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An Update on Methods for Revascularization and Expansion of the TASC Lesion Classification to Include Below-the-Knee Arteries: A Supplement to the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)

The TASC Steering Committee*

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Abstract

The Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) guidelines were last updated in 2007 (TASC II) and represented the collaboration of international vascular specialties involved in the management of patients with peripheral arterial disease (PAD). Since the publication of TASC II, there have been innovations in endovascular revascularization strategies for patients with PAD. The intent of this publication is to provide a complete anatomic lower limb TASC lesion classification, including the infrapopliteal segment, and an updated literature review of new endovascular techniques and practice patterns employed by vascular specialists today.

Keywords

angioplasty, arteries, claudication, critical limb ischemia, occlusion, peripheral artery disease, revascularization, stenosis, stents, surgery

Introduction

The TransAtlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC I), which in the subsequent version was named the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II), has previously provided expert recommendations on the diagnosis and treatment of peripheral arterial disease (PAD).[1,2] One highly utilized aspect of the TASC guidelines, originally published in 2000, is the TASC anatomic artery lesion classification. This anatomic classification provides a characterization of the various patterns of disease and guidance on treatment decisions regarding the optimal revascularization strategy (endovascular vs surgical) based on the complexity and location of the anatomic disease. The original classification stratified disease in the aortoiliac and femoropopliteal territories into categories, from A through to D. TASC A represented the least complex anatomic scenario (ie, focal stenosis) and TASC D reflected

the most complex revascularization scenario (ie, diffuse, occlusive). TASC A lesions were originally designated as most appropriately treated with an endovascular strategy, while TASC D lesions were recommended for surgical

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revascularization based on available evidence at the time. The optimal management strategy for TASC B and TASC C lesions could favor either approach based on factors such as the technical resources available, patient status, and physician experience. These guidelines also provided a framework for future studies needed to support a robust body of data for subsequent recommendations.

The TASC II guidelines were published in 2007 and included a revision of the original TASC classification for PAD, with a focus on the aortoiliac and femoropopliteal territories. TASC II also aimed to provide guidance on treatment decisions relating to the optimal revascularization strategy (endovascular vs surgical) based on the anatomic and clinical status of the patient. In general, this revision resulted in the reclassification of more complex anatomies into less severe categories of the TASC classification (eg, TASC C lesions reclassified as TASC B lesions with an associated shift from surgical to endovascular management). TASC A and B lesions were still recommended for primary endovascular revascularization, TASC D lesions for surgical revascularization, and TASC C lesions for surgical revascularization in patients with appropriate perioperative risk and available conduit. The influence of patient comorbidity, patient preference, and operator experience on decision-making was highlighted. Importantly, TASC I and TASC II primarily utilized an anatomic classification to guide revascularization treatment decisions. At the time, there were few head-to-head comparative effectiveness trials of endovascular vs surgical revascularization to provide evidence-based specific recommendations for each strategy. The recommendations were, therefore, based on practice patterns, technical considerations, the ease and lower morbidity of the endovascular approach, and a consensus of experts. In addition, the TASC II lesion classification did not include an infrapopliteal classification, which was subsequently criticized as an important omission given the expanding technologies and techniques for catheter-based tibial intervention for critical limb ischemia (CLI).

Since the publication of the TASC II document in 2007, a number of scientific publications and observational reports have utilized regional and national databases to document the rapid adoption of endovascular therapy as a primary strategy for the treatment of symptomatic PAD.[3–5] This rapid shift in clinical practice is presumably not related to a change in the patterns or natural history of arterial disease in the lower extremities. Rather, it appears to be due to the continued evolution of technology available for the endovascular treatment of PAD, including sheaths, catheters, wires, re-entry devices, balloons, stents, drug-device combinations, and debulking tools. In addition, improved vascular imaging techniques, the expanding skill level of many endovascular specialists across multiple disciplines, and the dissemination of these skills, have contributed significantly to this shift in treatment strategy. The overall result is that there has been an increase in adoption of the endovascular-first strategy for

even the most complex anatomies (ie, TASC D) in the clinical practice of endovascular specialists, decreasing the number of anatomies that are primarily referred for open surgical revascularization.[6] This shift was not clearly reflected in TASC II, a fact that has been criticized.[7,8] However, trials evaluating surgical relative to endovascular treatment are difficult to perform and are uncommon; therefore, there remains a lack of evidence to support either approach having a clear advantage over the other. Importantly, key trials addressing this deficit in evidence are now ongoing in Europe and the United States.

Based on advances in technology and change in practice patterns, the TASC Steering Committee convened a multispecialty panel meeting in Örebro, Sweden, in May 2009. The aim of the meeting was to gain an updated consensus on revascularization strategies for PAD and to develop a TASC lesion classification for infrapopliteal artery disease. This was considered as an intermediate step to keep TASC current and bridge to a more comprehensive update in TASC III. Subsequent to that meeting, a consensus was not achieved, particularly on the concept of recommending an "endovascular-first" approach as has been documented in the recent literature. Based on this lack of consensus, the focus of the current publication is to provide a literature update on endovascular and surgical revascularization strategies and techniques and to add a TASC infrapopliteal anatomic classification. The evident importance of secondary preventive measures for all PAD patients, exercise, and other noninterventional treatment of intermittent claudication as highlighted in TASC II is not discussed in detail here but should precede invasive treatment.

This update does not provide treatment recommendations since there remains a paucity of well controlled randomized clinical trials to make treatment decisions, particularly in the specific choice of utilizing an endovascular vs open or hybrid surgical approach in a particular patient.

Literature Review

Prior to the meeting in Sweden, the TASC group embarked upon a review of all relevant published literature since the completion of the TASC II guidelines (in addition to pertinent literature prior to that date). Medline and EMBASE databases were searched, utilizing key words including "peripheral arterial (artery) (occlusive) disease" and "peripheral vascular disease." A panel of 6 European and North American specialists in vascular surgery, vascular medicine, interventional radiology, and cardiovascular interventions evaluated the abstracts, and those pertaining to endovascular and surgical revascularization were selected. The review was divided into the 3 anatomic segments: aortoiliac, femoropopliteal, and the newly included infrapopliteal region. The literature review was subsequently updated by the TASC Steering Committee to

include publications up to 2015. Since the intent is to provide an update and not formal treatment recommendations, no grading system was applied to the reviewed references.

Aortoiliac Disease

There have been several recent publications using mostly observational data on the treatment of aortoiliac disease. Data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample from 2004 to 2007 included 4119 patients with aortoiliac occlusive disease, 1100 of which were treated with an endovascular procedure. The type of TASC lesion or severity of disease was not presented. Clinical and economic outcomes were assessed, and endovascular procedures were associated with lower complication rates, shorter length of stay, and lower hospital costs than surgical management.[9] A later systematic review and meta-analysis of a corresponding patient population demonstrated superior durability for open bypass compared with an endovascular approach, although surgery resulted in a longer hospital stay and increased risk for complications and mortality.[10]

Open Surgery vs Endovascular Intervention

No large-scale trials have compared surgical with endovascular intervention for the more complex TASC C and D lesions. Information is, however, available from small observational studies. In one series of 89 prospective TASC C–D aortoiliac lesions managed with percutaneous transluminal angioplasty (PTA) and stents, a 91% initial procedure success rate was demonstrated, with 3-year primary patency and limb salvage rates of 76% and 97%, respectively.[11] However, 24% of procedures included an additional open surgical component to revascularize the common femoral artery or as a method to facilitate a percutaneous approach. Thus, a hybrid approach may be utilized in one quarter of cases.

Another case series of TASC C and D aortoiliac disease was described in a 2-center retrospective comparison of 40 patients who underwent endovascular therapy and 32 patients who underwent surgical revascularization from 1998 to 2007. In this series, primary patency at 48 months was significantly better with surgery, but at a risk of more pulmonary complications.[12] Hospital length of stay was significantly longer in those patients treated with surgery (7±2 days in the surgical group vs 1±0.3 days in the stent group, p=0.0001). In 10% of the endovascular procedures, intraprocedural complications required a hybrid surgical approach.

Endovascular Intervention

A recent meta-analysis of aortoiliac endovascular interventions of TASC C–D lesions, including 19 nonrandomized

cohort studies, demonstrated a 4- to 5-year primary patency ranging from 60% to 86%, while secondary patency was up to 80% to 98%.[13] In another meta-analysis, the 12-month primary patency for TASC D lesions treated with stents was 87%.[14]
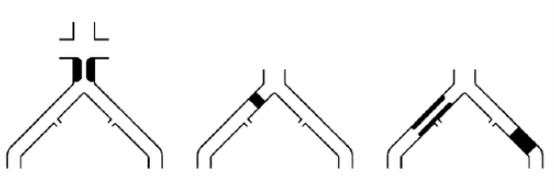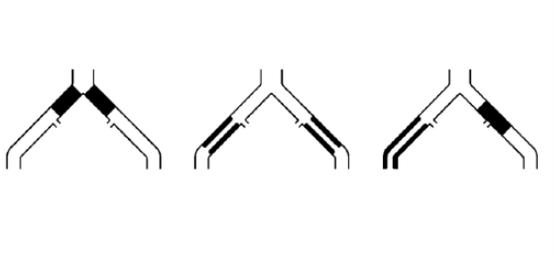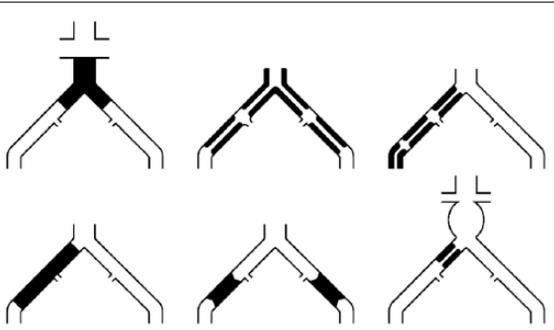
Subsequently, a prospective multicenter registry of 125 patients from 28 centers in the United States treated with a self-expanding iliac artery stent demonstrated primary 12 month patency of 94.4%, with an excellent safety profile.[15] Covered iliac stents have recently suggested improvement in the percutaneous management of complex aortoiliac bifurcation disease.[16,17] In a randomized controlled trial (RCT) of polytetrafluoroethylene (PTFE) covered stents compared with bare metal stents, there were statistically reduced restenosis rates with covered stents, particularly in the more complex TASC C–D aortoiliac lesions.[18] It should be noted that given the advances in percutaneous treatment of both abdominal and thoracic aortic aneurysms and aortic and mitral valve replacement, iliac artery stenosis may require treatment, even in asymptomatic patients, to facilitate passage of large bore catheters from the femoral artery to the target lesion. In a single center study of outcomes of balloon-expandable vs covered iliac artery stents, patency and target lesion revascularization (TLR) rates were superior for balloon-expandable stents.[19]

Exercise and Intervention

A prospective, multicenter randomized trial of optimal medical therapy, optimal medical therapy plus supervised exercise, and optimal medical therapy plus iliac artery stent placement sponsored by the United States National Institutes of Health demonstrated that walking time was superior in the group receiving supervised exercise at the 6-month primary endpoint.[20] Interestingly, the same cohort followed prospectively to 18 months suggested that walking times were equivalent between the exercise and primary stent cohorts.[21]

Choice of Revascularization Method

No contemporary RCTs have definitively established the magnitude and durability of the benefit of open surgical vs endovascular strategies. Comparisons within and between observational studies are prone to considerable bias. The choice of revascularization method must therefore to a great extent be based on each vascular center's competence and experience with the anatomic complexity, considering patient comorbidity and overall prognosis. In complicated cases, primary surgical or hybrid endovascular and open strategies may be more appropriate in a medically fit patient, as the durability of an open approach over time may be superior to an endovascular procedure. The TASC lesion classification for aortoiliac disease is illustrated in Figure 1.

Figure 1. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) classification of aortoiliac lesions. AAA, abdominal aortic aneurysm; CFA, common femoral artery; CIA, common iliac artery; EIA, external iliac artery.

Femoropopliteal Disease

Surgical revascularization has been the principal strategy for femoropopliteal disease and was comprehensively reviewed in TASC II. This treatment is relevant in cases with extensive femoral artery disease, particularly in the common femoral artery with extension into the deep femoral (profunda) artery. Direct comparisons of endovascular therapy with surgical revascularization need to be performed to provide a basis for recommending a particular strategy but are limited owing to variation in vascular anatomy. In fact, enrollment in appropriate comparative trials is very difficult. In a series of 100 patients considered for enrollment in a trial of PTFE femoropopliteal bypass graft surgery, compared with an endovascular approach (femoropopliteal intraluminal thrupass), only 4% of screened patients were truly eligible for participation in the proposed RCT.[22]

Open Surgery vs Endovascular Intervention

The most current randomized trial, published in 2005, comparing infrainguinal saphenous vein bypass to the above-knee or below-knee segment with PTA (BASIL) found that endovascular therapy equaled the results with surgery based on amputation-free survival at 6 months. Endovascular therapy was a less morbid procedure with equivalent quality of life outcomes and was significantly less costly than surgery.[23] At follow-up (3 to >5 years), there was a numerical trend for better overall survival and amputation-free survival for the surgical group compared to the endovascular group. A later subanalysis determined that in patients who lived for >2 years, there was a 7-month increase in overall survival for the bypass group without a significant difference in amputation-free survival.[24] Surgery after a failed angioplasty had a worse prognosis than primary surgery, perhaps reflecting a greater disease severity of this patient

population.[25] It should be noted at the time the BASIL trial was performed, the angioplasty group did not include stents or other adjunctive procedures; as such, the primary comparison between surgery and angioplasty may not reflect modern endovascular strategies.

Comparing the results of endovascular therapy (balloon angioplasty without stent)[5,26] with those of surgical revascularization is also difficult, as patients treated with endovascular interventions commonly present with symptoms of intermittent claudication, while those treated with surgical revascularization frequently have CLI. Patients with CLI have increased periprocedure morbidity and mortality and more diffuse arterial disease, including worse tibial runoff status.[27,28] Therefore, it would be expected that the clinical outcomes for those patients undergoing surgical intervention would be significantly worse based more on the characteristics of the patient and anatomy than the specific choice of revascularization strategy. Only a few superficial femoral artery (SFA) occlusions are included in endovascular trials. The BASIL trial[23] is the only study that has compared vein bypass and angioplasty in patients with severe ischemia. The PREVENT III trial[29] is useful as a large cohort study of CLI patients followed after bypass surgery, but it did not compare this therapy with any other revascularization intervention. The randomized SUPERB trial, comparing heparin-bonded endoluminal vs surgical femoropopliteal bypass, is ongoing and results are awaited.[30]

In a meta-analysis of observational studies, reviewing the literature from 1995 to 2012, no differences were found between endovascular and open surgical revascularization regarding all-cause mortality, amputation, or amputation-free survival at 2 years.[31] In femoropopliteal bypass procedures, PTFE grafts as a surgical conduit are expected to have worse patency than autologous vein grafts. A recent Cochrane analysis included 13 RCTs (2313 patients) and demonstrated a significantly improved primary patency for vein bypass grafts compared with PTFE grafts in the femoral above-knee popliteal setting.[32] This Cochrane report did not identify a trial comparing autologous vein grafts with a prosthetic graft in the femoral below-knee popliteal position. In a meta-analysis by Pereira et al[33] that included 49 retrospective and 24 prospective studies (6 of 24 were RCTs), the 5-year patency was similar for above-knee and below-knee vein bypasses in patients with CLI, while for claudicants, the above-knee position revealed a nonsignificant higher patency.

The PREVENT III trial did not report any difference in outcome for bypasses to the above-knee vs below-knee level. The analysis did find improved patency for shorter grafts, usually popliteal to distal bypass targets.[29] One-year follow-up data from the Swedish Vascular Registry (1997–2007), including 2873 above-knee and 2960 below-knee femoropopliteal bypasses, demonstrated patency rates of 73.7%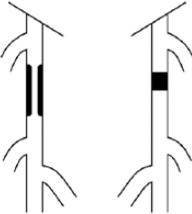 (above-knee) and 65.4% (below-knee) for vein bypass and 68.4% (above-knee) and 50% (below-knee) for prosthetic and composite grafts. Out of these 4833 procedures, 55% were performed for CLI and 45% for intermittent claudication.[34] It is important to note these are observational data reflecting different disease anatomies and clinical settings.

Endovascular Intervention

There have been multiple studies comparing nitinol stents with PTA or fabric-covered nitinol stents with bare nitinol stents[35] in the SFA. Three-year follow-up of complex TASC C and D SFA lesions in a RCT did not confirm any advantage of the fabric covered stent compared to the bare metal stent.[35] Technologic modifications, including coating the fabric with heparin, may offer some improvement in patency and outcomes; however, definitive data are still pending.[36] A prospective multicenter trial comparing bare nitinol stents (mean lesion length 7.1 cm) to PTA (mean lesion length 6.4 cm) suggested a statistical advantage of improved patency with stent over PTA alone in femoropopliteal lesions.[37] Three-year follow-up of this cohort demonstrated continued advantages of bare metal stents vs PTA.[38] Additionally, in one large meta-analysis evaluating subintimal angioplasty as a potential alternative to surgical revascularization, the technical success and limb salvage rates were comparable, with inferior primary patency rates in the subintimal angioplasty group.[39] However, the current evidence is insufficient to support a specific endovascular strategy, despite the current reports that 10- to 12-cm mean lesion lengths result in statistically superior patency and physical function outcomes with nitinol stents compared with PTA alone.[40] These studies included patients with lesion lengths up to 17 cm. A recent midterm report on the use of an interwoven nitinol stent (Supera) claims high patency rates in the treatment of long lesions.[41]

Literature has emerged regarding the role of primary atherectomy for femoropopliteal disease. Despite the different types of atherectomy devices (laser, directional, orbital),[42–47] there remain concerns regarding the risk of distal embolic debris and restenosis with this strategy. Publications of larger prospective multicenter trials are needed to highlight the role of atherectomy in femoropopliteal arterial disease.[48]

With the advent of paclitaxel-coated self-expanding nitinol stents, recent 2-year data have demonstrated superiority of this strategy compared to standard PTA.[49] Finally, considerable enthusiasm exists for the use of paclitaxel-coated balloon angioplasty catheters. Initial feasibility has been promising,[5,26] and the results of randomized multicenter trials of drug-coated vs bare balloons have begun to emerge.[50] Finally, the results of a large international prospective multicenter RCT of drug-coated balloon vs bare balloon angioplasty have been published, demonstrating a significant

TASC A lesions
- Single stenosis ≤10 cm in length
- Single occlusion ≤5 cm in length

TASC B lesions
- Multiple lesions (stenoses or occlusions), each ≤5 cm
- Single stenosis or occlusion ≤15 cm not involving the infrageniculate popliteal artery
- Heavily calcified occlusion ≤5 cm in length
- Single popliteal stenosis
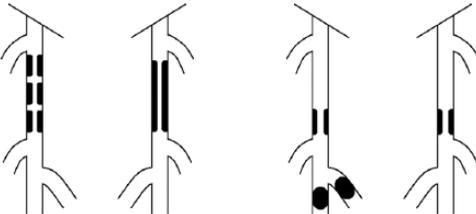
TASC C lesions
- Multiple stenoses or occlusions totaling >15 cm with or without heavy calcification
- Recurrent stenoses or occlusions after failing treatment
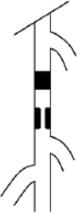
TASC D lesions
- Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery)
- Chronic total occlusion of popliteal artery and proximal trifurcation vessels
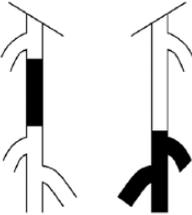
Figure 2. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) classification of femoral popliteal lesions. CFA, common femoral artery; SFA, superficial femoral artery.

advantage of the drug-coated balloon when analyzing patency and TLR.[51] It is anticipated that the results of the corresponding LEVANT 2 study will be published shortly.

Choice of Revascularization Method

In practical terms, although the level of evidence is low, the initial revascularization strategy for femoropopliteal disease is commonly an endovascular approach. Depending on numerous factors, namely lesion complexity, availability of autologous conduit, patient condition, and center experience, hybrid procedures may reduce the surgical trauma, while bypass surgery is commonly reserved for complex, extensive lesions, provided that the patient's health status suggests >2-year survival. This is supported by a recent meta-analysis of the published literature regarding endovascular vs surgical

revascularization for femoropopliteal disease. In this analysis, only 10 published RCTs were included, with only one considered high quality. Accepting these limitations, an endovascular-first strategy was suggested by the authors, particularly for those patients with limited life expectancy.[52] The TASC lesion classification for femoropopliteal disease is illustrated in Figure 2.

Infrapopliteal Disease

Revascularization of infrapopliteal disease is almost exclusively utilized for patients with CLI, which occurs in <10% of all patients with PAD.[53] Single-vessel tibial disease with patency of the other tibial arteries would not be expected to result in severe limb symptoms prompting the need for revascularization.

There is a significant body of literature pertaining to the surgical treatment of infrapopliteal disease, primarily using the greater saphenous vein as conduit, with various operative techniques (in situ, transposed, nonreversed, and reversed vein), or other autologous veins as conduit material. Less than ideal for the treatment of infrapopliteal disease is the use of spliced grafts, allograft material, or prosthetic material such as PTFE. Various inflow arteries have been used for the proximal anastomosis site of the grafts (ie, common femoral artery, SFA, popliteal artery) as well as multiple outflow targets (ie, tibial and pedal vessels), depending on the vascular anatomy and extent of atherosclerotic disease. One-year survival and limb salvage rates of 76% to 90% and 66% to 100%, respectively, have been reported.[54-57] The PREVENT III trial did provide outcomes for surgical bypass in the setting of a randomized multicenter clinical study of edifoligide, with a large cohort of patients with CLI (n=1404), in whom the distal anastomosis targets were at the tibial or pedal arteries in 65% of cases.[29,58] At 1-year follow-up, the primary patency rate for surgery and the survival and limb salvage rates were 61%, 83.8%, and 88.5%, respectively.

Major morbidity related to surgical bypass for infrapopliteal disease and CLI is clinically important. Although the BASIL[23] and PREVENT III[29] trials included patients with infrainguinal rather than isolated infrapopliteal disease, they offer the most relevant data in this regard. Periprocedure mortality occurred in 5.5% and 2.7% of patients, myocardial infarction in 7% and 4.7% of patients, and stroke in 1.5% and 1.4% of patients in the BASIL and PREVENT III trials, respectively. In addition, surgical wound complications were reported in 22% and 4.8% of patients, respectively.[23,29]

Objective performance goals in patients who present with CLI have been developed from large clinical trial databases and provide information on clinically important event rates. Objective performance goals have defined an important clinical outcome as the absence of 30-day mortality or major adverse limb events (amputation or reintervention).[59] Using patient-level data from 3 RCTs totaling 838 patients, a threshold for the primary efficacy endpoint rate of 76.9% and amputation-free survival rate of 76.5% was established. This type of analysis may be helpful in putting noncomparative, nonrandomized data from clinical trials in perspective.

A Japanese CLI registry reported data describing risk-adjusted outcomes for endovascular procedures.[60] It was determined that heart failure, wound infections, and being underweight (body mass index <18.5 kg/m^2) put patients at increased risk for a worse outcome, including a lower amputation-free survival. Patients with no adverse criteria were at low risk, those with one criterion were at intermediate risk, and those with 2 or 3 criteria were at high risk for an event.[60]

Percutaneous revascularization of infrapopliteal disease has been reported since the early 1990s,[61] and there has been widespread temporal adoption of an endovascular-first approach for CLI patients following the publication of the BASIL trial.[23] Technical success rates approaching 100% have been reported but likely suffer from case selection and reporting bias. In a large meta-analysis of series using PTA as the primary treatment modality that included many older series, the 3-year limb salvage rate was 82.4%.[62] This is comparable to open surgical results of 82.3% reported in a meta-analysis of popliteal-to-distal bypass using similar technique.[55] This comparative clinical efficacy was achieved despite significantly lower primary and secondary patency rates in the endovascular series.

New Technologies

There has been an evolution of newer technologies, specifically patency-enhancing drug coating for balloons and stents. In addition, several adjunctive endovascular devices, including atherectomy, cryoplasty, cutting balloons, and laser, have been shown to be feasible and safe in the infrapopliteal vessels but have failed to show superior efficacy when compared with conventional, less expensive therapies.[45,63–65] These devices add cost to the basic endovascular procedure, and therefore their added expense needs to be justified.[66] The data suffer from many of the limitations of the observational surgical series in that they largely represent the retrospective reports or uncontrolled registries, subject to selection bias, at individual centers.

Drug-Eluting Stents

In contrast to the adjunctive therapies mentioned above, there have been 4 RCTs (Table 1) and 4 meta-analyses analyzing the results of infrapopliteal drug-eluting stent (DES) vs either PTA or bare metal stents (BMS).[67–75] These studies are summarized below. Following BASIL, the preferred endovascular approach was PTA with BMS reserved to preserve patency in case of a dissection as a "bailout" technique. Clinical data suggested that BMS had little clinical advantage over successful balloon angioplasty in patients with CLI.[76,77] As DES platforms became established in the coronary bed, this encouraged acquisition of preliminary infrapopliteal data regarding primary DES.[78,79] These data led to the performance of 4 RCTs testing DES in infrapopliteal lesions.

The ACHILLES trial randomized 200 patients with infrapopliteal disease to PTA or DES (Cypher Select Sirolimus Eluting Stent; Cordis Corporation, Bridgewater, NJ, USA) and found superior patency rates at 1 year for the DES group (DES 75% vs PTA 57.1%, p=0.025).[73] There was no difference between the PTA or DES groups for death, amputation rates, or improved clinical status.

The Drug-Eluting Stents in the Critically Ischemic Lower Leg (DESTINY) study randomized 140 CLI patients

Table 1. Randomized Controlled Trials of Drug-Eluting Stents in Infrapopliteal Disease.

Study/Stent Type	N	CLI/IC	Control Arm	Follow-up, mo	Outcome	p
ACHILLES Sirolimus-eluting	200	CLI + IC	PTA	12	Primary patency 75% vs 57%	0.025
DESTINY Everolimus-eluting	140	CLI	BMS	12	Primary patency 85% vs 54%	<0.001
YUKON-BTX Sirolimus-eluting	161	CLI + IC	BMS	12	Primary patency 81% vs 56%	0.004
IDEAS Drug-eluting	50	CLI + IC	PCB	6	Restenosis 28% vs 58%	0.046

Abbreviations: BMS, bare metal stent; CLI, critical limb ischemia; IC, intermittent claudication; PCB, paclitaxel-coated balloon; PTA, percutaneous transluminal angioplasty.

with infrapopliteal disease to either a BMS (Multi-LinkVision; Abbott Vascular, Abbott Park, IL, USA) or a DES (Xience V; Abbott Vascular).[68] Over 12 months of follow-up, the DES group showed superior patency (DES 85% vs BMS 54%, p<0.001) and freedom from reintervention (DES 91% vs BMS 66%, p=0.001). They found no difference between groups for clinical Rutherford class improvement, major amputations, or mortality.

The YUKON-BTX trial randomized 161 patients to infrapopliteal treatment with BMS or DES (sirolimus-eluting YUKON stent; Translumina, Hechingen, Germany) and found superior patency at 12 months for the DES group but no difference in event-free survival.[72] Significant clinical benefit for the DES group was demonstrated when the trial follow-up was extended to 3 years, with an event-free survival for DES of 65.8% compared with 44.6% for BMS (p=0.02) and reduced amputation rates (DES 2.6% vs BMS 12.2%, p=0.03).[71]

The Paclitaxel-Coated Balloon Angioplasty vs Drug-Eluting Stenting for the Treatment of Infrapopliteal Long-Segment Arterial Occlusive Disease: The IDEAS Randomized Controlled Trial compared paclitaxel-coated balloons (PCB) vs DES in long (>70 mm) infrapopliteal lesions in patients with Rutherford categories 3 to 6. Fifty patients were randomized to infrapopliteal PCB angioplasty (25 arteries in 25 limbs) or primary DES placement (30 arteries in 27 limbs). At 6 months, 5 patients died (2 in PCB vs 3 in DES, p=1.0), and 3 suffered a major amputation (1 in PCB vs 2 in DES, p=1.0); the angiographic restenosis rate was significantly lower in DES [7 (28%) of 25 vs 11 (57.9%) of 19 in PCB, p=0.046]. There were no significant differences with regard to TLR [2 (7.7%) of 26 in DES vs 3 (13.6%) of 22 in PCB, p=0.65]. Compared with PCB in long infrapopliteal lesions, DES are associated with significantly lower residual immediate postprocedure stenosis and significantly reduced restenosis at 6 months.[75]

The 4 published meta-analyses of infrapopliteal DES compared with PTA and/or BMS demonstrated no benefit for primary infrapopliteal BMS over PTA, suggesting BMS

be reserved for bailout use to salvage patency in patients treated with PTA.[67,69,70,74] The preponderance of the evidence for infrapopliteal DES, however, has demonstrated significant benefit over both BMS and PTA for (1) patency, (2) reduced reinterventions, (3) reduced amputation, and (4) improved event-free survival. These results are not specific to CLI, as most trials have included severe claudicants into their populations. It is also likely that the lesions selected for randomized trials do not reflect "real-world" infrapopliteal lesions (eg, fewer lesions, more discrete lesions, less calcified lesions, and fewer occlusions). Despite these limitations, there is now Level 1 evidence from 4 randomized trials[71–73,75] and 4 meta-analyses[67,69,70,74] to support primary DES use in anatomically suitable infrapopliteal lesions causing symptomatic lower extremity ischemia.

There are only limited clinical data available on the below-knee applications of drug-eluting balloons (DEB). A registry of 104 patients treated with infrapopliteal angioplasty using a paclitaxel-eluting balloon (In.Pact Amphirion; Medtronic Cardiovascular, Santa Rosa, CA, USA) demonstrated favorable results compared to historical controls for restenosis reduction, and there were no safety issues noted.[80] The Drug-Eluting Balloon Evaluation for Lower Limb MUltilevel TreatMent (DEBELLUM) was a RCT of femoropopliteal (92, 75.4%) or below-the-knee (BTK) arteries (30, 24.6%). Patients were randomly assigned to the DEB (25 patients with 57 lesions; In.Pact Amphirion, Medtronic Cardiovascular) or PTA (25 patients with 65 lesions) group.[81,82] Overall, ankle-brachial index improved more in the DEB group: 0.81±0.3 vs 0.68±0.13 (p=0.02), and the Fontaine stage improved (from IIb to I): 80% DEB vs 56% PTA (p<0.05). For the BTK lesions, the overall late lumen loss was 0.66±0.9 mm in DEB patients vs 1.69±0.5 mm in the PTA arm (p=0.03).

The DEBATE-BTK trial randomized DEB (In.Pact Amphirion, Medtronic Cardiovascular) vs PTA in 132 diabetic patients with CLI and 158 infrapopliteal lesions.[83] Notably, the mean lesion length was 129±83 mm, which is dramatically (~100 mm) longer than lesions treated in the

infrapopliteal DES randomized trials. The primary endpoint, restenosis at 1 year, occurred in 20 (27%) and 55 (74.3%) lesions in the DEB and PTA groups, respectively (p<0.001). Target vessel occlusion occurred in 13 (17.6%) DEB-treated vs 41 (55.4%) PTA-treated vessels (p<0.001). Twelve-month major adverse events occurred less frequently in the DEB (31%) than in the PTA (51%) group (p=0.02), driven mainly by a reduction in TLR and better ulcer healing. However, there was no difference in the rates of amputation, limb salvage, or mortality between the groups.

The In.Pact Deep CLI trial outcomes resulted in the DEB (In.Pact Amphirion, Medtronic Cardiovascular) being withdrawn from the market worldwide by the sponsor.[84] The trial enrolled 358 CLI patients with infrapopliteal lesions and randomized them 2:1 to DEB and PTA, respectively. The primary efficacy endpoints were no different for (1) 12-month late lumen loss for the DEB (0.61±0.78 mm) group or the PTA (0.62±0.78, p=0.95) group and (2) the clinically driven TLR for the DEB (17.7%) group or the PTA (15.8%, p=0.66) group. There was a nonsignificant trend toward higher amputation rates in the DEB (8.8%) compared to the PTA group (3.6%, p=0.08). It seems clear that more data and more experience are needed to understand the relative benefits of DES vs DEB for infrapopliteal lesions.[84]

It is too early to recommend that infrapopliteal DEB should be used for infrapopliteal lesions, particularly given the superior comparative results of the DES. The DEB may have an advantage in very long lesions (including foot lesions), with demonstrated superiority over PTA in terms of restenosis and reintervention rates. Adverse periprocedure events with endovascular therapy for the treatment of infrapopliteal disease appear to be few, with mortality rates in observational series approaching <1%. However, in the PTA arm of the BASIL trial,[23] the periprocedure mortality was 3% compared with 5.5% in the surgical arm. Similarly, stroke and myocardial infarction are rarely reported in observational series but were reported in 0.4% and 2.5% of patients, respectively, in the PTA arm of the BASIL trial. In addition to these point estimates of risk, the confidence interval around these estimates needs to be considered to understand the potential risks when these procedures are performed in larger populations.

Choice of Revascularization Method

In practical terms, an "endovascular-first" approach is the current standard of care for symptomatic infrainguinal atherosclerotic disease strengthened by the recent technological advances of DES and DEBs. The Best Endovascular vs Best Surgical Therapy in patients with CLI (BEST-CLI) trial has just been launched and will answer the question of whether optimal surgery for selected patients with CLI and good quality saphenous vein available for bypass is a better choice than endovascular therapy.[85] With a corresponding aim, the BASIL 2 trial has recently been launched.[86]

The TASC infrapopliteal classification is illustrated in Figure 3. This classification has been developed to maintain consistency with the anatomic descriptions of the other vascular beds (aortoiliac, femoropopliteal). The classification acknowledges that patients with CLI have lesions in other tibial and inflow arteries.
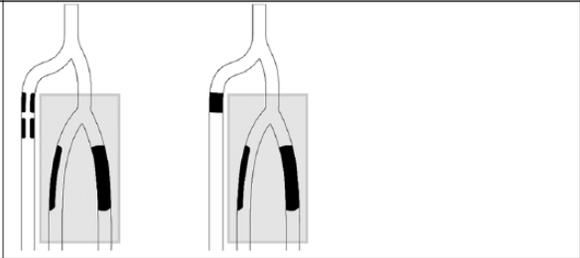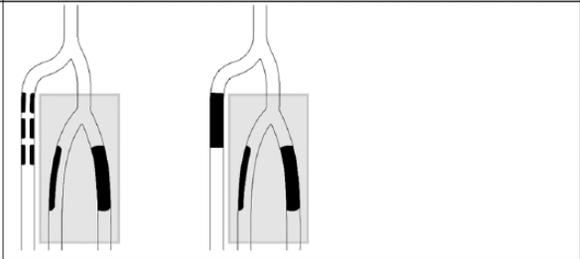
Hybrid Endovascular and Surgical Approaches

Given the advances in endovascular technology and techniques, the adoption of endovascular skills by vascular surgeons,[6] and the close cooperation between vascular surgeons and interventionists, revascularization strategies that employ both endovascular and surgical procedures are commonplace and may reduce the magnitude of the surgical trauma and systemic complications. The classic scenario is the patient with both inflow aortoiliac disease and infrainguinal disease.[87,88] A combined strategy might offer advantages, as inflow procedures may be managed by endovascular techniques, followed by infrainguinal surgical revascularization when appropriate. This scenario is usually found in patients with CLI, implying a more fragile patient.

Skill and Experience

Considering endovascular revascularization as the primary mode of therapy, the interventionist (regardless of specialty) has to be trained and thereafter possess appropriate technical expertise in the performance of complex endovascular revascularizations. Additionally, the interventionist must have access to all appropriate devices with adequate technology and up-to-date imaging modalities to achieve an optimal outcome. Likewise, the vascular surgeon must be trained and thereafter possess the technical skill and experience required to complete the surgical procedure efficiently and must have adequate conduit in order to achieve a successful outcome. The principal strategy must be to employ the least complex and most cost-effective procedure, thereby reducing the risk of complications and costs as much as possible. A fundamental caveat is that only experienced operators capable of efficient management of potential complications should employ the revascularization procedure.[89] Results of vascular and endovascular procedures should be recorded and be benchmarked in national databases to improve quality of care.

TASC Classifications

Together with the new infrapopliteal classification, the TASC II classifications, including the aortoiliac and femoropopliteal segments, are reproduced in this publication. Of note is

Figure 3. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC) classification of infrapopliteal lesions. The unshaded area represents the target lesion; area inside the shaded rectangle represents typical background disease (see text for further explanation).

that these 2 classifications are not changed from the TASC II version, except for a correction of an aortoiliac figure and clarification of some figure text. All 3 vascular territory classifications should be regarded as anatomic descriptions of the lesion patterns to enable comparison between various grades of complexity of lesions, but they are not sufficient on their own to guide clinical decisions regarding revascularization treatment strategies. Additional considerations to determine specific revascularization approaches include the hemodynamic condition in the limb, the overall health of the patient and the desired outcome, limb preservation and symptom relief in CLI, and improved limb function in all patients with PAD, which is a "patient-limb-lesion" approach.

The new infrapopliteal lesion classification incorporates several features that attempt to address the multivessel nature of possible infrapopliteal anatomies. Occlusive disease in a single tibial artery rarely leads to clinical signs or symptoms. Thus, a clinically significant reduction in distal arterial perfusion requires multivessel disease that can occur from multiple anatomic patterns of arterial occlusions. The figures include a shaded portion encompassing the peroneal and posterior tibial arteries that represent typical "background" disease, but this representation is not comprehensive and other patterns of 2 and 3-vessel disease that are associated with clinical consequences may occur. Based on these considerations, the figures provide a TASC A–D classification for the anterior tibial artery as the selected example, but similar patterns in various combinations would generally apply if the target vessel were the peroneal artery, posterior tibial artery, or the tibial-peroneal

trunk. Recently, the Society for Vascular Surgery proposed a lower extremity threatened limb classification in CLI based on wound, ischemia, and foot infection (WIfI).[90] This approach lends to evaluating the risks and benefits of a positive outcome for revascularization and the risks of amputation based on the severity of the components of the disease classification. TASC recommends the design of studies focusing on the interaction of the following key factors in making revascularization decisions: patient clinical stage and desired treatment outcome, lesion anatomy, limb hemodynamics, and systemic comorbidities.

Conclusion

Except for the BASIL trial, there is an absence of meaningful data comparing surgical to endovascular strategies for key outcomes, such as limb viability, wound healing, quality of life, survival, and costs in patients with CLI. Similar limitations exist for comparative effectiveness trials in patients with intermittent claudication. Most information on outcome is from observational studies, not infrequently in small series from single centers and industry sponsored, therefore resulting in an inferior level of evidence to make firm recommendations. With improving techniques and technologies, however, an increasing number of cases may now be managed with endovascular procedures. An important issue is that both for endovascular and open surgical procedures, there is a difference between what can be done in centers of excellence involved in the development of refined and simplified procedures and what should be completed in everyday practice. Appropriate training and benchmarking of outcomes is mandatory to improve the quality of care. TASC continues to highlight the limitations of the current endovascular and comparative surgical literature. It is critical that future clinical trials with appropriate design, inclusive of patients with common clinical and anatomic patterns of PAD, measure meaningful functional outcomes in addition to presenting information regarding anatomic patency.

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