Below-knee revascularization in patients with critical limb ischemia: long-term comparison of redo vs primary interventions

J CARDIOVASC SURG 2008;49:489-95

Below-knee revascularization in patients with critical limb ischemia: long-term comparison of redo vs *primary interventions*

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Aim. **The aim of this study was to evaluate the authors' experience in below-knee revascularization in patients with critical limb ischemia, comparing long-term outcomes in primary and secondary interventions.**
Methods. **From January 2000 to December 2006, 140 consecutive below-knee revascularizations in patients with critical limb ischemia were performed at the Department of Vascular Surgery of the University of Florence (Italy). In 105 patients (75%) a primary intervention was performed (Group 1). Early and long-term results in terms of survival, patency and limb salvage were compared with those obtained in the remaining 35 patients (25%) secondarily operated on in the same period for a late (>30 days) bypass graft thrombosis (Group 2).**
Results. **One patient died in the early postoperative period. Thirty-day thrombosis and amputation rates were poorer in Group 2 than in Group 1 (17.1% and 4.8%, P=0.02; 37.1% and 16.2%, P=0.01, respectively). Mean duration of follow-up was 25.1 months. At 60 months there were no differences between the two groups in terms of survival (90.1% in Group 1 and 90.9% in Group 2; P=NS), primary patency (43.5% in Group 1 and 31.9% in Group 2; P=NS) and secondary patency (48.4% in Group 1 *vs* 43.8% in Group 2; P=NS). Estimated 60-month limb salvage rate was significantly poorer in Group 2 than in Group 1 (64.1% and 77.7%, respectively; P=0.05). In Group 2 prosthetic graft material significantly affects 60-month limb salvage rate.**
Conclusion. **Redo below-knee revascularization in patients with critical limb ischemia provides acceptable long-term results in terms of primary and secondary patency; however, limb salvage appeared to be slightly worse in patients undergone redo surgery.**

KEY WORDS: Thrombosis - Ischemia - Leg.

Received on March 18, 2008.
Accepted for publication on June 6, 2008.

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Femoro-popliteal bypass represents a safe and effective procedure in order to modify natural history of patients affected by lifestyle-limiting claudication or critical limb ischemia (CLI), with good long-term rates of limb salvage.[1, 2] The main problem in infrainguinal revascularization is the not negligible rate of early and late failure. Data from meta-analysis and main mono- and multicentric series showed that the rate of graft failure ranges from 25% and 35% at 2-year follow-up.[3-5]

These results seem to be related to several factors concerning the patients' characteristics, the degree and the severity of peripheral arterial disease (PAD), the localization of atherosclerotic lesions and the surgical strategy, including the site of distal anastomosis.[6-8]

The fate of the occluded bypass grafts is still unclear.[9-11] When an early graft thrombosis occurs, the surgical revision is mandatory, whereas in the case of a late graft thrombosis different therapeutic options exist, such as surgical approach, thrombolytic treatment or medical therapy alone. In literature, results of secondary infrainguinal surgical reconstructions are limited.[9, 12]

The aim of this study was to evaluate the authors' experience in below-knee revascularizations in patients with critical limb ischemia, comparing long-term outcomes in primary and secondary interventions.

TABLE I.—*Preoperative clinical and anatomical patients' characteristics.*

	Group 1 (N.=105)	Group 2 (N.=35)	P
Median age (years)	74.1	71.9	NS
Male sex	69 (65.7%)	22 (62.9%)	NS
Smoking	61 (58.1%)	26 (74.3%)	NS
Diabetes	35 (33.3%)	14 (40%)	NS
Hypertension	79 (75.3%)	26 (74.3%)	NS
Coronary artery disease	44 (41.9%)	14 (40%)	NS
Hypercholesterolemia	32 (30.5%)	9 (25.7%)	NS
Hypertrygliceridemia	27 (25.7%)	8 (22.9%)	NS
Chronic renal failure	3 (2.9%)	0	NS
Tissue loss	53 (50.5%)	6 (17.1%)	0.001
Time of CLI (months)	2.2	1.4	NS
Poor run-off status (0-1 vessels)	58 (55.2%)	25 (71.4%)	NS

Materials and methods

From January 2000 to December 2006, 140 consecutive below-knee revascularizations in patients with critical limb ischemia were performed at our Department. Data from all the interventions were prospectively collected in a dedicated database, which included demographic data, preoperative risk factors, clinical and diagnostic assessment, intraoperative features and early and long-term outcomes.

In 105 patients (75%) a primary intervention was performed (Group 1). Early and long-term results in terms of survival, patency and limb salvage were compared with those obtained in the remaining 35 patients (25%) secondarily operated on in the same period for a late (>30 days) bypass graft thrombosis (Group 2).

All the patients preoperatively underwent clinical history and physical examination, a four-view chest X-ray, laboratory tests including complete blood count, coagulative parameters and blood chemistries, an electrocardiogram, a Duplex ultrasound scanning of lower limbs and extra-cranial vessels and an echocardiography with a cardiac consultation. Preoperative diagnostic evaluation was completed by a computed tomography angiography (CTA) of the lower limbs, reserving the digital subtraction angiography (DSA) in double projection in selected cases.

In all the cases the quality and diameter of the greater saphenous vein of the indexed limb was assessed. The authors preferred to use prosthetic graft in patients with absent or unsuitable autologous vein (proximal diameter <4 mm, presence of varicosity, previous thrombophlebitis).

At the end of the intervention completion study with DSA was routinely performed.

Follow-up program consisted of clinical and duplex scanning examination at 1, 6, 12 months and yearly thereafter. During the follow-up a clinical examination and a duplex-scanning assessment were performed in all the patients. For Duplex-scanning the Acuson Sequoia 512 Ultrasound System (Acuson Corporation, Mountain View, CA) with a 8L5 linear array probe with an operating frequency of 8.0 to 5.0 MHz was used in all the cases. Patency of the graft, status of anastomoses, inflow and ouflow vessels and contralateral femoro-popliteal axis were assessed.

Statistical analysis

Early (<30 days) results were assessed in terms of death, thrombosis and amputation rates and were compared in the two groups with χ^2 and Fisher's exact tests.

Long-term results were assessed in terms of survival, primary and secondary patency and limb salvage rates with Kaplan-Meyer curves. Uni- and multivariate analysis for the risk of amputation were performed by means of log-rank test and Cox regression analysis.

Results

The two groups were homogenous in terms of sex, age, common risk factors for atherosclerosis, duration of symptoms, comorbidities and run-off score. Patients in Group 2 had a significantly lower percentage of tissue loss than those in Group 1 (Table I). In Group 2, mean time from primary graft implantation was 22 months (range 4-90).

Concerning intraoperative details, the inflow vessel was always represented by the common femoral artery, while the site of distal anastomosis was in all cases infragenicular. Particularly, in patients of Group 2 distal anastomosis was more frequently performed on a tibial vessel than in patients of Group 1 (34.3% *vs* 18.1%, respectively; P=0.04). There were no differences in terms of graft material (prosthetic graft was used in 54.3% of patients in Group 1 and in 60% in Group 2; P=NS). Associated interventions were performed more often in Group 2 (14 cases-40% and 21 cases-20%, respectively, P=0.02). Concomitant procedures consisted of proximal or distal patching in 23 cases, endovascular treatment of inflow or out-

TABLE II.—*Intraoperative features.*

	Group 1 (N.=105)	Group 2 (N.=35)	P
Stop-flow thrombolysis	6 (5.7%)	4 (11.4%)	NS
Tibial anastomosis	19 (18.1%)	12 (34.3%)	0.04
Prosthetic graft material	57 (54.3%)	21 (60%)	NS
Associated intervention	21 (20%)	14 (40%)	0.02
— Proximal patching	3	0	
— Distal patching	10	10	
— Endovascular procedures	5	2	
— Thrombectomy	3	2	

TABLE III.—*Early (<30 days) results.*

	Group 1 (N.=105)	Group 2 (N.=35)	P
Death	1 (0.9%)	0	NS
Graft thrombosis	17 (16.2%)	13 (37.1%)	<0.001
Amputation	6/251 (2.4%)	7/60 (11.7%)	0.005

TABLE IV.—*Cumulative 60-months outcomes.*

	1-year (%)	3-year (%)	5-year (%)
Survival rate	99.2	92.1	90.3
Primary patency rate	66	51.3	41.1
Secondary patency rate	80.2	66.3	47.7
Limb salvage rate	84.9	75.8	74.1

flow vessels's stenoses in 7 patients and surgical thrombectomy in 5 patients. Intraoperative stop-flow thrombolysis [13, 14] was used in 10 patients, 6 in Group 1 and 4 in Group 2 (Table II).

All the interventions were performed under general anesthesia with intraoperative administration of 30 IU/kg of i.v. heparin at arterial clamping; postoperative drug protocol consisted of i.v. heparin administration (10 UI/kg/hr) followed by oral anticoagulants, maintaining the International Normalized Ratio (INR) between 2 and 3.

Early (<30 days) results are showed in Table III. In Group 1 one patient died in the early postoperative period for an acute myocardial infarction. Thirty early (<30 days) graft thromboses occurred (17 in Group 1 and 13 in Group 2) with a 30-day higher thrombosis rate in Group 2 than in Group 1 (37.1% *vs* 16.2%, P=0.01). All the early thromboses required an immediate reintervention during the same hospital stay,

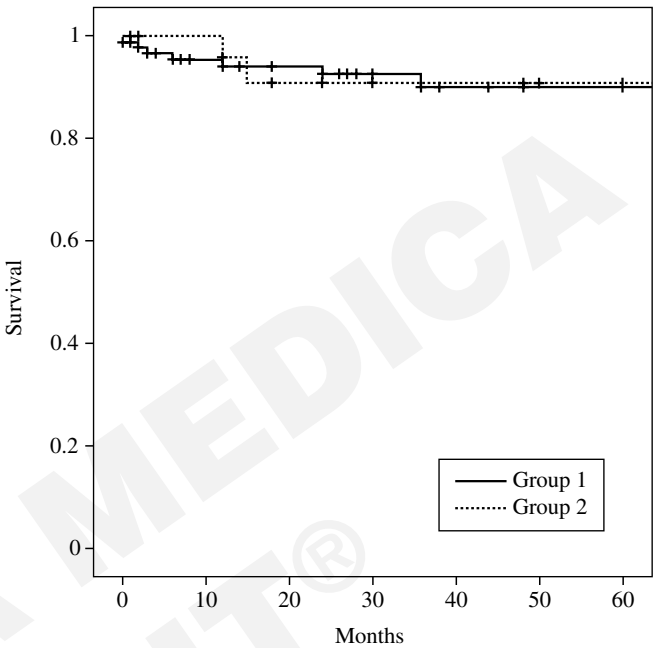

Figure 1.—Estimated 60-month survival rate (Kaplan-Meyer curve with number of patients at risk and standard error values).

which was unsuccessful in 13 cases; 11 out of these patients underwent major amputation (5 in Group 1 and 6 in Group 2), with a 30-day amputation rate higher in patients of Group 2 than in those of Group 1 (17.1% *vs* 4.8%, P=0.02).

Follow-up was available in 116 patients (82.9%) with a mean follow-up time of 25.1 months (range 1-96). In this period 11 deaths (7 in Group 1 and 4 in Group 2), 28 major amputations (17 in Group 1 and 11 in Group 2) and 66 graft thrombosis (45 in Group 1 and 21 in Group 2) occurred. All the deaths were not intervention-related.

Overall estimated survival, primary and secondary patency and limb salvage rates are reported in Table IV.

At 60 months there were no differences between the two groups in terms of survival (90.1% in Group 1 and 90.9% in Group 2; P=NS, log-rank 0.6) (Figure 1), primary patency (43.5% in Group 1 and 31.9% in Group 2; P=NS, log-rank 3) (Figure 2) and secondary patency (48.4% in Group 1 *vs* 43.8% in Group 2; P=NS, log-rank 0.8) (Figure 3). Estimated 60-month limb salvage rate was significantly poorer in Group 2 than in Group 1 (64.1% and 77.7%, respectively; P=0.05, log-rank 3.9) (Figure 4).

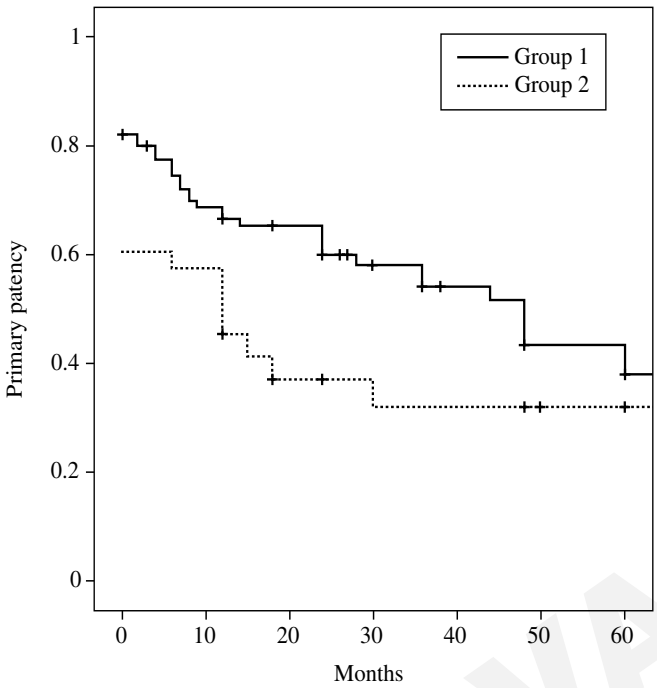

Figure 2.—Estimated 60-month primary patency rate (Kaplan-Meyer curve with number of patients at risk and standard error values).

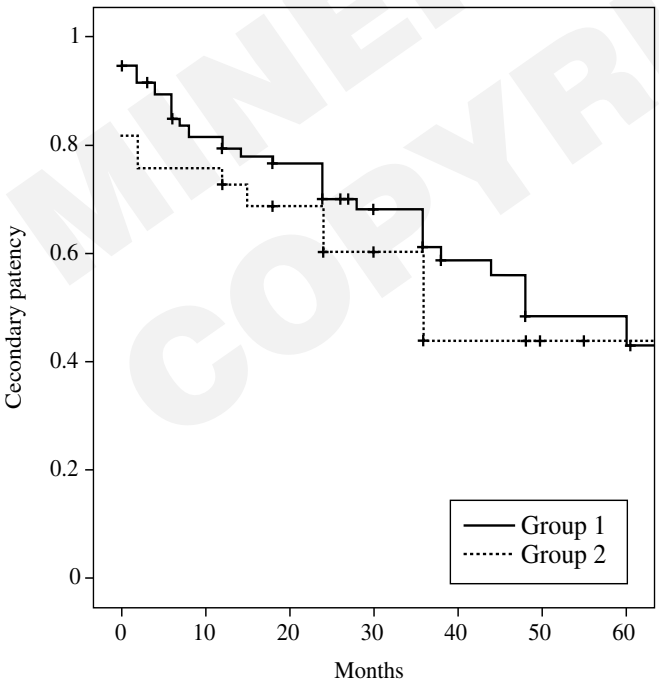

Figure 3.—Estimated 60-month secondary patency rate (Kaplan-Meyer curve with number of patients at risk and standard error values).

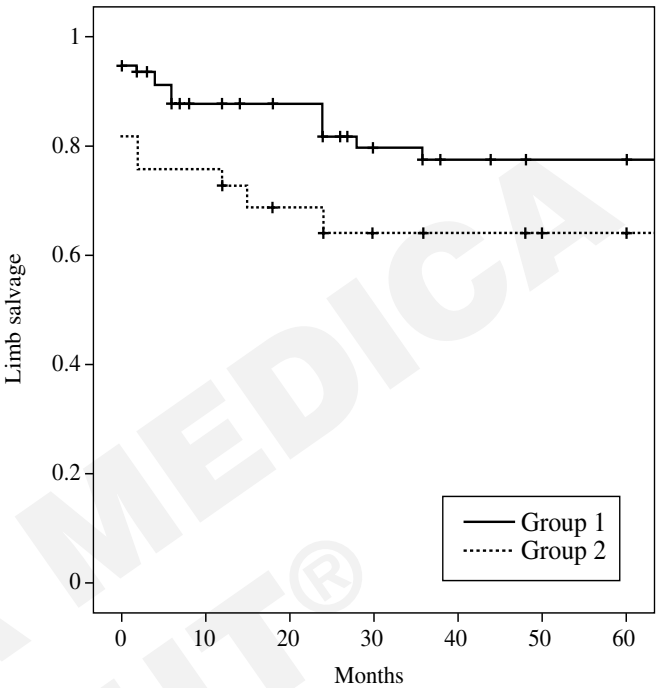

Figure 4.—Estimated 60-month limb salvage rate (Kaplan-Meyer curve with number of patients at risk and standard error values).

Univariate analysis for factors affecting 60-month limb salvage rate showed that only prosthetic graft material significantly increased the risk of amupation (Table V). At multivariate analysis the significance was confirmed (P=0.004, odds ratio 19.5; CI 95% 2.6-96.7).

Discussion

While environmental and medical therapies represent the first therapeutic choice in patients with intermittent claudication, in patients affected by CLI, open or endovascular intervention is mandatory in order to obtain limb salvage.[2]

In this background, surgical revascularization offers good early and long-term results in terms of patency and limb salvage rates, providing an improvement of quality of life of patients affected by PAD.[1, 3] Most series of primary femoro-popliteal bypasses report overall 5-year limb salvage rates up to 85%, with better results when autologous veins were used.[3]

The main problem in femoro-popliteal bypass is the not negligible rate of early and late failure, defined

as the impossibility of maintaining graft patency, away from clinical manifestations of graft occlusion. Data from metanalysis and main mono- and multicentric series showed that the rate of graft failure ranges from 25% and 35% at 2-year follow-up,[3-5] even if the rate of amputation remains lower. In the authors' experience, 5-year limb salvage rate was about 75%, a result in agreement with those obtained in other series.

While early graft thrombosis seems to occur mainly due to technical and surgical factors,[15, 16] late graft thrombosis (>30 days) may occur due to anastomotic miointimal hyperplasia, an inadequate medical therapy or progression of the atherosclerotic disease.[8] During follow-up, a significant proportion of the patients with occluded bypass graft develop CLI when the bypass fails; in these cases the intervention is mandatory.[16] Of interest is the observation that in this study group there was a significantly lower percentage of patients with tissue loss in Group 2 than in Group 1; this fact could be related to the shorter duration of symptoms of CLI in Group 2 and to the faster reconnaissance of a critical situation by a patient already operated on.

Traditional approach to this limb-threatening condition was historically represented by the balloon catheter thrombectomy associated to open or endovascular revision of causative lesions,[17] with not encouraging amputation and death rates (15-30%). Since the 1970s, the thrombolytic treatment has provided an alternative therapeutic approach to redo surgical therapy in patients with recently (<14 days) occluded bypass for a late graft thrombosis.[10, 11, 18, 19] In this series, all the patients with occluded bypass graft had CLI lasting more than 14 days, and preoperative thrombolysis was not attempted. The authors used in selected cases intraoperative stop-flow thrombolysis, particularly in patients with demonstrated preoperative severe tibial disease or when completion angiography showed an incomplete restoration of flow in distal vessels. This adjunctive therapy has been proposed and used by many authors [13, 14] and it seems to offer an improvement of early and late outcomes.

When these approaches are unsuccessful (no restoration of flow), a secondary revascularization remains the option of choice.

Data regarding results of secondary femoro-popliteal bypass after late graft thrombosis are limited and not well established; many authors [9, 20-22] report good long-term limb salvage rates (51% to 80%) not inferior to those obtained with primary femoro-popliteal bypasses, as other studies [12, 23] report discouraging rates (30-40%) of graft patency after secondary femoro-popliteal bypass. A possible explanation for these conflicting results could be the extreme heterogeneity of these studies, including both claudicants and patients with CLI. This study, including only patients with CLI, seems to suggest that results of secondary femoro-popliteal bypass are acceptable, with a satisfactory 5-year limb salvage rate of 64,1%, only slightly poorer than in patients undergone primary femoro-popliteal bypass.

Many factors has been described to affect early and long-term results of secondary femoro-popliteal bypass after late graft thrombosis. Henke *et al.*[12] stated that secondary infrainguinal bypasses are associated with an increased risk of graft failure and amputation, particularly in patients with critical limb ischemia with or without tissue loss, in female and when the patients

TABLE V.—*Group 2: univariate analysis for factors affecting 60-month limb salvage rate.*

	%	Log-rank	P
Sex			
— Male	61.1	0.1	NS
— Female	69.2		
Smoking			
— No	88.9	2.1	NS
— Yes	55.9		
Diabetes			
— No	57.8	1	NS
— Yes	74		
Hypertension			
— No	57.1	0.4	NS
— Yes	65.8		
Coronary artery disease			
— No	55.1	1	NS
— Yes	76.9		
Hypercholesterolemia			
— No	54.3	2.7	NS
— Yes	88.9		
Hypertrygliceridemia			
— No	56.5	1.8	NS
— Yes	87.5		
Tissue loss			
— No	66.8	0.3	NS
— Yes	50		
Run-off status (vessels)			
— 0-1	51.9	0.1	NS
— 2-3	66.1		
Tibial anastomosis			
— No	73.6	2.3	NS
— Yes	46.7		
Prosthetic graft material			
— No	84.6	3.6	0.05
— Yes	47.4		

have a history of early prior graft failure. Rossi *et al.*[20] concluded that redo bypass has a higher risk of failure, particularly in female patients. In the authors' experience, female gender did not represent a significant risk factor for early and late graft thrombosis after secondary femoro-popliteal bypass, and also the presence of skin ulcers did not affect 5-year results.

The only factor affecting long-term limb salvage rate in our study was the choice of graft material and the use of a prosthetic graft was associated with an increased risk of long-term limb loss. The site of distal anastomosis (tibial vessels) and the poor run-off status influenced long-term results in terms of limb salvage rate, even if they did not reach the statistical significance.

Data from the present study were similar to those reported in literature [3, 23] and confirmed the superiority of autologous veins over prosthetic grafts in below-knee revascularizations also in redo interventions. It is clear that an autologous saphenous vein should be used whenever possible; however, particularly in reinterventions, venous resources can be reduced and the use of prosthetic graft is unavoidable. In these situations, adjunctive procedures, such as distal venous patching, can be widely used to improve patency rates, and this was also the authors' policy. Some authors [24] suggested the use of arm vein as autologous conduit in lower extremity revascularization, reporting a better durability of arm vein over the prosthetic graft when an adequate greater saphenous vein is not available; the authors of the present study have no experience with this surgical technique.

Oral anticoaugulants were routinely administered to the patients in postoperative period; there is no evidence in literature concerning the best medical treatment in patients operated on for lower limb revascularization.[2, 25] However, the use of oral anticoagulants has been proposed by some authors in below-knee venous and prosthetic grafts,[25, 26] suggesting the patency rates of grafts to infrageniculate vessels may be improved by an effective anticoagulation. Such a therapeutical strategy, it is probably much more indicated in situations of higher risk of graft failure, such as critical limb ischemia and secondary bypass procedures.

Conclusions

Redo below-knee revascularization in patients with critical limb ischemia in the authors' experience provides acceptable long-term results in terms of primary and secondary patency rates, fairly comparable with those obtained in primary interventions; however, limb salvage rate appeared to be slightly worse in patients undergone redo surgery. The use of synthetic prosthesis affects late outcomes and the use of vein graft, whenever available, is recommended.

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