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Below-the-knee Interventions

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Introduction

Critical limb ischemia (CLI) is a limb- and life-threatening condition with a yearly incidence of around 220 new cases per million population. Infrapopliteal arterial occlusive disease, with or without concomitant inflow disease, is a leading source of CLI [1]. Especially in patients with diabetes, the risk of peripheral arterial disease (PAD) is 3- to 4-fold higher and it tends to be more aggressive than in patients without diabetes, with a major amputation rate 5–10 times higher, while typical below-the-knee (BTK) diabetic arterial disease is characterized by long, multilevel disease involving all three infrapopliteal vessels [2, 3].

The continuous advance in the field of vascular interventional radiology has facilitated infrapopliteal angioplasty through the development of low-profile balloon catheters, various small-caliber stents, steerable and hydrophilic guide wires, road map facilities, vasodilators, and antiplatelet medication. Infrapopliteal percutaneous endovascular methods, such as angioplasty and stenting, are currently supported by accumulated clinical data and therefore constitute a first line treatment for BTK arterial occlusive disease.

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Here we provide quality assurance guidelines concerning endovascular treatment of infrapopliteal chronic occlusive arterial disease. An algorithm for treatment is provided in Fig. 1 [1].

Definitions

The most common symptom associated with peripheral chronic atherosclerotic disease of the lower limb is intermittent claudication (IC), a cramping pain during walking caused by an inadequate supply of blood to the musculature of the lower limb. CLI is the final stage of PAD, with a typical clinical manifestation of chronic ischemic rest pain (of >2 weeks' duration), ischemic tissue loss of the limb (ulcers or gangrene), or both. CLI suggests chronicity and should be distinguished from acute limb ischemia [1].

Primary goals of CLI treatment are relief from ischemic pain, healing of neuroischemic ulcers, prevention of limb loss, improvement of patient function and quality of life, and amputation-free survival [1]. Some kind of revascularization, first endovascular and sometimes surgical, is usually necessary to achieve these goals. For some patients, primary amputation may be the only option. Treatment should also be directed toward the pain control, infection control, atherosclerosis control, anticoagulation, and cardiovascular risk management [1, 4].

Pretreatment Imaging

Modern preprocedural imaging includes digital subtraction angiography (DSA), multidetector computed tomography angiography, various techniques of contrast-enhanced magnetic resonance angiography (CE-MRA), and high-frequency

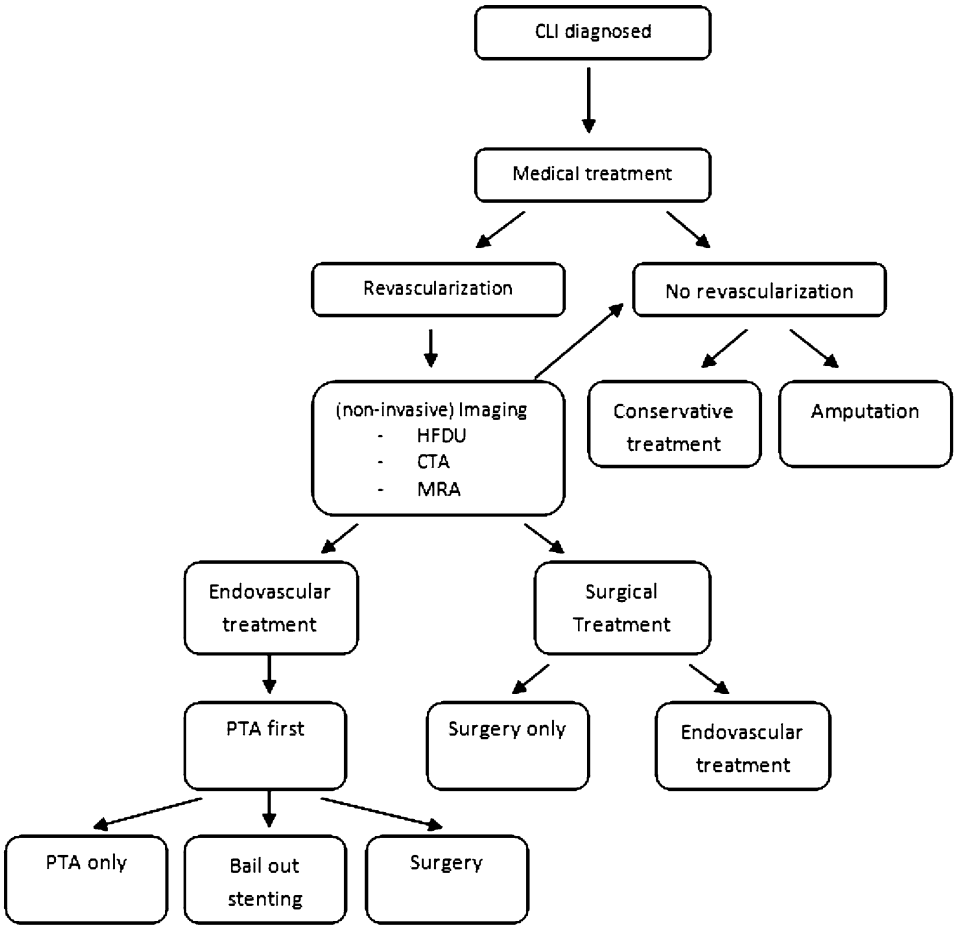

Fig. 1 Algorithm for treatment of patients with CLI. Modified from TASC II [1]

duplex ultrasound (HF-DU) [1, 5–7]. The choice of the optimal preprocedural imaging modality depends on the case and is based on the advantages and disadvantages of each particular method. Although all of the above-mentioned noninvasive modalities are appropriate in evaluating the large-diameter arterial bed above the knee, small-caliber BTK outflow vessels are best depicted by time-resolved CE-MRA and superselective DSA with the catheter positioned just above the infrapopliteal trifurcation [5, 8, 9]. CE-MRA has been reported to detect significantly more distal pedal arteries than selective DSA, even in patients with diabetes, a fact that could influence the pre- and intraprocedural BTK revascularization strategy [10]. Although DSA is an invasive imaging modality, it has the advantage that it can be combined with subsequent treatment during the same session.

MRA evaluation of in-stent stenosis is poor. Multidetector computed tomographic angiography is limited by small-caliber, calcified arteries, where the presence of calcium in the vessel wall may cause artifacts such as calcium blooming and beam hardening, which may hinder assessing the percentage of stenosis. HF-DU is operator dependent, and although the infrapopliteal arterial evaluation is compromised by inflow occlusions, obesity, and calcifications, it can be useful in assessing pedal artery morphology and detecting patent outflow pedal vessels [11]. In stage 3 or 4 chronic kidney disease and predialysis patients, sole preoperative HF-DU is recommended because intravenous (i.v.) administration of contrast agents containing iodine can cause contrast-induced nephropathy, and i.v. use of gadolinium may cause nephrogenic systemic fibrosis [12]. If HF-DU is unsatisfactory and further preprocedural imaging is necessary, gadobenate dimeglumine or gadopentetate dimeglumine time-resolved CE-MRA, nonenhanced MRA, or CO_2 angiography may be considered [13–15].

Pretreatment imaging in patients scheduled to undergo infrapopliteal interventions should provide accurate information regarding both the inflow and the infrapopliteal arterial status. Evaluation of the iliac, common, or superficial femoral and popliteal arteries is essential for the choice of treatment and procedural planning (access site, materials, procedural time). Patency of the iliac and common femoral arteries is of practical importance because it will determine the optimal strategy via an ipsilateral antegrade or contralateral retrograde common femoral approach.

Optimal preprocedural imaging should also identify the anatomical location and extent of the infrapopliteal arterial

lesion or lesions, providing detailed information about the distal foot vasculature. Especially in long occlusions, the reentry distal target vessel should be identified. It is important for the procedural technical and clinical success to identify and treat the infrapopliteal vessel, which contributes most to the blood supply of the foot, especially the part of the foot threatened by ischemia.

According to the angiosome concept, the ankle and foot are divided into six distinct three-dimensional vascular territories supplied by the posterior tibial artery, the anterior tibial artery, or the peroneal artery. Some authors report that in patients with ischemic wounds, direct revascularization of the source artery seems more effective than revascularization of a nonspecific artery with reliance on collateral arteries [16]. Other studies documented that the clinical outcome of the foot has been demonstrated to be favorably affected by increasing numbers of patent crural arteries at the end of endovascular treatment [17]. However, all of these results rely on retrospective data. Prospective studies are needed to validate these initial results, and therefore, in the meantime, any vessel providing sufficient pedal arch runoff should probably be revascularized.

Indications and Contraindications

The primary goal of infrapopliteal endovascular therapy is to obtain relief from the ischemic rest pain, facilitate healing of ulcer or gangrene, prevent limb loss or limit the extent of amputation, and permit wound healing after any type of amputation. Amputation above the ankle is generally defined as a major amputation; amputation at or below the ankle a minor amputation. In critically ill patients, patients unable to cooperate, and patients with recent myocardial infarction, severe arrhythmia, or electrolyte imbalance, treatment should be discussed and undertaken in the presence of cardiologist, the anesthesiologist, or both. In patients with impaired renal function, alternative CO_2 use instead of standard contrast media can be considered. The indications and contraindications for BTK endovascular treatment are listed in Table 1.

The intersociety consensus for the management of PAD (TransAtlantic InterSociety Consensus [TASC] II) classification is listed in Table 2. Generally, in infrapopliteal lesions classified as TASC A or B, endovascular treatment is preferred, while in TASC D lesions, surgical vein bypass is recommended. In TASC C lesions, surgery is the preferred treatment in good-risk patients while considering the patient's comorbidities and preferences, as well as the operator's success rates. However, in the absence of a suitable vein and/or adequate distal runoff vessels, and in high-risk surgical patients, endovascular treatment represents the only valid therapeutic option of CLI. Thus, in common practice with older and fragile patients, endovascular treatment is often the first treatment of choice and should be attempted even in difficult TASC C and D lesions. BTK angioplasty in patients with from severe, lifestyle-limiting, IC (< 10 m) remains controversial. However, it can be considered in selected cases of non-complex TASC A infrapopliteal lesions [1].

Table 1 Indications and contraindications of endovascular management for below-the-knee arterial occlusive disease

Indications
Critical limb ischemia; rest pain (Fontaine stage 3, Rutherford category 4) or nonhealing ulcer/gangrene (Fontaine stage 4, Rutherford category 5–6)
Significant flow-limiting stenosis of the anastomosis or outflow vessels in failing below-the-knee femoropopliteal or distal tibial bypass grafts
Absolute contraindications
Medically unstable patients
Life-threatening infected (wet) gangrene or/and life-threatening osteomyelitis of the target limb unless it is used to enable a more limited amputation
Uncorrectable bleeding disorders
Absent runoff vessels to and in the distal foot
Relative contraindications
Pregnancy
Inability of the patient to lie flat and immobile
Critically ill elderly patients with impaired mobility and dementia
Buerger disease
Impaired renal function (EGFR <30 ml/min/1.73 m^2)

EGFR epidermal growth factor receptor

Table 2 TASC classification of morphologic stratification of infrapopliteal lesions

TASC type A
Single stenoses shorter than 1 cm in the tibial or peroneal vessels
TASC type B
Multiple focal stenoses of the tibial or peroneal vessel, each less than 1 cm in length
One or two focal stenoses, each less than 1 cm long at the tibial trifurcation
Short tibial or peroneal stenosis in conjunction with femoropopliteal PTA
TASC type C
Stenoses 1–4 cm in length
Occlusions 1–2 cm in length of the tibial or peroneal vessels
Extensive stenoses of the tibial trifurcation
TASC type D
Tibial or peroneal occlusions longer than 2 cm
Diffusely diseased tibial or peroneal vessels

TASC TransAtlantic InterSociety Consensus

Patient Preparation

Assessments

Preprocedural laboratory examinations to consider ordering include baseline complete blood count and platelets, clotting profile (prothrombin time, partial thromboplastin time, and international normalized ratio [INR]), and renal function (serum creatinine or creatinine clearance).

Preprocedural clinical assessments include clinical history (including a differential diagnosis between acute, subacute, and chronic events and a history of allergy), detailed physical examination of the extremity (including color and temperature; skin and muscle changes; location and quality of pulses; presence of ulcers, in diabetes categorization into neuropathic, ischemic, or mixed-type ulcerations; photographic documentation of ulcers may be performed for follow-up purposes), and ankle–brachial index. In patients with ischemic ulcers, the ankle pressure is usually 50–70 mmHg, and in patients with ischemic rest pain 30–50 mmHg. However, in patients with diabetes, the ankle–brachial index may be within normal limits because of the relative noncompressibility of the calcified distal arteries. In addition, increased arteriovenous shunt flow due to autonomic neuropathy may result in a relatively warm foot [1]. Toe pressures should be assessed especially in patients with diabetes (critical level <50 mmHg, transcutaneous oxygen pressure, critical level <30 mmHg).

For cardiological assessment, in cases of impaired renal function (glomerular filtration rate [GFR] of <60 ml/min/1.73 m^2), patients should be treated according to the guidelines of the European Society of Urogenital Radiology international guidelines, which includes prophylactic hydration with saline infusion at a dosage of 1.0–1.5 mL/kg/h, 6 h before, during, and for 6 h after the procedure (Table 3) [12]. In outpatients, a sodium bicarbonate protocol can be applied because it is quicker than the isotonic saline regimen. Diabetes, renal disease, heart disease, and older age (>70 years) are associated with an increased risk of contrast-induced nephropathy [13, 14]. In patients receiving metformin treatment who have an GFR of ≥60 ml/min/1.73 m^2, metformin can be continued normally. If the GFR is 30–59 ml/min/1.73 m^2, to avoid lactic acidosis, metformin treatment should be stopped 48 h before the procedure and should be continued 48 h after the procedure only if the renal function has not deteriorated [18]. Patients with known allergic reactions to contrast material should be prepared according to the international guidelines [12]. If patients are unable to stay flat and immobile, general anesthesia should be considered.

Platelet count should be >75,000 mcL and INR <1.5. If these values are not met, the coagulation status must be corrected. Warfarin should be interrupted at least 3 days before the procedure; in heparinized patients, the infusion should be stopped at least 2 h before the procedure. INR and prothrombin time values should be checked before the intervention.

A functioning peripheral i.v. access (18 gauge if administration of blood products is expected) must be obtained, and the urinary bladder should be emptied before the procedure begins.

Table 3 Impaired renal function

Saline infusion (1.0–1.5 ml/kg/h), 6 h before and 6 h after the procedure, or intravenous sodium bicarbonate as an alternative
Stop metformin from 48 h before to 48 h after the procedure
Check renal function after the procedure

Defined as epidermal growth factor receptor <60 ml/min/1.73 m^2

Medication

Patients with CLI should receive cardiovascular risk reduction therapy (Table 4). Antithrombotic drugs, statins, and antihypertensive drugs should be administered to reduce cardiovascular events in all CLI patients, to prevent periprocedural complications, and to increase postprocedural patency rates. Aggressive blood glucose lowering is recommended in all patients with types 1 and 2 diabetes to reach glucose levels as close to normal as possible [1].

Acetylsalicylic acid (aspirin) is the standard antiplatelet therapy in CLI. This includes patients who undergo BTK endovascular treatment before, during, and after the procedure [19].

Although there is not enough evidence in the literature to support this, some authors recommend dual antiplatelet therapy of clopidogrel (75 mg/day) and aspirin (100 mg/day) 3 days before the intervention in patients who are not already receiving antiplatelet therapy. If the patients do not comply with the 3-day antiplatelet regimen, clopidogrel can be administered with a loading dose of 300 mg 12 h or 600 mg 2 h before the procedure [20].

Table 4 Medication for critical limb ischemia

In general
Antithrombotic drugs (aspirin)
Antihypertensive drugs
Statins
Blood glucose–lowering drugs in diabetes
Periprocedural
Intra-arterial heparin
Additional antithrombotic drugs (clopidogrel) (optional)
Intra-arterial nitroglycerin in cases of spasms

During the procedure, 3000–5000 IU of heparin is administered intra-arterially, and throughout the procedure, additional doses may be administered to maintain an activated clotting time at 200–250 s (Table 4).

Nitroglycerine (100–300 μg) can be administered routinely or therapeutically, selectively into the infrapopliteal arteries according to the systemic blood pressure, to prevent or resolve vasospasm (Table 4) [21]. The majority of BTK interventions can be performed under local anesthesia. Local analgesics such as lidocaine 1 % may be administered under US guidance to facilitate precise deposition [18]. Mild conscious sedation (usually up to 50–100 μg of fentanyl and 5 mg of midazolam are sufficient) may be required in anxious patients or for painful procedures. Data regarding the antiplatelet regime after BTK angioplasty and/or stenting are limited, and most protocols reported in the literature are based on coronary studies [22]. Although there is no consensus, double antiplatelet therapy with both aspirin (100 mg/day) and clopidogrel (75 mg/day) for 3–6 months and lifelong single therapy with either 75 mg clopidogrel or 100 mg aspirin is recommended (Table 4) [1, 21–26]. A more aggressive triple regimen including low-molecular-weight heparin for 14 days has been proposed, after treating complex lesions or deploying multiple stents [25]. Some patients are resistant to clopidogrel, and this could influence the clinical outcome. New drugs such as ticagrelor and prasugrel have been investigated in coronary studies, but data regarding their performance in PAD are missing [18, 27, 28].

Equipment

To perform infrapopliteal endovascular procedures, the use of a dedicated DSA C-arm unit adequately equipped with a large matrix providing high-quality imaging and sufficient magnification is indispensable The procedure must be performed in a well-organized hospital that provides essential internal services such as an intensive care unit and a surgical department; the contribution of an anesthesiologist and a vascular surgeon should be immediately available if needed.

The patient's vital signs must be constantly monitored. A complete backup of dedicated BTK materials is essential for the safety and effectiveness of infrapopliteal endovascular procedures. Standard materials include low-profile 0.018- and 0.014-inch, 1.5–4 mm semicompliant balloons up to and over 200 mm with long and extra-long shafts (150 mm for contralateral approaches) as well as "conical" (tapered) long balloons. Balloon-expandable and self-expandable stents 2.25–4 mm in diameter are necessary. Although both over-the-wire and monorail platforms may be used, over-the-wire platforms provide better pushability and allow contrast to be injected once the guide wire has been removed. In contrast, monorail balloons offer rapid exchange systems and provide a lower profile. Also in standard use are 4–5F, 0.035-inch hydrophilic catheters and dedicated 0.018- and 0.014-inch guide wires for BTK use. Support catheters, long sheaths, and guiding sheaths are used to provide better support. Also used are embolic materials (coils), small-caliber covered stents, foreign body retrieval devices, suction catheters, and thrombolytic agents for the management of intraprocedural thrombolysis (mainly for complications).

Percutaneous closure devices are of great value to obtain hemostasis in patients who have undergone antegrade puncture of the common femoral artery (CFA). It should be noted that in some of these devices, antegrade use may be off label.

Finally, micropuncture kits for distal popliteal, tibial, or peroneal approach are used, as is color Doppler ultrasound (US) for US-guided puncture.

Procedural Features and Variations of Techniques

Sterile skin preparation of both groins is advisable. The site and direction of the arterial access (antegrade ipsilateral or retrograde contralateral) depend on the inflow status.

Iliac disease can be treated in the same endovascular session via a contralateral retrograde CFA approach. It is also possible to gain ipsilateral retrograde access and invert the sheath, or to use popliteal or pedal access in the same session, depending on the local anatomical situation. The inflow needs to be corrected before the BTK intervention.

When concomitant ipsilateral CFA occlusive disease is present, surgical patch atherectomy and BTK angioplasty can be performed during the same session if an adequate angiography suite is present in the operating room. If this is not so, a contralateral puncture can be performed immediately or soon after atherectomy, or the endovascular treatment can be scheduled at least 2 weeks after surgery to facilitate the ipsilateral CFA or superior femoral artery (SFA) puncture with safety.

In nonobese patients without iliac, CFA, or very proximal SFA lesions, a direct antegrade puncture is preferable because it offers superior pushability and trackability of the materials to cross hard, calcified distal occlusions, while it allows easier catheter and guide wire maneuvers. Of note, the retrograde crossover technique can be almost impossible in cases of extremely tortuous iliac arteries, hostile aortic bifurcations, Y prosthesis, or abdominal aortic stent grafts. In contralateral access, a long sheath or a guide catheter positioned into the ipsilateral external iliac artery or the SFA allows selective angiographic visualization of the BTK vessels. Ideally, a 5F or 6F sheath can be placed because it enables check angiography during the procedure without retracting the balloon or stent. When these long sheaths are used, continuous irrigation with saline is

recommended to prevent sheath thrombosis. The aim of the intervention is to obtain at least one, but preferably two or even three, patent crural vessels down to the distal foot.

Procedural steps are as follows. US-guided puncture can be used to facilitate fast and precise arterial access. With US guidance, the operator can choose to access either the CFA or the SFA selectively. Puncture of the SFA has the advantage of a more direct route but is associated with more bleeding complications. In addition, puncture of the profunda femoral artery can be avoided. Popliteal and crural (pedal, anterior, or posterior tibial) access should be performed under US guidance. In case of vessel wall calcifications, fluoroscopic guidance may be used. A small real-time injection of contrast should be performed after sheath placement to adjust the position of the sheath in case it is occluding the inflow [26].

Baseline selective arteriograms of the whole limb are obtained to have a baseline to compare with the final result. The catheter is positioned at the level of the tibial trifurcation, and superselective DSA is performed. In general, optimal visualization of the upper and mid third tibial arteries is gained in an ipsilateral oblique projection. The origin of the anterior tibial artery is best visualized in the contralateral oblique projection. Imaging of the distal tibial arteries and the foot is best achieved in a contralateral oblique projection with foot abduction that produces a lateral arteriogram of the foot. The optimal projection to visualize the common plantar artery bifurcation, the dorsalis pedis artery, and the pedal–plantar loop is the lateral oblique projection. To visualize the pedal–plantar loop and the tarsal and metatarsal arteries, an anteroposterior projection of the foot should be obtained [10].

The target tibial vessel is catheterized either with an angled 4–5F catheter or a smaller (2.5–3.0F) support catheter. The stenoses are preferably crossed with a 0.018- or 0.014-inch guide wire. The 0.018-inch systems provide more column strength and pushability, whereas the 0.014-inch systems are less traumatic and have a lower profile. The more distal, the more the use of a 0.014-inch system should be considered. In very distal lesions, the guide wire may be supported by a low-profile 2- or 2.5-mm balloon catheter instead of a standard 4F catheter. In cases of subintimal crossing, a 0.035-inch hydrophilic or 0.018-inch guide wire is appropriate.

Over-the-wire balloon platforms demonstrate superior pushability and therefore efficiency in crossing very tight calcified lesions. These calcified vessels represent a challenge for both intraluminal (suboptimal inflation) and subintimal (difficulty in reentering into the true lumen, increased risk of rupture) angioplasties.

The balloon or stent dimensions are chosen according to the reference vessel diameter and lesion length by visual or quantitative vessel analysis.

Data regarding the duration of balloon dilatation are scarce; to our knowledge, there are no reliable studies on this topic in the literature. However, a dilatation time between 30 s and 1 min is usually sufficient. In case of a suboptimal angioplasty result due to inadequate dilation and/or elastic recoil, a second dilatation with a larger diameter balloon or a longer inflation time can be performed.

In cases of flow-limiting dissection, the balloon should be kept inflated for a period up to 3 min at the nominal balloon pressure or the lesion can be stented. If the dissection persists after additional balloon dilatation, bailout stenting is the only solution. The stent types available for BTK include balloon and self-expandable bare metal stents, as well as balloon expandable drug-eluting stents [20, 24].

Efforts should be made to improve the tibial runoff with additional below-the-ankle angioplasty of significant distal stenoses because the vessels may occlude rapidly without adequate outflow. Stenting in this specific area is not recommended.

A future surgical bypass is not precluded only if an undamaged, unstented landing zone is preserved.

A final check angiogram including the distal foot arteriogram is mandatory.

In cases where the antegrade approach has failed various retrograde techniques can be used as the ultimate resort for limb salvage (e.g., the safari technique via distal retrograde punctures, and the loop technique through the distal collaterals) [29–32]. In case of an occluded SFA that cannot be recanalized, antegrade popliteal access may also be considered. Efforts should be made to treat more than one tibial vessel, especially in cases of little additional procedural risk, as this has been reported to improve limb salvage [16]. In recurrent surgical anastomotic stenosis and tight calcified lesions, typical in patients with diabetes nonresponsive to conventional balloon angioplasty, cutting or high-pressure balloons may be used.

Postprocedural Care

Routine postangioplasty recovery is sufficient. Clinicians should check vital signs, puncture site, and distal extremity; obtain a full blood count; and obtain plasma creatinine levels. Although there is no evidence for clinical, morphological, or cost-effective benefit, patients usually enter a surveillance protocol that may include regular visits at 1, 3, 6, and 12 months and yearly after the index intervention for clinical assessment (adequate modification of risk factors, ankle–brachial index, patient mobility status, wound healing); and imaging follow-up comprising HF-DU, computed tomographic angiography, or MRA at 6 and 12 months and yearly thereafter, or earlier if clinical recurrence occurs (MRA is not

indicated in cases in which stents were used) [1]. In cases of clinical relapse of the symptomatology, preoperative assessment should be performed as previously indicated. Aggressive risk factor modification therapy for diabetes, hypertension, dyslipidemia, smoking, and sedentary lifestyle is highly recommended. Thus, a multidisciplinary team approach is especially advisable in patients with diabetes [21].

Outcomes

Percutaneous Transluminal Angioplasty

At present, percutaneous transluminal angioplasty (PTA) is the primary technique to consider in endovascular treatment of infrapopliteal occlusive disease.

Technical success rates of infrapopliteal PTA are reported to be as high as 80–100 % [33–39]. Success rates will depend on the definition of success, the severity (stenosis vs. occlusion) and length of the treated lesion, quality of inflow and outflow, and the presence of calcifications, diabetes, and renal insufficiency. Up to 80 % 2-year limb salvage rates after PTA are reported, but this will depend on the clinical and anatomical extent of disease [39].

To our knowledge, there are no prospective randomized trials comparing endovascular treatment and bypass surgery in patients with CLI and infrapopliteal occlusive disease.

In a meta-analysis of infrapopliteal angioplasty for chronic CLI, results of PTA were compared with those of a meta-analysis of popliteal-to-distal vein bypass grafts [37, 38]. Primary patency of PTA at 6 months (65 ± 7.0 %) and 12 months (58.1 ± 4.6 %) was significantly lower than of bypass surgery (85.8 ± 2.1 %, $p < 0.05$, and 81.5 ± 2.0 %, $p < 0.05$, respectively), but there was no significant difference between limb salvage at 6 months (88.2 ± 4.4 % vs. 90.9 ± 1.9 %) and 12 months (86.0 ± 2.7 % vs. 88.5 ± 2.2 %).

By preferentially using PTA for CLI and bypass surgery for those patients not suited for PTA, 2-year primary cumulative patency rates and limb salvage rates of 60 and 76 % were reported for 32 limbs with mainly (31 of 32 limbs) TASC D classification that underwent infrapopliteal PTA. In the 82 limbs that underwent infrapopliteal bypass surgery, primary cumulative patency was 53 % and limb salvage 57 %. At 30 days, the mortality and complication rates were higher for all patients undergoing infrainguinal bypass (5.2 and 35 %, respectively) than those undergoing infrainguinal PTA (2.7 and 8.3 %, respectively) [39].

A propensity score analysis of 1023 patients, of whom 262 underwent PTA and 761 surgical bypass, reported similar 5-year results for leg salvage (75.3 vs. 76.0 %), survival (47.5 vs. 43.3 %), and amputation-free survival (37.7 vs. 37.3 %) [40].

Thus, factors to consider when choosing between PTA and bypass surgery should include the anatomic extent and location of the disease and the anticipated morbidity and mortality of the procedure, which seems lower with endovascular treatment than with bypass surgery [1, 36, 38]. In a study that used the National Surgical Quality Improvement Program database, the 30-day composite mortality/major morbidity rate of infrainguinal bypass surgery was as high as 19.5 %, which made the authors conclude that "stringent indications for infra-inguinal bypass surgery should be maintained when considering the method of lower extremity revascularization" [41].

Drug-Eluting Balloons

Drug-eluting balloons have recently been introduced as local drug delivery–assisted angioplasty systems that are an alternative to drug-eluting stents. The advantage of these devices is that they offer the antiproliferative effect of local drug elution without leaving a metallic platform on the arterial wall. This could reduce restenosis rates and facilitate future reinterventions, especially at anatomical locations such as the infrapopliteal bifurcations and the distal tibial arteries, where stenting is not recommended [20]. The first data regarding BTK treatment with a paclitaxel-eluting balloon catheter were reported from a single-center study investigating 104 patients (82.6 % of whom had CLI) with at least one >80-mm-long lesion (mean ± SD lesion length 176 ± 88 mm). Clinical improvement was noted in 91.2 % and complete wound healing in 74.2 % of patients, while the 1-year target lesion revascularization and limb salvage rates were 17.3 and 95.6 %, respectively. The 3-month angiographic restenosis rate was significantly lower when compared to a historical control group treated with conventional balloon angioplasty (27.4 vs. 69 %, respectively) [42]. Several ongoing large multicenter randomized, controlled trials investigating drug-eluting balloon technology for the treatment of infrapopliteal disease are currently awaited.

Stents

The use of bare metal stents in the infrapopliteal arteries is generally reserved for patients with residual stenosis, flow-limiting dissections, or elastic recoil after PTA. Although the use of stents BTK is technically feasible and safe, there is no evidence to support direct or primary stent placement in all cases [43–45]. A small single-center prospective randomized study with 38 limbs in 35 patients with CLI found no statistically significant difference in survival (69.3 vs. 74.7 %), limb salvage (90 vs. 91.7 %), or primary (66 vs. 56 %) and secondary patency (79.5 vs. 64 %) at 1-year follow-up after PTA or primary stenting [46].

Enthusiastic results have been reported regarding the use of drug-eluting stents, especially sirolimus-eluting stents in the infrapopliteal arteries [47]. At present, all drug-eluting stents are balloon expandable and therefore of limited length. In a single-center, double-arm prospective registry comparing bailout after PTA with either a sirolimus-eluting stent or a bare metal stent, there was significantly better primary patency and fewer reinterventions after 1 and 3 years with sirolimus-eluting stents, but at 1 year's follow-up, there was no significant difference between both groups for mortality (13.8 vs. 10.3 %) and limb salvage (100 vs. 96 %) [29].

A prospective randomized multicenter double-blind trial compared infrapopliteal treatment with a polymer-free sirolimus-eluting stent and a bare metal stent in 161 patients with either CLI or IC. For all patients, the 1-year primary patency rate was significantly higher for sirolimus-eluting stents (80.6 %) than bare metal stents (55.6 %, $p = 0.004$). However, the limb salvage rate between both groups was comparable (98.4 vs. 96.8 %, $p = 0.61$). For patients with CLI only, 1-year primary patency rates did not differ significantly (75 vs. 56.5 %, $p = 0.23$) [48].

In the industry-initiated DESTINY trial, 140 patients with CLI (Rutherford categories 4 and 5) and a maximum of two focal de novo atherosclerotic target lesions in one or more infrapopliteal arteries were randomized to either a bare metal stent or an everolimus-eluting stent. Primary arterial patency, defined as absence of ≥50 % restenosis at 12 months, was significantly higher after treatment with the everolimus-eluting stents vs. bare metal stents (85 vs. 54 %) but was only obtained in 46 %. There was no difference in pain relief or limb salvage between both groups. The major amputation rate was only 3 % and the combined major amputation and death rate only 19 % at 12 months, which may be due to the selection of patients with short lesions—probably, as the authors state, atypical for patients with CLI [49].

Other randomized trials that investigate the use of drug-eluting stents BTK are the industry-initiated ACHILLES trial (sirolimus-eluting stent vs. PTA in patients with CLI and IC) and the investigator-initiated PADI trial (comparing paclitaxel-eluting stents with PTA in patients with CLI) [50]. Results of these trials remain to be published.

A prospective randomized multicenter study that compared the use of a bioabsorbable stents with PTA alone in 117 patients with CLI reported a significantly lower 6-month angiographic patency rate for lesions treated with a bioabsorbable stent than for those treated with PTA (patency rates 31.8 vs. 58 % $p = 0.013$) [51].

The use of carbon-coated stents (in combination with clopidogrel for 4 weeks) was compared with PTA (without administration of clopidogrel) in a prospective randomized multicenter study on 131 lesions in 88 patients. At 3 months, improved clinical results were found more often in the carbon-coated stent group (81.8 %) than in the PTA group (62.5 %). At 9 months, however, the clinical effect reversed. Clinical improvement at that date was found in 58.3 % of patients in the PTA group and 47.4 % of patients in the stent group. Although numerically the angiographic data at 9 months indicated inferior results in patients after PTA, these results were not statistically significant [52].

Complications and Management

Immediate complications occurring during or shortly after infrapopliteal endovascular procedures are reported in 2–10 % of cases [33–36]. Numbers of complications seem to depend on the definition that is used. Major and minor complications are often not defined, and separate results are often lacking. Major complications are usually observed in 3–4 % and minor complications in the remaining cases. Most frequently reported complications are vessel occlusion, puncture site hematomas, false aneurysms, and access site or retroperitoneal bleeding.

Vessel occlusion due to a flow-limiting dissection can be treated with a stent or prolonged (3 min or longer) inflation of the occluded segment with a PTA balloon. Vessel occlusion due to a thromboembolic event can be treated with percutaneous aspiration thrombectomy with a catheter or guiding sheath or with catheter directed thrombolysis with urokinase or recombinant tissue plasminogen activator. Vasodilators such as nitroglycerine may be administered when vessel narrowing or occlusion is thought to be caused by spasm.

A failed PTA does not seem to preclude subsequent bypass as long as an undamaged, unstented landing zone is preserved [1]. Pseudoaneurysms at the access site may be treated by US-guided injection of thrombin or US-guided pressure; surgery is reserved for exceptional cases. Retroperitoneal bleeding can be treated in the majority of cases with a covered stent or, in cases of endovascular failure, with surgical repair.

Transpedal access complications include bleeding, pseudoaneurysm formation, severe spasm, and vessel occlusion that may lead to limb loss.

Conclusions

Infrapopliteal endovascular techniques represent first-line treatment methods in patients with arterial occlusive disease BTK. Correct preprocedural investigation and planning, appropriate revascularization techniques, and adequate postprocedural follow-up and medical management are crucial to the desired clinical outcome.

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