

# Paper V

## The Outcome of Occluded Above-knee Femoropopliteal Prostheses Implanted for Critical Ischaemia

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**Objectives.** To investigate the impact of patient characteristics and treatment modality (graft thrombectomy vs thrombolysis) on the results of redo procedures for occluded above-knee prosthetic femoropopliteal grafts implanted for critical ischaemia.

**Material and methods.** Fifty-five procedures (thrombolysis 24 and thrombectomy 31) were performed on 24 prostheses (23 patients, 24 limbs) between January 1990 and December 2001. All cases were prospectively registered. Graft patency, limb salvage and survival rates were studied and subgroups of patients were compared. Risk factors were analysed with the use of log rank test and Cox proportional hazard analysis.

**Results.** Half of the 24 initial procedures to restored patency failed within one month. The outcome of second- or third-time redo procedures was similar. The primary patency rates of all 55 redo procedures were 32% at three months, 28% at six months and 12% at 12 months. The results of thrombectomy and thrombolysis were similar. Re-opened grafts additionally treated for an underlying anastomotic stenosis had significantly better patency as compared with re-opened grafts without a pre-existing stenosis on both univariate analysis ( $p = 0.024$ ) and multivariate analysis ( $p = 0.027$ , hazard ratio 2.813). The one-year limb salvage rate was 76%. The one- and five-year survival rates were 87% and 52%, respectively.

**Conclusions.** The results of redo procedures for occluded above-knee prosthetic grafts were disappointing. Grafts in which a graft-related stenosis was treated performed better than grafts in which occlusion could not be attributed to an underlying stenosis. Such cases should most likely be offered conservative treatment, amputation or a new arterial reconstruction.

**Keywords:** Occluded prosthetic grafts; Critical ischaemia; Graft thrombectomy; Thrombolysis.

### Introduction

The management of occluded prosthetic grafts is complex and represents a challenge for the vascular surgeon. The risk of amputation after a failed above-knee prosthetic bypass is high.<sup>1</sup> Occluded femoropopliteal prosthetic grafts may be re-opened either by graft thrombectomy or thrombolysis. Cases with an underlying inflow, outflow or anastomotic stenosis may be treated with patch angioplasty (open surgery) or percutaneous transluminal angioplasty (PTA) to eliminate the stenosis. Other treatment options in these patients are conservative, a new arterial reconstruction or amputation.

The aim of this study was to investigate the impact of patient characteristics and treatment modality (graft thrombectomy or thrombolysis) on the results of redo procedures for occluded above-knee prosthetic

femoropopliteal grafts implanted for critical limb ischaemia.

### Patients and Methods

One-hundred-and-eleven above-knee prosthetic femoropopliteal bypass operations for critical ischaemia were performed between Jan 1990 and Dec 2001. The operations were prospectively recorded into a vascular registry, run by the department. The results of these operations have previously been reported.<sup>2</sup> Fifty-three grafts occluded during follow-up of which 24 were subjected to a total of 55 redo procedures (24 thrombolysis and 31 thrombectomy). These redo procedures constitute the material of the present study. Twenty-nine cases were recorded with primary graft occlusion without being re-opened and the outcome of these was also studied.

The total number of femoropopliteal bypasses performed in Haukeland University Hospital in the same time period were 388, of which 279 were

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above-knee bypasses and 109 were below-knee. In above-knee femoropopliteal bypass, a vein was used as conduit in 27 cases whereas a prosthesis was used in 252 cases. Above-knee prosthetic bypass was performed for intermittent claudication in 141 cases and for critical ischaemia in 111 cases. For below-knee femoropopliteal bypass, an autologous vein was used in 75 cases, human umbilical vein in two cases, a composite graft in 13 cases and a prosthetic graft in 19 cases.

#### *Patient characteristics*

The mean and median age of the patients was 71 and 70 years (range 53–87). There were seven women and 16 men. The recorded preoperative patient characteristics are illustrated in Table 1. The indication for the primary operation was critical ischemia in all cases. Critical ischemia was defined according to the second European Consensus Document on chronic critical leg ischaemia.<sup>3</sup> Poor run-off score was defined as one patent crural artery or less, as seen on the preoperative angiogram. Poor run-off was recorded in 10 limbs (42%). In one case, graft implantation was performed without a preoperative angiography. Selection criteria for the treatment chosen were not clearly defined, but patients unfit for thrombolysis according to the recommendations of the Working Party on Thrombolysis in the Management of Limb Ischaemia were selected for thrombectomy.<sup>3</sup> Three cases of failed thrombolysis were subsequently subjected to open surgery.

#### *Thrombolysis*

The endovascular procedures ( $n = 24$ ) were performed with a crossover technique. The catheter was placed in the thrombus with constant release of thrombolytic agent. The catheter was re-positioned more distally as the thrombus dissolved. Until April 1997 Streptokinase (40 000 IE/hour) was used as thrombolytic agent. Recombinant human tissue-type plasminogen activator (rt-PA) was used in all later

procedures. A bolus dose of 5 mg was injected into the thrombus, followed by a continuous infusion (1.5 mg/hour). Cases complicated with distal embolization were managed with further thrombolysis or endovascular aspiration. Percutaneous transluminal angioplasty (PTA) after thrombolysis was successfully performed in six cases. In 18 cases, anastomotic stenoses were not found at completion angiography.

#### *Thrombectomy*

The open operations ( $n = 31$ ) were done with an incision over the distal anastomosis. The graft was incised and the anastomotic area was assessed intraluminally after thrombectomy. The thrombectomy was performed with a graft thrombectomy catheter. Anastomotic revision was performed in four cases. No evidence of graft stenosis had been identified during duplex surveillance of these 4 grafts. In the remaining 27 cases, freedom of stenosis was diagnosed with angiography in 20 cases and with duplex scanning in four cases. In three cases the only information regarding the anastomoses was that the balloon catheter passed the anastomoses without difficulty.

#### *Follow-up*

Postoperatively, all patients were given aspirin 160 mg daily on a permanent basis if tolerated. Follow-up included duplex scanning, ankle-brachial pressure measurement and clinical assessment at one, three, six and 12 months after surgery and annually thereafter. New procedures entered a new protocol for follow-up. The endpoints in this study were occlusion, major amputation and death. Graft occlusion was diagnosed by duplex scanning or by angiographic findings. The mean follow-up with respect to patency after re-opening procedures was 4 months (range 0–36 months). The mean follow-up with respect to limb salvage was 31 months (range 0–88 months) whereas the mean follow-up regarding survival was 59 months (0–137 months). Mortality data were obtained from The Registrars Office of Birth and Death.

#### *Statistics*

Patency, limb salvage and survival analyses were done using the product-limit method and illustrated as Kaplan-Meier curves. Calculations of patency were performed on an intention-to-treat basis. Univariate analysis of patency was performed with the log rank test whereas the Cox proportional hazard model

**Table 1. Patient characteristics in 23 patients with re-opened grafts originally implanted for critical ischaemia. (COPD = chronic obstructive pulmonary disease)**

Risk factor	$n =$ cases
Hypertension	9/21
Diabetes mellitus	3/21
COPD	7/21
Coronary disease	9/23
Cerebrovascular insult	3/23
s-Creatinin >125 mmol/l	4/22
Smoking	17/20

was applied for multivariate analysis of the recorded risk factors. Calculations of limb salvage and survival analysis were based upon the date of the first redo procedure. Comparisons of patency between groups were performed with log rank test. Categorical data were analysed with Fisher's exact test. The software program "SPSS for Windows 13.0" (SPSS Inc. (2004), Illinois, USA) was used for statistical computations. Differences were considered statistically significant at the 5% level ( $p < 0.05$ ).

**Results**

*Re-opening procedures*

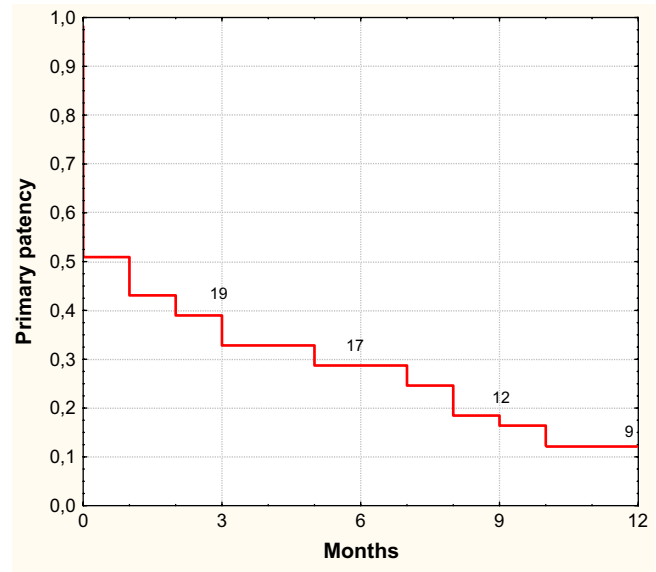
Twenty-four first-time redo procedures (graft thrombectomy 13 and thrombolysis 11) were performed. The mean and median time intervals from the primary graft implantation to the first redo procedure were 18 and 9 months (range 0–84). In Table 2, the grafts are categorised according to the number of re-opening procedures. Fifty-three of 55 redo procedures re-occluded during follow-up, leaving out one patient who died after thrombolysis and one patient lost to follow-up. There were no differences between first, second and third-time redo procedures with respect to patency. Twenty-nine re-occlusions (53%) occurred within one month after the re-opening procedure. The patency rates for all redo procedures were 32% at three months, 28% at six months and 12% at 12 months (Fig. 1). Graft thrombectomy and thrombolysis had similar patency rates ( $p = 0.90$ , log rank test) as did thrombolysis with streptokinase compared to rt-PA. None of the recorded patient characteristics influenced patency of the redo procedures.

*Anastomotic revisions*

Revision was done in 10 cases (six thrombolyses by PTA, four thrombectomies by patch angioplasty). Three of these grafts occluded within one month postoperatively. Three grafts were patent for 17, 34 and 36 months respectively and these were in the thrombectomy group. One case had no record of

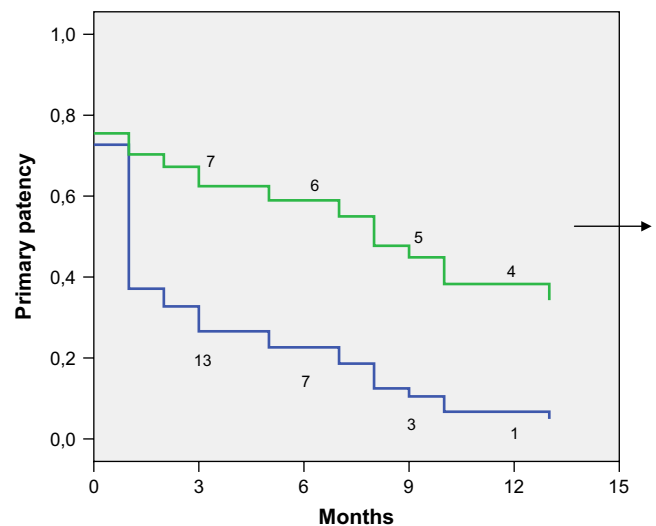
**Table 2. Grafts categorised according to how many times they were re-opened**

Procedure	1 Re-opening (n = 24)	2 Re-opening (n = 16)	3 or >Re-openings (n = 15)
Graft thrombectomy (n = 31)	n = 13	n = 10	n = 8
Thrombolysis (n = 24)	n = 11	n = 6	n = 7



**Fig. 1.** Kaplan-Meier curve: The patency rates of 55 re-opening procedures for occluded prosthetic above-knee femoropopliteal bypass. The numbers above the curve indicate the numbers at risk.

follow-up. At 12 months postoperatively, four out of 10 patients receiving redo procedures including anastomotic revision were alive with patent graft. Univariate analysis revealed anastomotic revision to be associated with improved patency ( $p = 0.024$ , log rank test) (Fig. 2). This association was also confirmed on multivariate analysis ( $p = 0.027$ , Cox regression analysis) with a hazard ratio of 2.813 (Table 3).



**Fig. 2.** Kaplan-Meier curve: The patency rates of 45 redo procedures for graft occlusions without a graft-related stenosis (lower curve) compared with 10 re-opening procedures in which also an anastomotic revision was done (upper curve). The numbers above and below the curves indicate the numbers at risk.

**Table 3. Cox regression analysis of risk factors for reduced patency in 55 redo procedures for occluded above-knee femoropopliteal prostheses implanted for critical ischaemia**

Risk factor	<i>p</i> -value	Hazard ratio	95% CI <sup>1</sup>
No presence of graft-related stenosis	0.027	2.813	1.125–7.038
Thrombectomy vs thrombolysis	0.127	1.594	0.875–2.902
Poor run-off score <sup>2</sup>	0.342	1.329	0.739–2.392
Tissue loss vs rest pain	0.584	0.841	0.453–1.561

<sup>1</sup> CI: Confidence Interval.

<sup>2</sup> Poor run-off score was defined as one patent crural artery or less as seen on the preoperative angiogram.

### *Limb salvage*

Thirteen limbs in 13 patients (57%) were subjected to major amputation. The limb salvage rates were 76% and 64% at one and two years respectively after re-opening procedures. None of the recorded patient characteristics influenced limb salvage. Twenty-nine cases with occluded grafts were not subjected to redo procedures, of which 14 limbs were amputated.

### *Survival*

One patient died two days postoperatively due to cerebral haemorrhage as a complication of thrombolysis. At 12 months, 20 of 23 patients were still alive (87%). The five-year survival rate was 52%. None of the recorded patient characteristics were significantly associated with reduced survival.

### *New arterial reconstruction*

Four patients received a new bypass. In one case a femoropopliteal vein graft was placed. This graft remained patent throughout follow-up. Three limbs were treated with a femorodistal vein bypasses of which all occluded and the patients subsequently required amputation.

## **Discussion**

The choice of treatment modality may be difficult when a patient presents with critical ischemia due to an occluded above-knee femoropopliteal graft. The treatment options are conservative, amputation, re-opening of the occluded graft or a new arterial reconstruction. The latter may be performed with subintimal angioplasty or a new bypass. Patients who originally receive a prosthetic graft for critical

ischemia are likely to develop recurrent critical ischemia in case of graft occlusion. This often demands intervention to avoid a major amputation or to relieve pain. There are reports of acceptable results of re-opening procedures for occluded above-knee femoropopliteal prostheses.<sup>4,5</sup> However, these studies include cases with intermittent claudication as well as critical ischaemia. In a study by AbuRahma *et al.*, limbs with less than two open tibial arteries were excluded, as were patients with inflow disease.<sup>4</sup> The indication for all graft implantations in the present study was critical ischemia and none were excluded.

The results of the present series are not encouraging. A previous paper reported a three-year patency of redo procedures of 12–20%.<sup>6</sup> Our department has previously reported a 12-month patency of 29% after redo operations for occluded above-knee prosthetic femoropopliteal bypass implanted for intermittent claudication.<sup>7</sup>

Re-opened grafts commonly re-thrombose. This was especially true for grafts that occluded without an underlying stenotic lesion, which was the case in 45 procedures. These grafts may have occluded because of low blood flow, possibly due to progression of distal atherosclerotic disease leading to high peripheral resistance. Low graft flow could also be due to inactivity or smoking (85% of the patients in the present series were smokers). According to a recently published meta-analysis, smokers have a three-fold risk of graft failure compared with non-smokers.<sup>8</sup> This could not be verified for the redo procedures in the present study, probably due to the overall very low patency rates and small sample size. In an earlier study, we found that smoking was significantly associated with reduced primary and secondary patency of the primary bypass operations.<sup>2</sup>

Primary occlusion of above-knee femoropopliteal prostheses occurring within 10 months has been associated with poor results of re-opening procedures.<sup>5,9</sup> The length of time before graft occlusion after primary implantation did not influence the results after re-opening in the present series. Surgical redo procedures have been reported superior to the results of endovascular treatment.<sup>4</sup> However, that conclusion was based only on patients treated for an additional stenotic lesion. Our results revealed no difference between the results of thrombolysis and graft thrombectomy. Redo procedures that included treatment of a stenotic anastomotic lesion resulted in prolonged patency in three cases. This may indicate that some patients may benefit from a redo procedure if a stenotic lesion is known prior to graft occlusion, which is in agreement with

a previous report.<sup>10</sup> Thus, knowledge of an anastomotic stenosis prior to graft occlusion may be important. This again may indicate a benefit of graft surveillance. However, the numbers in the present study are too small for conclusion in this respect. Obviously, the optimal treatment is PTA of a graft-related stenosis to prevent occlusion. A liberal policy regarding treatment of graft-related stenoses may be beneficial, but we have no data to support this.

Both hypertension and poor run-off has been associated with reduced patency of redo procedures for occluded grafts.<sup>11–13</sup> Neither comorbidity nor poor run-off were associated with reduced patency in the present study, probably due to small sample size.

Thirteen limbs were subjected to major amputation, giving a one-year limb salvage rate of 76%. This is consistent with results from a previous study.<sup>14</sup> Whether the repeated redo procedures influenced limb salvage or not remains unknown; 16 of 24 grafts were re-opened twice or more.

In the present series, ten limbs had poor run-off score in whom a femoropopliteal bypass may have been insufficient to treat critical ischaemia, as these patients most likely had multi-level disease.<sup>15</sup> Femorodistal bypass might have been more suitable for some of those patients. In the present series, femorodistal bypass was used as a last resort and the results of these procedures were poor.

The high prevalence of cardiac disease and other comorbidity illustrates that patients with critical ischemia are at high-risk following surgery and invasive procedures (Table 1). In the present series, one patient died within 30 days due to cerebral haemorrhage, underlining thrombolysis as a dangerous treatment.<sup>16</sup>

Even if a re-opened graft is patent only for a limited period of time, the patient may benefit from a pain-free interval and sustained ability to walk. Some patients may find such a result acceptable. However, one could claim that re-opening procedures only postpone an inevitable amputation. It might be better to amputate early, especially if the patient receives a walking prosthesis. This may be true only for younger patients, since elderly patients if amputated, will be constrained to a wheelchair and dependent on nursing facilities.

Adjunctive antithrombotic medication is recommended. Clopidogrel should be given to all patients with aspirin intolerance due to the fact that antiplatelet agents improve graft patency, especially in prosthetic grafts.<sup>17</sup> Clopidogrel may also be useful in addition to aspirin in cases with a marked tendency for thrombosis. However, this has not been proven in controlled trials. Warfarin has been reported to

improve patency of infrainguinal vein grafts, but not prosthetic grafts.<sup>18</sup>

In conclusion, both thrombolysis and surgical thrombectomy put a heavy strain on restricted resources.<sup>19</sup> The results of this study suggest that redo procedures for occluded above-knee prosthetic grafts are of limited value. Re-opening occluded above-knee prosthetic bypasses implanted for critical ischaemia cannot be recommended except in cases of a proven anastomotic lesion. Other cases needing re-intervention should be treated by amputation or a new arterial reconstruction.

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Accepted 21 June 2006

Available online 28 August 2006

