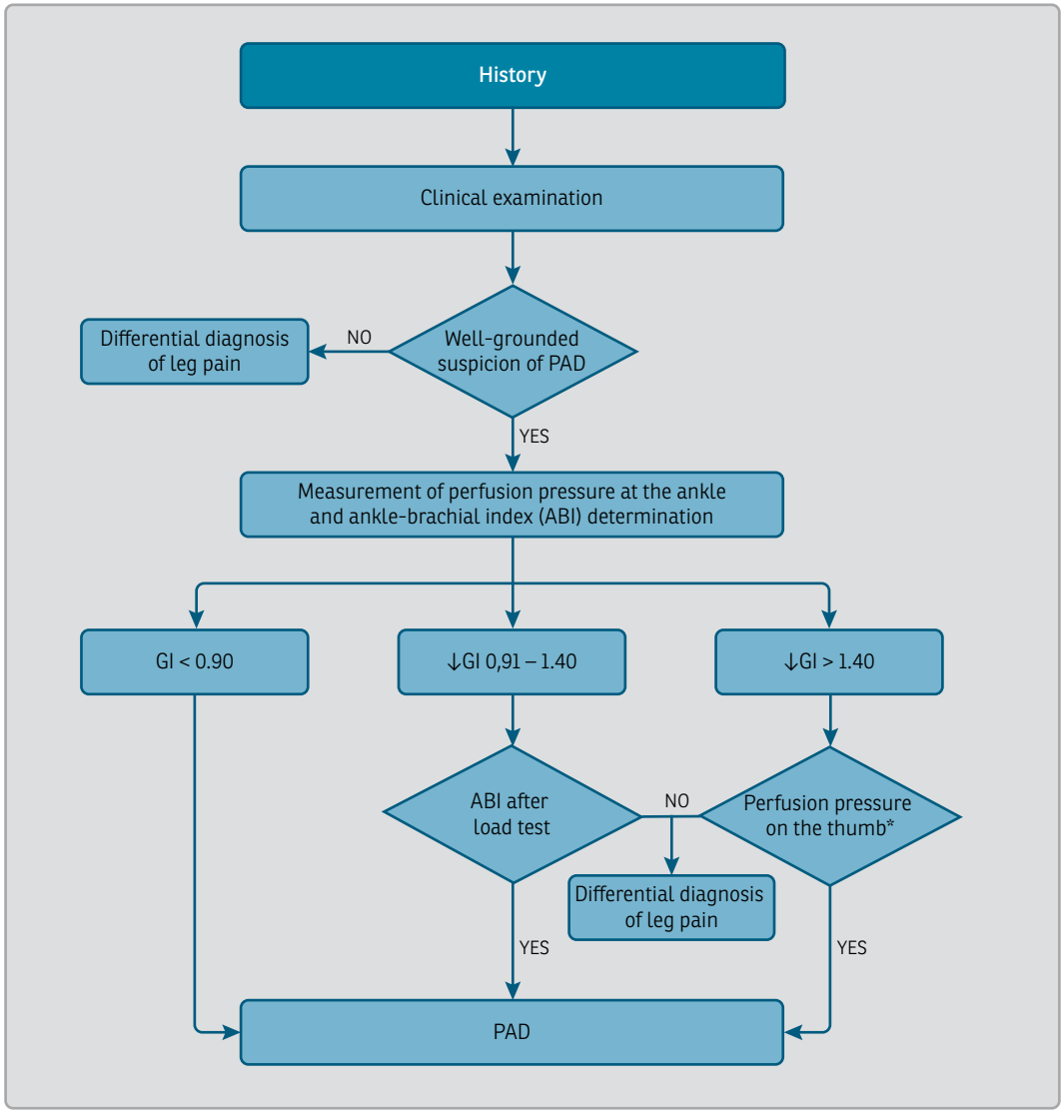

Figure 2: Diagnostic algorithm for suspected peripheral arterial disease (PAD). Adapted from 1 and 2. d.d. – differential diagnosis, obremen. – load test, perfuz. – perfusion. *In incompressible shin arteries, PAD can be also proven by ultrasonography of the arteries or by another imaging method.

Recommendation 18	**I C**
According to the TASC II criteria, endovascular intervention is recommended for the treatment of femoropopliteal disorders of type A and B, and as the first intervention in type C disorders.	

Recommendation 19	**IIb C**
According to the TASC II criteria, surgical treatment is recommended in type D disorders. In a patient with severe concomitant diseases, an endovascular intervention can be attempted, provided that it is performed by an experienced team of experts.	

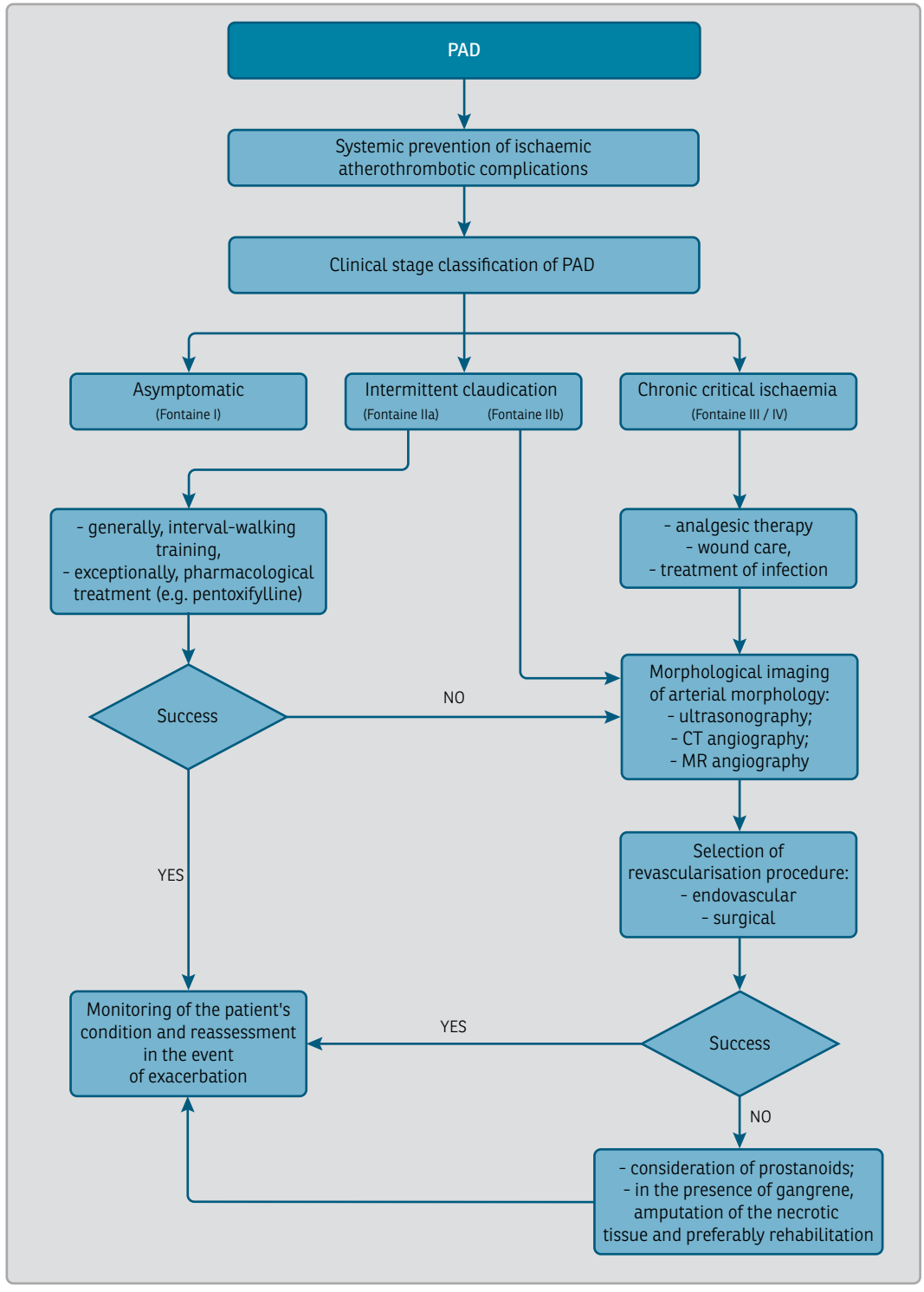

Figure 3: Algorithm for the treatment of peripheral arterial disease (PAD); adapted from 1 and 2.

Recommendation 20	IIa A
According to the TASC II criteria, vascular stent placement is recommended for the treatment of femoropopliteal type B disorders.	

In surgical revascularisation procedure in the femoropopliteal segment above the articular cavity of the knee, there are no major differences in the long-term patency of bypasses with the patient's vena safena magna and bypasses from synthetic materials, although long-term results are in favour of the use of the vena safena magna, whereas in bypasses under the articular cavity of the knee and on the lower-leg arteries an autologous vein functions much better than synthetic bypasses (1,2).

3.4.7. Revascularisation of the lower-leg segment

Revascularisation interventions in the shin arteries are indicated particularly in critical limb ischaemia when it is combined with femoropopliteal and iliacal segment involvement (1,2). The results of endovascular treatment of shin arteries are better in stenoses than in occlusions, as an unbridgeable occlusion of the distal part of shin arteries reduces the success of interventions (1). In surgical femorodistal bypass we choose the most preserved shin artery that should, as a rule, be transmitted to the foot (1,2). In bypasses to the shin arteries we use autologous vein, most often saphena magna vein (1,2).

In the treatment of critical limb ischaemia by revascularisation of the shin arteries, the percentage of limb preservation is slightly higher than the percentage of long-term patent shin arteries (2), which means that the improved perfusion of the limb is particularly important in the phase of ischaemic ulcer healing.

Recommendation 21	IIa C
For revascularisation treatment of the lower-leg arteries, an endovascular intervention is recommended as the treatment of choice.	

Recommendation 22	IIa C
In the endovascular treatment of the lower-leg arteries, balloon angioplasty is recommended; vascular stent placement is indicated only in the case of angioplasty failure.	

After every revascularisation procedure it is necessary to assess the success of the intervention and follow up clinical status of the patient. The first follow-up check is performed by non-invasive investigations immediately after the intervention, clinical examination and the determination of ankle-brachial index after 3–6 months, and after that at least once yearly or earlier in the case of subjective deterioration.

3.4.8. Limb amputation

Amputation of an ischaemic limb is necessary when a large gangrene is developing that poses a risk of an uncontrollable infection, or in rare cases, when ischaemic pain can not be controlled in any other way (1). Before amputation, we try to salvage the limb by revascularising interventions (1,2).

Primary amputation without a prior revascularisation attempt may be indicated in the following cases:

- when morphological investigation of the vessels shows evidence of an irreparable damage of the arteries (most often a large, multisegmental damage without preserved perfusion in the shin);
- in a bedridden patient with flexion contracture of the lower limb.

In a patient who was able to walk before the procedure, the amputation is usually followed by rehabilitation aimed at training him to walk with a prosthesis (1,2). The results of rehabilitation are better in transtibial than in transfemoral amputation, which is associated with more extensive peripheral arterial involvement and very often also with clinically expressed coronary and cerebrovascular disease (1,2).

4. Recognition and evaluation of evidence

The recommendations are written so as to take into account the results of the research obtained to-date in this field. We have considered the evaluation of those studies, which is presented in Table 6.

Tabele 6: Evaluation of recommendations

Recommendation level	
Level I	The procedure or treatment is recommended.
Level II	Opinions on the procedures or treatment are not fully reliable – there are also contradictory facts.
Level II a	Benefit is more likely – it makes sense.
Level II b	Benefit is questionable. No harm.
Level III	The procedure or treatment is harmful.
Evidence level	
A	Several randomised studies or meta analyses.
B	One randomised or several larger non-randomised studies.
C	Experts' opinion or the results of small-scale studies, data from registries.

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