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Part One: For the Motion. Lower Extremity Bypass versus Endovascular Therapy for Young Patients with Symptomatic Peripheral Arterial Disease☆

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Intermittent Claudication

Intermittent claudication caused by infrainguinal arterial disease can mostly be treated conservatively. Yet, when functional capacity is threatened, claudication may need to be treated by revascularisation. This should not be done too hastily as any kind of revascularisation may be an onset of a vicious cycle of repeated interventions, which may accelerate the otherwise benign course of PAD.[1] Furthermore, scientific evidence is lacking concerning the efficacy of endovascular therapy on claudication.[2]

Chronic Critical Ischemia

Patients with critical limb ischemia (CLI) represent less than 5% of symptomatic peripheral arterial disease. In younger age groups, CLI is encountered typically in diabetics and there are a number of ischemic and neuro-ischemic lesions in this group of patients which do not meet the strict definition of CLI. The risk for amputation at a metatarsal or higher level is 8-fold higher in diabetics compared to nondiabetics.[3] Additionally, type I diabetics reach a 86-fold increased risk for any nontraumatic amputation below the age of 65 years.[4] In addition, despite revascularization, ischemic lesions have a slow tendency for healing in diabetics.[5] In this patient group the 5-year survival of patients <65 years old was 60% while it was 48% in older patients in Helsinki.

This is why a durable revascularisation should be used to allow wound healing in this young group of patients. In-line arterial flow to the pedal level offers the best results in patients with CLI as shown by the 10-year data from Pomposelli et al. with results from 1032 limb salvage bypasses to dorsalis pedis artery in 865 patients.[6] In this study, the patency of saphenous vein grafts was better than any other conduit with a secondary patency rate of 67.6% at 5 years.[6] No comparable data are available for endovascular treatment.

Results Mean Everything[7]

Patency is a direct measure of revascularisation success when reopening or bypassing occlusions. Patency is the key criterion for judging the primary effectiveness of a revascularization but less often described than leg salvage and amputation-free survival, or even wound healing, quality of life and sustained ambulation. Patient-related outcomes are, of course, important but strongly affected by other measures than treatment modality itself.

Leg Survival or Leg Salvage

Leg salvage or foot preservation, a favoured and easy to retrieve endpoint of CLI studies, is problematic as a number of factors other than revascularisation affect the outcome. Leg salvage is an indirect measure of the success of revascularisation. The key question is what the leg outcome would be if untreated or treated conservatively. Indeed, in studies reporting outcome of patients with CLI unsuitable for revascularisation, one year leg survival rates of 54% (CLI verified by ankle pressure <50 mmHg or toe pressure <30 mmHg),[8] 58% for controls with spinal cord stimulation[9] and 66% in patients with ABI<0.5[10] were reported. In this last study, Marston et al[10] reported a wound healing rate of 52% at one year.

The results of any revascularisation should be compared with these data. Four large recent series of bypass surgery for CLI reported leg salvage rates of 88–92% at one year.[6,11–13] In these series, a 5-year leg salvage rate of 78% underlines the durability of bypass surgery.[6] Endovascular treatment has been found to have 82–86% leg salvage rates at one year.[14,15] Lu et al.[16] summed up the limited experience available in using distal venous arterialisation as the last resort procedure to avoid major amputation and even that method was associated with 71% leg salvage at one year (Fig. 1).

Mind the Gap!

We should be careful when considering the so-called patency/leg-salvage gap which seems wider in endovascular than in surgical series, i.e. occlusion of the revascularized segment leads to amputation less often after endovascular procedure than surgical bypass as summarized by Romiti et al.[14] This gap can be explained in different ways. One hypothesis is that leg salvage exceeding the

☆ Age is an issue. Younger patients have longer life expectancy and thus need more durable treatment solutions. Out of 1725 consecutive infrainguinal revascularisations for symptomatic peripheral arterial disease (PAD) in Helsinki University Central Hospital, as many as 482 (28%) belonged to this group of patients <65 years of age.

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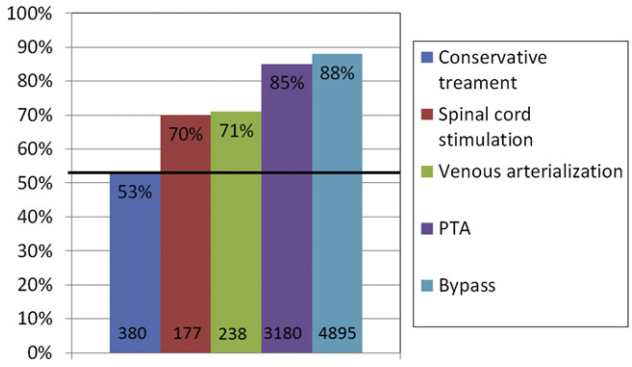

Figure 1. One-year leg survival after different modes of treatment for CLI (data from references [8–10] for conservative treatment, [9] for spinal cord stimulation, [16] for venous arterialization, [14–15] for PTA and [11–13] for bypass).

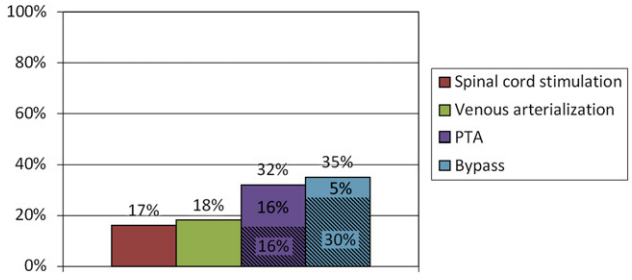

Figure 2. One-year leg salvage after different modes of treatment for CLI (leg salvage attributable to patent revascularization shown as shaded area of the column). Data from references [9] for spinal cord stimulation, [16] for venous arterialization, [14–15] for PTA and [11–13] for bypass).

patency of the revascularisation procedure is attributable to the early patency which provides adequate perfusion until ischemic lesions are healed. Thereafter the leg stays viable if infection is cleared and proper foot care sustained, especially with diabetic lesions. This concept may, of course, be partly true, but a more obvious explanation is that legs treated by endovascular methods have milder lesions as illustrated for instance by the impressive results of Faglia et al.[17] Leg salvage is actually the improvement achieved by therapeutic measures above natural leg survival (Fig. 2).

Apples and Oranges

Percutaneous transluminal angioplasty (PTA) was recommended for stenosis, and bypass for occlusions in the first TASC Document.[18] In the second TASC Document,[19] PTA was still recommended for stenosis and bypass for long occlusions, but there was no consensus on therapy for short and moderate occlusions (Table 1). Endovascular therapy for infrapopliteal arterial disease is gaining acceptance as a first-line method to improve ulcer healing and limb salvage, despite lack of evidence. In a recent meta-analysis on infrapopliteal surgery and infrapopliteal endovascular interventions[11,14] with 29 and 30 studies included respectively, 88% of patients were diabetics and 88% had tissue loss among the bypass group ($n = 2320$), whereas 61% were diabetics and 76% had tissue loss among the endovascular group ($n = 2653$). No distal pressure measurement was available in this study. Primary and secondary mid-term patency rates were better after bypass, but there was no difference in limb salvage. The results of this meta-analysis are biased by the heterogeneity of indications, risk factors, number of treated arterial segments, lesion type (occlusion vs. stenosis), lesion length, lesion characteristics, and outflow. In this setting, TASC II classification of femoropopliteal lesions is not very helpful.[20] Furthermore, many studies are flawed for a number of other reasons.[21,22] It is most likely that bypass groups include patients with more severe disease and only a rather small share of infrainguinal lesions are equally well treatable with either method (Table 1).

Data from Randomised Controlled Trials (RCT)

When both endovascular and surgical revascularisation are technically feasible, no significant difference was observed in symptomatic relief in the few RCT which included both supra- and infrainguinal revascularisations for mixed indications.[2] There are two RCTs including mostly claudicants with superficial femoral artery (SFA) occlusions, which suggest that surgical bypass gives better results than the endovascular approach.[23,24] Another RCT(25,26) including a large variety of lesions and mixed indications observed similar outcome after both approaches (Table 2).

The British Angioplasty vs. Surgery in Ischaemic Legs Trial (BASIL) is the only large RCT comparing endovascular revascularisation and bypass surgery.[27] Only patients with CLI or at least severe ischemia and potential candidates for either infrainguinal angioplasty or bypass were included. In this trial, 42% of patients were diabetics. Both approaches yielded similar results in terms of amputation-free survival up to two years. Surgery was associated with higher postoperative morbidity, more hospital days and higher costs and angioplasty was associated with higher need for further revascularisation procedures.[27] However, the long term results suggested that surgical repair was more durable[28] but no patency data was available. The results of BASIL Trial emphasize the role of bypass over PTA in fit patients with a saphenous vein available[28] and this was the case in 75% of the patients in BASIL Trial.

Table 1
Summary of recommendations of the TransAtlantic Inter-Society Consensus II Working Group.[22]

Level of disease	Segment/recommendation			
	Usually PTA (type A)	PTA preferred (type B)	Surgery preferred (type C)	Usually surgery (type D)
Femoropopliteal	SFA stenosis ≤10 cm or occlusion ≤5 cm	SFA stenosis or occlusion ≤15 cm; popliteal stenosis	SFA stenosis or occlusion >15 cm; recurrent disease	Complete SFA or popliteal occlusions
Crural	None[a]	None[a]	Stenoses ≤4 cm or occlusions ≤2 cm	Diffuse disease or occlusions >2 cm
Outcomes	Excellent[b]	Excellent[b]	PTA/stent only has modest results and is indicated when surgery is contraindicated for technical or patient reasons.	Endovascular approach is not advised unless symptoms are limb threatening and surgery is not possible.

[a] Crural interventions have severe outcomes if they go wrong; therefore there is no type A or B recommendation.
[b] Excellent results can be expected from an endovascular approach in all segments.

Table 2
Patency data in randomised controlled studies comparing infrainguinal surgical and endovascular revascularization.

Author, year (ref)	Centres, study period	Concealment	N	Degree of ischemia (Fontaine)	Lesions treated	Interventions	Lost to follow-up	Follow-up	Outcome and results	Significance	Comment	Cited in literature
van der Zaag et al 2004[23]	13 centres, 1995–1998	(+)	57	F II	SFA occlusions 5–15 cm (91%) and stenoses (9%)	PTA vs bypass (vein 79%)	10%	median 23 mos	PP: PTA 43%, bypass 82%	ARR by open surgery 31%	Poor recruitment, early termination	39
Adam et al. 2005[27]	27 centres, 1999–2004	+	452	F III-IV	infrainguinal lesions chosen for intervention on the basis of principle of equipose	PTA first (80% SFA) vs bypass first (vsm 75%, infrapopliteal outflow 33%) strategies	2%	66 mos	no difference in amputation free survival	Unadjusted hazard ratio: 1.07 (95% CI 0.72–1.6)	High quality and relevance Results beyond two years suggest superiority of bypass	474
Bradbury et al 2010[35]												41
Kedora et al. 2007[25]	single private centre, 2004–2005	–	86 (100 legs)	F II-IV	SFA stenoses and occlusions (TASC A-D)	PTFE endograft vs bypass (PTFE or polyester)	12%	median 18 mos	PP: PTA 74%, bypass 74% SP: PTA 84%, bypass 84%	ns ns	Two year results suggest a trend towards decreased endograft patency with higher TASC classification	84
McQuade et al 2009[26]												28
Lepäntalo et al 2009[24]	8 centres, 2003–2007	+	44	F II (89%) and F III-IV (11%)	SFA occlusions 5–25 cm	PTFE endograft vs bypass (PTFE)	14%	median 24 mos	PP: PTA 46%, bypass 84% SP: PTA 63%, bypass 100% (technical endograft failures excluded)	$p = 0.18$ $p = 0.05$	Poor recruitment, termination due to results of interim-analysis	10

(+) = concealment not clearly stated, F = Fontaine, SFA = superficial femoral artery, TASC = TransAtlantic Inter-Society Consensus II classification, PP = primary patency, SP = secondary patency.

The generalizability of the BASIL Trial was audited from a sample of 456 patients with infrainguinal lesions, 236 of whom underwent a revascularization procedure but only 29% of them were suitable for randomization, i.e. treatment by either method. This finding illustrates the narrow overlap of the indications for endovascular and surgical revascularization.

The same holds particularly true with the Scandinavian Thru-pass vs. Bypass Study, in which SFA occlusions were randomised between PTFE endografting and PTFE bypass grafting.[24] Only 4% of the SFA occlusions met the tight inclusion criteria chosen to exclude short occlusions and all lesions with unfavourable landing zones for an endograft. This illustrates the difficult balance between internal and external validity. But when comparable patients are analysed, bypass seems to give a better result.[23,24,28] These data are far less cited than those suggesting non-inferiority of endovascular methods (Table 2).

The findings of BASIL Trial suggest that whether to perform bypass or PTA first for CLI due to infrainguinal disease depends on life expectancy.[28] Long-term results favouring bypass were also observed in a large cohort study of 858 CLI patients with a propensity score analysis.[29]

Complications and Costs

Admittedly, bypass surgery is followed by a number of peri-operative and late complications. Recently LaMuraglia et al[30] reported a high incidence of complications related to bypass surgery according to an American private sector database with 2.7% mortality and 18.7% major complications including 7.4% of graft thrombosis. In this extended series, complications were associated with age >80 years and poor preoperative functional status.[31] Thus it is difficult to use these data directly to assess the risk of bypass for patients <65 years. The complications of PTA are said to be rare and minor and not to preclude a bypass at a later date. Yet, crural interventions may have severe non-correctable outcomes.[22] Furthermore, technical failure rates of 20% are associated with attempts to open infrapopliteal occlusions[32] and procedural complication rates of 7–17% have been reported.[14,15,31] Furthermore, an early death rate of 2.7% in a mixed series indicated that crural PTA first strategy is not without risk.[33] Finally the main predictor of outcome is not the approach used, but the risk profile of the patient. According to the BASIL Trial,[28] surgery was associated with higher number of days in hospital and the need for advanced postoperative care. The mean cost of inpatient treatment was by a third higher for bypass first than for PTA first strategy but this was true only during the first year. After two years the cost of repeated new interventions abolished this difference.[28] In addition, it is unclear what the costs of unnecessary interventions are.

Loss of ambulation is also an important cause of increase in costs. Goodney et al reported a 81% sustained ambulation rate at one year in patients treated by bypass for CLI.[12]

The approaches to maximize early detection and optimize therapy for PAD have been emphasized in the literature with the hope to lessen the number of patients with CLI.[34] This is absolutely true for risk factors and best medical treatment, but there is no data to show that indications for revascularisations should be extended. Regional data from southern Finland have shown that endovascular activity for CLI has been doubled during the past 5 years but without any positive effect on major amputation rates. An interesting, though biased analysis could be made using the present data to assess the effectiveness of the current practice (Figs. 1 and 2). To save one leg for a year, 3-4 legs should be treated by bypass operations and 6-7 legs by endovascular interventions. Indeed, scientific evidence is lacking to assess the true efficacy of endovascular therapy on critical ischemia.[2]

Conclusions

The aim is always to revascularize the leg properly, in CLI with resulting well perfused foot to allow ulcer healing. A durable solution can be achieved by bypass using good quality saphenous vein and by ascertaining good outflow. Bypass surgery and endovascular interventions are complementary techniques for revascularization. If endovascular and bypass procedure were possible with equal outcomes, then endovascular treatments would be preferred. However the main issue, especially in younger patients, is the durability of the revascularisation, better to trust a bypass with a good vein to an artery with good outflow. Despite early peripheral arterial disease in patients <65 years old, the longevity is not shortened to an extent to allow the second best treatment of choice to be selected.

Endovascular techniques and equipment are developing rapidly but scientific evidence of these new methods is scarce. Level one evidence concerning subintimal angioplasty, drug eluting balloon, cryoplasty and other latest endovascular innovations do not exist. When available, scientific data includes mainly short case-series, and since new techniques are introduced all the time, the target is moving too rapidly to collect proper scientific data.

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