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ADJUVANT ARTERIOVENOUS FISTULA FOR INFRAPOPLITEAL BYPASS PATENCY

Katariina Laurila

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Helsinki 2008

To my family

1. CONTENTS

2. LIST OF ORIGINAL ARTICLES

This thesis is based on the following original articles. The studies will be referred to in the text by their Roman numerals.

I Laurila K, Lepäntalo M, Teittinen K, Kantonen I, Forssell C, Vilkko P, Nielsen OM, Railo M, Lehtola A for the ScanPAC Study Group. Does an adjuvant AV-fistula improve the patency of a femorocrural PTFE bypass with distal vein cuff in critical leg ischaemia?
-A prospective randomised multicentre trial. European Journal of Vascular and Endovascular Surgery 2004; 27: 180-185.

II Laurila K, Aho PS, Albäck A, Teittinen K, Kantonen I, Lepäntalo M. The impact of adjuvant av-fistula on cuffed femorocrural PTFE bypass grafting: flow and pressure response. European Journal of Vascular and Endovascular Surgery 2005; 29: 425-428.

III Tukiainen E, Laurila K, Kallio M, Lorenzetti F, Kantonen I, Lepäntalo M. Internal arteriovenous fistula within a radial forearm flap – A novel technique to increase femorodistal bypass graft flow to the diabetic foot and flap covering ischaemic tissue loss. European Journal of Vascular and Endovascular Surgery 2006; 31: 423-430.

IV Laurila K, Aho PS, Vikatmaa P, Tukiainen E, Lepäntalo M.
Enlarged outflow bed to a pedal bypass established by a previous free flap transfer.
Submitted 2007.

V Laurila K, Luther M, Roth W-D, Vilkko P, Kantonen I, Teittinen K, Sihvo EI, Ihlberg L, Albäck A, Lepäntalo M. Adjuvant arteriovenous fistula as means of rescue for infrapopliteal venous bypass with poor runoff. Journal of Vascular Surgery 2006; 44: 985-992.

3. ABBREVIATIONS

ABI	Ankle-brachial index
ADP	Arteria dorsalis pedis
AK	Above knee
APP	Assisted primary patency
ASA	Acetylsalicylic acid
ATA	Arteria tibialis anterior
ATP	Arteria tibialis posterior
Avf	Arteriovenous fistula
BK	Below knee
CAD	Coronary artery disease
CAPRIE	Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events Study
CASPAR	Clopidogrel and Acetylsalicylic acid in bypass Surgery for Peripheral ARterial disease Study
CLI	Critical leg ischaemia
CO	Common ostium
CRP	C-reactive protein
CTA	Computer tomography angiography
DM	Diabetes mellitus
DSA	Digital substraction angiography
DUAM	Duplex ultrasound arterial mapping
HUV	Human umbilical vein
LD	Latissimus dorsi muscle
LMWH	Low molecular weight heparin
LS	Leg salvage
MFC	Maximum flow capacity
MRA	Magnetic resonance angiography
NS	Not significant, $p > 0.05$
PAD	Peripheral arterial disease
PP	Primary patency
PTFE	Polytetrafluoroethylene
PVR	Pulse volume recording
S	Survival
SCanPAC	SCandinavian Prothesis, Av-fistula and Cuff Study
SFA	Superficial femoral artery
SE	Standard error
SLI	Symptomatic leg ischaemia
SP	Secondary patency
TASC	Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease
TTV	Thrombotic threshold velocity
Vmax	Maximum flow velocity
Vsm	Vena saphena magna

4. ABSTRACT

Background

A lack of suitable venous graft material or poor outflow is an increasingly encountered situation in peripheral vascular surgery. Prosthetic grafts have clearly worse patency than vein grafts in femorodistal bypass surgery. The use of an adjuvant arteriovenous fistula (av-fistula) at the distal anastomosis has been postulated to improve the flow and thus increase prosthetic graft patency. In theory the adjuvant fistula might have the same effect in a compromised outflow venous bypass. A free flap transfer also augments graft flow and may have a positive effect on an ischaemic limb.

Aims of the study

The aim of this study was to evaluate the possible benefit of an adjuvant av-fistula and an internal av-fistula within a free flap transfer on the patency and outcome of an infrapopliteal bypass. The effect of the av-fistula on bypass haemodynamics was also assessed along with possible adverse effects.

Patients and methods

1. A prospective randomised multicentre trial comprised 59 patients with critical leg ischaemia and no suitable veins for grafting. Femorocrural polytetrafluoroethylene (PTFE) bypasses with a distal vein cuff, with or without an adjuvant av-fistula, were performed. The outcome was assessed according to graft patency and leg salvage.
2. Haemodynamic measurements were performed to a total of 50 patients from Study I with a prolonged follow-up.
3. Nine critically ischaemic limbs were treated with a modified radial forearm flap transfer in combination with a femorodistal bypass operation. An internal av-fistula was created within the free flap transfer to increase flap artery and bypass graft flow.
4. The effect of a previous free flap transfer on bypass haemodynamics was studied in a case report.
5. In a retrospective multicentre case-control study, 77 infrapopliteal vein bypasses with an adjuvant av-fistula were compared with matched controls without a fistula. The outcome and haemodynamics of the bypasses were recorded.

Main results

1. The groups with and without the av-fistula did not differ as regards prosthetic graft patency or leg salvage.
2. The intra- and postoperative prosthetic graft flow was significantly increased in the patients with the av-fistula. However, this increase did not improve patency. There was no difference in patency between the groups, even in the extended follow-up.
3. The vein graft flow increased significantly after the anastomosis of the radial forearm flap with an internal av-fistula.
4. A previously performed free flap transfer significantly augmented the flow of a poor outflow femoropedal bypass graft.
5. The adjuvant av-fistula increased the venous infrapopliteal bypass flow significantly. The increased flow did not, however, lead to improved graft patency or leg salvage.

Conclusion

1. An adjuvant av-fistula does not improve the patency of a femorocrural PTFE bypass with a distal vein cuff.
2. The av-fistula increased the flow values, both in the intraoperative measurements and during the immediate postoperative surveillance. The increased flow values nevertheless did not improve patency. The adjuvant av-fistula did not cause any adverse effects.
3. In a group of diabetic patients, the flow in a vascular bypass graft was augmented by an internal av-fistula within a radial forearm flap.
4. In a patient with a previous free flap transfer, a high intraoperative graft flow was achieved due to the free flap shunt effect.
5. The adjuvant av-fistula increased graft flow significantly in a poor outflow venous bypass, but this effect did not result in clinical benefit.

5. INTRODUCTION

Atherosclerosis is a systemic disease. Disturbances in the balance between blood, flow and the arterial wall lead to thrombus formation in low flow states to the diseased arterial wall. The occlusive lesions caused by atherosclerosis with superimposed thrombosis in the arteries of the lower extremities lead to the symptoms of chronic leg ischaemia and the entity called peripheral arterial disease (PAD). Reduced blood flow to the extremity causes claudication or, in a more critical stage, rest pain or tissue loss, thus threatening the viability of the limb. This latter entity is called chronic critical leg ischaemia (CLI). The incidence of CLI varies according to different estimations between 500-1000/million/year (Norgren et al. 2007).

The manifestations of ischaemia were first defined into the four categories by Fontaine's classification (Fontaine et al. 1955). Asymptomatic disease (class I) or claudication (class II) seldom leads to limb loss (Dormandy et al. 1991), whereas patients with rest pain (class III) and those with ulcer or gangrene (class IV) are at risk of losing their limb. The main objective of vascular procedures is to prevent limb loss and sustain the patient's ambulatory status and quality of life.

Along with bypass surgery, endovascular procedures offer an alternative. The revascularization policy is shifting from traditional bypass surgery towards endovascular procedures both in primary and secondary procedures (Nasr et al. 2002, Kudo et al. 2004). According to the latest TASC II recommendations (Norgren et al. 2007), bypass surgery is still the golden standard for long multisegmental lesions. In a randomised study, bypass and angioplasty in critical ischaemia were compared, and it was concluded that due to the high failure and re-intervention rate of endovascular procedures, bypass surgery provides a more durable result than angioplasty (Adam et al. 2005). Thus, despite the constantly developing endovascular techniques, there are still patients with extensive infrainguinal disease and critical ischaemia beyond the endovascular therapy options.

The mean age of the patients, as well as the prevalence of diabetes is increasing (Onkamo et al. 1999). The progression of the atherosclerotic disease and graft failure result in recurrence of critical ischaemia in an elderly patient population with numerous co-morbidities and previous vascular procedures. In this patient population the graft material

is often sparse and the outflow tract limited. Co-morbidities present a challenge because they increase postoperative morbidity and the risk of mortality. The extensive ulcers with tissue necrosis and infection in diabetic patients may require a vascularised free tissue transfer in addition to a bypass to achieve wound healing (Tukiainen et al. 2006). In a situation where the bypass graft is poor, the outflow limited, and tissue loss is extensive, the feasibility of the bypass operation can be questioned. However, an aggressive policy in vascular surgery, especially infrainguinal reconstructions, has been shown to reduce amputation rates (Eskelinen et al. 2004, Winell et al. 2006) and to be cost-effective in terms of salvaged limbs and sustained ambulatory status of the patient (Luther 1997a).

Saphenous vein bypass is the gold standard of infrainguinal bypass surgery. In patients with critical ischaemia, the best long-term results in both bypass patency and leg salvage are achieved with autologous vein bypass (Veith et al. 1986, Shah et al. 1995b). Even alternative sources of autologous vein perform better than prosthetic grafts (Faries et al. 2000, Chew et al. 2001, Curi et al. 2002).

Infrapopliteal prosthetic bypass may be an alternative to primary amputation to ensure limb salvage in patients with critical leg ischaemia and no suitable autologous conduits. The patency of a prosthetic bypass is inferior to that of a venous bypass (Veith et al. 1986, Sayers et al. 1998) and therefore adjunctive methods to improve patency and outcome have been developed. Vein cuff interposition was introduced to facilitate the anastomosis between the non-compliant graft and a native artery (Miller et al. 1984, Tyrrel & Wolfe 1991). The true mechanism behind the protective effect of the vein cuff is unclear, but it is thought that the vein cuff reduces the mismatch in compliance between the recipient artery and the prosthetic graft. The venous endothelium may also have a beneficial effect against the formation of myointimal hyperplasia (Norberto et al. 1995). Hyperplasia accumulates in areas of low shear stress in an anastomosis. It has been shown in an experimental model that the vein cuff alters the flow, which results in the shifting of sites of low shear stress away from critical sites of the anastomosis (How et al. 2000).

Prosthetic materials are highly thrombogenic, and thus low flow in a poor run-off graft further increases the risk of thrombosis. Sauvage first hypothesised thrombotic threshold velocity, i.e. a velocity below which thrombosis occurs (Sauvage et al. 1979). An adjuvant

av-fistula ideally increases the flow velocity above the thrombotic threshold, increases shear stress, and counteracts vessel shrinkage and stenosis.

Most diabetic wounds are neuropathic. Neuropathy may cause a lesion, which is often complicated by infection, and healing is prevented by inadequate tissue perfusion caused by ischaemia (Oyibo et al. 2002, Heikkinen et al. 2007). Radical wound excisions and skin grafting are seldom sufficient to achieve ulcer healing. A vascularised free flap transfer in combination with an infrainguinal reconstruction may therefore be indicated to prevent major amputation (Tukiainen et al. 2000, Vermassen et al. 2000, Illig et al. 2001).

Diabetic vascular disease was proposed to cause microangiopathy and affect the small arteries of the foot. This view has nevertheless been contradicted by numerous studies focusing on the pattern of PAD in diabetics. The tibial vessels are often affected in the leg, whereas the arteries of the foot are less frequently involved (LoGerfo & Coffman 1984, Diehm et al. 2006). An angiographic study of run off showed that the small arteries of the foot in both diabetics and non-diabetics were similarly affected (Karacagil et al. 1989b). The dorsal pedal artery is often spared to allow a bypass (Andros 2004) and with crural vessel involvement, bypasses from the popliteal level to pedal arteries can be performed to achieve leg salvage (Shah et al. 1995a, Biancari et al. 2000a).

A bypass to a foot artery often offers a limited run off. A free flap transfer in combination with a vascular bypass procedure significantly increases the outflow bed and consequently bypass graft flow (Lorenzetti et al. 2001). Therefore, in these patients a free flap transfer can be used with two aims: as tissue coverage and as an aid to maintain bypass graft patency.

Outflow is one of the strongest determinants of bypass outcome in infrainguinal bypass surgery (Albäck et al. 1998, Seeger et al. 1999). In patients with critical ischaemia, the outflow is often compromised, and even worse in redo surgery. The status of the outflow artery may be worse than anticipated, or the flow achieved by the bypass may indicate a high-risk graft. There may also be situations in which the extremity requires a free flap in adjunction with a bypass graft to cover the ischaemic tissue loss. Some encouraging reports have been published on a prosthetic bypass and av-fistula (Dardik et al. 1991, Harris et al. 1993, Biancari et al. 2001). Because low graft flow predicts also infrainguinal

vein graft failure (Albäck et al. 2000), the rationale to create an adjuvant av-fistula was that it might be beneficial not only in a prosthetic bypass, but also in a venous bypass. An internal av-fistula was created within a radial forearm free flap transfer with the intention to increase flap flow and thus possibly also bypass graft flow. The haemodynamic changes caused by a patient's previous free flap transfer were evaluated.

This study has been carried out mostly among an aged patient population with critical leg ischaemia and numerous co-morbidities. These patients were presented with suboptimal bypass grafts and a poor outflow bed. The aim of the study was to assess the possible benefit of an adjunctive av-fistula on both prosthetic and venous bypass graft patency, to assess possible adverse effects that the av-fistula may cause, to assess the effects of a previously reconstructed free flap on graft flow, and to present a novel method of free flap transfer with an internal av-fistula.

6. REVIEW OF THE LITERATURE

6.1 VEIN GRAFT BYPASS

6.1.1 The saphenous vein bypass

The saphenous vein is the conduit of choice for infrapopliteal bypass. Infrapopliteal bypass is mainly performed for limb salvage, and therefore the long-term performance of the graft is essential (Rafferty et al. 1987, Leather et al. 1988, Belkin et al. 1996). In a large patient series studied by Shah et al. (1995b) more than 2000 patients were followed for over 10 years, giving a secondary patency rate of 91%, 81% and 70% respectively, at one, five and 10 years. The limb salvage rate was 97%, 95% and 90% during the same period. 91% of the patients in the study had critical leg ischaemia and 67% had Fontaine IV lesions, indicating that surgery was mainly performed to achieve limb salvage.

The excellent performance of the saphenous vein graft has also been seen in the reports of Veith et al. (1986) and Sayers et al. (1998). Compared to a prosthetic popliteal, infrapopliteal and femorotibial bypass, the vein bypass performed far better and gave better results in the long run. At four years the primary patency of infrapopliteal vein bypass was 49% compared to 12% of PTFE grafts in the report by Veith and coworkers (1986). In a study by Rafferty et al. (1987) the three-year patency was 43% for femorotibial vein bypasses and 19% for prosthetic bypasses. In Sayers's study (1998) the primary patency was 54% at two years of vein grafts, compared to 31% of PTFE grafts. These studies concluded that femorotibial bypass provided good long-term results, and that saphenous vein graft is the optimal choice for these bypasses.

The saphenous vein can be used both in situ and as a reversed vein. It was proposed that the in situ technique would yield better patency, because the graft is manipulated less and the vasculature thus remains untouched, and possibly the endothelium better preserved. Bush and coworkers (1983) suggested that increased operative blood flow and postoperative patency were achieved by the in situ technique. In an endovascular in situ bypass series of Rosenthal et al. (1994) additional benefits were achieved by the endovascular technique in the form of reduced hospital stay, fewer wound-related complications and shorter recovery. In a large series investigated by Taylor et al. (1990),

however, 516 reversed vein bypasses were reported to have equal patency when compared with the in situ technique, i.e. secondary patency above 76% at five years. In a number of other large series with both reversed and in situ saphenous vein grafts, there was no difference between the groups, irrespective of the method used (Londrey et al. 1991, Morris et al. 1993, VA Group 1988). Finally, in two randomised series studied by Wengerter et al. (1991) and Harris et al. (1993) the in situ vein bypass was compared to a reversed vein infrapopliteal bypass. Equal patency rates were achieved by both methods; therefore, currently it is generally accepted that the saphenous vein is the optimal graft, regardless of whether it is used in situ or reversed.

6.1.2 Alternative vein bypass

Wengerter et al. (1991) noted that in their series, 30% of the patients requiring infrapopliteal bypass had no suitable vein for the in situ technique. Alternative sources of graft material were thus often searched. In the absence of the ipsilateral saphenous vein, the question arises which vein to use as the primary alternative. Some believe that the contralateral saphenous vein should be saved for the subsequent revascularization of the contralateral leg or for coronary artery bypass surgery, while others emphasize minimizing operative injury to the revascularized leg, and prefer to use the contralateral saphenous vein (Chew et al. 2002). Nevertheless, long enough segments of arm vein can also be harvested to allow crural bypass.

Holzenbein et al. (1996) reported a series of 250 arm vein bypasses to infrapopliteal arteries. They achieved a three-year patency of 52% and a leg salvage rate of 92%. The authors concluded that the arm veins were easily accessed and vein configuration or splicing did not affect patency rates, but that the vein quality should first be confirmed by angioscopy. Results on 520 arm vein bypasses were reported by Faries et al. (2000), yielding a five-year patency rate of 58% and leg salvage of 72%. Single-segment and spliced veins resulted in equal patency and, on the whole, the long-term performance of the arm vein bypass was superior to that reported for prosthetic or cryopreserved grafts.

All autogenous graft material can be used in almost all instances if graft material is actively searched, as proposed by Kent et al. (1989). Chew et al. (2001) reported a series of 165 autogenous composite vein bypasses with a five-year secondary patency of 65% and leg

salvage of 81%. Good long-term results could thus be achieved, but spliced vein grafts required surveillance and revision more often than one-segment grafts (Gentile et al. 1996, Chew et al. 2001).

Curi and coworkers (2002) compared an autogenous spliced vein graft to a single-segment saphenous vein graft, as well as to a prosthetic graft. In the infrapopliteal position the autogenous spliced graft performed equally well in the long run as the saphenous vein graft, and was far superior to the prosthetic conduit.

Gentile et al. (1996) reported a large retrospective series of 919 patients with ipsilateral or contralateral saphenous vein or alternative autogenous vein bypass. The alternative vein bypass required revision more often, but still the five-year patency and leg salvage rate with an alternative autogenous vein was similar to that of a single-segment saphenous vein bypass.

The lesser saphenous vein is also relatively easily harvested, but often requires splicing due to its inadequate length (Weaver et al. 1987, Shandall et al. 1987). It is claimed to be easier to handle than arm veins, which tend to be thin-walled. Problems in wound healing sometimes occur, because in distal bypasses skin flaps result from harvesting the lesser saphenous vein. Suction drains and exposition with the aid of duplex mapping has been suggested to overcome these problems (Chang et al. 1992).

Schulman and coworkers (1987) first introduced deep veins as arterial grafts in a randomised study. Femoral-popliteal veins performed equally well as saphenous vein grafts in this study of femoropopliteal bypasses. Venous morbidity has been shown to be minimal despite the deep vein harvest in later series of superficial femoral vein grafts (Wells et al. 1999, Modrall et al. 2004).

6.1.3 Outflow level

Good long-term patency and leg salvage has been achieved in a series of vein bypasses to crural arteries. Even bypasses to a single artery outflow have yielded acceptable results. A number of patients have stenosis or occlusions in the superficial femoral artery and popliteal artery, and therefore the crural arteries offer the most proximal site for the

distal anastomosis. Ideally a bypass should be done to the first artery in continuity with the pedal arch (LoGerfo & Gibbons 1996, Andros 2004). (Table I)

Excellent results are reported also with pedal artery bypass. Pomposelli and his coworkers (2003) published a series of 1000 patients with pedal artery bypass and long-term follow-up. Even emergency pedal artery bypass has been reported; in cases of acute thromboembolism or ischaemia a pedal artery bypass was attempted without preoperative angiographic imaging to achieve foot salvage (Hofmann et al. 2003). (Table II)

Bypasses to plantar and tarsal artery branches with a vein graft have also been reported. In these series the patients have had either previous pedal artery bypass, or no visible pedal artery in preoperative angiography. Acceptable leg salvage rates have been achieved even in these series. (Table III)

According to the literature a vein graft, both a single-segment and a spliced vein graft, performs well in a distal outflow site and in a compromised outflow bed. However, contradictory reports exist as well. Poor outflow and especially an occluded pedal arch predicted poor patency of femorodistal and pedal bypasses in the studies of Karacagil et al.(1990) and Albäck et al. (2000).

Table I
Outcome after crural artery bypasses with vein grafts

Author	No.of bypasses	PP 1-year	PP 2-year	PP 3-year	PP 4-year	PP 5-year	SP 1-year	SP 2-year	SP 3-year	SP 4-year	SP 5-year	LS 1-year	LS 2-year	LS 3-year	LS 4-year	LS 5-year	S 1-year	S 2-year	S 3-year	S 4-year	S 5-year
Bergamini et al 1991	246	75	66	63	-	-	89	86	85	-	-	-	-	-	-	-	-	-	-	-	-
Hickey et al 1991	239	-	-	-	-	-	84	-	83	-	82	-	-	-	-	-	81	-	62	-	60
Anderson et al 1992 *	228	-	-	-	-	-	62-82	-	60-79	-	-	78-90	-	74-85	-	-	-	-	-	-	-
Cheshire et al 1992	89	-	-	54	-	-	-	-	72	-	-	-	-	-	-	-	-	-	-	-	-
Schneider et al 1993	203	-	-	61	-	-	-	-	79	-	-	-	-	87	-	-	-	-	64	-	-
Darling et al 1995	732	84	-	75	-	70	89	-	83	-	78	96	-	-	-	93	-	-	-	-	-
Shah et al 1995b **	1271	77-85	-	-	-	66-78	86-95	-	-	-	76-86	97	-	-	-	94	86	-	-	-	51
Eslami et al 1997	130	-	-	-	-	50	-	-	-	-	70	-	-	-	-	79	-	-	-	-	55
Luther&Lepäntalo 1997	209	57	-	53	-	47	69	-	66	-	53	81	-	76	-	71	-	-	-	-	-
Sayers et al 1998 ***	251	63	54	-	-	-	66	56	-	-	-	81	73	-	-	-	84	74	-	-	-
vanDamme et al 2003	90	-	-	-	80	-	-	-	-	86	-	-	-	-	88	-	-	-	-	54	-

Outcome endpoints are reported in percentages
PP= primary patency, SP= secondary patency, LS= leg salvage, S= survival
* divided into groups according to crural outflow artery
** divided into groups according to outflow artery, in leg salvage and survival pedal bypasses also included
*** in leg salvage and survival, prosthetic bypasses also included

Table II
Outcome after pedal artery bypasses

Author	No.of bypasses	PP 1-year	PP 2-year	PP 3-year	PP 5-year	PP 10-year	SP 1-year	SP 2-year	SP 3-year	SP 5-year	SP 10-year	LS 1-year	LS 2-year	LS 3-year	LS 5-year	LS 10-year	S 1-year	S 2-year	S 3-year	S 5-year	S 10-year
Davidson&Callis 1993	43	89	-	79	-	-	92	-	82	-	-	94	-	86	-	-	-	-	-	-	-
Schneider et al 1993	53	-	-	58	-	-	-	-	82	-	-	-	-	92	-	-	-	-	61	-	-
Tordoir et al 1993*	30	67	-	55	-	-	75	-	64	-	-	-	-	82	-	-	-	-	-	-	-
Bergamini et al 1994	99	74	70	70	-	-	77	77	77	-	-	83	83	-	-	-	-	-	-	-	-
Gloviczki et al 1994	100	67	-	60	-	-	78	-	69	-	-	85	-	79	-	-	90	-	83	-	-
Isaksson&Lundgren 1994	33	76	-	-	-	-	89	-	-	-	-	89	-	-	-	-	82	-	-	-	-
Darling et al 1995	238	82	-	71	57	-	86	-	78	67	-	94	-	-	86	-	-	-	-	-	-
Robison et al 1995	111	-	-	-	57	-	-	-	-	61	-	-	-	-	64	-	-	-	-	-	-
Shah et al 1995b	152	82	-	-	68	-	92	-	-	77	-	-	-	-	-	-	-	-	-	-	-
Abou-Zamzam et al 1996	46	63	-	49	-	-	-	-	-	-	-	70	-	70	-	-	84	-	69	-	-
Eckstein et al 1996	56	65	55	-	-	-	71	62	-	-	-	77	71	-	-	-	89	78	-	-	-
Luther&Lepäntalo 1997a	109	-	-	-	-	-	59	59	59	-	-	-	60	60	-	-	80	69	54	-	-
Biancari et al 1999 **	162	43	-	34	-	-	50	-	41	-	-	66	-	60	-	-	76	-	55	-	-
Dorweiler et al 2002	49	-	-	-	89***	-	-	-	-	-	-	-	-	-	87***	-	-	-	-	-	-
Frankini& Pezzella 2003	43	-	-	-	-	-	58	-	39	-	-	56	-	46	-	-	-	-	-	-	-
Pomposelli et al 2003	1032	-	-	-	57	38	-	-	-	63	42	-	-	-	78	58	-	-	-	49	24
Staffa et al 2005	54	-	-	-	76 ****	-	-	-	-	78 ****	-				81****	-	-	-	-	-	-

Outcome endpoints are reported in percentages
PP= primary patency, SP= secondary patency, LS= leg salvage, S= survival
*30 pedal bypasses in a series of 141, patency calculated for the whole group, leg salvage for pedal bypasses only
** 20 patients with PTFE or combined bypass included
*** patency and leg salvage at four years
**** patency and leg salvage at 54 months

Table III
Outcome after plantar artery bypasses

Author	No.of bypasses	PP 1-year	PP 2-year	PP 3-year	PP 5-year	SP 1-year	SP 2-year	SP 3-year	SP 5-year	LS 1-year	LS 2-year	LS 3-year	LS 5-year	S 1-year	S 2-year	S 3-year	S 5-year
Ascer et al 1988	20	89	81	-	-	-	-	-	-	85	85	-	-	-	-	-	-
Andros et al 1989	20 (24)	73*	-	-	-	-	-	-	-	89	-	-	-	81	-	-	-
Quinones-Baldrich et al 1993	24 (46)**	-	72	-	-	-	-	-	-	-	89	-	-	-	-	-	-
Gloviczki et al 1994	34 (100)***	67	-	60	-	78	-	69	-	85	-	79	-	90	-	83	-
Luther&Lepäntalo 1997a	20 (109)***	-	-	-	-	59	59	59	-	-	60	-	-	80	69	54	-
Roddy et al 2001	18	74	-	-	-	-	-	-	-	74	-	-	-	-	-	-	-
Friedman et al 2002	22	-	72	-	-	-	-	-	-	-	82	-	-	-	-	-	-
Connors et al 2003	24	-	70	-	-	-	-	-	-	-	78	-	-	-	-	-	-
Frankini&Pezzella 2003	20 (43)***	-	-	-	-	58	-	39	-	56	-	46	-	-	-	-	-
Aulivola&Pomposelli 2004	124	67	-	-	41	70	-	-	50	75	-	-	69	-	-	-	-
Hughes et al 2004	98	67	-	-	41	70	-	-	50	75	-	-	69	91	-	-	63

Outcome endpoints are reported in percentages
- numbers in brackets are the total number of bypasses in the series
PP= primary patency, SP= secondary patency, LS= leg salvage, S= survival
* SE exceeds 10%
** Life Table data for the whole series, but there were no differences between the subgroup analysis
*** Life Table data for the whole series, pedal bypasses included

6.2 PROSTHETIC BYPASS

Prosthetic grafts are widely used in bypasses performed for symptomatic leg ischaemia. They perform acceptably well in the above-knee (AK) position, when used in claudication patients with good run-off (Rosenthal et al. 1990, Ballotta et al. 2003). Dacron, polytetrafluoroethylene (PTFE) or human umbilical vein (HUV) grafts are available as prosthetic material, and the grafts come with standard or special coatings. Graft coatings are under active research by the graft industry. One of the latest developments is the heparin-bonded prosthetic graft claimed to have superior patency, i.e. close to the patency rates achieved by vein grafts (Peeters et al. 2006). However, there is lack of evidence to support the superiority of one over the other.

Results comparable to those with vein grafts have been achieved in patients with good run-off. Some authors therefore suggest that the saphenous vein should be saved for later use, because in most vascular patients the disease progresses and requires repeated surgery (Prendville et al. 1990, Rosen et al. 1986, Patterson et al. 1990, Quinones-Baldrich et al. 1992). Two randomised studies were published in 2000 describing the performance of AK prosthetic bypass. Burger et al. (2000) reported the PTFE graft to have acceptable short-term patency, and therefore it would be a reasonable alternative in the AK position. Johnson et al. (2000) reported the initial performance of the prosthetic grafts to be similar to vein grafts, but during long-term follow-up, it became clear that the vein bypasses fared better even in the AK position.

The performance of different grafts in the AK position has been tested. In a randomised trial, no difference was found between Dacron and PTFE grafts in the AK position (Post et al. 2001). In a multicentre trial, HUV and PTFE were compared in a femoropopliteal bypass yielding equal patency (McCollum et al. 1991). A Scandinavian multicentre study showed that polyester grafts fared at least as well as PTFE at two-year follow-up (Jensen et al. 2007).

It has been estimated that 30% of patients with critical ischaemia have no suitable saphenous vein to allow autogenous graft bypass. In addition, half of the patients with secondary procedures have no autogenous graft material available (Belkin et al. 1995,

Rossi et al. 2003). In the early 1990s prosthetic grafts were used more liberally than currently, because in the earlier reports prosthetic grafts seemed to perform well. After long-term follow-up, however, it has become evident that autogenous graft material fares better in the long run.

The reason for using prosthetic grafts is that in critically ischaemic patients there is no autogenous graft material to be used. The Veterans Administration Cooperation Study Group (1989) compared PTFE, umbilical vein and vein bypass in 596 patients who had a below-knee (BK) or crural bypass. Two-year patency was 76% for a vein bypass and 64% for a prosthetic bypass in BK position, and 73% and 30% for tibial/peroneal bypasses, respectively. In a study by Eickhoff et al. (1987) the performance of HUV grafts was found to be superior to that of PTFE grafts in the below-knee position. Dardik and coworkers (2002) presented a large series of HUV bypasses from comparative decades. The HUV graft was reported to offer an alternative when the autologous vein is not available, giving acceptable long-term outcome even in the crural position. In most of the studies, the prosthetic bypass to crural arteries is associated with worse patency than the autologous bypass, and therefore prosthetic bypass is justified only to avoid amputation (Wolfe &Tyrrell 1991, Jacobsen et al. 1998, Feinberg et al. 1990, Londrey et al. 1991, Schweiger et al. 1993, Parsons et al. 1996). (Table IV)

Table IV
Outcome after prosthetic crural bypasses

Author	No.of patients	CLI / SLI	Outflow	Type of bypass	PP	PP	PP	PP	PP	SP	SP	SP	SP	SP	LS	LS	LS	LS
					1-year	2-year	3-year	5-year	8-year	1-year	2-year	3-year	5-year	8-year	1-year	2-year	3-year	5-year
Flinn et al 1988	75	97/3	Crural	PTFE	-	45	37*	-	-	-	-	-	-	-	-	75	-	-
VA study 1988	135	90/10	BK 50	PTFE or	-	64	-	-	-	-	-	-	-	-	-	85	-	-
			Crural 50	HUV	-	30	-	-	-	-	-	-	-	-	-	58	-	-
Feinberg et al 1990	87	97/3	Crural	PTFE or	35	30	-	-	-	-	-	-	-	-	62	-	-	-
	21			HUV**	12	6	-	-	-	-	-	-	-	-	33	-	-	-
Londrey et al 1991	45	92/8	Crural	Comp	-	-	-	-	-	55	49	44	28	-	-	-	-	82
	33			PTFE***	-	-	-	-	-	63	38	26	7	-	-	-	-	-
Quinones-Baldrich et al 1992	322	59/41	AK 68	PTFE	-	-		-	63	-	-	-	-	72	-	-	-	-
			BK 23	PTFE	-	-	-	-	38	-	-	-	-	-	-	-	-	-
			Crural 9	PTFE	-	-	22		-	-	-	-	-	-	-	-	37	-
Dardik et al 1993	167	91/9	AK 12	HUV	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			BK 37	HUV	-	-	-	-	-	83	77	72	65	-			-	73
			Crural 51	HUV	-	-	-	-	-	77	70	58	45	-	-	-	-	56
Morris et al 1993	201	96/4	Crural	PTFE	-	-	21	-	-	-	-	-	-	-	74	-	64	-
Schweiger et al 1993	211	100/0	Crural	PTFE	51	46	37	27	-	63	60	45	34	-	-	63	-	51
Parsons et al 1996	66	100/0	Crural	PTFE	71	47	35	28	-	78	61	55	43	-	84	71	71	66
Jakobsen et al 1998	40	100/0	BK 20	PTFE	63	50	-	-	-	63	53	-	-	-	80	75	-	-
			Crural 80	PTFE****	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dardik et al 2002	283	90/10	AK 12	HUV	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			BK 29	HUV	-	-	-	-	-	90	85	81	71	-	-	-	-	80
			Crural 59	HUV*****	-	-	-	-	-	83	75	66	56	-	-	-	-	65

Outcome endpoints are reported in percentages
CLI= critical leg ischaemia, SLI= symptomatic leg ischaemia, AK=above knee, BK=below knee, HUV=human umbilical vein graft
PP= primary patency, SP= secondary patency, LS= leg salvage
* Primary patency at four years
** PTFE-composite or HUV-composite bypass
***Composite or PTFE bypass
****Crural PTFE bypass with distal vein cuff or av-fistula
***** Crural HUV bypass with adjuvant av-fistula

6.3 FACTORS AFFECTING BYPASS OUTCOME

A number of factors affect the outcome of a bypass graft. The causes of graft occlusion can be divided into immediate, early and late causes. Immediate graft failure is often caused by poor patient selection. Technical error and thrombogenity of the graft material are the other causes of immediate graft failure. Early graft failure is caused by a technical error, intimal hyperplasia or blood rheology, and late graft failure by intimal hyperplasia, bypass deterioration or progression of the atherosclerotic disease. Blood coagulation and thrombocyte aggregation can be affected by adjunctive medication. Treatment of concomitant diseases and risk factors prevents the complications caused by the diseases, and consequently the progression of the atherosclerotic disease (Burns et al. 2003, Chobanian et al. 2003, Critchley & Capewell 2003, Baigent et al. 2005, Dormandy et al. 2005).

6.3.1 Graft-related causes

The graft material has an important role on the outcome. In a study by Rutherford et al. (1988) the material of the bypass graft was found to be the most important predictor of long-term outcome, its influence being the greater, the more distal the bypass was. In studies with comparative cohorts, prosthetic graft material predicted poor prognosis in the series studied by Londrey et al. (1991) and Tordoir et al. (1993). Carsten et al. (1998) suggested that a prosthetic graft should not be used in crural bypasses due to the poor outcome of these grafts.

Albäck and coworkers (1998) studied the immediate failure of femoropopliteal saphenous vein grafts and found that almost half of the immediate occlusions were graft-related and almost as many were due to technical causes. They concluded that a number of occlusions could be avoided if these matters were carefully addressed. A study by Donaldson et al. (1992) showed that in 63% of primary saphenous vein graft bypasses, failure was caused by the graft itself. In the rest of the cases, compromised inflow, outflow and hypercoagulability were the causes of failure. Panayitopoulos et al. (1997) studied factors predicting failure of a femorodistal bypass graft and found graft material and outflow status to be strongest predictors of outcome. In a series of Varty et al. (1993) the only independent risk factor for immediate vein graft failure was peripheral resistance, but

a poor quality vein was found to be a risk factor for subsequent graft stenosis. In a study by Ihlberg et al. (2001) low graft flow was found to predict the development of de novo stenosis in a vein graft.

In conclusion, the bypass graft itself, whether prosthetic or vein, is a significant factor in the outcome of infrainguinal bypass surgery. With careful patient and graft selection and graft monitoring, i.e. intraoperative graft quality control and postoperative surveillance, a considerable number of occlusions can be avoided (Harward et al. 1994, Idu et al. 2005).

6.3.2 Co-morbidities

Vascular patients typically have a number of co-morbidities. These often determine the fate of the patient regardless of the fate of the bypass graft. Severe coronary artery disease, previous stroke, long-term dialysis and diabetes with co-existing infection were found to be risk factors for both limb loss and mortality in a study by Biancari et al. (2000b). An increased level of postoperative c-reactive protein (CRP) was predictive of amputation in a study by Mätzke et al. (2001), possibly indicating an inflammatory state in these patients. Patients with ulcer and gangrene had higher CRP values, as did patients with subsequent amputation.

Patients in long-term dialysis and those with coronary artery disease have a poor outcome according to survival, even if the bypass surgery is successful. Biancari and coworkers (2002) and Peltonen et al. (1998) concluded that revascularization should not be attempted in patients on dialysis due to the poor survival and high amputation rate of these patients. When several risk factors are present, the fate of the patient is poor. Biancari and coworkers (2007) introduced a risk score for patients with critical limb ischaemia. Diabetes, coronary artery disease, foot gangrene and urgent operation were each assigned one point, and a risk score was thus determined. This risk score can be used to predict postoperative outcome, for example with a high risk score of four, the 30-day mortality/amputation rate was 22.2%.

Diabetes is present in about half of the vascular patients who require bypass surgery. In a series where diabetics were compared to non-diabetics in terms of patency and outcome, no significant difference was found between the groups, except for survival (Wolfle et al.

2003). In a study by Luther and Lepäntalo (1997b) diabetes and female gender were prognostic of poor outcome as to patency and limb salvage. In a series of patients with popliteal-to-distal bypasses, Biancari et al. (2000a) found that diabetes had no effect on patency, but that survival and amputation-free survival rates of diabetics were significantly inferior. Carsten et al. (1998) described a series of patients who had limb loss despite a patent graft. In their patient material, persistent diabetic infection was the cause of early limb loss, and chronic ulcer and osteomyelitis were the causes of late limb loss. Diabetes was found to be predictive of amputation also in a study by Seeger et al. (1999), due to poor wound healing.

Virkkunen and coworkers (2004) studied diabetes as a risk factor for postoperative complications. There were more Fontaine IV lesions and more distal bypasses in the group of diabetics, and diabetes was found to be a risk factor for early BK amputation but not for mortality. Urgency of operation was a significant predictor of adverse outcome in diabetics. The same was noted by Biancari and coworkers (2007). An urgent operation may be connected to the concurrent severe infection in a diabetic patient, the infection itself being a predictor of poor outcome (Mätzke et al. 2001).

6.3.3 Outflow

6.3.3.1 Assessment of outflow

Perhaps the most important predictive factor of bypass graft outcome is the outflow status, a factor that cannot be controlled. The status is sometimes so poor that the overall possibility of the reconstruction can be questioned. The predictive role of the outflow has been addressed in a number of studies. In series where bypass graft failure has been studied, poor outflow is often one of the main causes of failure (Donaldson et al. 1992, Panayitopoulos et al. 1997, Varty et al. 1993).

Ways of describing the outflow have been searched to determine a uniform scoring system to aid in decision-making when a distal bypass is planned. The run-off has been assessed from the angiographic images by grading the outflow. In the traditional classification, the run-off was graded from excellent to poor, depending on the status of the popliteal artery and its tributaries (Linton & Darling 1962). A classification based on three risk groups has

been used subsequently, presenting a status of isolated popliteal outflow, one-vessel outflow, or two- to three-vessel outflow (Miller et al. 1990). In a study by Prendville et al. (1990) with femoropopliteal prosthetic grafts, patients with poor run-off (0-1 patent crural vessel) had a significantly worse outcome compared to patients with better run-off. In a series by Schweiger et al. (1993) the number of patent crural vessels and the patency of the plantar arch predicted the patency of a prosthetic graft.

6.3.3.2 Run-off score

The run-off score is a scoring system that grades the outflow based on angiographic findings and the planned site of the distal anastomosis. The guidelines determing the run-off score were first published by the Ad Hoc Committee in 1986 and the revised version in 1997 (Rutherford et al. 1986 and 1997). Depending on the status of the outflow arteries, the run-off receives a value from one to ten, one indicating normal outflow and ten blind outflow. Unfortunately the validity of the run-off score depends on the quality of the images, so the accuracy of the score can be questioned. Yet, the run-off score has been widely used as a descriptive method of the outflow tract and its predictive value has been tested in a number of studies.

Tordoir et al. (1993) reported a series of 121 patients with an infrainguinal bypass. In their report the run-off score, determined according to the guidelines of the Ad Hoc Committee, had no predictive value on graft patency. Prosthetic graft material was the only tested parameter that predicted poor outcome. Takolander et al. (1995) tested the predictive value of the run-off score in 53 infrainguinal bypass patients. They found that the run-off score had no effect on the patency at one year. In a study of peroneal bypasses by Plecha et al. (1993), the run-off score was not a predictor of the outcome.

The intraoperative determinants of graft failure were studied by Blankensteijn et al. (1995). A run-off score of more than one, i.e. other than normal run-off, predicted early failure in their study; on the other hand, no graft with a normal run-off failed. Okadome et al. (1991) also found the run-off score to be predictive of femoropopliteal bypass outcome with a cut-off value of 4.5. The run-off score predicted the immediate outcome of a femoropopliteal graft in a study by Albäck et al. (1998) and the fate of a femorocrural graft in a report by Biancari et al. (1999a). Seeger et al. (1999) studied the potential predictors of outcome in

a series of 210 patients, and found the run-off score to be the strongest predictor of outcome in terms of survival, amputation and graft patency.

Karacagil et al. described their own method of scoring the run-off and found it to be predictive of patency in both femoropopliteal (1989a) and femorodistal bypass (1990). In their report, the Ad Hoc scoring method did not predict the outcome. Their revised scoring method did predict patency also in later reports of femoropopliteal and femorodistal grafts (Ljungman et al. 2000, Ulus et al. 2001).

It is difficult to compare the reports when the Ad Hoc scoring method is used. Some of the series are small, some retrospective, and the patients differ according to outflow artery and bypass graft material. The contradictory findings of these series may be explained by the fact that legs with the most difficult outflow are excluded from operative therapy, as demonstrated by the small number of pedal bypasses in all the reports.

6.3.3.3 Other means of defining the outflow

Other means to define the outflow have also been described due to the problems inherent in angiography. Angiography is an invasive examination with a certain, although low, complication risk, and sometimes it fails to visualise the outflow tract precisely. Doppler can be used to demonstrate the patency of pedal vessels not seen in angiography, as proposed by Pomposelli et al. (1990). In a study by Wilson et al. (1997) Doppler, angiography and duplex ultrasound were used to assess the outflow, and duplex was found to be most accurate in the crural area. Newer high frequency colour duplex devices are especially effective in visualising distal arteries. Extremely calcified vessels may visualize poorly, but in most cases a more accurate image can be obtained with duplex imaging than with contrast angiography (Hingorani et al. 2007).

Scott et al. (1989) used a pulse-generated Doppler run-off score and compared it to the angiographic scores. They found that the pulse-generated Doppler score was more accurate in the crural area in defining the outflow. When Davies and coworkers (1996) used the same method, they found that the run-off score was strongly associated with the outcome of the bypass. A pre-operative hand-held Doppler run-off score was described by Stewart et al. (2002), and this Doppler score correlated with the outcome.

Stirnemann et al. (1994) described a method to measure flow during the operation and found this intraoperative flow to be a predictor of the outcome. A very low flow value and a prosthetic graft resulted in poor outcome.

Peripheral resistance can be calculated from the graft flow intraoperatively. Ascer et al. (1987) measured peripheral resistance in femoropopliteal and femorodistal reconstructions and found the outflow resistance to predict patency and limb salvage. Davies et al. (1993) reported intraoperative graft resistance and flow to be predictive of early outcome.

Intraoperative flow can be measured by the transit time flowmeter. It was introduced and validated in clinical practice in 1996 (Albäck et al. 1996, Laustsen et al.1996). High peripheral resistance and low graft flow predicted adverse graft outcome in a study by Lundell & Bergqvist (1993). Intraoperative graft flow was found to be a predictor of the outcome also by Albäck et al. (2000). Poor intraoperative flow predicted subsequent de novo stenosis of a vein graft in a study by Ihlberg et al. (2001).

A run-off score based on Doppler flow measurement of the graft was introduced by Scwierz et al. (2003). Currently colour duplex is becoming increasingly popular in the imaging of the peripheral arterial tree. Duplex ultrasound arterial mapping (DUAM) is a safe and relatively accurate alternative to contrast angiography (Mazzariol et al. 2000, Hingorani et al. 2004).

Even though the outflow strongly affects the outcome, bypasses to poor outflow have been attempted. Series of bypasses to an isolated popliteal segment have been described (Roddy et al. 2002, Mosimann & Stirnemann 1995). Desai and coworkers (2001) reported a series of 274 patients in whom the outflow score was 10, i.e. blind outflow in one third of the patients. Acceptable patency was achieved even with blind outflow, which nevertheless was a predictor of subsequent limb loss, as shown by the worse limb salvage in the group with the blind outflow.

6.3.3.4 When to reconstruct

The question remains, when to reconstruct, and when should the attempt be considered too risky. The bypass graft may be suboptimal, the patient may have a number of co-morbidities, and the outflow may be poor. The Second European Consensus Document (1991) proposed that a 25% amputation-free survival rate achieved by surgery justifies attempts for limb salvage. Because this rate is close to the one achieved with conservative treatment, a higher success rate of 75% should be attained to justify bypass surgery instead of primary amputation according to Robison & Beard (1999). In reports from national vascular registries, similar rates have been achieved in the treatment of critical leg ischaemia (The Vascular Surgical Society of Great Britain and Ireland 1995, Tröeng et al. 1994).

The outcome of a patient with unreconstructed CLI is poor; only 46% of these patients are alive at one year, and 28% are alive with a non-amputated leg (Lepäntalo & Mätzke 1996). In other studies of conservative treatment at 18-24 months, 54% of the patients have had an amputation (Jivegård et al. 1995, Klomp et al. 1999). On the other hand, if certain risk factors are present as described by Biancari et al. (2000b), the patient is prone to both limb loss and life loss. The failure of infrainguinal surgery leads to a poor outcome, particularly in patients with immediate graft failure and tissue loss. A limb salvage rate of 34% has been reported in these patients after graft failure (Baldwin et al. 2004).

Critical ischaemia often demands repeated surgery. Luther studied the costs of reconstruction versus amputation in CLI patients. Despite the need for repeat surgery, reconstructive surgery was found to be cost-effective in potentially mobile patients who are likely to regain their independent living status, incurring lower costs than amputation when calculated on the basis of cost/survival year (Luther 1997a). In a study of outcome and cost analysis (Panayiotopolous et al. 1997), bypass grafting was found to be cost-effective, because the costs of revascularisation are low compared to amputation. However, in patients with severe disease, repeat surgery is needed, thus increasing the costs, and therefore primary amputation may be justified in some patients. Due to the number of repeated surgical procedures that these demanding patients require, Goshima et al. (2004) proposed that traditional reporting standards underestimate the expenses and efforts to attain limb salvage.

The outcome of failed bypass is poor. Therefore in a situation with a high failure risk due to the poor graft or outflow, means to predict or detect graft failure are searched. In a series of 631 grafts under surveillance for an average of 28 months, 26% developed secondary failure (Baldwin et al. 2004). On the other hand, when long-term results of vein graft revision were studied, 30.9% of the revised vein grafts developed additional lesions, leading the authors to conclude that ongoing surveillance is mandatory (Nguyen et al. 2004).

The true benefit of graft surveillance has been studied in randomised studies. In contrast to the initial observation by Lundell et al. (1995), Ihlberg et al. found in a randomised trial (1998) and its extension (1999) that there was no difference in the outcome in the groups with duplex or conventional graft surveillance. This was also observed in the Vein Graft Surveillance Randomised Trial (Davies et al. 2005); the graft surveillance programme did not show any benefit in terms of limb salvage, but it did increase the costs.

6.4 ADJUNCTIVE METHODS FOR BETTER BYPASS PATENCY

In CLI patients, adjunctive methods to improve bypass performance are searched in suboptimal situations. The poor graft material or outflow entail risk to the bypass. Adjunctive medication is used to prevent graft thrombosis when a thrombogenic graft is used or a low-flow graft is at risk. Vein cuffs were introduced to improve prosthetic graft performance. Means to improve the outflow have been introduced in the form of an adjunctive av-fistula and free flap transfer.

6.4.1 Medication

The role of anti-platelet or anticoagulation medication on graft patency has been studied, but only in few randomised controlled trials. In some centres anticoagulation is routinely used in conjunction with prosthetic bypass to improve graft patency. Flinn et al. (1988) reported improved results from a prosthetic bypass with the use of warfarin. In a retrospective series the 4-year patency rate was 37% in a series of 75 patients with few late complications from the adjunctive medication. In a randomised trial conducted by Sarac et al. (1998), combination therapy with warfarin and acetylsalicylic acid (ASA)

improved the outcome of infrainguinal bypasses with high risk for failure, i.e. poor graft, outflow or redo surgery.
The overview of randomised trials by the Anti-platelet Trialists' Collaboration (1994) showed that anti-platelet therapy succeeded in reducing the risk of vascular occlusion irrespective of the anti-platelet regimen used.

Tangelder et al. (1999) published a review of randomised controlled trials of using ASA and oral anticoagulants. A meta-analysis showed that the absolute risk of graft occlusion was reduced by 8.2% when anti-platelet therapy was applied, and by 16.2% when anticoagulation therapy was used. None of the reviewed series, however, provided proof of which modality was most effective, nor conclusive evidence on the reduction of the risk of stroke, myocardial infarction or death among vascular patients.

The Dutch BOA study (2000) was a large randomised trial comparing oral anticoagulants with ASA in infrainguinal bypass surgery. A total of 2690 patients were randomised and followed for a mean of 21 months, graft occlusion being the primary outcome. Both treatments were effective irrespective of the level of the distal anastomosis. In a subgroup analysis, oral anticoagulation was more effective than ASA in preventing infrainguinal vein bypass failure, but it caused more bleeding episodes. ASA was superior in preventing non-venous graft occlusion, contrary to a number of local policies, by which ASA is commonly used in all vascular patients and warfarin only in high-risk patients.

The recommendations of the APCC conference (2004) for vascular patients include administration of ASA for all patients with chronic ischaemia, intermittent claudication, and patients undergoing vascular reconstructions (Clagett et al. 2004). ASA is recommended for patients with prosthetic bypass, but routine use of anticoagulation is not recommended for venous bypass patients, presumably for fear of noncompliance and bleeding in this elderly multimorbid patient population. Anticoagulation and ASA both are recommended for high-risk patients only.

Clopidogrel is the latest anti-platelet agent with proved benefit in cardiovascular patients in terms of risk reduction of vascular events (CAPRIE Steering Committee 1996). A randomized trial by Smout et al. (2004) gave evidence to support long-term clinical combination of ASA and clopidogrel in patients with peripheral vascular bypass grafts. The

data from the CASPAR trial showed that when clopidogrel was combined with ASA, the outcome in the group of prosthetic grafts was improved. There was no overall beneficial effect of the use of clopidogrel and ASA for infrapopliteal venous bypass (Belch et al. 2007). Currently, clopidogrel is recommended only to patients intolerant of ASA or with a history of coronary artery stenting (Dagher et al. 2007). A recently observed problem is the nonresponsiveness to ASA or especially to clopidogrel in a number of patients with atherothrombotic disease (Lepäntalo A et al. 2004).

6.4.2 Vein cuff

Due to the fact that a prosthetic graft is a suboptimal bypass graft, attempts to improve it have been searched. A rigid non-compliant prosthesis is difficult to anastomose to a small recipient artery. Furthermore, it was noted that intimal hyperplasia accumulated strongly on the anastomosis area, especially in areas of low shear stress, i.e. at the heel and at the floor of the anastomosis (How et al. 2000). Siegman first introduced the reconstruction of a vein cuff at the distal anastomosis in 1979. Miller (1984) developed this idea further to a venous collar, later called Miller cuff, at the distal anastomosis. The cuff aided the suturing of the distal anastomosis because both the heel and the toe of the anastomosis were clearly visible. Subsequently, different configurations of cuffs were introduced: the Tyrrel/Wolfe cuff or St.Mary's boot (Tyrrel & Wolfe 1991) and the Taylor patch (Taylor et al. 1992) among others. The rationale of the cuff was to inhibit intimal hyperplasia and thus graft occlusion, even though it was not clear what caused the hyperplasia.

The effect of the venous cuff was also the focus of experimental studies. Tyrrel et al. (1990) proposed that the vein cuff protected the anastomosis from mechanical distortion and possibly acted as a reservoir for the flow. In their canine model, Norberto et al. (1995) compared the compliant vein cuff with a jacketed non-compliant cuff, and found no difference in the formation of hyperplasia. They concluded that the protective effect of the cuff was not mechanical in origin. Kissin and coworkers (2000) compared the vein cuff with a prosthetic cuff and with an end-to-side anastomosis without a cuff in an experimental study. The vein cuff altered the site of the intimal hyperplasia thus sparing the recipient artery. Despite the same configuration of the prosthetic cuff, it did not have the same protective effect, leading to the conclusion that biological properties of the autologous tissue were responsible for the protective effect.

The haemodynamic studies by Cole et al. (2002) showed that the vein cuff caused unfavourable flow conditions predisposing to intimal hyperplasia. The protective effect of the cuff was therefore assumed to be caused by the venous material. In contrast to this, How et al. (2000) compared cuffed and non-cuffed anastomosis in an experimental model and showed that the altered site of shear stress in a cuffed anastomosis caused redistribution of the myointimal hypeplasia away from the critical sites.

To determine the role of the distal vein cuff in adjunction with a PTFE graft, a randomised controlled trial was published by Stonebridge et al. (1997). They reported on a group of 261 bypasses, 37% to below knee popliteal and 6% to crural vessels, which were randomised to either the vein cuff group or the control group. There was no difference in patency between the groups in the above knee bypasses, but in the below knee position, the vein cuff resulted in significantly better patency and in 20% higher limb salvage. The protective effect of the vein cuff was explained to be technical, facilitating the reconstruction of the distal anastomosis.

Prosthetic bypass without adjunctive methods gives poor long-term results. Even though the protective effect of the vein cuff has not been thoroughly explained, the results on series with vein cuffs and on a randomised trial, indicate that the use of a vein cuff is justified in a PTFE bypass to crural arteries. (Table V)

Table V
Outcome of prosthetic bypasses with a vein cuff

Author	No.of bypasses	CLI/SLI	Cuff type	Outflow	PP 1-year	PP 2-year	PP 3-year	PP 4-year	PP 5-year	PP 8-year	SP 1-year	SP 2-year	SP 3-year	LS 1-year	LS 2-year	LS 3-year	LS 4-year	LS 5-year	LS 8-year
Taylor et al 1992	256	72/28	Taylor patch	34% AK	91*	-	81*	-	71*	54*	-	-	-	96*	-	-	-	88*	80*
				34% BK	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				32% IP	74	-	58	-	54	-	-	-	-	-	-	-	-	-	-
Harris et al 1993a	43	100/0	avf+ Miller cuff	100%IP	-	61	-	-	-	-	-	62	-	61	-	-	-	-	-
Raptis&Miller 1995	489	49/51	cuff or patch	57% AK	85	-	69	-	-	-	-	-	-	-	-	-	-	-	-
				43% BK	83	-	57	-	-	-	-	-	-	-	-	-	-	-	-
Sidawy	80	100/0	Taylor patch	100%IP	82	78	70	63	-	-	-	-	-	88	83	79	79	-	-
Stonebridge et al 1997	133	89/11	Miller cuff	57% AK	80	72	-	-	-	-	-	-	-	86	84	-	-	-	-
				37% BK	80	52	-	-	-	-	-	-	-	86	82	-	-	-	-
				6% IP	47	**	-	-	-	-	-	-	-	**	**	-	-	-	-
Pappas et al 1998	42***	98/2	Miller cuff	16% AK	-	75	-	-	-	-	-	-	-	-	92	-	-	-	-
				33% BK	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
				51% IP	-	62	-	-	-	-	-	-	-	-	65	-	-	-	-
Kreienberg et al 2000	59****	100/0	Vein cuff	12% BK	96	45	38	-	-	-	98	47	47	92	92	92	-	-	-
				88% IP	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Outcome endpoints are reported in percentages
CLI= critical leg ischaemia, SLI= symptomatic leg ishaemia, avf=av-fistula, AK= above knee, BK= below knee, IP= infrapopliteal bypasses
PP= primary patency, SP= secondary patency, LS= leg salvage
* patency for popliteal grafts and leg salvage for all grafts
** n too small to allow calculations
*** Warfarin in 69% of patients, patency and leg salvage calculated for popliteal and infrapopliteal subgroups
**** results for all grafts

6.4.3 AV-fistula

End-to-side anastomosis between the graft and the recipient artery is most commonly used in infrainguinal bypass surgery. This configuration allows blood to circulate both through the new bypass conduit and through the remaining patent native vasculature. Especially in the distal anastomosis, an end-to-side anastomosis allows blood to circulate both antegrade and also retrograde if the outflow is compromised. Fisher et al. (2004) studied the outflow distribution at the distal anastomosis of a bypass. The mean outflow distribution was 75% to the distal direction and 25% to the proximal direction, with the distal flow decreasing more, the more distally that the anastomosis was placed. These observations suggest that when the distal outflow is poor, most of the flow is directed retrograde to a limited outflow tract resulting in poor bypass graft flow.

Sauvage et al. introduced the theory of thrombotic threshold velocity (TTV) in 1979. According to their theory and observations, there was a certain flow velocity for each graft material below which thrombosis of the graft would occur. Prosthetic grafts required a significantly higher flow to remain patent, whereas autologous arterial grafts remained patent with almost no flow. Based on the TTV hypothesis, an adjuvant av-fistula was combined to a prosthetic bypass to improve graft flow. The idea of the av-fistula is to increase flow by reducing peripheral resistance. The fistula shunts part of the flow to the low resistance venous circuit, short-circuiting the inadequate run-off, thus preventing stagnant flow and thrombosis.

The adjuvant arteriovenous fistula was first used in experimental studies. The first experimental canine models demonstrated increased graft flow (McGovern et al. 1985, Gwynn et al. 1988), but also led to venous hypertension and retrograde distal flow. Due to the worsened distal perfusion, the authors concluded that av-fistulas should not be used in clinical practice.

In an experimental setting, Parvin et al. (1984) showed a flow increase of 900% in the bypass graft when the av-fistula was made between the deep vein and artery proximal to the site of the anastomosis. An electromagnetic flowmeter showed that the artery offered adequate resistance between the distal anastomosis and proximal fistula, thus improving the distal perfusion. In this study the optimal configuration of the fistula was determined by

comparing different sizes and locations of the fistula. All fistulas increased bypass graft flow, but distal perfusion was found to benefit most from the proximal av-fistula.

Paty et al. (1990) experimented with different sized distal av-fistulas and found that increasing the fistula size caused a reversal of flow. In a 3 mm calibre artery, a 3-5mm long av-fistula increased graft flow without reversing distal flow, which was noted with a 7mm long av-fistula. In their clinical series, a distal av-fistula increased graft flow and distal perfusion, which was evidenced by duplex examination.

In addition to distal flow impairment, other adverse effects of the fistula were feared. Steal is a phenomenon caused by the av-fistula when most of the graft flow is directed to the low resistance venous outflow and the distal perfusion is compromised. When there is no proximal stenosis, i.e. the inflow is adequate, steal does not occur (Moody et al. 1991, Nielsen et al. 1996). Only anecdotal reports of excessive shunting exist (Teittinen et al. 1999). On the other hand, when the flow through the fistula increases, the distal perfusion is impaired. In a study by Kallakuri et al. (2003) a flow above 1 l/min decreased distal perfusion significantly. Such high flow values are, however, rarely encountered in combination with bypass surgery and av-fistulas; usually even limited flow to the outflow tract reverses the ischaemic state of the limb (Dardik et al. 1991).

Venous hypertension and extremity oedema may be encountered when the deep veins are filled with arterial flow from the bypass graft. This rarely occurs if the deep vein system is patent and the fistula flow is directed to the deep and not the superficial venous system (Moody et al. 1991, Harris et al. 1993a). Banding of some portion of the av-fistula has been proposed by some authors to prevent venous hypertension and steal (Jacobs et al. 1992, Ascer et al. 1996). In an experimental model Kallakuri and coworkers suggested banding of the fistula in all cases to achieve a distal graft pressure of 100 mmHg (Kallakuri et al. 2003). In clinical series the banding of the fistula has rarely been necessary (Dardik et al. 1996).

Even cardiac overload is possible if the fistula is too large, causing shunting of excessive amounts of blood. Flow values of 2 l/min or a 20% increase in cardiac output are needed to increase the preload to the right ventricle and to cause cardiac failure. Generally cardiac failure with adjuvant fistulas is rare, and has been described only in case reports (Teittinen

et al. 1999). Adjuvant av-fistulas are usually well tolerated. The reported cardiac problems have arisen from therapeutic av-fistulas in haemodialysis patients (Engelberts et al. 1995).

Ibrahim et al. (1980) presented one of the first series of patients in which clinical benefit was achieved in conjunction with the use of an av-fistula: out of 13 patients with human umbilical vein bypass in combination with an adjuvant fistula, limb salvage was achieved in 10 patients, and only one patient displayed the steal phenomenon. On the other hand, Snyder's group (1985) reported a series of 30 bypasses with initially augmented graft flow, but poor long-term outcome, with a rate of only 20% leg salvage at two years. In a more recent clinical series better outcome was achieved with the adjunctive fistula. (Table VI)

Table VI
Outcome of infrapopliteal prosthetic bypasses with av-fistula

Author	No.of bypasses	CLI/SLI	Type of bypass	Outflow	PP 1-year	PP 2-year	PP 3-year	SP 1-year	SP 2-year	SP 3-year	LS 1-year	LS 2-year	LS 3-year
Paty et al 1990	16	100/0	PTFE +avf	crural	67	-	-	-	-	-	75	-	-
Moody et al 1991	80	100/0	HUV+avf	crural	39	36	30	-	-	-	43	38	36
Jacobs et al 1992	30	100/0	PTFE+avf	crural,	71	-	-	-	-	-	83	-	-
				2 pedal	-	-	-	-	-	-	-	-	-
Harris et al 1993a	76	100/0	PTFE+avf	crural	-	25	-	-	28	-	38	35	-
	43		PTFE+avf+cuff	crural,	-	61	-	-	62	-	62	55	-
				1 pedal	-	-	-	-	-	-	-	-	-
Ascer et al 1996	68	100/0	PTFE+avf+cuff	crural,	78	70	62	-	-	-	89	86	78*
				3 pedal	-	-	-	-	-	-	-	-	-
Dardik et al 1996	290	100/0	HUV+avf	crural	-	-	-	77	69	61	81	79	75
Sogaro et al 1996	91	100/0	HUV+avf	crural	54	40	40	72	60	57	73*	62*	62*
Eagleton et al 1999	43	100/0	PTFE+avf	crural,	-	46	-	-	65	-	-	64	-
				3 pedal	-	-	-	-	-	-	-	-	-
Kreienberg et al 2000	48	100/0	PTFE+avf	10% BK	86	73	48	86	73	48	84	76	76
				90% crural	-	-	-	-	-	-	-	-	-
Biancari et al 2001**	12	100/0	PTFE+avf	crural	67	-	-	-	-	-	100	-	-

Outcome endpoints are reported in percentages
CLI= critical leg ischaemia, SLI= symptomatic leg ischaemia, HUV= human umbilical vein graft, avf= av-fistula, BK= below knee
PP= primary patency, SP= secondary patency, LS= leg salvage
*SE > 10%
** redo bypasses

Different types of fistula configurations have been described. Dardik et al. (1996) described the common ostium av-fistula in combination with a human umbilical vein bypass. In a report by Moody et al. (1991) the configuration of the fistula, either common ostium or proximal, had no effect on patency. Sogaro et al. (1996) introduced a pantaloon technique of an adjuvant fistula with HUV. Jacobs et al. reported (1992) a series of 30 patients with a PTFE crural bypass, a common ostium av-fistula and proximal vein ligation. In a series by Ascer et al. (1996) an av-fistula was created first, after which the PTFE graft was anastomosed to the hood of the av-fistula, and the distal vein was then ligated. (Figure 1)

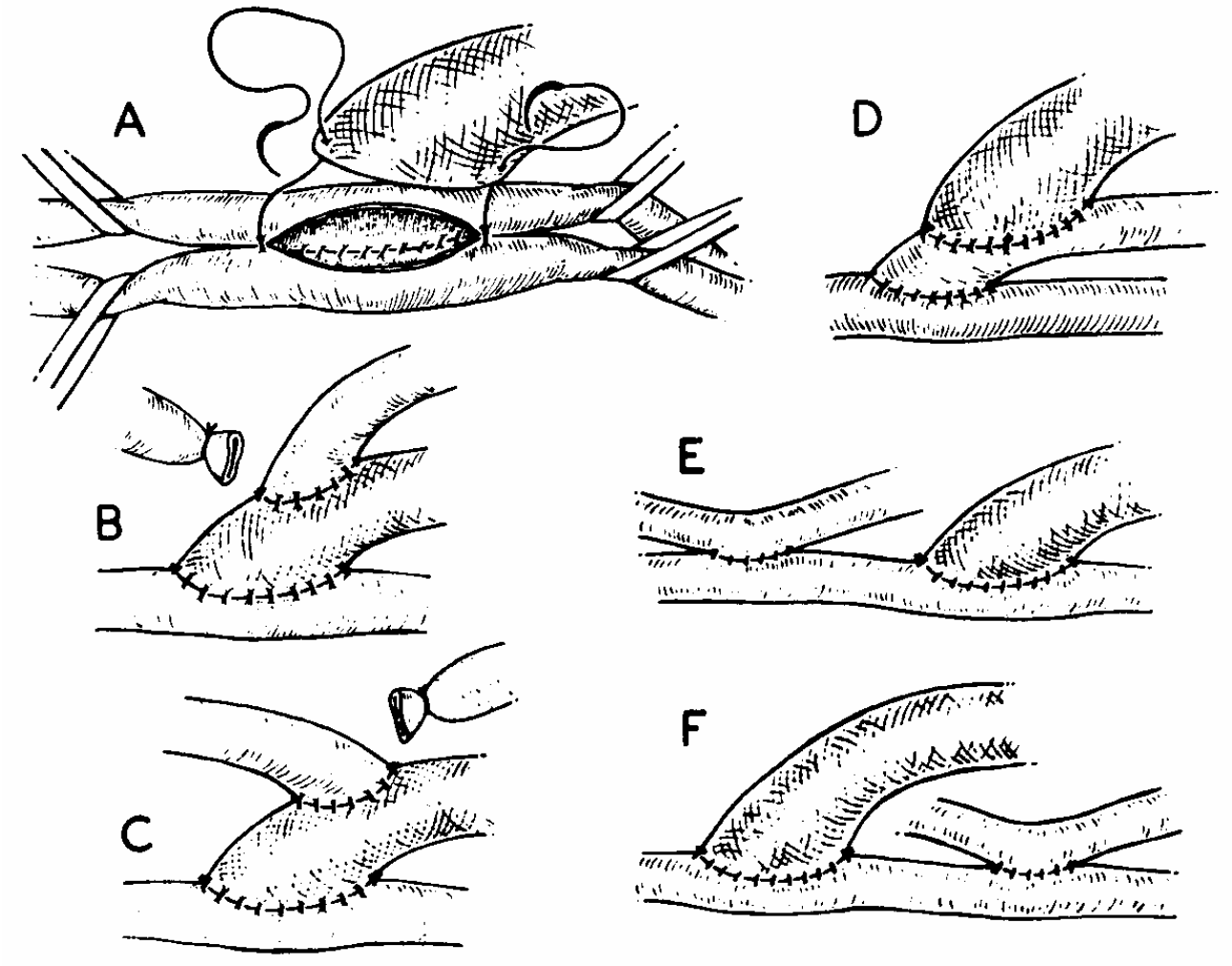


Figure 1. Different types of av-fistulas
A Common ostium av-fistula, B Proximal vein piggyback, C Distal vein piggyback, D Vein interposition av-fistula, E Distal av-fistula, F Proximal av-fistula (modified from D'Andrea et al. 1998)

The haemodynamic changes caused by the fistula have also been investigated in clinical series. Dardik et al. (1991) showed that the bypass graft flow improved, as demonstrated by both angiogram and duplex examination, always with antegrade distal flow. His group has also recorded the patency of the adjunctive fistula. Their observations demonstrated that the fistula patency decreased during the follow-up, but this had no direct effect on the graft patency, i.e. a number of grafts stayed patent despite the thrombosed fistula.

Jacobs et al. (1992) demonstrated the improved distal perfusion by ABI measurements. In his later study of 26 patients with PTFE bypass with or without an av-fistula, the patients with the av-fistula displayed significantly better patency and leg salvage. The microcirculation of the foot was also improved as shown by the augmented capillary perfusion (Jacobs et al. 1993).

Harris' group (1993a) compared a PTFE bypass with an av-fistula to a cuffed PTFE bypass and av-fistula and to a venous bypass. The patency of the cuffed PTFE bypass with adjunctive fistula approached that of a venous bypass and was significantly better than the non-cuffed PTFE bypass. They concluded that the two adjunctive methods, the vein cuff and the av-fistula, might be synergistic.

Kreienberg et al. (2000) compared a PTFE bypass with either a vein cuff or an av-fistula, and found limb salvage to be better in the vein cuff group. This was explained by the better opportunity of revision in the case of failure in the vein cuff group.

Biancari and coworkers reported a series redo infrapopliteal bypasses in 2001 (Biancari et al. 2001). In their series, the adjuvant av-fistula seemed to augment redo bypass graft patency, but the survival of the patients with an av-fistula was significantly poorer than of the patients without a fistula.

All these studies suggest that the av-fistula offers some benefit in terms of improved flow and patency. The studies were, however, small case series. A randomised trial comparing the av-fistula in adjunction with a PFTE bypass is needed.

The introduction of the in situ saphenous vein bypass technique allowed the effect of residual av-fistulas to be studied, as a number of in situ grafts inevitably had residual

connections from the arterialised vein to the venous tree. In comparison with reversed vein bypass, it was anticipated that the residual av-fistulas would have a negative impact, if any, on the outcome, contrary to the idea of improving flow in a prosthetic bypass with an adjuvant fistula.

Chang et al. (1989) reported a series of 216 in situ bypasses which were followed up by duplex examination. The flow through the fistula decreased significantly during the first postoperative year, and was of haemodynamic significance in only 6.5% of the bypasses. Haemodynamic significance was determined as persistent increasing fistula flow with or without oedema and decreased distal resting flow or pressure measured by duplex or pulse volume recording (PVR). When the haemodynamic criteria were met and fistula ligation performed, distal bypass flow improved. In this study it was concluded that in the majority of patients, the residual fistula had no clinical significance, whereas in patients with reduced flow capacity, the redistribution of flow caused by the av-fistula was poorly tolerated.

Lundell et al.(1999) studied 98 in situ bypasses for critical ischaemia. Residual av-fistulas were found in 56% of the patients. About a quarter of these were surgically corrected due to decreased flow velocity in the grafts distal to the residual av-fistula. The majority of the residual fistulas did not require any procedures. Even though the distal flow velocity decreased due to the residual fistulas, this did not always affect the distal perfusion as demonstrated by the non-affected ABI. The criteria for a haemodynamically significant residual fistula were therefore not clear.

Van Dijk et al. (1997) reported a series of 35 closed in situ bypasses. A total of 216 side branches were coil-embolised and after this 39 residual av-fistulas were detected, and of these, 11 symptomatic ones were treated. On the basis of these figures it was concluded that it is unlikely for the av-fistulas to cause symptoms and thus repeat procedures.

The assumption made in all these studies was that residual av-fistulas would cause decreased distal perfusion. The distal flow was shown to decrease in some cases, but the ABI was not affected. However, none of these reports focused on the possible positive effects of an av-fistula on venous bypass.

6.4.4 Free flaps

The soft tissues in an ishaemic foot are limited, and rarely allow direct closure of tissue defects. An ischaemic extremity may have a tissue defect that is so large that the wound will not heal with conventional methods of revision and split thickness skin grafting. Local cutaneous flaps of pedicular flaps can seldom be used due to the poor perfusion of the limb. The reconstructive ladder presents the various options to achieve wound healing from simple direct closure to microvascular free flaps (Mathes & Nahai 1997). In a PAD patient the free flap may be the only alternative. Different types of free flaps have been described to reconstruct foot tissue defects (Kaplan et al. 1998).

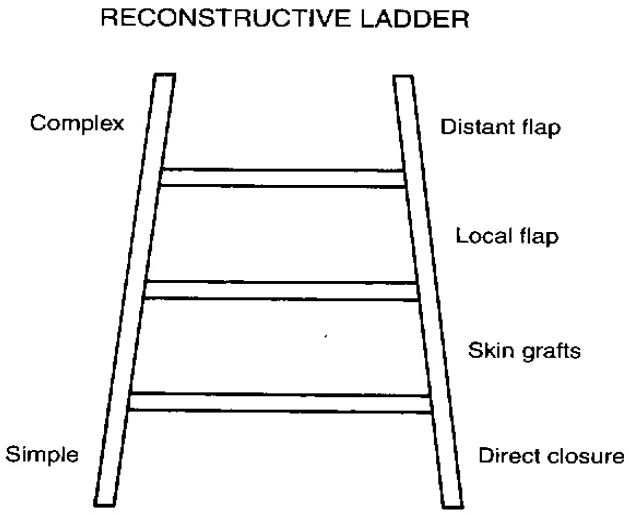


Figure 2. The reconstructive ladder (Mathes & Nahai 1997)

Special features are required from free flaps in the foot to allow healing of ulcers and tissue defects and to achieve ambulation of the patient. Fasciocutaneous flaps are proposed to provide the best contour in foot reconstructions (Rautio et al. 1989), but may not tolerate ambulation well. There is a shearing effect between the fascia plane and the skin and subcutaneous tissues during weight bearing. Therefore it has also been suggested that a muscle flap with split thickness skin grafting yields best results in weight bearing areas (Rainer et al. 1999).

Shestak et al. (1990) reported an indirect method of vascularisation of the extremity by free flap transfer: When conventional bypass was not feasible, a vascularised flap was placed to an ischaemic extremity, achieving foot salvage and resolution of symptoms. The flap effect was explained by the improved run-off achieved by the flap. The “nutrient flap”

was also described by Mimoun et al. (1989). In addition to providing a tissue cover, the flap also provided supplementary blood flow to ischaemic areas, assisted in venous drainage, and induced the formation of a capillary network.

Simultaneous vascular bypass and free flap transfer have been described in a number of studies (Briggs et al. 1985, Gooden et al. 1997, Cronenwett et al. 1989, Lepäntalo &Tukiainen 1996, Quinones-Baldrich et al. 2000). It has also been proposed that the surgery should be staged: the vascular bypass should be done first, followed by the free flap transfer (Greenwald et al. 1990). Simultaneous surgery extends the limits of limb salvage with a cumulative 2-year limb salvage of 77-88% (Tukiainen et al. 2000, Vermassen et al. 2000) and corresponding 5-year rates of 57-66% (Illig et al. 2001,Tukiainen et al. 2006). Due to the demanding nature of this combined surgery, however, patient selection is crucial. The presence of diabetes and renal failure are strong predictors of poor outcome. Illig and coworkers therefore suggested that these patients should not be considered candidates for combined surgery (Illig et al. 2001). The presence of heel ulcers and calcanear osteomyelitis are predictive of amputation, despite combined surgery (Tukiainen et al. 2006).

Free flap transfer indirectly revascularises the extremity even without direct vascular bypass. Serletti et al. (1995) found that in a number of cases in their series, combined vascular bypass and flap transfer was not possible. They thus directed the vein graft inflow to the free flap only, still achieving limb salvage. In a series by Tukiainen et al. (2006) a subgroup of 13 patients did not have a suitable distal recipient artery; the bypass graft was therefore anastomosed end-to-end to the flap artery directly. The limb salvage of this subgroup did not differ from that of the rest of the patients. This procedure has been described in case reports and explained by the ingrowth of the flap and resulting neovascularisation into the surrounding tissues (van Landuyt et al. 1996a, Mätzke et al. 1997).

The blood flow in free flaps has been studied. Experimental models have demonstrated that free muscle flap blood flow and capillary perfusion increase postoperatively. This is thought to be caused mainly by the denervation of the flap (Chen et al. 1991, Siemionow et al. 1994). Lorenzetti et al. (1999) studied blood flow in latissimus dorsi flaps, and noted that the postoperative flap flow increased in the immediate postoperative period also in a

clinical setting. This phenomenon helps to keep the microanastomosis open and is also beneficial for wound healing. Flap flow in different types of flaps differs significantly. The flow depends on the different tissue components of the flap, but it has also been noted that the flap flow is not dependent on the recipient artery flow. The flow varies according to the requirements of the free flap (Lorenzetti et al. 2001a).

When free flap transfer is connected to a bypass graft, the free flap has a significant positive effect on the bypass graft flow. Van Landyut et al. (1996b) reported augmentation of the graft flow, and suggested that the free flap increases the distal outflow bed without the disadvantages of a conventional av-fistula, i.e. without shunting away of arterial blood and causing venous hypertension. Lorenzetti et al. (2001b) reported a series of free flap reconstructions in combination with a pedal vein graft bypass. In their study, the free flap connected to the bypass increased the vein graft flow significantly. The free flap received about a third of the total graft flow, the vein graft flow still being augmented. Thus the free flap did not compromise the distal perfusion of the limb. It was proposed that the free flap acted as an av-fistula, increasing the outflow bed and reducing peripheral resistance.

In a compromised situation the free flap connected to the vascular bypass graft seems to improve the outflow status. It offers a flow reservoir by multiple possible mechanisms: the ingrowth of the flap forms a capillary network, and the denervation of the flap causes opening of subcutaneous av-shunts and increased flow through the transferred tissue, which thus functions as an av-fistula. These phenomena seem to make the free flap a haemodynamically promising method in augmenting vascular bypass graft flow by enlarging the outflow bed.

7. AIMS OF THE STUDY

The study investigates the effect of an adjuvant av-fistula on compromised infrapopliteal prosthetic and venous bypass patency, and the possible impact of an adjuvant fistula on leg salvage.
The following questions were posed:

1. The effect of an adjuvant av-fistula on prosthetic graft bypass patency.
2. The haemodynamic effects of an adjuvant av-fistula on a prosthetic bypass and its possible adverse effects.
3. Effect of a radial forearm flap with an internal av-fistula connected to a vein bypass graft on bypass graft haemodynamics and patient outcome.
4. Effect of a previous free flap transfer on a vascular bypass.
5. Potential benefit of an adjuvant av-fistula on a vein graft bypass with poor outflow.

8. PATIENTS AND METHODS

All the patients in this study were operated on either by vascular surgeons, or in case of a hybrid surgical procedure, together by a vascular and a plastic surgeon. The study design was prospective in three studies (I, II, III), one study was a case report (IV) and one a retrospective study (V).

8.1 PATIENTS

Study I: In this prospective randomised multicentre trial, 59 patients with critical leg ischaemia and no suitable veins for grafting were recruited to receive a femorocrural PTFE bypass with distal vein cuff, with or without an adjuvant av-fistula. 31 patients were randomised to have an av-fistula, and 28 patients having a femorocrural bypass and distal vein cuff without a fistula served as a control group.

Study II: A total of 50 patients from the two Finnish centres, i.e., Department of Vascular Surgery, Helsinki University Central Hospital, and Department of Surgery, Etelä-Karjala Central Hospital, that were involved in a prospective randomised trial, underwent an extended follow-up including haemodynamic measurements. They comprised the patient group in Study II.

Study III: Nine patients were treated with a modification of a standard technique of a radial forearm flap. The flap included an internal av-fistula, and the free flap was used to cover a tissue defect. All patients had large non-healing distal ulcers requiring both a vascular bypass and free flap transfer. All the patients underwent a hybrid operation by a team consisting of a vascular surgeon and a plastic surgeon at the Department of Vascular and Plastic Surgery, Helsinki University Central Hospital.

Study IV: This study was a case report of a patient previously operated on for complicated wound infection with a free flap transfer. The patient later needed a pedal bypass for CLI.

Study V: This study group comprised 77 patients who underwent an infrapopliteal autogenous bypass procedure, which was complemented by an adjuvant av-fistula,

because the bypass was considered to be at high risk for failure due to poor outflow. The study was a retrospective multicentre study. Control patients randomly retrieved from the three centres were matched with each case according to the outflow artery and run-off score. The cases and controls were operated on during the same period. Table VII presents data on operative activity in each of the study centres.

Table VII
Background data on the operative activity of the study population

	Institutions involved	Retrieval period	No. of operations for CLI	Patients included	% of all operations
Study I	Helsinki, Lappeenranta Västerås, Hillerod	1997-2000	983*	59	6
Study II	Helsinki, Lappeenranta	1997-2003	453**	50	11
Study III	Helsinki	1998-2003	40 / 790 ***	9	23 / 1.1
Study IV	Helsinki	2005	case report	1	
Study V	Helsinki, Lappeenranta Vaasa	1996-2003	1813*	77+77	4+4

* number of all infrainguinal bypasses for CLI during the study period
** number of all femorocrural bypasses for CLI during the study period
*** number of combined infrainguinal bypasses and free flap transfers / number of all infrainguinal bypasses for CLI during the study period

Demographics

Demographic data on the patients were collected according to the risk factors recorded in the national vascular registry, Finnvasc database (Salenius 1992). The data were collected prospectively, except for Study V which was a retrospective study. The data are presented in Table VIII.

Table VIII
Demographics of the study groups

Variable	Study I Avf group	Control group	Study II Avf group	Control group	Study III	Study IV	Study V Avf group	Control group
No. of patients	31	28	26	24	9	1	77	77
Sex: M / F	15 / 16	10 / 18	13 / 13	7 / 17	7 / 2	- / 1	42 / 35	37 / 40
Age: mean (range)	74 (49-93)	73 (46-88)	76 (50-93)	74 (47-89)	56 (37-78)	71	74 (39-90)	75 (46-93)
Coronary artery disease	22 (71)	14 (50)	23 (88)	12 (50)	2 (22)	-	45 (61)	42 (55)
Diabetes	12 (39)	12 (43)	12 (46)	12 (50)	9 (100)	+	52 (70)	44 (57)
Hypertension	15 (48)	14 (50)	14 (54)	11 (46)	1 (11)	+	31 (42)	28 (36)
Renal failure	2 (6)	2 (7)	2 (8)	1 (4)	1 (11)	-	13 (18)	12 (16)
Preoperative ABI: Median	0.3*	0.36*	0.32*	0.40*	0.57	0.42	0.40	0.37
Run-off score**: median (range)	6 (1-10)	5 (1-8.5)	6 (2-10)	5 (2-8.5)	8 (4-10)	-	7.5 (4-10)	7.5 (4-10)
Indication: Rest pain	8 (25)	11 (39)	8 (31)	7 (29)		-	7 (9)	14 (18)
Ulcer	16 (52)	14 (50)	14 (54)	14 (58)	9 (100)	+	47 (61)	44 (57)
Gangrene	7 (23)	3 (11)	4 (15)	3 (13)		-	23 (30)	19 (25)

Avf = arteriovenous fistula
Numbers in parentheses are percentages
*mean ABI of the patient group
** Defined by the standards proposed by the Ad Hoc Committee (Rutherford et al. 1997)

- Hypertension defined as blood pressure>165/95 mmHg or medication
- Renal failure defined as serum-creatinine>150ug/ml

8.2 METHODS

8.2.1 Angiographic run-off score

The angiographic run-off score was determined according to the standards proposed by the Ad Hoc Committee (Rutherford et al. 1997).

Studies I & II: The run-off score was evaluated preoperatively in 51 (86%) patients in Study I and in 42 (84%) patients in Study II. The run-off was evaluated for both the recipient crural artery and the pedal arch. Eight patients had poor angiographic data that did not allow outflow scoring.

Study III: The extent of the vascular disease was assessed by angiography. DSA images were scored by the method proposed by the Ad Hoc Committee (Rutherford et al. 1997).

Study V: The angiographic images were scored retrospectively by an experienced angioradiologist blinded as to patient data. Intraoperative angiographic studies were used as an aid for scoring in cases where the preoperative angiographic images were not sufficient for scoring. The run-off scores were available for 56 (73%) patients from the patient group with the av-fistula. Run-off data were available for the entire retrieved control group. Control patients for the cases without a run-off score were selected from a sample of controls with run-off scores ranging from four to ten. The frequency of the different run-off scores in the av-fistula group was thus matched with that of the control group.

8.2.2 Surgical procedure

Studies I & II: The surgical procedure was carried out with a 6 mm externally supported PTFE prosthesis. An interposition vein cuff was constructed in all cases at the distal anastomosis. Patients randomised to the fistula group received an av-fistula of either the common ostium type or proximal type according to the surgeon’s discretion. The patients were operated on as a part of daily hospital routine. Any vascular surgeon with previous experience of three or more av-fistulas was accepted to perform these operations.

Study III: A two-team approach was used in all cases. First, a radical wound excision was performed. The operation was then continued in two separate fields. The vascular surgeon performed the distal bypass, and the plastic surgeon raised the fasciocutaneous radial forearm flap. The internal fistula within the flap was created by performing an end-to-end anastomosis between the distal end of the radial artery and the cephalic vein, or the concomitant vein of the radial artery. The flap artery was anastomosed end-to-side to the vein graft in eight cases, and in one case the flap artery was directly connected to the vein graft because a distal bypass was not possible. The outflow of the flap was directed to a deep vein of the limb. The flap was fixed into place and the wound closure was completed with a meshed split thickness skin graft if necessary.

Study IV: In this case study a femoropedal bypass was performed with a saphenous vein graft in a patient who 13 years earlier had been operated on for a complicated ankle fracture with a latissimus dorsi (LD) free flap transfer.

Study V: An infrapopliteal vein graft bypass was performed in all cases. Only patients with an autogenous vein graft bypass to either a crural or a pedal artery with an adjuvant av-fistula were included in the study group. The patients in the control group were matched according to the outflow artery.

The vein cuffs used in this study were either the Miller cuff or St. Mary's boot (Miller et al. 1984, Tyrrel & Wolfe 1991). The av-fistula configurations were of the common ostium, proximal or modified type (see Figure1: A, D, F). The internal av-fistula within the radial forearm flap was created between the distal end of the radial artery and the cephalic vein (Figure 3). The operative data are presented in Table IX.

Systemic heparin was given to all patients before arterial cross clamping. A prophylactic antibiotic was administered according to hospital routine, or to bacterial cultures in patients with infection. Low molecular weight heparin (LMWH) was administered postoperatively until the patients became ambulatory. ASA medication was started for life, unless the patient was on anticoagulation medication.

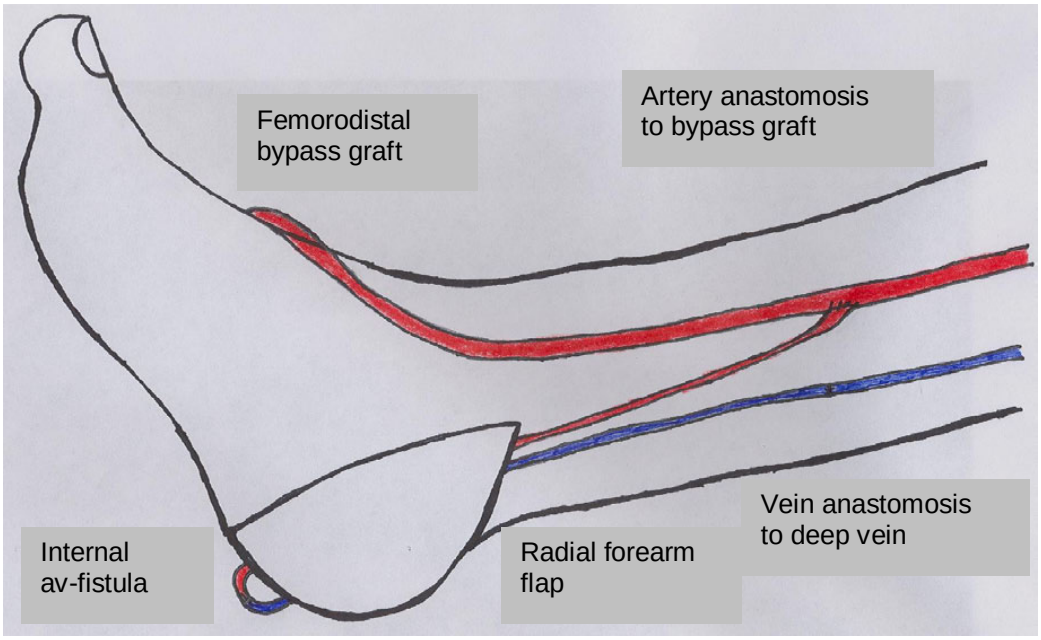
The free flap transfer patients were monitored in the intensive care unit or the recovery room for the first 24 hours to ensure the vitality of the flap. These patients were kept in bed

rest for seven days with the limb elevated. Ambulation was started gradually with exercises in standing position, and weight bearing was allowed only after four to six weeks.

Table IX
Operative data

Variable	Study I Avf group	Control group	Study II Avf group	Control group	Study III	Study V Avf group	Control group
No. of bypasses	31	28	26	24	9	77	77
Inflow: Common femoral	31	23	26	20	4	28	42
Prosthesis*	-	5	-	4	-	-	-
SFA	-	-	-	-	2	29	16
AK popliteal	-	-	-	-	-	5	3
BK popliteal	-	-	-	-	3	15	16
Outflow: ATA	13	13	9	12	-	5	5
ATP	8	7	7	5	3	6	6
Fibularis	10	8	10	7	1	8	8
ADP	-	-	-	-	2	42	42
Plantaris	-	-	-	-	2	16	16
Other**	-	-	-	-	1	-	-
Graft: PTFE	31	28	26	24	1***	-	-
Vsm	-	-	-	-	8	63	67
Arm vein	-	-	-	-	1***	9	2
Spliced vein	-	-	-	-	-	5	8
Cuff: Miller	16	16	14	16	-	-	-
St. Mary's boot	11	9	8	5	-	-	-
Other	4	3	4	3	-	-	-
Av-fistula: Common ostium	25	-	20	-	-	60	-
Proximal	6	-	6	-	-	9	-
Other	-	-	-	-	9[a]	8[b]	-

Avf = arteriovenous fistula
* inflow from a previous prosthesis at the femoral level
** outflow from the vein graft directly to the flap artery
*** femoropopliteal PTFE graft with an arm vein jump graft
[a] internal av-fistula in the radial forearm flap
[b] a modified fistula: the fistula was made directly on the vein graft on the distal anastomosis without re-doing the entire anastomosis



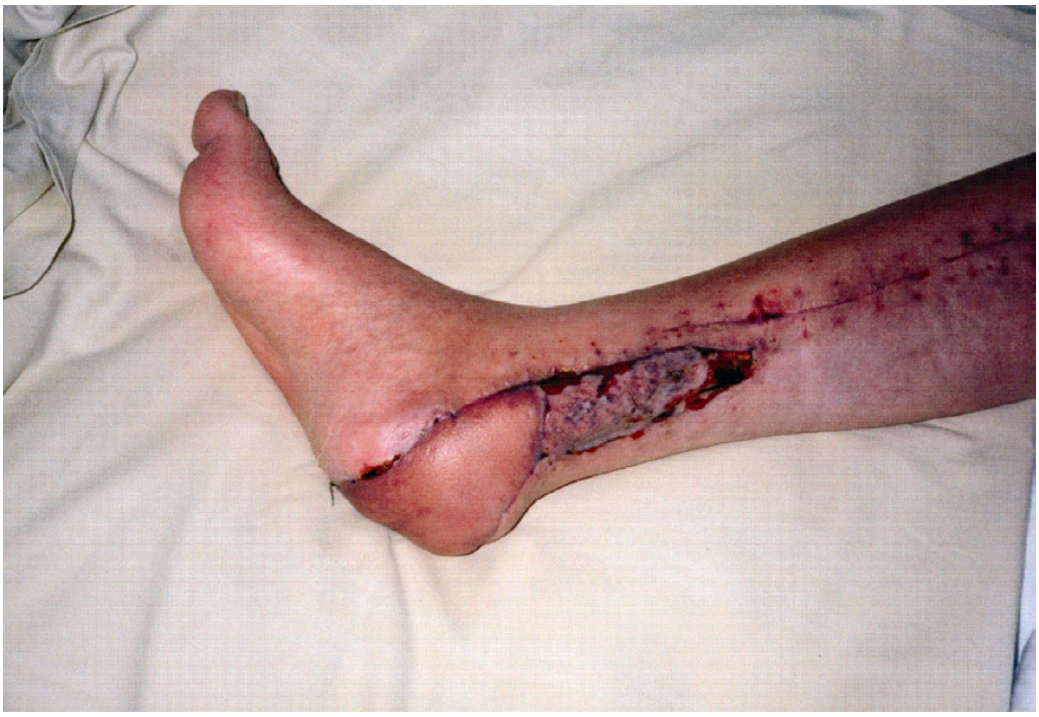


Figure 3. Schematic illustration of the modified radial forearm flap with the internal av-fistula and a patient with the modified radial forearm flap covering calcanear defect.

8.2.3 Intraoperative flow measurements

Study II: Intraoperative flow measurements were done to evaluate the haemodynamic effect of the fistula. The flow measurements were performed with a transit time flowmeter (CardioMed CM4006, Medistim A/S, Oslo, Norway) at the end of the operation when the distal anastomosis was completed and flow opened and stabilised. Outflow to the recipient artery and to the fistula was recorded separately, as well as the maximal flow capacity after intragraft injection of papaverin hydrochloride (40 mg). The maximal flow capacity was recorded with the fistula closed in the av-fistula group. Systemic blood pressure and pressure at the inflow artery were registered intra-arterially to reveal a possible gradient indicating proximal stenosis.

Study III: Flow measurements were recorded during the surgery. A transit time flowmeter was used. The flow in the radial artery was measured when the flap was raised while the vascular pedicle was intact, with the fistula both open and closed. The graft flow was recorded prior to the flap transfer. After the flap was fixed on the foot, anastomoses were completed and the flow stabilised. The flow to the graft and to the flap artery were recorded with the av-fistula both open and closed.

Study IV: The flow was recorded after the completion of the distal anastomosis according to hospital routine, using a transit-time flowmeter.

Study V: In this study the flow was recorded with a transit-time flowmeter after the completion of the distal anastomosis. If the patient was considered haemodynamically stable, the maximal flow capacity (MFC) was recorded after an intra-arterial injection of papaverin hydrochloride (40 mg). In 12 patients with an av-fistula, flow recordings were taken both prior to and after the reconstruction of the av-fistula. Flow measurement recordings were available in 39 cases in the av-fistula group and in 61 cases in the control group, because the data were collected retrospectively.

8.2.4 Follow-up

Study I: The follow-up was at regular intervals according to a surveillance schedule. Clinical outpatient visits with ABI measurements and duplex graft surveillance took place at 7 days, 1, 3, 6, 9, 12, 18 and 24 months postoperatively.

Study II: The same schedule was applied, with extended follow-up every six months after two years. Duplex examinations with graft velocity measurements were performed and the circumference of the legs was recorded in addition to other clinical data. The follow-up time ranged from 40 to 75 months.

Study III: The first follow-up visit was at 1 to 2 months postoperatively, and thereafter at 3, 6 and 12 months, and once a year, depending on the healing of the foot. The follow-up time varied between 14 and 51 months.

Study IV: The patient was assigned a follow-up schedule according to hospital routine: at 1, 3 and 6 months, and every 6 months thereafter.

Study V: All three units utilised the same graft surveillance schedule. During the first postoperative year the visits were at 1, 3 and 6 months, after which the patients were generally surveyed every 6 months with clinical outpatient visits, ABI measurements and duplex examinations of the grafts. The follow-up time ranged from 2 months to 8 years.

8.2.5 Statistical analysis

The statistical analyses were conducted with SPSS statistical software (ver 9.0, 11.0, 14.0, SPSS Inc, Chicago, Ill., USA). Primary and secondary patency, leg salvage and patients alive with a leg were analysed by the life table method. Kaplan-Meier analysis and the log-rank test were applied to test for statistical significance (I, II, III, V). Fisher's exact test was used for the analysis of categorical data (I). The Mann-Whitney U test and Chi-square test were used for the analysis of nonparametric and categorical data, as appropriate. Correlation analysis was done using bivariate correlation and Spearman's correlation coefficient (II). The Chi-square test, the Wilcoxon test and the Mann-Whitney U test were used in analysis of the nonparametric data and the parametric data with a skewed distribution (III, V). Statistically significant differences were given with p-values less than 0.05 (I, II, III, V).

9. RESULTS

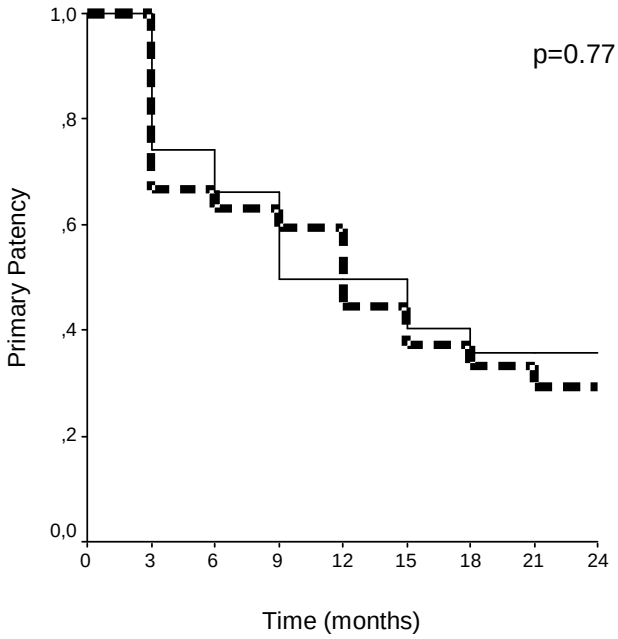
Study I

Our results revealed that there was no difference between the av-fistula group and the control group in terms of patency. The cumulative primary and secondary patencies were 29% and 40% in the av-fistula group, and 36% and 40% in the control group at two years (p=0.77 and 0.89). (Figure 4)

Leg salvage at two years was 65% and 68%, respectively. 54% of the patients in the av-fistula group, and 48% in the control group were alive without amputation in the same period. (Figure 5)

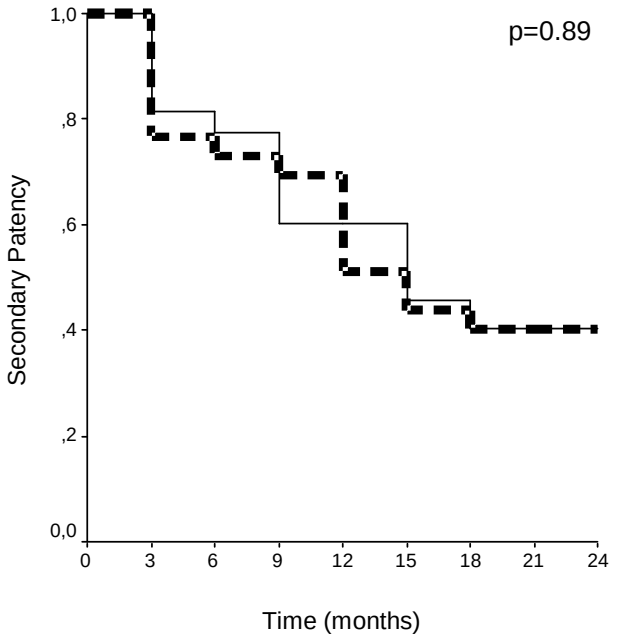
The av-fistula did not have negative effects on the distal perfusion, as shown by the average ABI increase from the preoperative level of 0.55 in the av-fistula group and 0.57 in the control group at one month.
The operation lasted 222 minutes (median) in the av-fistula group, and 180 minutes in the control group (p=0.04).

The patency of the av-fistula was recorded by duplex surveillance in 19 patients available for surveillance at one year. Four of the original 31 av-fistula patients were amputated, three were dead, three had occluded grafts, and two patients were not available for surveillance. In six cases there was an occlusion of the av-fistula, and in only one case this resulted in graft thrombosis, which after reoperation led to leg salvage. Five patients had a record of a previously patent fistula but had had graft failure at one year. These data on fistula patency indicated that the patency of the graft was not dependent on the patency of the fistula (p=0.02).



Patients at risk:

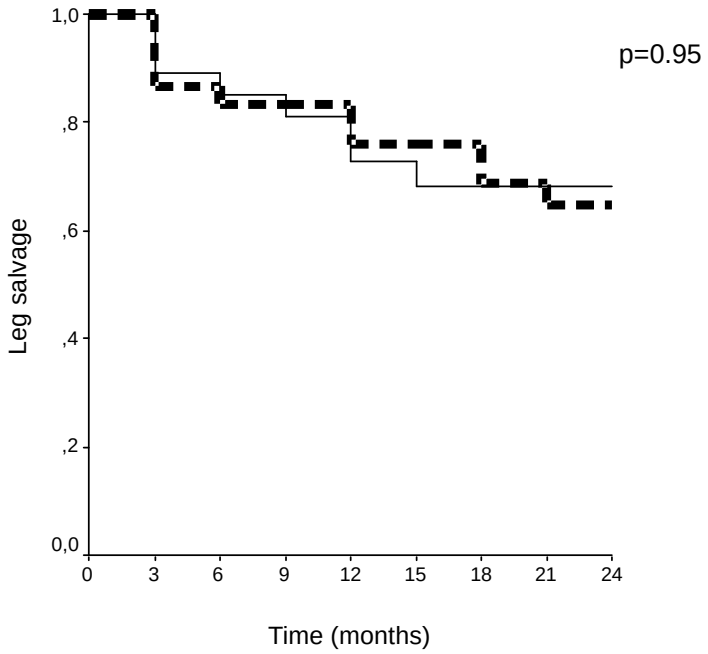
Avf group	31	19	17	16	12	10	9	7	6
Controls	28	19	16	12	11	9	7	7	7



Patients at risk:

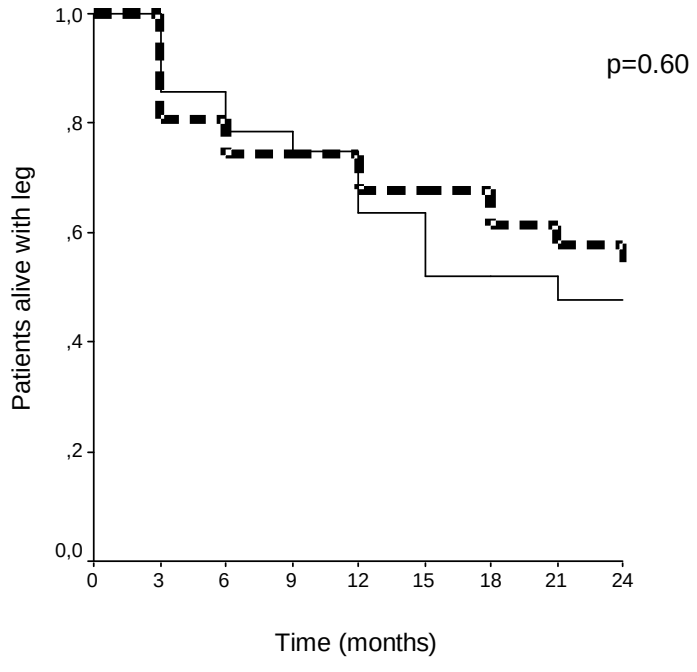
Avf group	31	22	20	19	14	12	11	10	9
Controls	28	21	18	14	13	9	7	7	7

Figure 4. Primary and secondary patency in the av-fistula (- -) and control groups (—). (Study I)



Patients at risk:

Avf group	31	25	23	23	21	21	19	16	14
Controls	28	24	21	20	17	13	12	11	11



Patients at risk:

Avf group	31	25	23	23	21	21	19	16	14
Controls	28	24	21	20	17	13	12	11	11

Figure 5. Leg salvage and patients alive with salvaged limb, av-fistula group (- -), controls (—). (Study I)

Study II

Long-term patency

At three years, the primary and secondary graft patency rates in the av-fistula group were 21% and 24%, and in the control group 33% and 43 %, respectively. The difference did not reach statistical significance. (Tables X & XI)

Table X
Primary patency rates in the av-fistula group and the control group (Study II)

AVF group

Interval (mo)	No. at risk	No. failed	No. withdrawn	Cumulative patency rate	Standard error (%)
0-1	26	5	1	0.81	7.8
1-3	20	2	2	0.72	8.9
3-6	16	1	0	0.68	9.4
6-9	15	3	0	0.54	10.3
9-12	12	2	0	0.45	10.4
12-18	10	2	0	0.36	10.1
18-24	8	1	3	0.32	9.8
24-30	4	1	1	0.21	10.8
30-36	2	0	1	0.21	10.8

Control group

Interval (mo)	No. at risk	No. failed	No. withdrawn	Cumulative patency rate	Standard error (%)
0-1	24	5	1	0.79	8.3
1-3	18	1	0	0.75	8.9
3-6	17	4	0	0.57	10.3
6-9	13	1	0	0.53	10.4
9-12	12	0	1	0.53	10.4
12-18	11	3	0	0.38	10.4
18-24	8	0	1	0.38	10.4
24-30	7	1	1	0.33	10.2
30-36	5	0	0	0.33	10.2

Table XI

Secondary patency rates in the av-fistula group and the control group (Study II)

AVF group

Interval (mo)	No. at risk	No. failed	No. withdrawn	Cumulative patency rate	Standard error (%)
0-1	26	2	1	0.92	5.3
1-3	23	2	2	0.84	7.3
3-6	19	1	0	0.80	8.2
6-9	18	4	0	0.62	10.1
9-12	14	2	0	0.53	10.4
12-18	12	2	0	0.44	10.4
18-24	10	0	3	0.44	10.4
24-30	7	1	2	0.35	11.5
30-36	4	1	1	0.24	12.3

Control group

Interval (mo)	No. at risk	No. failed	No. Withdrawn	Cumulative patency rate	Standard error (%)
0-1	24	3	1	0.88	6.8
1-3	20	1	0	0.83	7.7
3-6	19	3	1	0.69	9.7
6-9	15	1	0	0.65	10.1
9-12	14	0	1	0.65	10.1
12-18	3	4	1	0.43	11.1
18-24	8	0	1	0.43	11.1
24-30	7	0	1	0.43	11.1
30-36	6	0	0	0.43	11.1

Leg salvage

The groups fared equally well as regards leg salvage and survival. Three-year leg salvage was 64% for the av-fistula group and 71% for the control group (p=0.44). At three years, 58% and 54% of the patients were alive, respectively. At five years the survival rate was 49% and 36%, respectively. Altogether 35% and 42% of the patients were alive with a salvaged leg at three years, respectively. (Figure 6)

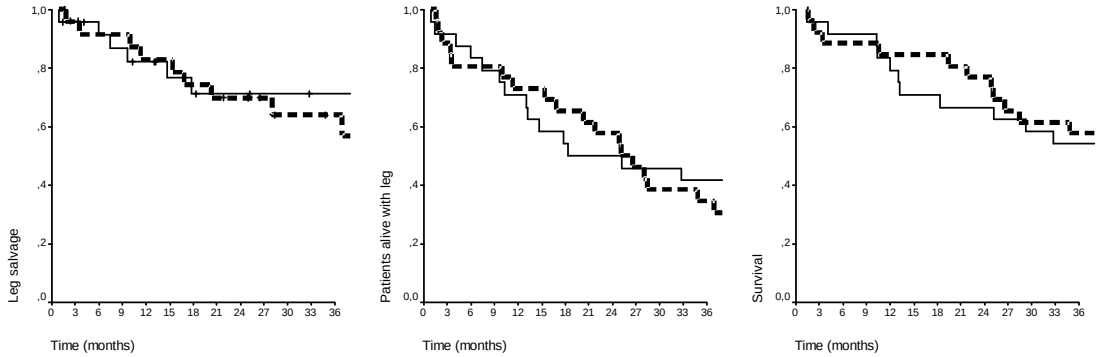


Figure 6. Long-term leg salvage, survival, and patients alive with a salvaged leg: av-fistula group (- - -), controls (——). (Study II)

Haemodynamic measurements

Intraoperative graft flow

The intraoperative graft flow values varied widely, the median being 110 ml/min (range 11-600). There was no significant proximal gradient between systemic and inflow artery blood pressure (mean 7.9 mmHg). There were 8 immediate graft failures (<30 days). The median flow value in the immediate success group was 115 ml/min (range 20-600) compared to 65 ml/min (range 11-250) in the group of 8 failed grafts (p=0.1).

The flow values in patients with an av-fistula were significantly higher (p=0.009) than in the control group (181 vs 80 ml/min). However, when flow directed to the outflow vessel was registered separately with the fistula closed, this difference in outflow values between the groups disappeared (93 vs 80 ml/min, p=0.59). (Figure 7)

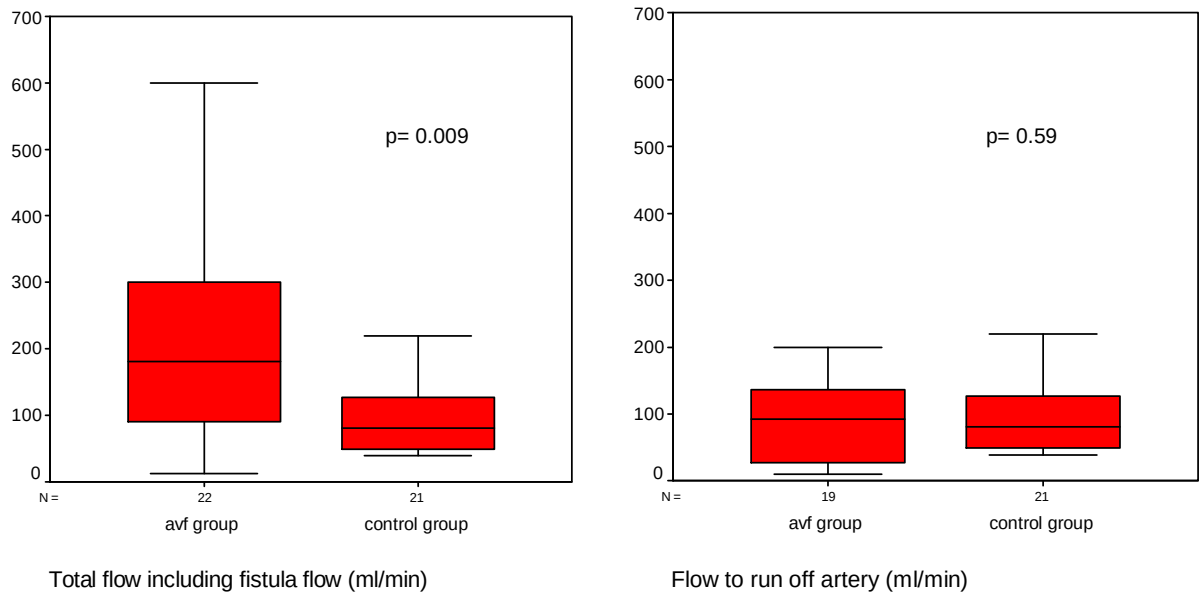


Figure 7. Total graft flow in the av-fistula group and the control group, and flow to the outflow artery, when the av-fistula was temporarily closed in both groups. (Study II)

There was no difference between the patients with or without an av-fistula in terms of maximal flow capacity after papaverin injection (125 vs 131 ml/min, p=0.55). The group of patients with immediately patent grafts responded better to papaverin (131 vs 65 ml/min). This points to a better run-off and thus a better prognosis in terms of patency (p=0.08). (Figure 8)

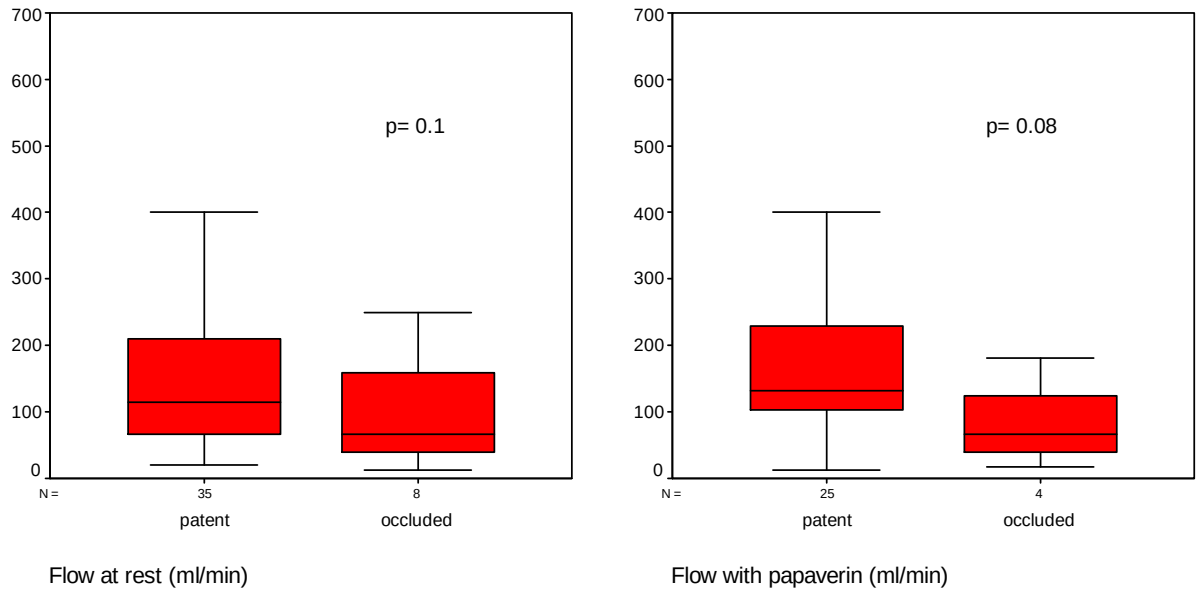


Figure 8. Graft flow at rest and after i.a. injection of papaverin in subsequently patent and occluded grafts. (Study II)

When the flow values were compared to the preoperative run-off scores, no correlation was found (r=0.17, p=0.25).

In the group of patients with an av-fistula the flow values of the failed and patent grafts did not differ (189 vs 115 ml/min, p=0.23). Furthermore, whether most of the flow was directed to the fistula or to the outflow vessel had no effect on patency. When a low flow value of 50 ml/min was used as a cut-off point, patients with a flow level higher than 50 ml/min had significantly better immediate patency than patients with a flow beneath this level (p=0.025).

Postoperative graft flow

In the postoperative duplex surveillance, there was a statistically significant difference in terms of maximum flow velocity (Vmax) between the av-fistula and control groups at one month (104 vs 65 cm/s, p=0.04), which disappeared in the subsequent examinations (82 vs 89.5 cm/s, p=0.83 at three months). When the Vmax values for the grafts that later occluded were compared with the grafts that remained open, there was no statistical difference between the two groups. Under the 12-month surveillance period the median Vmax value for the av-fistula group was 80 cm/s (range 39-200) and 65 cm/s (range 0-

180) in the control group (p=0.08). Median Vmax values for the patent and later occluded grafts were 80 cm/s (30-200) and 70 cm/s (0-180), respectively (p=0.30). (Figure 9)

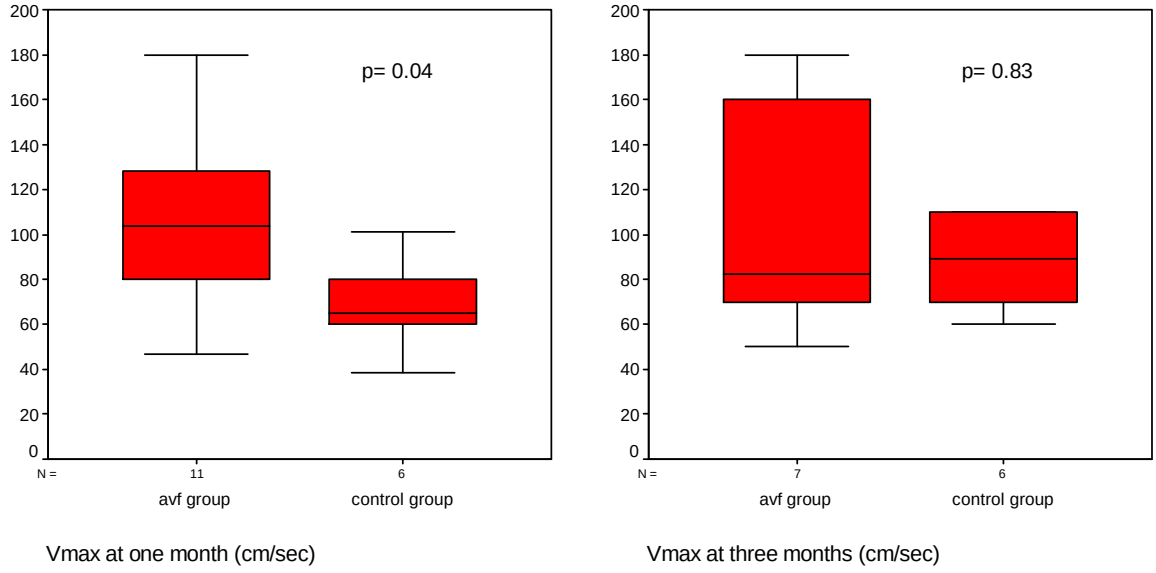


Figure 9. Graft flow in the duplex examination at one and at three months in the av-fistula group and the control group. (Study II)

In the immediate postoperative period, the greater graft flow correlated with the circumference of the leg in the av-fistula group (r= 0.68, p=0.03). This was not observed in later measurements.

Pressure response

An average ABI increase of 0.61 was recorded in the av-fistula group, and of 0.54 in the control group immediately after operation. Toe pressure was increased by an average of 47 and 50 mmHg in both groups, respectively. The ABI increase was similar in the groups of grafts that stayed patent, as well as in those with subsequent early failure (p=0.22).

Adjuvant av-fistula patency

In a subgroup of patients under surveillance for patency of the av-fistula, the graft was found patent in 41% at one year, whereas patency of the fistula was only 30%. At two years 24% of the fistulas were still open, i.e. 40% of the open grafts had an open fistula. (Figure 10)

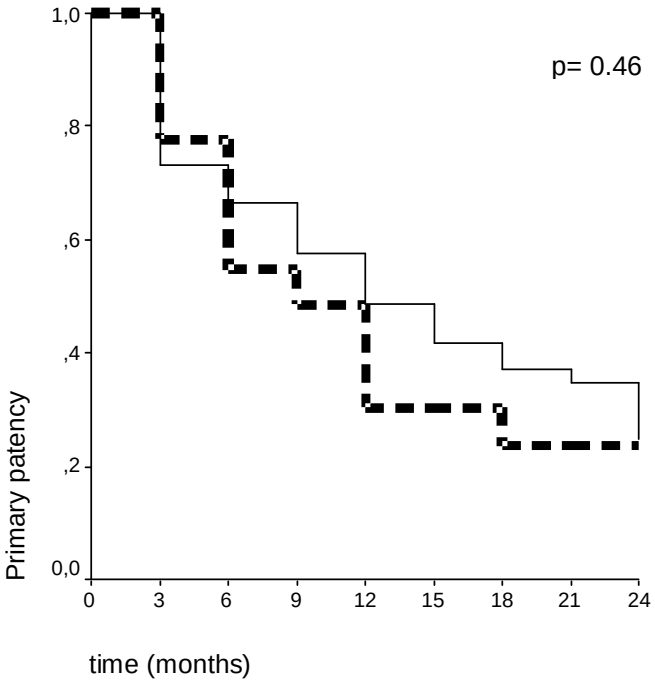


Figure 10. Primary patency of the av-fistula (- -) vs graft patency (—). (Study II)

Table XII
Av-fistula patency rates

Interval (mo)	No. at risk	No. failed	No. withdrawn	Cumulative patency rate	Standard error (%)
0-1	18	1	0	0.94	5.4
1-3	17	4	1	0.72	10.6
3-6	12	3	0	0.54	12.0
6-9	9	2	0	0.42	12.0
9-12	7	2	0	0.30	11.2
12-18	5	1	1	0.24	10.4
18-24	3	0	3	0.24	10.4

Leg circumference

Calf and ankle circumferences were measured at each visit to find out possible oedema caused by the av-fistula. The greatest circumference of the operated leg was compared to that of the non-operated leg to standardise the measurement. The difference between these was the parameter to be followed. In subsequent measurements, the circumference of the operated leg tended to be greater than the preoperative measurement in the av-fistula group, but this difference did not reach statistical significance. When the circumference of the operated leg was compared to that of the non-operated leg at every measurement point, the only difference that was nearly statistically significant was found at 12 months when the difference in circumference was greater in the av-fistula group than in the control group (p=0.05). (Figure 11)

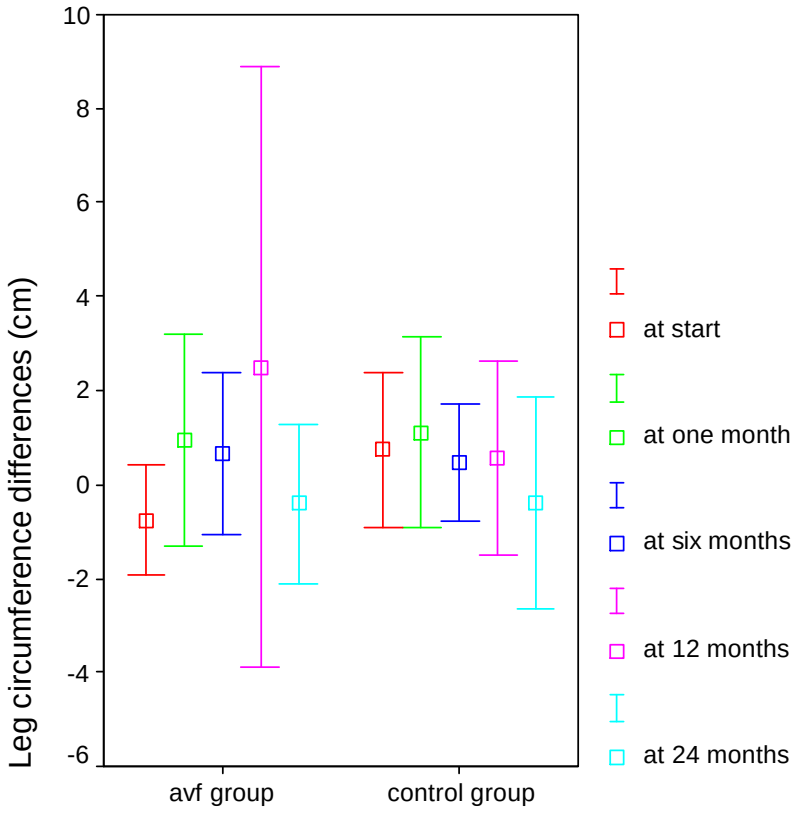


Figure 11. Leg circumference measured in both groups up to 24 months. (Study II)

Adverse effects

One patient with an av-fistula had static excema and swelling in the operated leg. At one month the diameter of the operated leg was 7 cm greater than that of the non-operated leg. At re-operation, the flow in the fistula was found to be 700 ml/min. The patient's

symptoms resolved after closure of the fistula, and the leg circumference returned to the preoperative level.

Study III

Patency of the flap artery and bypass graft

There was one immediate (<30 days) flap failure. Despite the patent bypass graft, the flap artery thrombosed and the flap was lost.

In one patient the vein graft occluded two months after the operation. The graft occlusion led to flap artery occlusion, and later to below knee amputation.

Flap artery and graft patency were thus 78% and 89%, respectively, at two years.

Leg salvage

Two patients underwent below knee amputation in the immediate postoperative period because of persistent infection despite patent grafts and vital flaps. Another major amputation was required due to infection at 13 months.

Altogether four limbs were amputated during the follow-up: in addition to the one limb lost due to flap artery thrombosis, three limbs had to be amputated due to infection. The limb salvage rates at one and two years were 67% and 53% respectively.

Impact of internal fistula on flap artery and bypass graft flow

Median flow through the radial forearm flap while it was still in the arm was 8 ml/min (range 4-12) and it increased to a median of 58 ml/min (range 31-110) after the internal av-fistula was created.

Median vein graft flow prior to flap transfer was 44 ml/min (range 20-60). The vein graft flow increased almost twofold after the radial forearm flap anastomosis, the median flow being 76 ml/min (range 32-105, p=0.016).

The flow through the flap artery after the anastomosis to the foot was 45 ml/min (range 13-108) with the av-fistula open, but when the av-fistula was temporarily closed, the flow was only 9 ml/min (range 3-15). There was no difference in the flow values of the artery of the flap regardless of whether it was on the arm or transplanted to the foot (p=0.43).

The median flows in the bypass graft and in the flap artery were significantly higher (76 ml/min and 45 ml/min, respectively) with a patent fistula than when the fistula was temporarily closed (30 ml/min and 9 ml/min, p=0.016 and p=0.004, respectively).
(Figure 12)

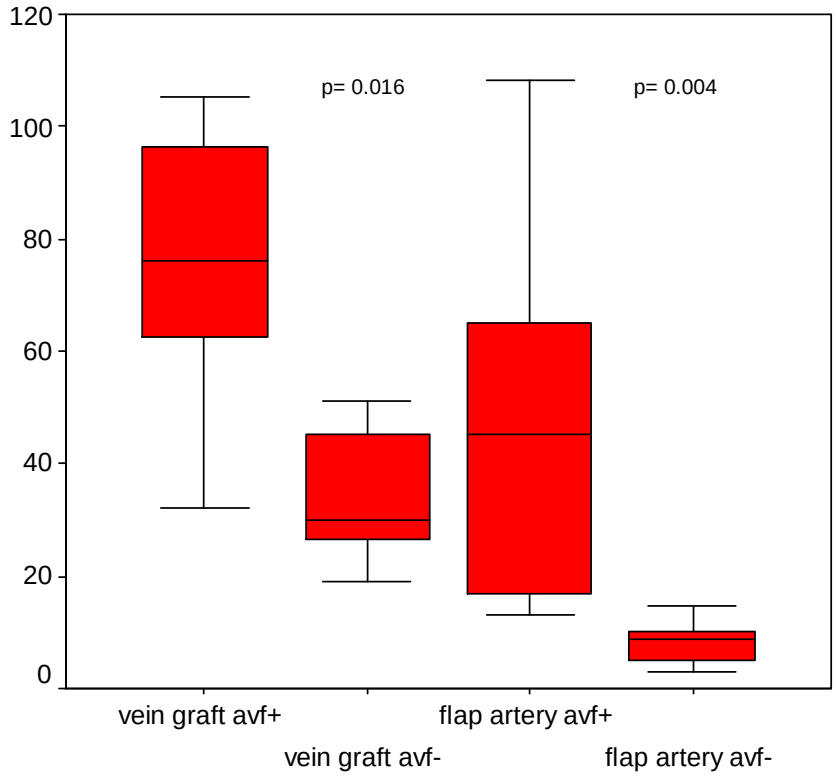


Figure 12. Flow in the vein graft and the flap artery with the internal av-fistula open (+) and temporarily closed (–). (Study III)

Study IV

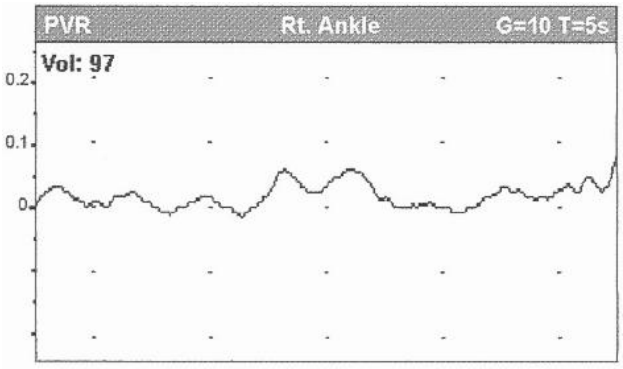
After the completion of a femoropedal bypass, a high flow value for a pedal bypass graft of 200 ml/min was measured with a transit time flowmeter. A completion angiogram revealed poor outflow but a patent vein graft.

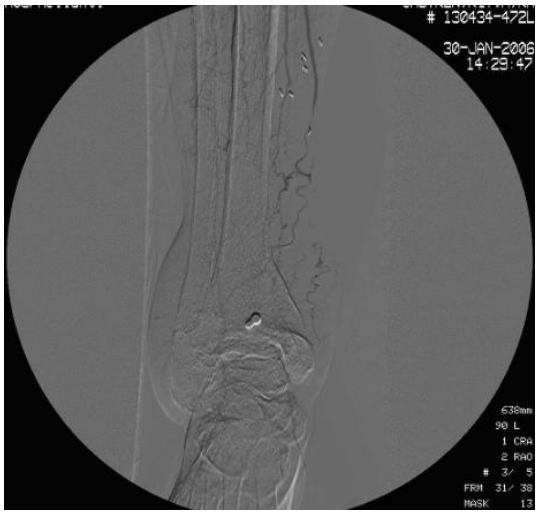
The postoperative ABI was 1.09 and the toe pressure 118 mmHg. A very high amplitude pulse volume recording was seen in the postoperative ABI measurements. (Figure 13)
A high flow of 100 cm/s was measured in the postoperative duplex ultrasonography examination in the bypass graft at one month.

During the follow-up the ABI increase was sustained with ABI of 1.38 and toe pressure of 124 mmHg. The status of the graft was checked with duplex ultrasonography and the graft was found patent with a flow of 70-100 cm/s.

Figure 13. Pre- and postoperative pulse volume recordings and pre- and postoperative angiograpy in the patient in Study IV.

Pre





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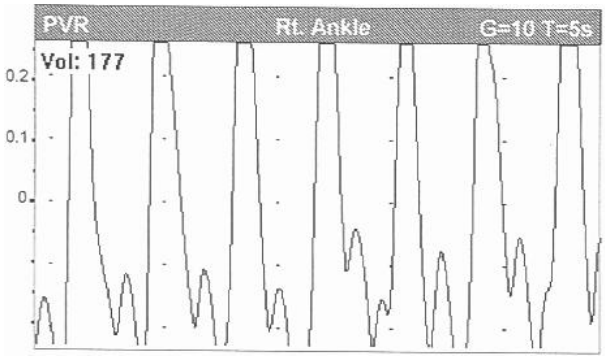
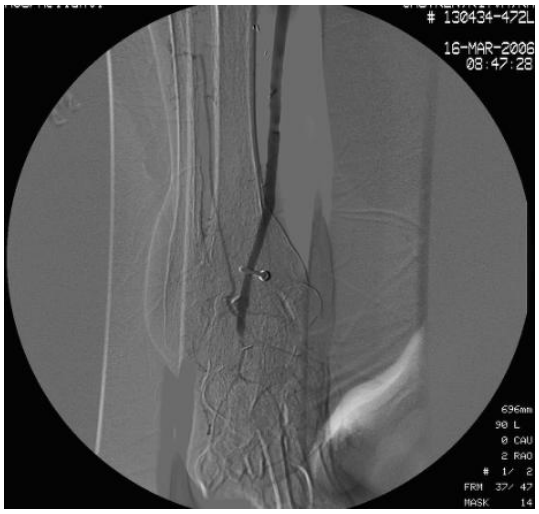




Study V

Patency

There was no difference in patency between the two groups during the follow-up. Primary patency of the vein graft was 61% and 49% at one and three years, respectively, in the av-fistula group, and 57% and 46% in the control group during the same time period. Assisted primary patency and secondary patency were 67% and 75% at one year and 58% and 62% at three years, respectively, for the av-fistula group. Assisted primary patency and secondary patency for the control group were 70% and 71% at one and three years, respectively. (Figure 14)

Leg salvage

The leg salvage rate was 83% and 76% at one year and three years in the av-fistula group compared to the 87% leg salvage rate of the control group. The survival of the patients was 79% and 52% at one and three years, respectively, for the av-fistula group, and 85% and 58% for the control group. Accordingly, the amputation-free survival for the av-fistula group was 64% and 40% at one and three years, and 77% and 54% for the control group in the same time period. (Figure 15)

Impact of run-off score on patency

In the group of patients with an av-fistula, 49 (88%) out of 56 angiographies sufficient for scoring had a run-off score of seven or more. The run-off scores of the control group were similar to those of the av-fistula group. There was no difference in the run-off score between the patients with patent grafts and immediately occluded grafts ($p=0.79$) in either group, nor in the analysis of the whole patient population. When a cut-off value of seven was tested, there was no difference in terms of patency between the patients with the run-off score of at least seven or lower than seven ($p=0.92$). Furthermore, the patients with a completely obstructed pedal arch (giving a run-off score of 10) achieved patency rates equalling those of the rest of the study group.

Pressure response

The median increase in ABI was similar in both groups: 0.6 in the av-fistula group and 0.62 in the control group.

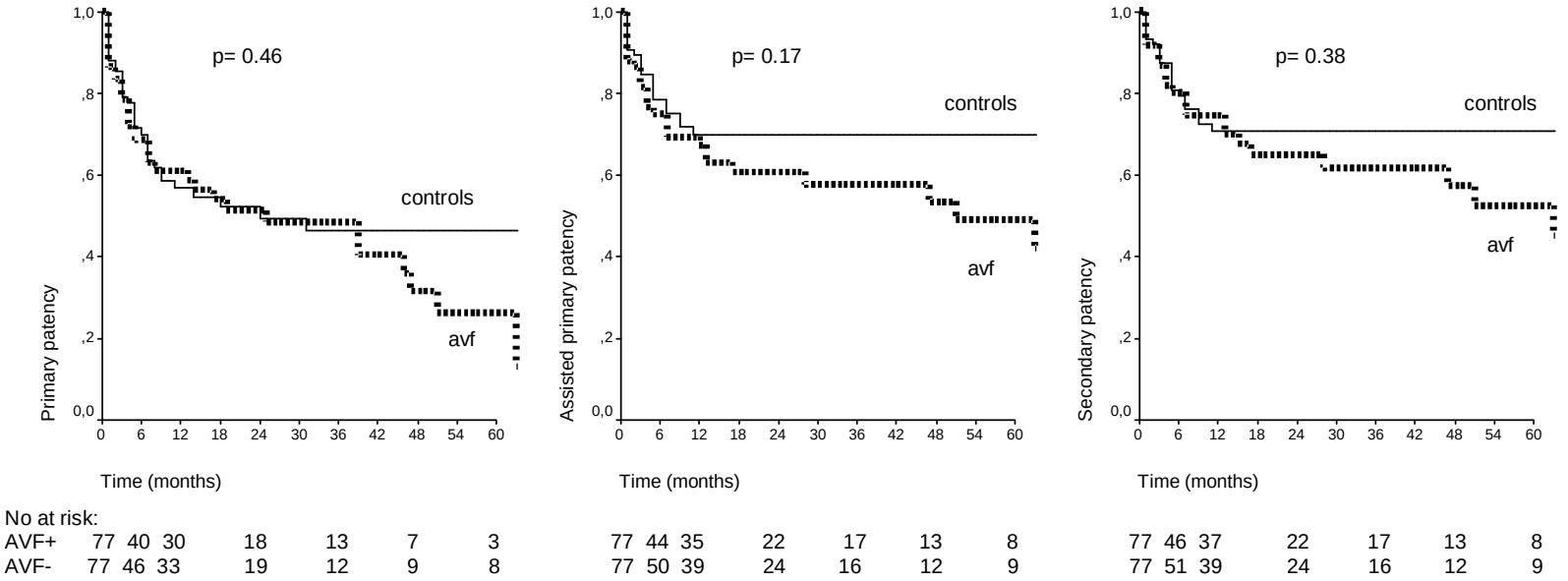
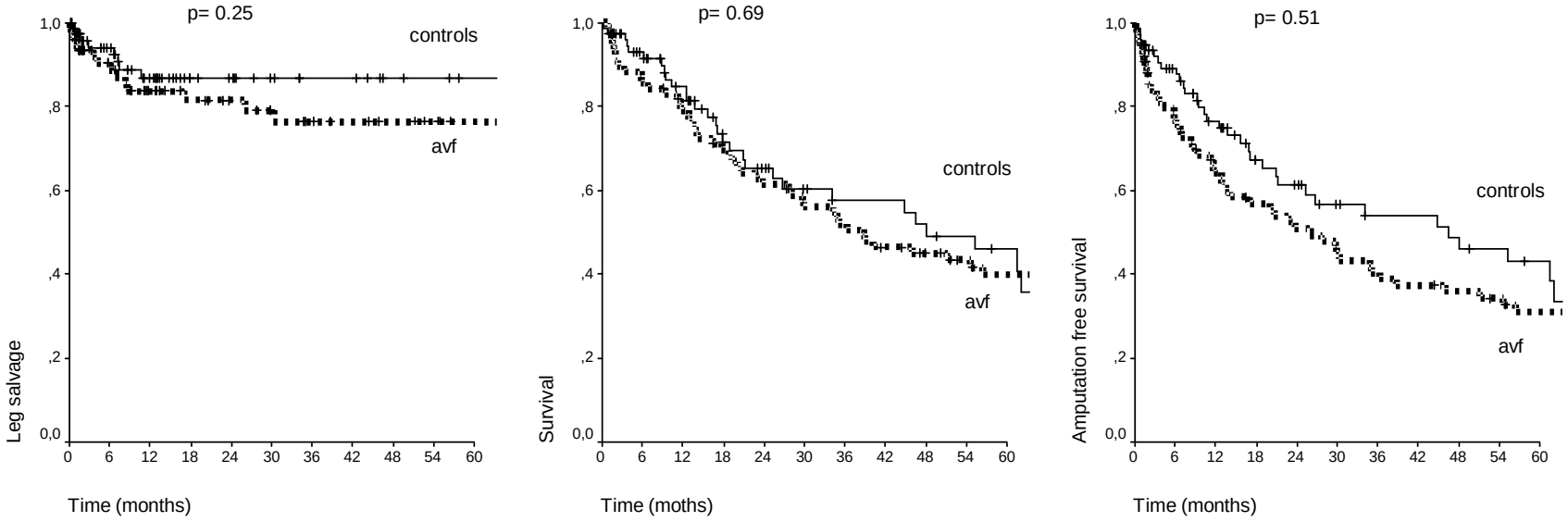


Figure 14. Primary patency, assisted primary patency and secondary patency rates of the av-fistula (- - -) and control groups (——). (Study V)



No at risk:

AVF+	77 54 44	34	27	23	18	77 66 59	45	38	29	22	77 54 44	34	27	23	18
AVF-	77 54 40	25	17	13	10	77 61 49	29	20	17	14	77 59 46	29	20	17	14

Figure 15. Leg salvage, survival and amputation free survival in the av-fistula (- - -) and control groups (——). (Study V)

Flow

The median graft flow after the completion of the fistula was significantly higher in the av-fistula group than the in the control group (110 ml/min (range 10-400) vs 60 ml/min (range 10-176, p=0.001). In a subgroup of 12 patients the flow was measured both prior to the reconstruction of the fistula and after it, giving median flow values of 20 ml/min (range 10-60) and 115 ml/min (range 10-350) respectively. The difference was statistically significant (p=0.003).

Regardless of the av-fistula, after the papaverin-induced vasodilatation, the flow values increased equally in the two groups according to recorded MFC. (Figure 16)

The patency rates did not differ between the pedal and the crural bypasses in either the av-fistula or the control group (p=0.84), even though there was a significant difference in the respective median graft flows (60 ml/min vs 93 ml/min, p=0.003).

The patients whose grafts had failed immediately tended to have lower flow values (29 ml/min vs 80 ml/min, p=0.07). Despite the reconstruction of the fistula, the flow values did not increase in some patients in the group of failed grafts. In the control group, three patients had a low flow value (<20 ml/min) after the completion of the distal anastomosis; this would have been considered an indication to reconstruct an av-fistula in the av-fistula group. However, these patients had, a good vasodilatation response to papaverin.

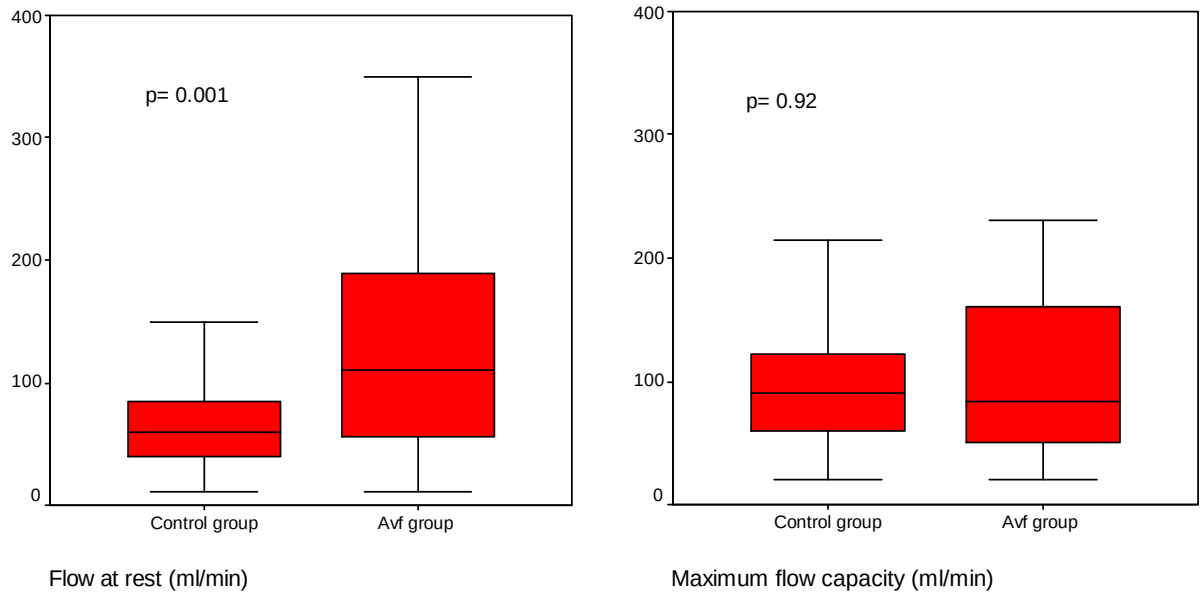


Figure 16. Graft flow in both groups at rest, and the maximum flow capacity after intra-arterial papaverin injection. (Study V)

10. DISCUSSION

10.1 LIMITATIONS OF THE STUDY

Studies I and II: A total of 59 patients were recruited to a randomised prospective trial with strict inclusion and exclusion criteria. This Scandinavian multicentre pilot trial was undertaken to compare a 6 mm PTFE graft with a distal vein cuff, and an adjuvant av-fistula with a similar graft without a fistula. The aim was to find out whether patients with the adjuvant fistula might have better 2-year graft patency and leg salvage, and if so, whether the results would indicate a need to shed light on the causes of the difference in a larger multicentre study with sample size calculations aided by the results of this pilot study. Since there was no difference between the groups at two years, and another study had also revealed similar outcome results (Hamsho et al. 1999), there was no reason to start planning a randomised major scale study despite the possibility of a type two statistical error.

Study III: A novel technique of flap coverage was introduced in this study and therefore the number of patients is very small. The results were presented with the life table analysis, the validity of which is open to criticism in this kind of small series.

Study IV: This study is a case report. Objective observations were made on a single patient, so generalizations cannot be made on the basis of these findings.

Study V: This was the first reported series of vein graft bypasses with an adjuvant av-fistula. Because the series was a retrospective case series with matched controls, it is able to provide level III evidence at best. Due to the small sample size, the study may be prone to a type two statistical error.

10.2 GENERAL DISCUSSION

In suboptimal circumstances, adjunctive methods to improve the outcome are searched. With a prosthetic graft or with poor outflow and a low graft flow, the risk for failure is high. The adjuvant av-fistula is believed to increase graft flow, hopefully to a level that results in improved long-term patency. The av-fistula was first used in combination with thrombogenic prosthetic grafts, and it seemed to improve patency and outcome. In clinical series, augmented graft flow was achieved with hardly any adverse effects. The true effect of the fistula needed to be determined more specifically, however.

Our randomised controlled study revealed that the av-fistula did not improve the outcome of the prosthetic bypass with a distal vein cuff. This was a result which we had not anticipated. Hamsho and coworkers (1999) came to the same conclusion in their randomised study. The distal perfusion was improved in haemodynamic measurements despite the adjuvant fistula, and the flow values were significantly augmented. The distal flow was antegrade, the ABI increased, and only one patient had symptoms indicating adverse effects of venous hypertension. The only significant finding in the flow measurements was, however, that a low flow value below 50 ml/min predicted graft failure and was significant according to the outcome. This applied to both the av-fistula group and the control group.

The patency of the av-fistula was also recorded. These data showed that even when the av-fistula thrombosed, the graft could remain patent. In a patient with a large fistula causing venous stasis, the fistula was ligated without subsequent occlusion. In contrast to the results presented here, Dardik et al. (1991) showed that graft patency was accompanied by fistula patency. They concluded that increased graft flow caused by the fistula aided graft patency. Ascer et al. (1996) reported that the patency of the adjuvant fistula declined. Their interpretation was that in the early phases the fistula patency aided the graft patency and later on despite the thrombosis of the av-fistula, the threshold of the graft to tolerate low flow would increase. The benefit of the fistula on prosthetic graft patency is unclear, as there is no evident clinical benefit to be shown. The higher graft flow might nevertheless help to keep some risky bypasses open long enough for the ischaemic lesions to heal. It is known that some patients, whose skin lesions have healed, may

tolerate graft failure even though operated on for critical ischaemia. This has recently been a commonly used argument to advocate endovascular treatment, although lacking sound evidence and open to serious debate (Lepäntalo et al. 2007). Since the av-fistula does not improve prosthetic graft patency, the only indication to use a prosthetic graft in infrapopliteal bypass surgery would be to avoid amputation in patients who have no autogenous graft material.

Both distal ischaemia causing extensive tissue damage and concurrent infection resulting in microthrombosis decrease the distal outflow bed. This may lead to the development of a very limited outflow tract. The free flap transfer functions as a large av-fistula with open av-shunts due to the vasodilatation caused by the denervation of the flap. The flows in the muscle flaps differ. For instance, the LD flap has a flow of 50 ml/min, and thus it can be seen as a well functioning av-fistula (Lorenzetti et al. 1999). The radial forearm flap acts as a poor av-fistula, and we therefore introduced a new technique by which an internal av-fistula was created within a radial forearm flap. The rationale of this was to decrease the resistance in the poor run-off situation. The low-flow radial forearm flap was transformed into a high-flow flap to augment the bypass graft flow. Acceptable results were achieved in a small patient group: the radial forearm flap doubled the bypass graft flow. In a previous series of Lorenzetti et al. (2001) the latissimus dorsi musculocutanous flap increased the graft flow by 50%. The LD flap is a high-flow muscle flap, but a radial forearm flap with an internal av-fistula functioned as an even better av-fistula by increasing the graft flow by 100%.

The free flap transfer has, however, also other properties by which it affects the outcome. The ingrowth of the flap results in a microcirculatory capillary network that improves the outflow bed. The flap carries nutrients and antibiotics to the infected wound bed and thus aids in the wound healing (Mimoun et al. 1989).

The published studies have shown that free flap transfer in combination with a vascular bypass augments graft flow intraoperatively (Lorenzetti et al. 2001). The long-term effect of a free flap, however, has not been assessed thus far. In our case report the effect of a free flap transfer performed 13 years earlier was recorded. The preoperative angiogram visualised almost no outflow bed, and despite this, a very high bypass graft flow and pulse volume recordings indicating a large av-fistula were achieved. The LD flap had grown into

the recipient wound bed forming a capillary network which functioned as a large av-fistula enabling a high graft flow.

The free flap transfer may have the positive effects of an adjuvant av-fistula without the adverse effects of the latter. The denervated free flap causes vasodilatation and reduced resistance, leading to improved bypass graft flow. The negative effects of an av-fistula such as steal or venous hypertension are not, however, encountered because the free flap functions as a transplanted organ with its own circulatory bed. In selected cases the free flap transfer may therefore be significant to the patient by increasing the bypass graft flow sufficiently to result in leg salvage.

Despite the development and possibilities of imaging techniques, the outflow bed of a distal bypass cannot be accurately determined. The flow in very small arteries can be identified by the duplex technique. However, this technique is not able to give an exact morphological image. Whenever contrast media is used, whether in digital subtraction angiography (DSA), computer tomographic angiography (CTA) or magnetic resonance angiography (MRA), there is a possibility that not all vessels are visualised due to wrong timing, arterial spasm, low concentration of the contrast media or other technical problems (Hingorani et al. 2007). Four-planar DSA is imperative for obtaining the best possible data on pedal vasculature. The assessment of the outflow is as accurate as the imaging technique. The outflow is unfortunately one of the main determinants of outcome, so an exact image would help in the planning of a bypass.

Due to problems in imaging techniques, there are clinical situations in which the status at the operation is worse than anticipated. Consequently, means of rescue are needed to avoid immediate vein graft failure. It can, of course, be questioned whether this is due to poor patient selection. However, in these situations an adjuvant av-fistula again may offer an option to achieve better flow and thus possibly a better outcome. There are no previous reports of an adjuvant av-fistula in combination with venous bypass, and this is partly because a vein graft tolerates relatively low flow.

In these extremely poor situations encountered in our clinical series, we attempted to achieve better results by using an adjuvant fistula. The results obtained with the av-fistula group were promising with relatively good patency and leg salvage, taking into account the

outflow status. There was, however, no significant difference between these patients and the matched controls in regard to either patency or leg salvage. Even in a patient group with poor run-off, acceptable long-term patency and leg salvage was achieved. This justifies the active policy concerning the use of infrapopliteal autogenous bypass in the study centres.

Vein grafts may remain patent even with very low flow, as demonstrated by Stirnemann et al. (1994). In Sauvage's experimental study, an arterial allograft stayed patent even with no flow (1979). Intraoperative flow values of crural bypasses were predictive of outcome in a study by Albäck et al. (2000), but no significant cut-off value was found for pedal bypasses. This may reflect the difficulty to determine the outflow potential of very distal bypasses. The large muscles in the crural area provide an additional outflow bed, which is not present in the pedal area.

Dardik and his coworkers reserve the use of an adjuvant fistula to human umbilical vein bypasses to a limited outflow in the crural area. The compliant HUV prosthesis is proposed to perform better than a noncompliant PTFE, and thus give better results. The compliance of a graft is therefore suggested to be critical to patency. Because autogenous veins are compliant, an adjunctive fistula in these bypasses would rarely be necessary, but in selected cases it might prevent failure according to Dardik et al. (2007).

The angiographic run-off score did not predict patency in our study, as even grafts with an extremely poor angiographic score and occluded pedal arch stayed patent. The quality of the angiographic images may, of course, be questioned, as four-planar images were not available on the outflow tract at the foot level during the study period. Additionally, angiographic images provide only morphological information, which cannot be directly interpreted as a functional measure of the distal arterial tree.

Intraoperative flow and peripheral resistance may provide better assessment of the true run-off capacity. In their study, Peterkin et al. (1988) found that the peripheral resistance correlated, to a limited extent, with the angiographic images. They observed that a number grafts stayed patent despite limited run-off in angiography and high peripheral resistance. In contrast, Lundell and Bergqvist (1993) found a high peripheral resistance and low flow to be predictive of graft failure. In our present study the graft flow was significantly

increased in the intraoperative flow measurements in the group with the fistula. The maximal outflow capacity was, however, equal in the two groups despite the av-fistula. The flow in the group of failed grafts was lower than in the grafts that stayed patent. It thus seemed that a high enough rest flow and the vasodilatation effect predicted good patency. A good response in maximal flow capacity measurements caused by an intra-arterial injection of papaverin predicted graft patency in a study by Albäck et al. (2000). Davies and coworkers (1993) also used the maximal flow value and found that patients with a good haemodynamic response had a better outcome. In our study, it was obvious that the adjuvant av-fistula augmented the graft flow in intraoperative measurements, but this did not result in clinical benefit. The vasodilatation effect was equal in both groups, possibly indicating that the outflow bed has a certain capacity beyond which it cannot be manipulated by adjunctive measures. The papaverin response might therefore be the best predictor of graft patency, as it seems to reflect the maximal outflow capacity of the bypass.

With the caveat of statistical type II error, it seems that an adjuvant av-fistula does not offer any benefit on the outcome of either prosthetic or autologous vein bypass grafting.
The internal av-fistula in a free flap transfer or a large free flap function in a manner similar to that of an av-fistula, i.e. they increase the outflow bed and thus the bypass graft flow. There is no evidence, however, on the true effect of the free flap on graft patency, which should be determined in a larger scale study with flow measurements and long-term follow up. Enormous effort would be needed to launch and follow through a randomised multicentre study with a large number of patients in order to determine the effect of an av-fistula on bypass grafting with statistically valid results. Because these patients are rather infrequent, managing such a study would be unrealistic.

11. CONCLUSIONS

1. An adjuvant av-fistula does not improve the patency of a femorocrural PTFE bypass with a distal vein cuff.

2. In combination with a prosthetic bypass the av-fistula increases the flow values both in the intraoperative measurements and during immediate postoperative surveillance. This increase in flow values does not, however, bring clinical benefit. Low intraoperative flow and a poor papaverin response may predict poor graft patency. The reconstruction of an adjuvant fistula caused marked adverse effects in only one patient, and after fistula closure the symptoms resolved.

3. In a group of diabetic patients a radial forearm flap with an internal av-fistula markedly increased the bypass graft flow. This method can be useful in selected cases with poor run-off and large ischaemic lesions.

4. A free muscle flap connected to a vascular bypass graft functions as a large av-fistula, circulating blood at a high velocity through the bypass graft. Consequently the distal perfusion is improved.

5. The adjuvant av-fistula increases graft flow significantly in a poor outflow venous bypass. Regardless of this, the av-fistula does not improve the outcome. This result is in agreement with our results achieved with an av-fistula and a prosthetic graft.

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13. REFERENCES

Abou-Zamzam AM Jr, Moneta GL, Lee RW, Nehler MR, Taylor LM Jr, Porter JM. Peroneal bypass is equivalent to inframalleolar bypass for ischemic pedal gangrene. Arch Surg. 1996; 131: 894-898.

Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, Fowkes FGR, Gillespie I, Ruckley CV, Raab G, Storkey H; Basil trial participants. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet 2005; 366(9501): 1925-1934.

Albäck A, Biancari F, Saarinen O, Lepäntalo M. Prediction of the immediate outcome of femoropopliteal saphenous vein bypasses by angiographic runoff score. Eur J Vasc Endovasc Surg. 1998; 15: 220-224.

Albäck A, Lepäntalo M. Immediate occlusion of in situ saphenous vein bypass grafts: a survey of 329 reconstructions. Eur J Surg. 1998; 164: 745-750.

Albäck A, Mäkisalo H, Nordin A, Lepäntalo M. Validity and reproducibility of transit time flowmetry. Ann Chir Gynaecol. 1996; 85: 325-331.

Albäck A, Roth W-D, Ihlberg L, Biancari F, Lepäntalo M. Preoperative angiographic score and intraoperative flow as predictors of the mid-term patency of infrapopliteal bypass grafts. Eur J Vasc Endovasc Surg. 2000; 20: 447-453.

Anderson CB, Stevens SL, Allen BT, Sicard GA. In situ saphenous vein for lower extremity revascularization. Surgery. 1992; 112: 6-10.

Andros G, Harris RW, Salles-Cunha SX, Dulawa LB, Oblath RW. Lateral plantar artery bypass grafting: defining the limits of foot revascularization. J Vasc Surg. 1989; 10: 511-519.

Andros G. Diagnostic and therapeutic arterial interventions in the ulcerated diabetic foot. Diabetes Metab Res Rev. 2004; 20 Suppl 1:S29-33.

Ascer E, Gennaro M, Pollina RM, Ivanov M, Yorkovich WR, Ivanov M, Lorensen E. Complementary distal arteriovenous fistula and deep vein interposition: a five-year experience with a new technique to improve infrapopliteal prosthetic bypass patency. J Vasc Surg. 1996; 24: 134-143.

Ascer E, Veith FJ, Gupta SK. Bypasses to plantar arteries and other tibial branches: An extended approach to limb salvage. J Vasc Surg. 1988; 8: 434-441.

Ascer E, White SA, Veith FJ, Morin L, Freeman K, Gupta SK. Outflow resistance measurement during infrainguinal arterial reconstructions: a reliable predictor of limb salvage. Am J Surg. 1987; 154: 185-188.

Aulivola B, Pomposelli FB. Dorsalis pedis, tarsal and plantar artery bypass. J Cardiovasc Surg. 2004; 45: 203-212.

Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment Trialists' (CTT) collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005; 366(9493): 1267-1278.

Baldwin ZK, Pearce BJ, Curi MA, Desai TR, McKinsey JF, Bassiouny HS et al. Limb salvage after infrainguinal bypass graft failure. J Vasc Surg. 2004; 39: 951-957.

Ballotta E, Renon L, Toffano M, Da Giau G. Prospective randomized study on bilateral above-knee femoropopliteal revascularization: polytetrafluoroethylene graft versus reversed saphenous vein. J Vasc Surg. 2003; 38: 1051-1055.

Belch JJF, Dormandy J, Biasi G, Cairols M, Diehm C, Eikelboom B et al. Clopidogrel and Acetylsalicylic acid in bypass Surgery for Peripheral Arterial disease: Results of the CASPAR Trial. Preprint 2007.

Belkin M, Conte MS, Donaldson MC, Mannick JA, Whittemore AD. Preferred strategies for secondary infrainguinal bypass. Lessons learned from 300 consecutive reoperations. J Vasc Surg. 1995; 21: 282-295.

Belkin M, Knox J, Donaldson MC, Mannick JA, Whittemore AD. Infrainguinal arterial reconstruction with nonreversed greater saphenous vein. J Vasc Surg. 1996, 24: 957-962.

Bergamini TM, George SM, Massey HT, Henke PK, Klamer TW, Lambert GE Jr et al. Pedal or peroneal bypass: which is better when both are patent? J Vasc Surg. 1994; 20: 347-355.

Bergamini TM, Towne JB, Bandyk DF, Seabrook GR, Schmitt DD. Experience with in situ saphenous vein bypasses during 1981 to 1989: determinant factors of long-term patency. J Vasc Surg. 1991; 13: 137-147.

Biancari F, Albäck A, Ihlberg L, Kantonen I, Luther M, Lepäntalo M. Angiographic runoff score as a predictor of outcome following femorocrural bypass surgery. Eur J Vasc Endovasc Surg. 1999a; 17: 480-485.

Biancari F, Albäck A, Kantonen I, Luther M, Lepäntalo M. Predictive factors for adverse outcome of pedal bypasses. Eur J Vasc Endovasc Surg. 1999b; 18: 138-143.

Biancari F, Kantonen I, Albäck A, Ihlberg L, Lehtola A, Lepäntalo M. Popliteal-to-distal bypass grafts for critical leg ischaemia. J Cardiovasc Surg. 2000a; 41: 281-286.

Biancari F , Kantonen I, Albäck A, Mätzke S, Luther M, Lepäntalo M. Limits of infrapopliteal bypass surgery for critical leg ischemia- When not to reconstruct. World J Surg. 2000b; 24: 727-733.

Biancari F, Kantonen I, Mätzke S, Albäck A, Roth WD, Edgren J, Lepäntalo M. Infrainguinal endovascular and bypass surgery for critical leg ischemia in patients on long-term dialysis. Ann Vasc Surg. 2002;16: 210-4.

Biancari F, Railo M, Lundin J, Albäck A, Kantonen I, Lehtola A, Lepäntalo M. Redo bypass surgery to the infrapopliteal arteries for critical leg ischaemia. Eur J Vasc Endovasc Surg. 2001;21: 137-142.

Biancari F, Salenius JP, Heikkinen M, Luther M, Ylönen K, Lepäntalo M. Risk-scoring method for prediction of 30-day postoperative outcome after infrainguinal surgical revascularization for critical lower-limb ischemia: a Finnvasc registry study. World J Surg. 2007; 31: 217-225.

Blankensteijn JD, Gertier JP, Brewster DC, Cambria RP, LaMuraglia GM, Abbott WM. Intraoperative determinants of infrainguinal bypass graft patency: A prospective study. Eur J Vasc Endovasc Surg. 1995; 9: 375-382.

Briggs SE, Banis JC Jr, Kaebnick H, Silverberg B, Acland RD. Distal revascularization and microvascular free tissue transfer: an alternative to amputation in ischemic lesions of the lower extremity. J Vasc Surg. 1985; 2: 806-811.

Burger DHC, Kappetein AP, van Bockel JH, Breslau PJ. A prospective randomised trial comparing vein with polytetrafluoroethylene in above-knee femoropopliteal bypass grafting. J Vasc Surg. 2000; 32: 278-283.

Burns P, Gough S, Bradbury AW. Management of peripheral arterial disease in primary care. BMJ 2003; 326(7389): 584-588.

Bush HL Jr, Corey CA, Nabseth DC. Distal in situ saphenous vein grafts for limb salvage. Increased operative blood flow and postoperative patency. Am J Surg. 1983;145: 542-548.

CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet. 1996; 348(9038):1329-1339.

Carsten CG 3rd, Taylor SM, Langan EM 3rd , Crane MM.. Factors associated with limb loss despite a patent infrainguinal bypass graft. Am Surg. 1998; 64: 33-37.

Chang BB, Leopold PW, Kupinski AM, Kaufman L, Leather RP, Shah DM. In situ bypass hemodynamics. The effect of residual A-V fistulae. J Cardiovasc Surg. 1989; 30: 843-847.

Chang BB, Paty PS, Shah DM, Leather RP. The lesser saphenous vein: an underappreciated source of autogenous vein. J Vasc Surg. 1992; 15: 152-156; discussion 156-157.

Chen LE, Seaber AV, Bossen E, Urbaniak JR. The effect of acute denervation on the microcirculation of skeletal muscle: rat cremaster model. J Orthop Res. 1991; 9: 266-274.

Cheshire NJ, Noone MA, Wolfe JH. Re-intervention after vascular surgery for critical leg ischaemia. Eur J Vasc Surg. 1992; 6: 545-550.

Chew DK, Conte MS, Donaldson MC, Whittemore AD, Mannick JA, Belkin M. Autogenous composite vein bypass for infrainguinaal arterial reconstruction. J Vasc Surg. 2001; 33: 259-265.

Chew DK, Owens CD, Belkin M, Donaldson MC, Whittemore AD, Mannick JA, Conte MS. Bypass in the absence of ipsilateral greater saphenous vein: safety and superiority of the contralateral greater saphenous vein. J Vasc Surg. 2002; 35: 1085-1092.

Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung and Blood Institute; National High Blood Pressure Education Progman Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42: 1206-1252.

Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systemic review. JAMA 2003; 290: 86-97.

Clagett GP, Sobel M, Jackson MR, Lip GY, Tangelder M, Verhaeghe R. Antithrombotic therapy in peripheral arterial occlusive disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004; 126(3 Suppl):609S-626S.

Cole JS, Watterson JK, O'Reilly MJG. Is there a haemodynamic advantage associated with cuffed arterial anastomoses? J Biomech. 2002; 35: 1337-1346.

Collaborative overview of randomised trials of antiplatelet therapy--II: Maintenance of vascular graft or arterial patency by antiplatelet therapy. Antiplatelet Trialists' Collaboration. BMJ. 1994; 308(6922): 159-168.

Connors JP, Walsh DB, Nelson PR, Powell RJ, Fillinger MF, Zwolak RM, Cronenwett JL. Pedal branch artery bypass: a viable limb salvage option. J Vasc Surg. 2000; 32: 1071-1079.

Cronenwett JL, McDaniel MD, Zwolak RM, Walsh DB, Schneider JR, Reus WF, Colen LB. Limb salvage despite extensive tissue loss. Free tissue transfer combined with distal revascularization. Arch Surg. 1989; 124: 609-615.

Curi MA, Skelly CL, Woo DH, Desai TR, Katz D, McKinsey JF, Bassiouny HS, Gewertz BL, Schwartz LB. Long-term results of infrageniculate bypass grafting using all-autogenous composite vein. Ann Vasc Surg. 2002;16: 618-623.

D'Andrea V, Lepäntalo M, Kantonen I, Biancari F, DiMatteo FM, Bartolucci R, Spyrou M, de Antoni E. Adjuvant arteriovenous fistula in infrapopliteal bypasses. G Chir. 1998; 19: 117-119.

Dagher NN, Modrall JG. Pharmacotherapy before and after revascularization: anticoagulation, antiplatelet agents, and statins. Semin Vasc Surg. 2007 ; 20: 10-14.

Dardik H. The second decade of experience with the umbilical vein graft for lower-limb revascularization. Cardiovasc Surg. 1995; 3: 265-269.

Dardik H. Regarding " Adjuvant arteriovenous fistula as a means of rescue for infrapopliteal venous bypass with poor runoff ". J Vasc Surg. 2007; 45: 1091.

Dardik H, Silvestri F, Alasio T, Berry S, Kahn M, Ibrahim IM, Sussman B, Wolodiger F. Improved method to create the common ostium variant of the distal arteriovenous fistula for enhancing crural prosthetic graft patency. J Vasc Surg. 1996; 24: 240-248.

Dardik H, Berry SM, Dardik A, Wolodiger F, Pecoraro J, Ibrahim IM, Kahn M, Sussman B. Infrapopliteal prosthetic graft patency by use of the distal adjunctive arteriovenous fistula. J Vasc Surg. 1991; 13: 685-691.

Dardik H, Wengerter K, Qin F, Pangilinan A, Silvestri F, Wolodiger F, Kahn M, Sussman B, Ibrahim IM. Comparative decades of experience with glutaraldehyde-tanned human umbilical cord vein graft for lower limb revascularization: An analysis of 1275 cases. J Vasc Surg. 2002; 35: 64-71.

Darling RC 3rd, Chang BB, Paty PSK, Lloyd WE, Leather RP, Shah DM. Choice of peroneal or dorsalis pedis artery bypass for limb salvage. Am J Surg. 1995; 170: 109-112.

Davidson JT, Callis JT. Arterial reconstruction of vessels in the foot and ankle. Ann Surg. 1993; 217: 699-708.

Davies AH, Hawdon AJ, Sydes MR, Thompson SG, on behalf of the VGST Participants. Is Duplex surveillance of value after leg vein bypass grafting? Principal results of the vein graft surveillance randomised trial (VGST). Circulation. 2005; 112: 1985-1991.

Davies AH, Magee TR, Baird RN, Horrocks M. Intraoperative measurement of vascular graft resistance as a predictor of early outcome. Br J Surg. 1993; 80: 854-857.

Davies AH, Magee TR, Parry R, Horrocks M, Baird RN. Evaluation of distal run-off before femorodistal bypass. Cardiovasc Surg. 1996; 4: 161-164.

Desai TR, Meyerson SL, Skelly CL, MacKenzie KS, Bassiouny HS, Katz D, McKinsey JF, Gewertz BL, Schwartz LB. Patency and limb salvage after infrainguinal bypass with severely compromised ("blind") outflow. Arch Surg. 2001; 136: 635-642.

Diehm N, Shang A, Silvestro A, Do DD, Dick F, Schmidli J, Mahler F, Baumgartner I. Association of cardiovascular risk factors with pattern of lower limb atherosclerosis in 2659 patients undergoing angioplasty. Eur J Vasc Endovasc Surg. 2006; 31: 59-63.

Donaldson MC, Mannick JA, Whittemore AD. Causes of primary graft failure after in situ saphenous vein bypass grafting. J Vasc Surg. 1992; 15: 113.118.

Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene Am, Tan MH, Lefebre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Koranyi L, Laakso M, Mokan M, Norkus A, Pirags V, Podar T, Scheen A, Scherbaum W, Schernthaner G, Schmitz O, Skrha J, Smith U, Taton J; PROactive investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial. Lancet 2005; 366(9493): 1279-1289.

Dormandy JA, Murray GD. The fate of the claudicant- A prospective study of 1969 claudicants. Eur J Vasc Surg 1991; 5: 131-133.

Dorweiler B, Neufang A, Schmiedt W, Oelert H. Pedal arterial bypass for limb salvage in patients with diabetes mellitus. Eur J Vasc Endovasc Surg. 2002; 24: 309-313.

Dutch Bypass Oral anticoagulants or Aspirin (BOA) Study Group. Efficacy of anticoagulants compared with aspirin after infrainguinal bypass surgery (The Dutch Bypass Oral anticoagulants or Aspirin Study): a randomised trial. Lancet. 2000; 355: 346-351.

Eagleton MJ, Ouriel K, Green RM. Femoral-infrapopliteal bypass with prosthetic grafts. Surgery. 1999; 126: 759-764.

Eckstein HH, Schumacher H, Maeder N, Post S, Hupp T, Allenberg JR. Pedal bypass for limb-threatening ischaemia: an 11-year review. Br J Surg. 1996; 83:1554-1557.

Eickhoff JH, Broome A, Ericsson BF, Buchardt Hansen HJ, Mouritzen C, Kvernebo K et al. Four years' results of a prospective, randomised clinical trial comparing polytetrafluoroethylene and modified human umbilical vein for below-knee femoropopliteal bypass. J Vasc Surg. 1987; 6: 506-511.

Engelberts I, Tordoir JHM, Schreij G. High-output cardiac failure due to excessive shunting in a hemodialysis access fistula: an easily overlooked diagnosis. Am J Nephrol. 1995; 15: 323-326.

Eskelinen E, Lepäntalo M, Hietala EM, Sell H, Kauppila L, Maenpaa I et al. Lower limb amputations in Southern Finland in 2000 and trends up to 2001. Eur J Vasc Endovasc Surg. 2004;27:193-200.

Eslami MH, Belkin M, Mannick JA, Whittemore AD, Donaldson MC. Optimal methods for autogenous bypass to the anterior tibial artery. Am J Surg. 1997; 174: 198-201.

Faries PL, Arora S, Pomposelli FB Jr, Pulling MC, Smakowski P, Rohan DI, Gibbons GW, Akbari CM, Campbell DR, LoGerfo FW. The use of arm vein in lower-extremity revascularization: results of 520 procedures in eight years. J Vasc Surg. 2000; 31: 50-59.

Feinberg RL, Winter RP, Wheeler JR, Gregory RT, Snyder SO, Gayle RG, Parent FN, Adcock GD. The use of composite grafts in femorocrural bypasses performed for limb salvage: A review of 108 consecutive cases and comparison with 57 in situ saphenous vein bypasses. J Vasc Surg. 1990; 12: 257-263.

Fisher RK, How TW, Bakran A, Brennan JA, Harris PL. Outflow distribution at the distal anastomosis of infrainguinal bypass grafts. J Biomech. 2004; 37: 417-420.

Flinn WR, Rohrer MJ, Yao JST, McCarthy WJ, Fahey VA, Bergan JJ. Improved long-term patency of infragenicular polytetrafluoroethylene grafts. J Vasc Surg. 1988; 7: 685-690.

Fontaine R, Klm M, Kieny R. Die chirurgische behandlungen der peripheren durchblutnungsstörungen. Helv Chir Acta.1955; 36: 499-533.

Frankini AD, Pezzella MW. Foot revascularization in patients with critical limb ischemia. Rev Port Cir Cardiotorac Vasc. 2003; 10: 75-81.

Friedman SG, Safa TK. Pedal branch arterial bypass for limb salvage. Am Surg. 2002; 68: 446-448.

Gentile AT, Lee RW, Moneta GL, Taylor LM, Edwards JM, Porter JM. Results of bypass to the popliteal and tibial arteries with alternative sources of autogenous vein. J Vasc Surg. 1996; 23: 272-279.

Gloviczki P, Bower TC, Toomey BJ, Mendonca C, Naessens JM, Schabauer AM et al. Microscope-aided pedal bypass is an effective and low-risk operation to salvage the ischemic foot. Am J Surg. 1994; 168: 76-84. Review.

Gooden MA, Gentile AT, Mills JL, Berman SS, Demas CP, Reinke KR, Hunter GC. Free tissue transfer to extend the limits of limb salvage for lower extremity tissue loss. Am J Surg. 1997; 174: 644-649.

Goshima KR, Mills JL, Hughes JD. A new look at the outcomes after infrainguinal bypass surgery: traditional reporting standards systematically underestimate the expenditure of effort required to attain limb salvage. J Vasc Surg. 2004; 39: 330-335.

Greenwald LL, Comerota AJ, Mitra A, Grosh JD, White JV. Free vascularized tissue transfer for limb salvage in peripheral vascular disease. Ann Vasc Surg. 1990; 4: 244-254.

Gwynn BR, Shearman CP, Simms MH. Anastomotic arteriovenous fistulae- Are they worth it? Eur J Vasc Surg. 1988; 2: 71-76.

Hamsho A, Nott D, Harris PL. Prospective randomized trial of distal arteriovenous fistula as an adjunct to femoro-infrapopliteal PTFE bypass. Eur J Vasc Endovasc Surg. 1999; 17: 197-201.

Harris PL, Bakran A, Loai E, Nott DM. ePTFE grafts for femoro-crural bypass- Improved results with combined adjuvant venous cuff and arteriovenous fistula? Eur J Vasc Surg. 1993a; 7: 528-533.

Harris PL, Veith FJ, Shanik GD, Nott D, Wengerter KR, Moore DJ. Prospective randomised comparison of in situ and reversed infrapopliteal vein grafts. Br J Surg. 1993b; 80: 173-176.

Heikkinen M, Salmenperä M, Lepäntalo A, Lepäntalo M. Diabetes care for patients with peripheral arterial disease. Eur J Vasc Endovasc Surg. 2007; 33: 583-591.

Hickey NC, Thomson IA, Shearman CP, Simms MH. Aggressive arterial reconstruction for critical lower limb ischaemia. Br J Surg. 1991; 78: 1476-1478.

Hingorani A, Ascher E, Markevich N, Kallakuri S, Hou A, Schutzer R, Yorkovich W. Magnetic resonance angiography versus duplex arteriography in patients undergoing lower limb revascularization: Which is the best replacement for contrast angiography. J Vasc Surg. 2004; 39: 717-722.

Hingorani A, Ascher E, Marks N. Preprocedural imaging: new options to reduce need for contrast angiography. Semin Vasc Surg. 2007; 20: 15-28.

Hofmann WJ, Walter J, Cerny M, Magometschnigg H. Emergency pedal artery bypass grafting. Eur J Vasc Endovasc Surg. 2003; 26: 643-648.

Holzenbein TJ, Pomposelli FB Jr, Miller A, Contreras MA, Gibbons GW, Campell DR et al. Results of a policy with arm veins used as the first alternative to an unavailable ipsilateral greater saphenous vein for infrainguinal bypass. J Vasc Surg. 1996; 23: 130-140.

How TV, Rowe CS, Gilling-Smith GL, Harris PL. Interposition vein cuff anastomosis alters wall shear stress distribution in the recipient artery. J Vasc Surg. 2000; 31: 1008-1017.

Harward TR, Govostis TM, Rosenthal GJ, Carlton LM, Flynn TC, Seeger JM. Impact of angioscopy on infrainguinal graft patency. Am J Surg. 1994; 168: 107-110.

Hughes K, Domenig CM, Hamdan AD, Schermerhorn M, Aulivola B, Blattman S et al. Bypass to plantar and tarsal arteries: an acceptable approach to limb salvage. J Vasc Surg. 2004; 40: 1149-1157.

Ibrahim IM, Sussman B, Dardik I, Kahn M, Israel M, Kenny M, Dardik H. Adjunctive arteriovenous fistula with tibial and peroneal reconstruction for limb salvage. Am J Surg. 1980; 140: 246-251.

Idu MM, Ubbink D, Legennate DA. The fate of unrevised stenoses in infrainguinal autologous vein grafts as detected by intraoperative duplex scanning. Vasc Endovascular Surg. 2005; 39: 317-325

Ihlberg L, Luther M, Albäck A, Kantonen I, Lepäntalo M. Does a completely accomplished duplex-based surveillance prevent vein-graft failure? Eur J Vasc Endovasc Surg. 1999; 18: 395-400.

Ihlberg L, Luther M, Tierala E, Lepäntalo M. The utility of duplex scanning in infrainguinal vein graft surveillance: results from a randomised controlled study. Eur J Vasc Endovasc Surg. 1998; 16: 19-27.

Ihlberg LH, Albäck NA, Lassila R, Lepäntalo M. Intraoperative flow predicts the development of stenosis in infrainguinal vein grafts. J Vasc Surg. 2001; 34: 269-76.

Illig KA, Moran S, Serletti J, Ouriel K, Orlando G, Smith A, Shortell CK, Green RM. Combined free tissue transfer and infrainguinal bypass graft: an alternative to major amputation in selected patients. J Vasc Surg. 2001; 33: 17-23.

Isaksson L, Lundgren F. Vein bypass surgery to the foot in patients with diabetes and critical ischaemia. Br J Surg. 1994; 81: 517-520.

Jacobs M, Gregoric I, Reul G. Prosthetic graft placement and creation of a distal arteriovenous fistula for secondary vascular reconstruction in patients with severe limb ischemia. J Vasc Surg. 1992; 15: 612-618.

Jacobs M, Reul G, Gregoric I, Ubbink DT, Tordoir JHM, Kitslaar PJ, Reneman RS. Creation of a distal arteriovenous fistula improves microcirculatory hemodynamics of prosthetic graft bypass in secondary limb salvage procedures. J Vasc Surg. 1993; 18: 1-9.

Jakobsen HL, Baekgaard N, Christoffersen JK. Below-knee and distal bypass with PTFE and vein cuff. Eur J Vasc Endovasc Surg. 1998; 15: 327-330.

Jensen LP, Lepäntalo M, Fossdal JE, Roder OC, Jensen BS, Grenager O, Fasting H, Myhre HO, Baekgaard N, Nielsen OM, Helgstrand U, Schroeder TV. Dacron or PTFE for above-knee femoropopliteal bypass. A multicenter randomised study. Eur J Vasc Endovasc Surg. 2007; 34: 44-49.

Jivegård L, Augustinsson LE, Carlsson CA, Holm J. Long-term results by epidural spinal electrical stimulation (ESES) in patients with inoperable severe lower limb ischaemia. Eur J Vasc Surg. 1995; 1: 345-349.

Johnson WC, Lee KK and members of the Department of Veterans Affairs COOP study 141. A comparative evaluation of polytetrafluoroethylene, umbilical vein and saphenous vein bypass grafts for femoral-popliteal above-knee revascularization: A prospective randomised Department of Veterans Affairs cooperative study. J Vasc Surg. 2000; 32: 268-277.

Kallakuri S, Ascher E, Hingorani A, Jacob T, Salles-Cunha S. Hemodynamics of infrapopliteal PTFE bypasses and adjunctive arteriovenous fistulas. Cardiovasc Surg. 2003; 11: 125-129.

Kaplan I, Ada S, Ozerkan F, Bora A, Ademoglu Y. Reconstruction of soft tissue and bone defects in lower extremity with free flaps. Microsurgery. 1998; 18: 176-81.

Karacagil S, Almgren B, Bergström R, Bowald S, Eriksson I. Postoperative predictive value of a new method of intraoperative angiographic assessment of runoff in femoropopliteal bypass grafting. J Vasc Surg. 1989a; 10: 400-407.

Karacagil S, Almgren B, Bowald S, Eriksson I. A new method of angiographic runoff evaluation in femorodistal reconstructions: Significant correlation with early graft patency. Arch Surg. 1990; 125: 1055-1058.

Karacagil S, Almgren B, Bowald S, Eriksson I. Arterial lesions of the foot vessels in diabetic and non-diabeetic patients undergoing lower limb revascularization. Eur J Vasc Surg. 1989b; 3: 239-244.

Kent KC, Whitteomore AD, Mannick JA. Short-term and midterm results of an all-autogenous tissue policy for infrainguinal reconstruction. J Vasc Surg.1989; 9: 107-114.

Kissin M, Kansal N, Pappas PJ, DeFouw DO, Duran WN, Hobson RW. Vein interposition cuffs decrease the intimal hyperplastic response of polytetrafluoroethylene bypass grafts. J Vasc Surg. 2000; 31: 69-83.

Klomp HM, Steyerberg EW, van Urk H, Habbema JD, ESES Study Group. Spinal cord stimulation is not cost-effective for non-surgical management of critical limb ischaemia. Eur J Vasc Endovasc Surg. 2006; 31: 500-508.

Kreienberg PB, Darling RC, Chang BB, Paty PS, Lloyd WE, Shah DM. Adjunctive techniques to improve patency of distal prosthetic bypass in polytetrafluoroethylene with remote arteriovenous fistulae versus vein cuff. J Vasc Surg. 2000; 31: 696-701.

Kudo T, Chandra F, Kwun W-H, Haas B, Ahn S. Changing pattern of surgical revascularization for critical limb ischemia over 12 years: Endovascular vs open bypass surgery. J Vasc Surg. 2004; 44: 304-313.

Laustsen J, Pedersen EM, Terp K, Steinbruchel D, Kure HH, Paulsen PK, Jorgensen H, Paaske WP. Validation of a new transit time ultrasound flowmeter in man. Eur J Vasc Endovasc Surg. 1996; 12: 91-96.

Leather RP, Shah DM, Chang BB, Kaufman JL. Resurrection of the in situ saphenous vein bypass. 1000 cases later. Ann Surg. 1988; 208: 435-440.

Lepäntalo A, Virtanen KS, Heikkilä J, Wartiovaara U, Lassila R. Limited early antiplatelet effect of 300 mg clopidogrel in patients with aspirin therapy undergoing percutaneous coronary interventions. Eur Heart J. 2004; 25: 476-483.

Lepäntalo M, Heikkinen M, Eskelinen E, Albäck A. Surgical treatment of the diabetic foot. In: More Vascular and Endovascular Challenges, 29th International Symposium Charing Cross 2007.

Lepäntalo M, Mätzke S. Outcome of unreconstructed chronic critical leg ischaemia. Eur J Vasc Endovasc Surg. 1996; 11: 153-157.

Lepäntalo M, Tukiainen E. Combined vascular reconstruction and microvascular muscle flap transfer for salvage of ischaemic legs with major tissue loss and wound complications. Eur J Vasc Endovasc Surg. 1996; 12: 65-69.

Linton RR, Darling RC. Autogenous saphenous vein bypass grafts in femoropoliteal arterial disease. Surgery 1962; 51: 62.

Ljungman C, Ulus AT, Almgren B, Bergström R, Hellberg A, Bergqvist D, Karacagil S. A multivariate analysis of factors affecting patency of femoropopliteal and femorodistal bypass grafting. Vasa. 2000; 29: 215-220.

LoGerfo FW, Coffman JD. Current concepts. Vascular and microvascular disease of the foot in diabetes. Implications for foot care. N Engl J Med. 1984; 311: 1615-1619. Review.

LoGerfo FW, Gibbons GW. Vascular disease of the lower extremities in diabetes mellitus. Endocrinol Metab Clin North Am. 1996; 25: 439-445. Review.

Londrey GL, Ramsey DE, Hodgson KJ, Barkmeier LD, Sumner DS. Infrapopliteal bypass for severe ischemia: Comparison of autogenous vein, composite and prosthetic grafts. J Vasc Surg. 1991; 13: 631-636.

Lorenzetti F, Salmi A, Ahovuo J, Tukiainen E, Asko-Seljavaara S. Postoperative changes in blood flow in free muscle flaps: A prospective study. Microsurgery. 1999; 19: 196-199.

Lorenzetti F, Suominen S, Tukiainen E, Kuokkanen H, Suominen E, Vuola J, Asko-Seljavaara S. Evaluation of blood flow in free microvascular flaps. J Reconstr Microsurg. 2001a; 17: 163-167.

Lorenzetti F, Tukiainen E, Albäck A, Kallio M, Asko-Seljavaara S, Lepäntalo M. Blood flow in a pedal bypass combined with a free muscle flap. Eur J Vasc Endovasc Surg. 2001b; 22: 161-164.

Lundell A, Bergqvist D. Prediction of early graft occlusion in femoropopliteal and femorodistal reconstruction by measurement of volume flow with transit time flowmeter and calculation of peripheral resistance. Eur J Vasc Surg 1993; 7: 704-708.

Lundell A, Lindblad B, Bergqvist D, Hansen F. Femoropopliteal-crural graft patency is improved by an intensive surveillance program: a prospective randomized study. J Vasc Surg. 1995; 21: 26-33.

Lundell A, Nyborg K. Do residual arteriovenous fistulae after in situ saphenous vein bypass grafting influence patency? J Vasc Surg. 1999; 30: 99-105.

Luther M, Lepäntalo M. Arterial reconstructions to the foot arteries – a viable option? Eur J Surg. 1997a; 163: 659-665.

Luther M, Lepäntalo M. Femorotibial reconstructions fot chronic critical leg ishaemia- Influence on outcome by diabetes, gender and age. Eur J Vasc Endovasc Surg. 1997b; 13: 569-577.

Luther M. Surgical treatment for chronic critical leg ischaemia: a 5 year follow-up of socio-economic outcome. Eur J Vasc Endovasc Surg. 1997a; 13: 452-459.

Luther M. Treatment of chronic critical leg ischaemia- a cost benefit analysis. Ann Chir Gynaecol Suppl. 1997b; 213: 1-142.

Mathes SJ, Nahai F. In: Mathes SJ, Nahai F. Reconstructive Surgery: Principles, Anatomy, and Technique. Churchill Livingstone, New York, 1997.

Mäztke S, Biancari F, Ihlberg L, Albäck A, Kantonen I, Railo M, Lepäntalo M. Increased preoperative c-reactive protein level as a prognostic factor for postoperative amputation after femoropopliteal bypass surgery for CLI. Ann Chir Gynaecol. 2001; 90: 19-22.

Mäztke S, Tukiainen EJ, Lepäntalo MJ. Survival of a microvascular muscle flap despite the late occlusion of the inflow artery in a neuroischaemic diabetic foot. Scand J Plast Reconstr Surg Hand Surg. 1997; 31: 71-75.

Mazzariol F, Ascher E, Hingorani A, Gunduz Y, Yorkovich W, Salle-Gunha S. Lower-extremity revascularisation without preoperative contrast arteriography in 185 cases: lessons learned with duplex ultrasound arterial mapping. Eur J Vasc Endovasc Surg. 2000; 19: 509-515.

McCollum C, Kenchington G, Alexander C, Franks PJ, Greenhalgh RM. PTFE or HUV for femoro-popliteal bypass: a multi-centre trial. Eur J Vasc Surg.1991; 5: 435-443.

McGovern PJ, Jain KM, Kerr JC, Swan KG, Rocko JM. Haemodynamics of an anastomotic arteriovenous fistula. Am J Surg. 1985; 149: 368-370.

Miller JH, Foreman RK, Ferguson L, Faris I. Interposition vein cuff for anastomosis of prosthesis to small artery. Aust. N.Z. J. Surg 1984; 54: 283-285.

Miller J, Walsh JA, Foreman RK, Dupont PA, Luethke R, James MJ, Iannos J. Vascular outflow resistance and angiographic assesment of lower limb arterial reconstructive procedures. Aust N Z J Surg. 1990; 60: 275-281.

Mimoun M, Hilligot P, Baux S. The nutrient flap: a new concept of the role of the flap and application to the salvage of arteriosclerotic lower limbs. Plast Reconstr Surg. 1989; 84: 458-467.

Modrall JG, Sadjadi J, Ali AT, Anthony T, Welborn MB, Valentine RJ, Hynan LS, Clagett GP. Deep vein harvest: predicting need for fasciotomy. J Vasc Surg. 2004; 39: 387-394.

Moody AP, Al Fagih S, Edwards PR, Campbell H, Harris PL. The use of adjuvant arterio-venous shunt in prosthetic femoro-crural bypass. Eur J Vasc Surg. 1991; 5: 327-332.

Morris GE, Raptis S, Miller JH, Faris IB. Femorocrural grafting and regrafting: Does polytetrafluoroethylene have a role? Eur J Vasc Surg. 1993; 7: 329-334.

Mosimann UP, Stirnemann P. Chronic critical leg ischemia: revascularization of the isolated popliteal segment in comparison with femoro-distal bypass. Vasa. 1995; 24: 49-55.

Nasr MK, McCarthy RJ, Hardman J, Chalmers A, Horrocks M. The increasing role of percutaneous transluminal angioplasty in the primary management of critical limb ischaemia. Eur J Vasc Endovasc Surg. 2002; 23: 398-403.

Nguyen LL, Conte MS, Menard MT, Gravereaux EC, Chew DK, Donaldson MC, Whittemore AD, Belkin M. Infrainguinal vein bypass graft revision: factors affecting long-term outcome. J Vasc Surg. 2004; 40: 916-923.

Nielsen TG, Djurhuus C, Pedersen EM, Laustsen J, Hasenkam JM, Schroeder TV. Arteriovenous fistulas aggravate the hemodynamic effect of vein bypass stenoses: An in vitro study. J Vasc Surg. 1996; 24: 1043-1049.

Norberto JJ, Sidawy AN, Trad KS, Jones BA, Neville RF, Najjar SF, Sidawy MK, DePalma RG. The protective effect of vein cuffed anastomoses is not mechanical in origin. J Vasc Surg. 1995; 21: 558-564.

Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FRG on behalf of the TASC II Working Group. Inter-Society Consensus fot the management of peripheral arterial disease (TASC II). J Vasc Surg. 2007; 45 Suppl S:S5-67.

Okadome K, Onohara T, Yamamura S, Mii S, Sugimachi K. Evaluation of proposed standards for runoff in femoropopliteal arterial reconstructions: correlation between runoff score and flow waveform pattern. A preliminary report. J Cardiovasc Surg. 1991; 32: 353-359.

Onkamo P, Väänänen S, Karvonen M, Tuomilehto J. Worldwide increase in the incidence of type I diabetes: the analysis of the data on published incidence trends. Diabetologia 1999; 42: 1395-1403.

Oyibo SO, Jude EB, Voyatzoglou D, Boulton AJM. Clinical characteristics of patients with diabetic foot problems: changing patterns of foot ulcer presentation. Pract Diabetes Int. 2002; 19: 10-12.

Panayiotopoulos YP, Tyrrell MR, Owen SE, Reidy JF, Tylor PR. Outcome and cost analysis after femorocrural and femoropedal grafting for critical limb ischaemia. Br J Surg. 1997; 84: 207-212.

Pappas PJ, Hobson RW, Meyers MG, Lee JB, Silva MBJr, Goldberg MC, Padberg FT. Patency of infrainguinal polytetrafluoroethylene bypass grafts with distal interposition vein cuffs. Cardiovasc Surg. 1998; 6: 19-26.

Parsons RE, Suggs WD, Veith FJ, Sanchez LA, Lyon RT, Marin ML, Goldsmith J, Faries PL, Wengerter KR, Schwartz ML. Polytetrafluoroethylene bypasses to infrapopliteal arteries without cuffs or patches: A better option than amputation in patients without autologous vein. J Vasc Surg. 1996; 23: 347-356.

Parvin SD, Bentley S, Asher MJ, Pryherch DR, Evans DH, Bell PRF. Haemodymanics of the adjunctive arteriovenous fistula in femorodistal bypass grafting: an experimental study. Br J Surg. 1984; 71: 502-505.

Patterson RB, Fowl RJ, Kempczinski RF, Gewirtz R, Shukla R. Preferential use of EPTFE for above-knee femoropopliteal bypass grafts. Ann Vasc Surg. 1990; 4: 338-343.

Paty PSK, Shah DM, Saifi J Chang BB, Feustel PJ, Kaufman Jl, Leather RP, Wengerter KR, Ascer E, Gupta SK, Veith FJ. Remote distal arteriovenous fistula to improve infrapopliteal bypass patency. J Vasc Surg.1990; 11: 171-178.

Peeters P, Verbist J, Deloose K, Bosiers M. Results with heparin bonded polytetrafluoroethylene grafts for femorodistal bypasses. J Cardiovasc Surg. 2006; 47: 407-413.

Peltonen S, Biancari F, Lindgren L, Mäkisalo H, Honkanen E, Lepäntalo M. Outcome of infrainguinal bypass surgery for critical leg ischaemia in patients with chronic renal failure. Eur J Vasc Endovasc Surg. 1998; 15: 122-127.

Peterkin GA, Manabe S, LaMorte WW, Menzoian JO. Evaluation of a proposed standard reporting system of preoperative angiograms in infrainguinal bypass procedures: angiographic correlates of measured peripheral resistance. J Vasc Surg. 1988; 7: 379-385.

Plecha EJ, Seabrook GR, Bandyk DF, Towne JB. Determinants of successful peroneal artery bypass. J Vasc Surg. 1993; 17: 97-105.

Pomposelli FB Jr, Jepsen SJ, Gibbons GW, Campbell DR, Freeman DV, Miller A, LoGerfo FW. Efficacy of the dorsal pedal bypass for limb salvage in diabetic patients: short-term observations. J Vasc Surg. 1990; 11: 745-751.

Pomposelli FB, Kansal N, Hamdan AD, Belfield A, Sheahan M, Campbell DR, Skillman JJ, LoGerfo FW. A decade of experience with dorsalis pedis artery bypass: analysis and outcome in more than 1000 cases. J Vasc Surg. 2003; 37: 307-315.

Post S, Kraus T, Muller-Reinartz U, Weiss C, Kortmann H, Quentmeier A, Winkler M, Husfeldt KJ, Allenberg JR. Dacron vs polytetrafluoroethylene for femoropoliteal bypass: a prospective randomised multicentre trial. Eur J Vasc Endovasc Surg.2001; 22: 226-231.

Prendville EJ, Yeager A, O'Donnell TF Jr, Coleman JC, Jaworek A, Callow AD, Mackey WC, Deterling RA. Long-term results with the above-knee popliteal expanded polytetrafluoroethylene graft. J Vasc Surg. 1990; 11: 517-524.

Quinones-Baldrich WJ, Colburn MD, Ahn SS, Gelabert HA, Moore WS. Very distal bypass for salvage of the severely ischemic extremity. Am J Surg. 1993; 166: 117-123.

Quinones-Baldrich WJ, Kashyap VS, Taw MB, Markowitz BL, Watson JP, Reil TD, Shaw WW. Combined revascularization and microvascular free tissue transfer for limb salvage: A six-year experience. Ann Vasc Surg. 2000; 14: 99-104.

Quinones-Baldrich WJ, Prego AA, Ucelay-Gomez R, Freischlag JA, Ahn SS, Baker JD, Machleder HI, Moore WS. Long-term results of infrainguinal revascularization with polytetrafluoroethylene: A ten-year experience. J Vasc Surg. 1992; 16: 209-217.

Rafferty TD, Avellone JC, Farrell CJ, Hertzer NR, Plecha FR, Rhodes RS, Sharp WV, Rogers JM. A metropolitan experience with infrainguinal revascularization. Operative risk and late results in northeastern Ohio. J Vasc Surg. 1987 Oct;6(4):365-71.

Rainer C, Schwabegger AH, Bauer T, Ninkovic M, Klestil T, Harpf C, Ninkovic MM. Free flap reconstruction of the foot. Ann Plast Surg. 1999; 42: 595-606.

Raptis S, Miller JH. Influence of vein cuff on polytetrafluoroethylene grafts for primary femoropopliteal bypass. Br J Surg.1995; 82: 487-491.

Rautio J, Asko-Seljavaara S, Harma M, SundellB. Reconstruction of the foot using free flaps. Handchir Mikrochir Plast Chir. 1989; 5: 227-234.

Robison J, Beard JD. Is there a place for primary amputation? In: Branchereau A, Jacobs M. Critical limb ischemia. Futura Publishing Company, Armonk, 1999: Pp. 239-246.

Robison JG, Cross MA, Brothers TE, Elliott BM. Do results justify an aggressive strategy targeting the pedal arteries for limb salvage? J Surg Res. 1995; 59: 450-454.

Roddy SP, Darling RC 3rd, Chang BB, Kreienberg PB, Paty PS, Lloyd WE, Shah DM. Outcomes with plantar bypass for limb-threatening ischemia. Ann Vasc Surg. 2001; 15: 79-83.

Roddy SP, Darling RC III, Ozsvath KJ, Kreienberg PB, Chang BB, Mathew TS, Paty PS, Mehta M, Shah DM. Composite sequential arterial reconstruction for limb salvage. J Vasc Surg. 2002; 36: 325-329.

Rosen RC, Johnson WC, Bush HL Jr, Cho SI, O'Hara ET, Nabseth DC. Staged infrainguinal revascularization: initial prosthetic above-knee bypass followed by a distal vein bypass for recurrent ischemia. A valid concept for extending limb salvage? Am J Surg. 1986; 152: 224-230.

Rosenthal D, Dickson C, Rodriguez FJ, Blackshear WM Jr, Clark MD, Lamis PA, Pallos LL. Infrainguinal endovascular in situ saphenous vein bypass: ongoing results. J Vasc Surg. 1994; 20: 389-394; discussion 394-395.

Rosenthal D, Evans RD, McKinsey J, Seagraves MA, Lamis PA, Clark MD, Daniel WW. Prosthetic above-knee femoropoliteal bypass for intermittent claudiacation. J Cardiovasc Surg. 1990; 31: 462-468.

Rossi PJ, Skelly CL, Meyerson SL, Bassiouny HS, Katz D, Schwartz LB, McKinseyJF, Gewertz BL, Desai TR. Redo infrainguinal bypass: Factors predicting patency and limb salvage. Ann Vasc Surg. 2003; 17: 492-502.

Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, Jones DNRecommended standards for reports dealing with lower extremity ischaemia: Revised version. J Vasc Surg. 1997; 26: 517-538.

Rutherford RB, Flanigan DP, Gupta SK, Johnston KW, Karmody A, Whittemore AD, Baker JD, Ernst CB, Jamieson C, Mehta S. Suggested standards for reports dealing with lower extremity ischemia. J Vasc Surg. 1986; 4: 80-94.

Rutherford RB, Jones DN, Bergentz SE, Bergqvist D, Comerota AJ, Dardik H, Flinn WH, Fry WJ, McIntyre K, Moore WS. Factors affecting the patency of infrainguinal bypass. J Vasc Surg. 1988; 8: 236-246.

Salenius JP. National vascular registry in Finland. FINNVASC Study Group. Ann Chir Gynaecol.1992; 81: 257-260.

Sarac TP, Huber TS, Back MR, Ozaki CK, Carlton LM, Flynn TC, Seeger JM. Warfarin improves the outcome of infrainguinal vein bypass grafting at high risk for failure. J Vasc Surg. 1998; 28: 446-457.

Sauvage LR, Walter MW, Berger K, Robel SB, Lischko MM, Yates SG, Logan GA. Current arterial prostheses. Experimental evaluation by implantation in the carotid and circumflex coronary artery of the dog. Arch Surg. 1979; 114: 687-691.

Sayers RD, Raptis S, Berce M, Miller JH. Long-term results of femorotibial bypass with vein or polytetrafluoroethylene. Br J Surg. 1998; 7: 934-938.

Schneider JR, Walsh DB, McDaniel MD, Zwolak RM, Besso SR, Cronenwett JL. Pedal bypass versus tibial bypass with autogenous vein: a comparison of outcome and hemodynamic results. J Vasc Surg. 1993; 17: 1029-1038; discussion 1038-1040.

Schulman ML, Badhey MR, Yatco R. Superficial femoral-popliteal veins and reversed saphenous veins as primary femoropopliteal bypass grafts: a randomised comparative study. J Vasc Surg. 1987; 6: 1-10.

Schweiger H, Klein P, Lang W. Tibial bypass grafting for limb salvage with ringed polytetrafluoroethylene prostheses: Results of primary and secondary procedures. J Vasc Surg. 1993; 18: 867-874.

Schwierz T, Pricop T, Ebner C, Havlicek W, Schmöller F, Nesser HJ, Böhmig HJ, Fugger R. The evaluation of run-off prior to infra-inguinal bypass reconstruction – A modified scoring system based on flow measurement. Eur J Vasc Endovasc Surg. 2003; 26: 52-58.

Scott DJ, Hunt G, Beard JD, Hartnell GG, Horrocks M. Arteriogram scoring systems and pulse generated run-off in the assessment of patients with critical ischaemia for femorodistal bypass. Br J Surg. 1989; 76: 1202-1206.

Second European Consensus Document on chronic critical leg ischemia. Circulation. 1991; 84(IV Suppl): IV1-26.

Seeger JM, Pretus HA, Carlton LC, Flynn TC, Ozaki CK, Huber TS. Potential predictors of outcome in patients with tissue loss who undergo infrainguinal vein bypass grafting. J Vasc Surg. 1999; 30: 427-35.

Serletti JM, Deuber MA, Guidera PM, Herrera HR, Reading G, Hurwitz SR, Jones JA, Ouriel K, Green RM. Atherosclerosis of the lower extremity and free-tissue reconstruction for limb salvage. Plast Reconstr Surg. 1995; 96: 1136-1144.

Shah DM, Darling RC 3rd, Chang BB, Bock DEM, Leather RP. Durability of short bypasses to infragenicular arteries. Eur J Vasc Endovasc Surg. 1995a; 10: 440-444.

Shah DM, Darling RC 3rd, Chang BB, Fitzgerald KM, Paty PS, Leather RP. Long-term results of in situ saphenous vein bypass. Analysis of 2058 cases. Ann Surg. 1995b; 4: 438-446.

Shandall AA, Leather RP, Corson JD, Kupinski AM, Shah DM. Use of the short saphenous vein in situ for popliteal-to-distal bypass. Am J Surg. 1987; 154: 240-244.

Shestak KC, Hendricks DL, Webster MW. Indirect revascularization of the lower extremity by means of microvascular free-muscle flap. A preliminary report. J Vasc Surg. 1990; 12: 581-585.

Sidawy AN. Infrapopliteal prosthetic bypasses: Does distal venous tissue interposition improve their patency? In 28th Global: Vascular and Endovascular Issues, Techniques and Horizons.

Siegman FA. Use of a venous cuff for graft anastomosis. Surg Gynecol Obstet. 1979; 148: 930.

Siemionow M, Andreasen T, Chick L, Lister G. Effect of muscle flap denervation on flow hemodynamics: a new model for chronic in vivo studies. Microsurgery. 1994;15: 891-894.

Smout JD, Mikhailidis DP, Shenton BK, Stansby G. Combination antiplatelet therapy in patients with peripheral vascular bypass grafts. Clin Appl Thromb Hemost. 2004; 10: 9-18.

Snyder SO Jr, Wheeler JR, Gregory RT, Gayle RG. Failure of arteriovenous fistulas at distal tibial bypass anastomotic sites. J Cardiovasc Surg. 1985; 26: 137-142.

Sogaro F, Galeazzi E, Amroch D, Ganassin L. Pantaloon vein graft technique in tibial revascularization with arteriovenous fistula for limb salvage. Cardiovasc Surg. 1996; 4: 377-380.

Staffa R, Leypold J, Kriz Z. Pedal bypass for limb salvage. Acta Chir Belg. 2005;105: 491-496.

Stewart AHR, Lucas A, Smith FCT, Baird RN, Lamont PM. Pre-operative hand-held doppler run-off score can be used to stratify risk prior to infra-inguinal bypass surgery. Eur J Vasc Endovasc Surg. 2002; 23: 500-504.

Stirnemann P, Ris HB, Do D, Hämmerli R. Intraoperative flow measurement of distal runoff: A valid predictor of outcome of infrainguinal bypass surgery. Eur J Surg. 1994; 160: 431-436.

Stonebridge PA, Prescott RJ, Ruckley CV. Randomized trial comparing infrainguinal polytetrafluoroethylene bypass grafting with and without vein interposition cuff at the distal anastomosis. J Vasc Surg 1997; 26: 543-550.

Takolander R, Fischer-Colbrie W, Jogestrand T, Ohlsen H, Olofsson P, Swedenborg J. The “Ad Hoc” estimation of outflow does not predict patency of infrainguinal reconstructions. Eur J Vasc Endovasc Surg. 1995; 10: 187-191.

Tangelder MJD, Lawson JA, Algra A, Eikelboom BC. Systematic review of randomized controlled trials of aspirin and oral anticoagulants in the prevention of graft occlusion and ischemic events after infrainguinal bypass surgery. J Vasc Surg. 1999; 30: 701-709.

Taylor LM Jr, Edwards JM, Porter JM. Present status of reversed vein bypass grafting: five-year results of a modern series. J Vasc Surg. 1990; 11: 193-205.

Taylor RS, Loh A, McFarland RJ, Cox M, Chester JF. Improved technique for polytetrafluoroethylene bypass grafting: long-term results using anastomotic vein patches. Br J Surg. 1992; 79: 348-354.

Teittinen K, Alback A, Biancari F, Lehtola A, Tukiainen E, Lepäntalo M. Congestive heart failure due to adjuvant arteriovenous fistula in a femoroperoneal bypass. J Cardiovasc Surg. 1999; 40: 571-572.

The Vascular Surgical Society of Great Britain and Ireland. Critical limb ischaemia: mangement and outcome. Report of a national survey. The Vascular Surgical Society of Great Britain and Ireland. Eur J Vasc Endovasc Surg. 1995; 10: 108-113.

Tordoir J, van der Plas J, Jacobs M, Kitslaar P. Factors determining the outcome of crural and pedal revascularisation for critical limb ischaemia. Eur J Vasc Surg. 1993; 7: 82-86.

Tröeng T, Bergqvist D, Janson L. Incidence and causes of adverse outcomes of operation for chronic ischaemia of the leg. Eur J Surg. 1994; 160: 17-25.

Tukiainen E, Biancari F, Lepäntalo M. Lower limb revascularization and free flap transfer for major ischemic tissue loss. World J Surg. 2000; 24: 1531-1536.

Tukiainen E, Kallio M, Lepäntalo M. Advanced leg salvage of the critically ischemic leg with major tissue loss by vascular and plastic surgeon teamwork: Long-term outcome. Ann Surg. 2006; 244: 949-957; discussion 957-958.

Tyrrell MR, Chester JF, Vipond MN, Clarke GH, Taylor RS, Wolfe JHN. Experimental evidence to support the use of interposition vein collars/patches in distal PTFE anastomoses. Eur J Vasc Surg. 1990; 4: 95-101.

Tyrrell MR, Wolfe JHN. New prosthetic venous collar anastomotic technique: combining the best of other procedures. Br J Surg 1991; 78: 1016-1017.

Ulus AT, Ljungman C, Almgren B, Hellberg A, Bergqvist D, Karacagil S. The influence of distal runoff on patency of infrainguinal vein bypass grafts. J Vasc Surg. 2001: 35: 31-35.

van Damme H, Zhang L, Baguet E, Creemers E, Albert A, Limet R. Crural artery bypass with the autogenous greater saphenous vein. Eur J Vasc Endovasc Surg. 2003; 26: 635-642.

van Dijk LC, van Urk H, Lameris JS, Wittens CHA. Residual arteriovenous fistulae after “closed” in situ bypass grafting: an overrated problem. Eur J Vasc Endovasc Surg. 1997; 13: 439-442.

van Landuyt K, Monstrey S, Blondeel P, Tonnard P, Vermassen F. Revascularisation by ingrowth of a free flap: fact or fiction? Microsurgery. 1996a; 17: 417-422.

van Landuyt K, Vermassen F, Monstrey S, Tonnard P, van den Brande F, Matton G. Single-stage revascularization and free flap coverage in the treatment of ischemic lower limb lesions. Eur J Plast Surg. 1996b; 19: 245-252.

Varty K, London NJ, Brennan JA, Ratliff DA, Bell PR. Infragenicular in situ vein bypass graft occlusion: a multivariate risk factor analysis. Eur J Vasc Surg. 1993; 7: 567-571.

Veith FJ, Gupta SK, Ascer E, White-Flores S, Samson RH, Scher LA, Towne JB, Bernhard VM, Bonier P, Flinn WR. Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. J Vasc Surg. 1986; 3: 104-114.

Vermassen FE, vanLanduyt K. Combined vascular reconstruction and free flap transfer in diabetic arterial disease. Diabetes Metab Res Rev. 2000; 16 (suppl 1): S33-S36.

Veterans Administration Cooperative Study Group 141. Comparative evaluation of prosthetic, reversed and In Situ vein bypass grafts in distal popliteal and tibial-peroneal revascularization. Arch Surg. 1988; 123: 434-438.

Virkkunen J, Heikkinen M, Lepäntalo M, Metsänoja R, Salenius JP; Finnvasc Study Group. Diabetes as an independent risk factor for early postoperative complications in critical limb ischemia. J Vasc Surg. 2004; 40: 761-767.

Weaver FA, Barlow CR, Edwards WH, Mulherin JL Jr, Jenkins JM. The lesser saphenous vein: autogenous tissue for lower extremity revascularization. J Vasc Surg. 1987; 5: 687-692.

Wells JK, Hagino RT, Bargmann KM, Jackson MR, Valentine RJ, Kakish HB, Clagett GP. Venous morbidity after superficial femoral-popliteal vein harvest. J Vasc Surg. 1999; 29: 282-289; discussion 289-291.

Wengerter KR, Veith FJ, Gupta SK, Goldsmith J, Farrell E, Harris PL, Moore D, Shanik G. Prospective radomized multicenter comparison of in situ and reversed vein infrapopliteal bypass. J Vasc Surg. 1991; 13: 189-199.

Wilson YG, George JK, Wilkins DC, Ashley S. Duplex assessment of run-off before femorocrural reconstruction. Br J Surg. 1997; 84: 1360-1363.

Winell K, Niemi M, Lepäntalo M. The national hospital discharge register data on lower limb amputations – quality indicator for diabetes care. Eur J Vasc Endovasc Surg. 2006; 32: 66-70.

Wolfe JHN, Tyrrell MR. Justifying arterial reconstruction to crural vessels- even with a prosthetic graft. Br J Surg. 1991; 78: 897-899.

Wolfle KD, Bruijnen H, Loepecht H, Rumenapf G, Schweiger H, Grabitz K, Sandmann W, Lauterjung L, Largiader J, Erasmi H, Kasprzak PM, Raithel D, Allenberg JR, Lauber A, Berlakovich GM, Kretschmer G, Hepp W, Becker HM, Schulz A. Graft patency and clinical outcome of femorodistal arterial reconstruction in diabetic and non-diabetic patients: results of a multicentre comparative analysis. Eur J Vasc Endovasc Surg. 2003; 25: 229-234.

14. ORIGINAL PUBLICATIONS