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Natural History of Infrainguinal Vein Bypass Stenoses: Early Lesions Increase the Risk of Thrombosis

T. G. Nielsen*

Department of Vascular Surgery RK, Rigshospitalet, National University Hospital, Copenhagen, Denmark

Objectives: *To describe the natural history of stenoses in infrainguinal vein bypasses and to identify factors predicting outcome.*
Methods: *Forty-two patients with non-revised vein bypass stenoses were followed prospectively by ultrasound Duplex scanning and ankle blood pressure measurements.*
Results: *During a median follow-up of 8(range 0–22) months 18(43%) (95% confidence limits 28–59%) bypasses thrombosed and 6(14%) (95% confidence limits 5–29%) patients were amputated. Bypass patency was lower in 12 patients with stenoses associated with reduction in ankle brachial index (ABI) exceeding 0.15 than in 30 patients with no or only marginal reduction in ABI (12 month patency 33% vs. 68%, p = 0.005). Among the 30 patients without distal pressure reduction, stenoses identified within 3 months from surgery were associated with an increased risk of thrombosis as compared to stenoses identified at a later stage (12 month patency 51% vs. 92%, p = 0.03).*
Conclusion: *Time interval from surgery to stenosis detection seems to be an independent parameter influencing outcome in patients with vein bypass stenoses.*

Key Words: Autologous vein; Infrainguinal bypass; Graft stenosis; Duplex ultrasound.

Introduction

Vein bypass is an established procedure in the management of critical limb ischaemia.[1] Graft stenoses due to myointimal hyperplasia occur in 20–30% of vein bypasses[2–4] and is the predominant cause of reconstruction failure during the first year after surgery.[5] The positive benefit of intensive bypass surveillance with early revision of failing, but patent, grafts has been shown in a recent randomised study by Lundell *et al.*[6] Not all stenoses, however, progress to occlusion and the criteria for bypass revision remain controversial.[7–9] In this study patients with conservatively treated stenoses were followed prospectively in order to describe the natural history of vein bypass stenoses and to identify subgroups in whom prophylactic reintervention is justified.

Materials and Methods

Since 1991 patients undergoing infrainguinal vein bypass surgery at the Vascular Service, Rigshospitalet in Copenhagen have been included in a 2 year surveillance regime based on ultrasound Duplex scanning and ankle blood pressure measurements. During an 18 month period from January 1 1993 until June 30 1994, a total of 1508 Duplex examinations were carried out in 356 patients. In 63 (18%), the examinations revealed an increase in the peak systolic velocity by a factor 2.5 or more indicative of significant stenosis.[10,11] Among the 63 patients with Duplex verified stenoses 30 (48%) had no or only marginal reduction in ankle brachial index (ABI-reduction ≤ 0.2) and were treated conservatively. In another 12 (19%) patients with stenoses associated with interval reduction of ABI exceeding 0.2 reintervention was not carried out for the following reasons. Cardiac disease (5) and wound infection (1) contraindicated prophylactic surgery in six, and six other patients with diffusely diseased grafts were considered to be technically inoperable. Eleven surgical revisions and eight percutaneous transluminal angioplasties (PTA) were performed in 17 (27%) patients with stenoses causing a distal pressure reduction of more than 0.2. In four (6%) additional cases elective intervention was planned but the bypasses thrombosed median 15

*Please address all correspondence to: Tina G. Nielsen, Department of Vascular Surgery RK 3111, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark.

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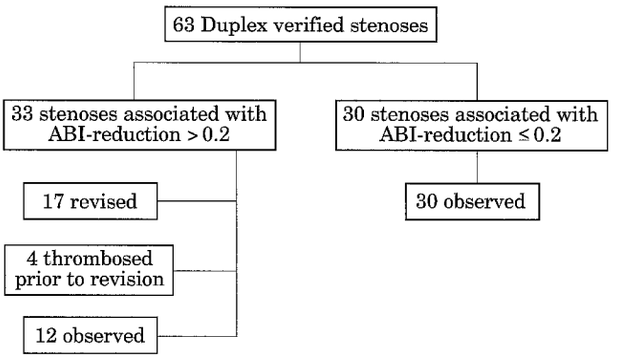

Fig. 1. The management of 63 patients with Duplex verified vein bypass stenoses.

(4-47) days after detection of stenoses before revision was carried out. These 21 patients in whom bypass revision was planned were excluded from the study (Fig. 1).

Thus 42 non-revised patients were available for analysis. The median age of these 28 males and 14 females was 74 (range 50–88) years. Three (7%) had insulin dependent diabetes and six (14%) non-insulin dependent diabetes. The indication for surgery was claudication in seven (17%), critical ischaemia in 34 (81%) and a symptomatic popliteal aneurysm in one (2%). Sixteen (38%) bypasses were femoropopliteal and 26 (62%) femoroinfrapopliteal grafts. Time interval from bypass surgery to detection of the stenosis is shown in Fig. 2. The stenoses were located at the proximal anastomosis in six (14%), in the body of the graft in 24 (57%) and at the distal anastomosis in 12 (29%). Thirty-seven (88%) stenoses were asymptomatic, while two (5%) patients had experienced recurrent claudication and three (7%) developed rest pain at the time of diagnosis.

Non-revised patients were included in a surveillance protocol consisting of ultrasound Duplex scanning and ankle blood pressure measurements at 6 weeks and 3, 6, 9, 12, 18 and 24 months. All patients with patent grafts were followed for at least 6 months. The Duplex examinations were performed with a B&K Medical 3535 Duplex scanner using a 7.5 MHz linear array or a 5 MHz convex array transducer and the following waveform parameters determined: midgraft peak systolic velocity (PSVmidgraft), ratio of peak systolic velocity in the stenosis and adjacent normal graft segment (PSV-ratio) and end diastolic velocity in the stenosis (EDV). Resting ankle blood pressure was determined by Doppler technique. A reduction in ABI between two examinations of more than 0.15 was regarded a significant pressure reduction and an indicator for disease progression.

Statistics

Bypass patency was calculated by the life-table method and patency rates between groups compared by log rank test. Proportions among two groups were compared by Fischer's exact test. A confidence limit of less than 0.05 was regarded as significant.

Results

During a median follow-up of 8 (range 0–22) months, six patients died. Eighteen (43%) (95% confidence limits 28–59%) bypasses thrombosed resulting in a cumulative 12 month patency rate of 58% (95% confidence limits 39–77%) (Fig. 3). Sixteen of the 18 patients presented with recurrent symptoms in relation to the bypass occlusion: claudication in four and

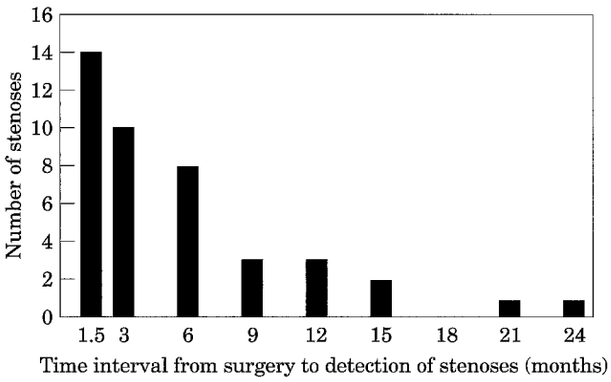

Fig. 2. Time interval from surgery to the detection of stenoses in 42 patients with non-revised vein bypasses.

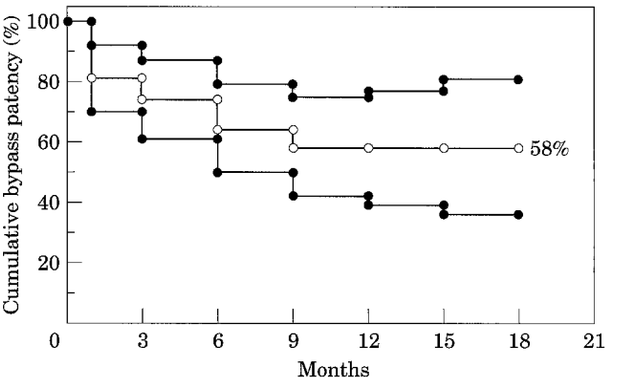

Fig. 3. Cumulative bypass patency in 42 patients with non-revised vein bypasses (● = 95% confidence intervals).

Table 1. Patient outcome at follow-up according to progression of stenosis

	Asymptomatic	Claudication	Critical ischaemia
Regressed/unchanged stenosis (n=16)	16	0	0
Progressed stenosis (n=8)	5	2	1
Bypass occlusion (n=18)	2	4	12
Total (n=42)	23 (55%)	6 (14%)	13 (31%)

critical ischaemia in 12, of which five had a major and one a minor amputation (Table 1).

Bypass patency was lower in the 12 patients with an initial pressure reduction as compared to the 30 patients without a pressure reduction at the time of initial examination (12 month patency 33% *vs.* 68%, $p = 0.005$) (Fig. 4). However, bypass failure occured without precedent ABI-reduction in seven patients, of which six had developed stenoses within 3 months and one 6 months postoperatively. Patients who developed stenoses within 3 months from surgery had a higher risk of bypass thrombosis than patients who developed stenoses at a later stage (12 month patency 40% *vs.* 83%, $p = 0.01$). This association between early development of stenosis and poor outcome was also present among the 30 patients with non-haemodynamically significant stenoses (12 month patency 51% *vs.* 92%, $p = 0.03$) (Fig. 5). All six amputations occured in the group of patients with stenoses appearing early ($\leq$ 3 months).

No significant correlation between bypass patency and age, diabetes, level of distal anastomosis, the location of the stenosis or PSVmidgraft could be demonstrated. However an EDV exceeding 75 cm/s

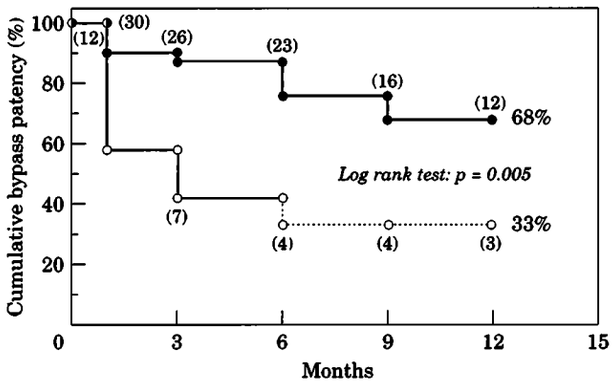

Fig. 4. Cumulative bypass patency in 12 patients with haemodynamically significant stenoses (ABI-reduction > 0.15) (○) and in 30 patients with non-haemodynamically significant stenoses (ABI-reduction $\leq$ 0.15) (●).

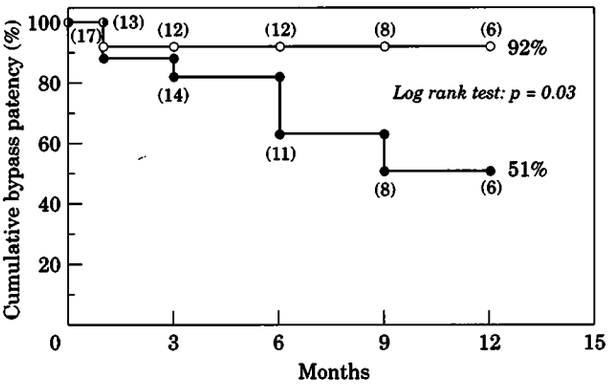

Fig. 5. Cumulative bypass patency in 17 patients with non-haemodynamically significant stenoses detected within 3 months (○) and in 13 patients with non-haemodynamically significant stenoses detected more than 3 months from surgery (●).

was associated with an increased risk of occlusion (12 month patency 29% *vs.* 73%, $p = 0.003$).

Discussion

Though graft related stenoses are common following infrainguinal vein bypass surgery, few studies have addressed the fate of uncorrected stenoses. In this study 42 patients with Duplex-verified non-revised stenoses were followed prospectively for up to 22 months to describe the natural history of vein bypass stenoses and to identify parameters predicting outcome. As observation of haemodynamically significant stenoses in our opinion is unethical the study group predominantly consisted of patients with non-haemodynamically significant stenoses as well as a minor group of patients with stenoses fulfilling our criteria for revision, but in whom reintervention for various causes was not carried out.

In the literature the incidence of bypass occlusion in patients with stenoses ranges from 13% to 39%, depending on the degree of stenosis and length of follow-up.[2,4,8,12,13] Though the present selected patient population may not be fully representative, our finding of a 12 month patency of only 58% confirms the general opinion that conservatively treated vein bypass stenoses are associated with a considerable risk of occlusion. Reconstruction failure, however, did not inevitably result in loss of the extremity as the majority of patients avoided amputation following bypass occlusion. Considering this relatively benign course the best approach towards vein bypass stenoses seem to be selective revision of subgroups at increased risk.

Confirming the observations of Green *et al.*,[8] ABI-

reduction was found to be highly predictive of graft failure. In a smaller series Moody *et al.* observed that stenoses detected early tended to progress to occlusion more often than later stenoses, though the difference did not reach statistical significance.[2] We also found an increased risk of bypass thrombosis in patients with stenoses identified within 3 months postoperatively. Early lesions accounted for 15 of the 18 occlusions and all six amputations. Furthermore six of the seven occlusions not preceded by distal pressure reduction occurred in this group. Therefore patients with early stenoses appear to benefit from revision even in the absence of ABI-reduction. The majority of vein graft stenoses occuring during the first year after surgery are caused by myointimal hyperplasia. The initiating event is believed to be intraoperative endothelial injury leading to an accelerated healing response, which involves platelet aggregation and smooth muscle cell proliferation and results in progressive luminal narrowing.[14] Thus, it is likely to assume that the development of stenoses in all cases begins at the time of surgery, and that stenoses reaching the threshold of diagnosis in the early postoperative period represent rapidly progressing lesions,[15] whereas stenoses identified later represent more slowly progressing lesions. The finding that all patients with late stenoses progressing to occlusion had developed sufficient collateral supply to avoid amputation, supports the assumption that disease progression is slower in this group.

In contrast to the high incidence of occlusions in patients with early lesions only one of 13 bypasses with late non-haemodynamically significant stenoses thrombosed during follow-up. In a recent study Mills *et al.*[16] observed that most stenoses developed at sites of early flow abnormalities and that de novo stenoses rarely occured after 3 months. These authors used a velocity ratio of 1.5 for detection of stenoses compared to our threshold of 2.5. This difference may explain the higher indicence of *de novo* stenoses detected after 3 months in our series. It is possible that minor flow disturbances might have been present earlier in the cases we classified as late *de novo* stenoses. Nevertheless our finding of a low rate of reconstruction failure in patients with non-haemodynamically significant stenoses identified more than 3 months postoperatively indicates that revision is not justified in this subgroup and hence supports Mills conclusion that the value of Duplex scanning is highest during the first postoperative months.

The risk of occlusion following detection of stenoses was highest during the first month and in four cases strictured bypasses occluded before planned revision was carried out. Based on this experience our policy has been modified so that angiography and bypass revision are carried out within a few days after detection of a stenosis. Likewise, follow-up of patients not subjected to immediate revision should be very close with intervals of no more than a few weeks.

In summary, ankle blood pressure as well as time of stenosis detection are independent risk factors for graft failure in patients with vein bypass stenoses. Based on these findings patients may be separated in three risk groups (1) patients with haemodynamically significant (ABI-reduction > 0.15) stenoses who undoubtedly benefit from revision (2) patients with early (≤ 3 months) non-haemodynamically significant stenoses in whom quick revision should also be considered and (3) patients with late non-haemodynamically significant lesions in whom continued surveillance is warranted.

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