View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Elsevier - Publisher Connector

Intraoperative flow predicts the development of stenosis in infrainguinal vein grafts

Leo H. M. Ihlberg, MD,[a] N. Anders Albäck, MD,[a] Riitta Lassila, MD,[b] and **Mauri Lepäntalo, MD,[a]**
Helsinki, Finland

Objective: **There are data to suggest that the development of myointimal hyperplasia is affected by long-term alterations in blood flow. However, the clinical relevance of these findings has not been demonstrated.**
Methods: **In this retrospective clinical study, intraoperative volume flow measurement with transit time flowmeter was performed in 257 infrainguinal vein grafts carried out in 241 patients. The patients were enrolled in an intensive duplex scanning–based surveillance program. The relationship between the intraoperative graft flow and subsequent occlusion or development of stenosis was evaluated and controlled for other pertinent risk factors.**
Results: **The median follow-up time was 13.6 months. A graft stenosis was found in 58 grafts. The mean graft flow for event-free grafts was 98 mL/min, which was significantly higher compared with 78 mL/min for stenosed or 69 mL/min for occluded grafts. The patients were divided into four groups according to quartiles of the sample distribution of graft flow measurements. The respective 2-year primary and assisted primary patency rates in the lowest to the highest graft flow groups were 39%, 49%, 47%, and 72% ($P = .003$) and 55%, 67%, 71%, and 84% ($P = .01$). Analogous significant differences were observed for maximal flow capacity measurements. Female sex ($P = .009$) and low graft flow in maximal flow capacity measurements ($P = .003$) were independent predictors of stenosis development in the multiple regression model.**
Conclusion: **Intraoperative graft volume flow is a predictor of bypass occlusion after infrainguinal bypass. In addition, this study verifies an association between the development of clinically evident graft stenoses and low graft flow. (J Vasc Surg 2001;34:269-76.)**

Infrainguinal arterial bypass reconstructions are routinely performed on patients with severe lower limb vascular disease. Autologous vein is the preferred conduit, especially for bypasses extending below the knee.[1] Unfortunately, the failure rate has remained high, and the outcome of an occluded bypass after a take-back procedure is bleak. In the immediate postoperative period, reconstructions fail mainly because of technical or graft-related defects, as well as because of compromised runoff.[2,3] Most midterm bypass occlusions are due to the development of focal stenoses within the conduit or at the anastomotic areas, with an incidence of 20% to 35% within 1 to 2 years after surgery.[4,5]

Myointimal hyperplasia, which is usually a self-limiting process, is the universal response of a vein graft to insertion into the arterial circulation. In focal areas, it can proceed to a significant stenosis, leading to graft failure.[6,7] Because the pathophysiologic cause of myointimal hyperplasia is unknown, no effective clinical regimen to limit its development is available.[6] Thus, the treatment strategy has been surgical or endovascular correction of already established stenoses.[8,9] The detection of remediable lesions by rigorous duplex surveillance programs has gained wide acceptance.[10-12] At present, the whole population of infrainguinal vein grafts are surveyed because no clear risk groups have been defined.

Interestingly, evidence from several experimental studies suggests that in a state of a low flow and a low shear stress, the formation of myointimal hyperplasia is accelerated.[13-18] The purpose of this study was to evaluate the value of graft volume flow measured during operation in predicting the survival of infrainguinal vein grafts and, moreover, whether it is predictive for the development of de novo graft stenoses.

METHODS

Intraoperative flow measurements were performed in 276 infrainguinal vascular reconstructions with an autologous vein graft at the Division of Vascular Surgery, Helsinki University Central Hospital, from July 1994 through June 1999, of which 257 infrainguinal vascular reconstructions carried out in 247 patients are included in this study. These represented 52% of all infrainguinal vein graft reconstructions performed during this period. The measurements were performed with a transit time flowmeter (CardioMed CM4006, Medistim A/S, Oslo, Norway). The ultrasonic transit-time flowmeter is based on ultrasonic pulsed-beam technique and measures volume flow within the conduit. A precalibrated probe is placed around the vein graft of a size to fit the graft (from 3-5 mm). The flow measurements have been found to be highly valid and reproducible and are not dependent on vessel diameter,

From the Departments of Vascular Surgery,[a] and Internal Medicine,[b] Helsinki University Central Hospital.
Competition of interest: nil.
Supported by a grant from Finska Läkaresällskapet.
Reprint requests: Leo Ihlberg, Department of Vascular Surgery, Helsinki University Central Hospital, PO Box 340, FIN – 00029 HYKS (e-mail: leo.ihlberg@hus.fi).
Copyright © 2001 by The Society for Vascular Surgery and The American Association for Vascular Surgery.
0741-5214/2001/$35.00 + 0 **24/1/115812**
doi:10.1067/mva.2001.115812

Table I. Indication for revascularization

Indication	*No. (%)*
Intermittent claudication	28 (11)
Rest pain	52 (20)
Ischemic ulcer	104 (40)
Gangrene	63 (25)
Popliteal aneurysm	5 (2)
Acute-on-chronic ischemia	3 (1)
Graft infection	2 (1)

wall thickness, or hematocrit changes.[19,20] The variability in in vivo testing has been between 1.1% and 4.4%.[19] The graft flow was measured from the proximal part of the graft after the distal anastomosis was completed, and the flow was opened and stabilized. The measurement was repeated after injection of 40 mg of papaverine hydrochloride into the graft. This acts as a smooth muscle relaxant that causes a transient vasodilation of the distal vascular bed, and maximal flow capacity (MFC) is registered. This was performed at the preference of the operating surgeon and only in patients who were considered hemodynamically stable and with a good diuresis. Overall, the MFC was measured in 189 of 257 grafts. During operation the reconstruction was evaluated with on-table angiography, angioscopy, and invasive pressure measurements when necessary and on the basis of the preference of the operating surgeon. If the intraoperative assessment prompted corrective measures to technical issues within the bypass, the flow measurements were repeated thereafter, and the final values were taken into the analysis.

The patients were enrolled into a prospective graft surveillance protocol at outpatient visits that included physical examination, ankle/brachial index measurements, and color-flow duplex scanning at 4 to 6 weeks and 3, 6, 9, 12, 18, and 24 months after operation. The duplex examinations were performed by means of a 7.5-MHz transducer with either an ATL Ultramark 9 (Advanced Technology Laboratories, Bothell, Wash) or an HP Image Point (Hewlett Packard, Andover, Mass) ultrasound scanner. The whole graft, including a few centimeters of inflow and outflow arteries, was serially scanned, and specific structural abnormalities or exceptional flow patterns in color-flow images were searched for. Peak systolic velocity (PSV) measurements were performed routinely at multiple sites along the course of the graft and especially at sites of abnormal flow patterns.

The noninvasive criteria for a failing graft included a decrease in ankle/brachial index greater than 0.15, PSV less than 45 cm/s throughout the graft, or a focal disturbance where the V_2/V_1 ratio exceeded 2.0 (V_2 is the PSV at the site of the stenosis, and V_1 is the PSV at a nonstenosed point within 2 cm on either side of the stenosed segment). For these grafts confirmatory arteriography was usually performed before graft revision. During the last 2 years of the study period, the revision was performed on the basis of duplex findings alone, on the condition that the stenosis was clearly found and that it was limited to the graft.

The patients were identified through the hospital's vascular registry database, and the clinical records were retrospectively reviewed. In 19 patients an adjuvant arteriovenous fistula (AVF) was applied to the distal anastomosis, and they were excluded from the analysis.

Data on patient demographics, risk factors, and procedure specifications were entered into a computerized database. The series was composed of 138 men and 119 women with a mean age of 71 years (range, 21-95 years). The pertinent risk factors included a history of smoking (30% of patients), diabetes mellitus (50%), hypertension (42%), coronary artery disease (44%), history of cerebrovascular accident (16%), chronic obstructive pulmonary disease (10%), chronic renal insufficiency (14%), and previous vascular reconstruction or amputation (43%). The indication for revascularization was critical leg ischemia in 85% of patients (Table I).

The bypass types were as follows: 73 (28%) femoral-popliteal, 102 (40%) femoral-crural, 44 (17%) femoral-pedal, and 38 (15%) popliteal-distal. In three reconstructions a microvascular free flap muscle transfer was anastomosed to the bypass in the same operation. In situ vein was used as bypass conduit in 117 grafts, and reversed or translocated nonreversed greater saphenous vein, as well as spliced/alternative vein grafts, was used in 140 grafts.

The subsequent graft patency and duplex information at the outpatient visits were recorded. Details about the location and the length of the stenosis, V_2/V_1 ratio, and time of occurrence were also recorded, as well as time and type of revision operation. Only the first stenosis was recorded, that is, if a recurrent stenosis developed at the same bypass later during the follow-up, it was not added to the total sum of stenoses. The end points of primary patency were graft revision or occlusion.

Statistical analysis was performed with the aid of the SPSS statistical software package (SPSS for Windows version 9.0, SPSS, Chicago, Ill). Continuous variables are presented as a mean, SD, and SEM, if not otherwise stated. Because the distribution of flow values was skewed, they are presented as a geometrically corrected mean. The primary patency, assisted primary patency, and free-of-stenosis rates were calculated by Kaplan-Meier survival estimates (according to the guidelines of the Society for Vascular Surgery/International Society for Cardiovascular Surgery[21]), and comparison was performed with the log-rank test. A multivariate analysis with a Cox proportional hazard model was used to identify independent associations for significant group differences for free-of-stenosis survival (Table II). Statistical significance was considered for P values less than .05.

RESULTS

The median postoperative follow-up period was 13.6 months. Seventy-one grafts (28%) occluded during the study period (median, 16 days; interquartile range, 3-108

Table II. Univariate correlation of preoperative and intraoperative clinical parameters with the free-of-stenosis survival

Parameter		*No. of patients*	*2-year free-of-stenosis rate (%)*	*Log rank* P *value*
Sex	Female	117	61	
	Male	138	77	.009
Diabetes mellitus	Yes	128	62	
	No	127	72	.114
Smoking	Yes	76	62	
	No	179	69	.615
Hypertension	Yes	108	67	
	No	147	71	.353
Cardiac risk	Yes	113	66	
	No	142	71	.97
Cerebrovascular disease	Yes	42	72	
	No	213	69	.792
Chronic pulmonary disease	Yes	27	55	
	No	226	71	.152
Renal insufficiency	Yes	37	67	
	No	216	70	.951
Previous vascular operation	Yes	110	64	
	No	145	74	.093
Preoperative ABI	< 0.60	154	64	
	= 0.60	25	68	.9
Indication	CLI	217	66	
	Other	38	75	.124
Grafting technique	In situ	116	76	
	Other	139	64	.069
Bypass anatomy	Femoropopliteal	72	72	
	Femorocrural	101	63	
	Femoropedal	44	70	
	Popliteal-distal	38	63	.258
Graft flow	=130 mL/min	192	64	
	> 130 mL/min	63	82	.04
Maximal flow capacity	= 200 mL/min	140	62	
	> 200 mL/min	47	89	.003

ABI, Ankle/brachial index.

days). Graft stenosis developed in 58 (23%) grafts (median, 186 days; interquartile range, 95-279 days). The location of these stenoses were categorized as follows: 2 (3%) at the inflow artery; 4 (7%) at the proximal anastomosis; 10 (17%) in the proximal graft; 29 (48%) in the distal graft; 11 (18%) at the distal anastomosis; and 2 (3%) at the outflow artery. The temporal occurrence of the stenoses is depicted in Fig 1. The mean V_2/V_1 ratio was 5.4 (range, 2-15). Of the detected stenoses 44 were revised (Table III). In 14 grafts no revision procedure was performed, of which 10 were mild stenoses that were treated with intensified surveillance. Three grafts with detected high-degree stenoses occluded before the scheduled angiogram, and on one occasion the leg was amputated with an open but stenosed graft resulting from extensive foot gangrene.

For the whole series, the intraoperative graft flow and the MFC were 86 mL/min (SD 74 mL/min; SEM 82-89 mL/min) and 136 mL/min (SD 130 mL/min; SEM 129-143 mL/min), respectively. The mean increase in the flow after papaverine injection was 88%. When grouped on the basis of survival, the grafts with event-free outcomes had a higher graft flow (98 mL/min [SD 77; SEM 91-104]) than grafts that either developed a stenosis (77 mL/min [SD 43; SEM 72-83]) or occluded (68 mL/min [SD 88; SEM 57-79]). MFC was also higher for event-free grafts (158 mL/min [SD 144; SEM 143-171]) than for stenosed or occluded grafts (115 mL/min [SD 76; SEM 104-127]) and 106 mL/min (SD 138; SEM 93-129), respectively). The respective mean flow and MFC values for in situ grafts were 86 and 143 mL/min and for non–in situ grafts were 85 and 130 mL/min.

Table III. Type of revision procedure on 44 grafts

Procedure	*No. (%)*
Vein patch angioplasty	16 (36)
Interposition graft	12 (27)
Distal extension jump graft	8 (18)
Percutaneous transluminal angioplasty	7 (16)
Endarterectomy	1 (2)

A total of 207 grafts had their first scheduled duplex scan performed. In this group 46 graft stenoses were detected, of which 10 were identified in the first scan. The development of de novo stenoses, defined as those that occurred after 2 months after graft implantation and a

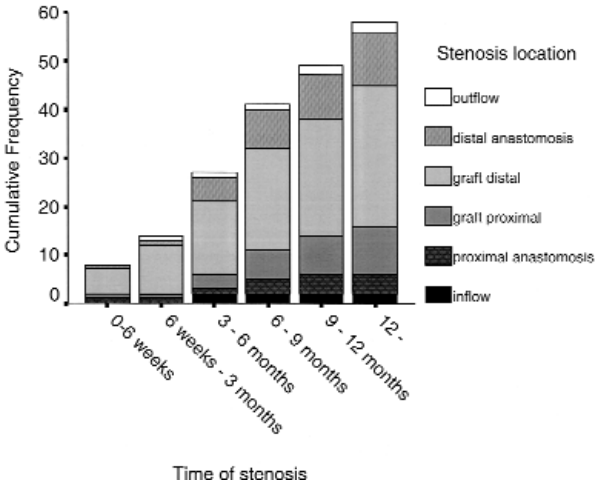


Fig 1. Fifty-eight graft stenoses were detected. Most of them were located in body of graft.

normal first scheduled duplex scan, was recorded in 36 grafts. For these grafts, the graft flow and MFC were lower than those for the event-free grafts (75 mL/min [SD 36, SEM 70-81] and 123 mL/min [SD 81; SEM 109-138], respectively).

The overall primary and assisted primary patency rates were 59% and 72% at 1 year and 52% and 70% at 2 years, respectively. The sample for graft flow was divided into quartiles (groups 1-4). The 25%, 50%, and 75% percentiles were at 61 mL/min, 90 mL/min, and 130 ml/min, respectively. After operation the ankle/brachial index increased with a mean of 0.46, 0.45, 0.49, and 0.38 for groups 1 through 4, respectively (NS). At 24 months the primary patency rates were 39%, 49%, 47%, and 72%, respectively ($P = .0038$), and the assisted primary patency rates were 55%, 67%, 71%, and 84%, respectively ($P = .011$) (Figs 2 and 3). The 24-month free-of-stenosis rates for groups 1 through 4 were 59%, 66%, 68%, and 82%, respectively ($P = .040$). The sample of MFC values was in a similar manner divided into quartiles. The results of survival analysis were analogous to graft flow. The 2-year free-of-stenosis survival rate for the lowest through highest MFC quartile was 61%, 62%, 64%, and 90% ($P = .027$) (Fig 4).

In addition to flow variables, only sex was a predictor of graft stenosis ($P = .009$). Multiple regression analysis indicated that sex and MFC were independent risk factors.

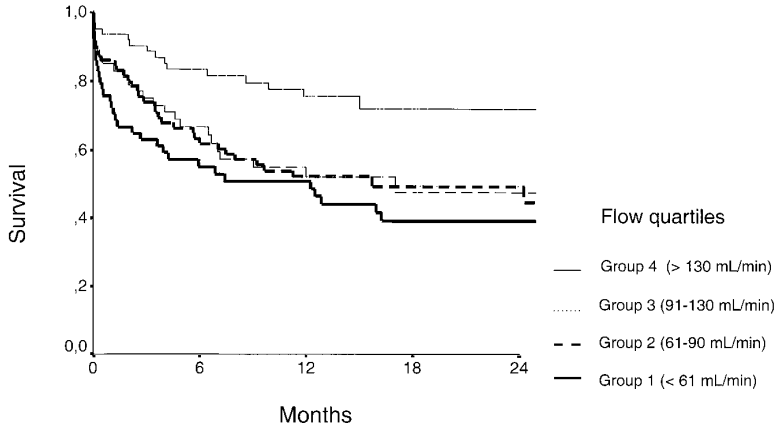
DISCUSSION

In an effort to reduce vein graft failure in infrainguinal revascularization, intense investigation has been directed to the detection and treatment of graft stenosis. Serial duplex surveillance has been used as a means of detecting these developing graft lesions, allowing timely repair before graft failure. This strategy has gained widespread acceptance, even though it is not known to what extent the detected stenoses necessarily threaten graft patency.[22] However, it is demonstrated that duplex scanning is an accurate and reliable method to detect focal graft lesions.[23,24]

An association between the development of vein graft stenoses and several risk factors has been studied. Systemic variables that might associate with graft stenosis are lipoprotein (a), smoking and plasma fibrinogen,[25] hyperhomocystinemia,[26,27] and antibodies to cardiolipin.[28] The importance of vein quality has been also studied. The hypothesis of preimplantation morphologic changes in the saphenous vein as an etiologic factor of vein graft stenosis is disputed.[29-31] A small internal diameter of the vein has been documented to increase the risk for vein graft stenosis.[32,33] In our study the vein diameter was not measured during operation. The measurement of vein graft diameter is a bit problematic, and comparison of studies on vein size is difficult because the intraoperative timing and the location where the measurements is taken varies, and usually it is not stated. Ideally, the internal diameter should be measured because the thickness of the vein wall is variable. By contrast, we found that stenoses were significantly more common in women, which is in accordance with a recent finding in a European multicenter study.[34] This fact may relate to a smaller vein diameter or to a higher prevalence of venous disease in women.[35] In the trial by Idu et al,[32] where small graft diameter was found to be a sole risk factor for graft stenosis, the impact of sex was not controlled in their risk analysis model.

Because it has been suggested that preexisting intrinsic abnormalities in vein grafts form the basis of progressive hyperplastic lesions, attempts to identify promoters already at the time of operation for subsequent development of graft stenosis have been made. Bandyk et al[36] studied the fate of moderate duplex abnormalities that were encountered during operation but were left untreated. A revision was needed in 18 of 40 such grafts (45%). The follow-up, however, was only 3 months, and the study was not blinded. Wilson et al[37] and Olojugba et al[38] have studied the predictive value of predischarge duplex scanning for risk graft identification with conflicting results. To sum up the information available, efforts to allocate grafts into high- and low-risk categories in relation to the stenosis development have not been successful, and still no method of decreasing the number of grafts undergoing surveillance exists.

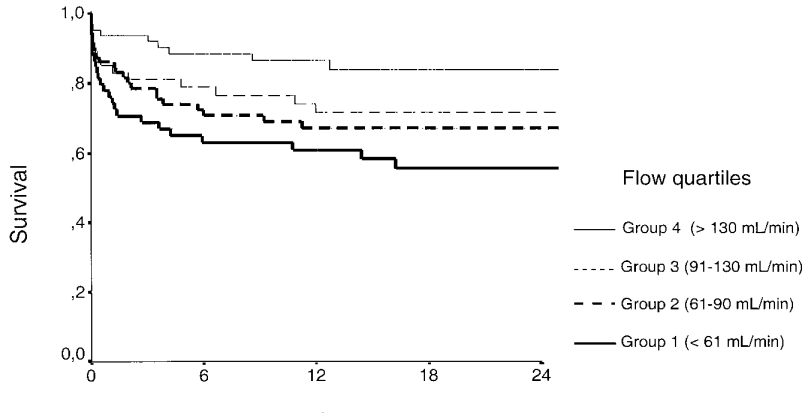
Since the advent of transit time flowmeter measurements, it has been easy to measure graft volume flow accurately and reliably during surgery.[19,20] As a method for intraoperative assessment of the technical adequacy of the bypass, its role is dubious. When the in situ grafting technique is used, unligated side branch AVFs are easily detected.[39] Otherwise the potential technical errors of the bypass cannot be assessed sufficiently with flow measurement only.[40] With current methods, the graft volume flow can be accurately measured only during operation. It can be derived from postoperative duplex scanning velocity measurements, but they are shown to be unreliable and



Number of grafts at risk

	0 to 3	3 to 6	6 to 9	9-12	12 to 18	18-24	S.E. (%) at 24 Months
Group 4	63	53	48	40	34	15	6.5
Group 3	54	37	29	24	21	9	8.1
Group 2	72	49	41	36	29	16	6.5
Group 1	65	34	26	23	23	14	7.0

Fig 2. Kaplan-Meier analysis of primary patency as function of intraoperative graft flow. At 2 years, primary patency rates were 39%, 49%, 47%, and 72% for groups 1 through 4 ($P < .0038$).



Number of grafts at risk

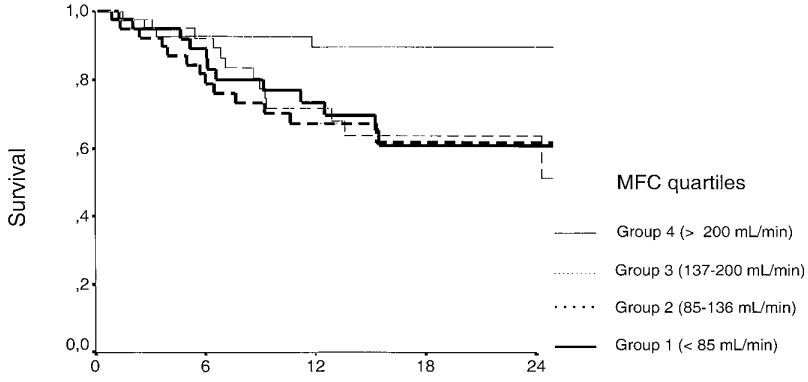
	0 to 3	3 to 6	6 to 9	9-12	12 to 18	18-24	S.E. (%) at 24 Months
Group 4	63	55	51	44	40	18	5.1
Group 3	54	40	35	33	29	14	6.5
Group 2	72	52	46	41	34	21	5.8
Group 1	66	38	30	29	28	18	7.0

Fig 3. Kaplan-Meier analysis of assisted primary patency for flow quartiles also showed improved survival with increasing intraoperative graft flow. Assisted primary patency rates at 2 years were 55%, 67%, 71%, and 84% for groups 1 through 4 ($P < .011$).

poorly reproducible.[41] The calculation of flow varies in relation to the fourth power of the radius of the vessel. This means that small inaccuracy in diameter measurement alters the derived flow value dramatically.

As a predictor of outcome, it has previously been demonstrated that low graft flow increases the risk of graft thrombosis not only in the immediate postoperative period, but also later in the follow-up.[42,43] Our data confirm these findings because the difference in the assisted primary patency rate at 2 years between lowest and highest flow quartile was 36%, with an increasing tendency during the first postoperative year.

The biomedical background with regard to how hemodynamic alterations affect the development of myo-



Number of grafts at risk

	0 to 3	3 to 6	6 to 9	9-12	12 to 18	18-24	S.E. (%) at 24 Months
Group 4	47	39	37	32	29	16	5.0
Group 3	46	37	32	25	21	12	8.6
Group 2	45	35	29	25	21	9	9.0
Group 1	49	35	30	26	20	11	9.2

Fig 4. Free-of-stenosis survival rates for lowest through highest MFC quartile were 61%, 62%, 64%, and 90% at 2 years ($P = .027$).

intimal hyperplasia is intriguing. It has increasingly been recognized that the vascular endothelium is a living organ in which the metabolism and synthetic activities of different vasoactive factors are altered as a response to biomechanical forces generated by the blood flow.[44] In normal arteries the flow-induced remodeling results in changes in arterial diameter that return wall shear stress toward normal in a negative feedback manner.[45] Furthermore, Fillinger et al[46] demonstrated that the same phenomenon takes place in vein grafts; in response to changes in shear stress 1 year after operation, the small-diameter veins were remodeled to a final diameter that was not significantly different from larger veins. This remodeling might contribute to the pathophysiological condition of neointimal hyperplasia because it is shown that shear stress can regulate endothelial smooth muscle cell migration and proliferation.[47] It is probable that this is mediated by nitric oxide, a potential vasodilator that causes vessel wall atrophy. In an experimental in vivo model, the endothelial nitric oxide synthesis was induced in high-flow graft intima.[48]

Furthermore, the synthesis of tissue-type plasminogen activator is known to be triggered dependently by shear force.[49] It is plausible that the more efficient the initial fibrinolytic activity is, the less stabilized the fibrin form is on the new conduit surface. The activity of the fibrinolytic system is linked to cardiovascular tissue remodeling and pathophysiologic study of myointimal hyperplasia.[50] In later stages of myointimal hyperplasia, the upregulation of fibrinolytic and its regulatory enzymes is induced.[51]

Therefore, an appealing idea is to augment flow in the graft with a distal AVF. Faulkner et al[52] demonstrated in the 1970s that the application of AVF decreases the amount of subendothelial proliferation in vein grafts in dogs. In clinical outcome studies the interest has concentrated on combining adjuvant AVF with a prosthetic infrainguinal bypass, but the potential additional clinical advantage of this method is still undetermined.[53,54] The clinical value of AVF as an adjunct to vein bypass grafting has remained unexplored. We have gained some limited experience combining adjuvant AVFs to vein bypass grafts. This has not been, however, a common practice and has been reserved as a last option in extreme cases, where a successful outcome of the reconstruction has been judged as unlikely. They were excluded from this analysis because potentially these grafts with elevated flow rates would have biased the results. On the other hand, their number was too small to allow meaningful subanalysis.

It would be beneficial to find flow criteria for risk group stratification for future surveillance programs. On the basis of the data reported herein, it seems that high graft flow is protective against the development of de novo graft stenosis because only four grafts in the highest quartile had development of a stenosis after a normal duplex scanning result within 6 weeks. It is a matter of discussion whether this risk is acceptably low, so that discontinuation of surveillance for grafts with high flow and normal early duplex scanning results can be recommended. At this point, however, the merits of the data presented in this series should be viewed as preliminary clinical verification that the myointimal growth and regression in infrainguinal vein grafts are regulated by blood flow. In our opinion a larger sample size is needed for more reliable risk and best cutoff point calculation before clinical guidelines can be drawn.

In conclusion, this study confirms that intraoperative graft flow is a predictor of bypass occlusion after infrainguinal bypasses after the immediate postoperative period. Interestingly, it also indicates that the development of clin-

ically evident graft stenoses may be induced by low graft flow. Further experience is needed with a greater number of patients and longer follow-up, before it is evident whether these findings have consequences in clinical practice.

We thank Hanna Oksanen, MSc, PhD, for her valuable consulting aid with the statistical analysis.

REFERENCES

1. TASC Working Group. Management of peripheral arterial disease (PAD). J Vasc Surg 2000:31(Suppl 1):S233-6.
2. Albäck A, Lepäntalo M. Immediate occlusion of in situ saphenous vein bypass grafts: a survey of 329 reconstructions. Eur J Surg 1998;164:745-50.
3. Donaldson MC, Mannick JA, Whittemore AD. Causes of primary graft failure after in situ saphenous vein bypass grafting. J Vasc Surg 1992;15:113-8.
4. Mills JL, Fujitani RM, Taylor SM. The characteristics and anatomic distribution of lesions that cause reversed vein graft failure: a five-year prospective study. J Vasc Surg 1993;17:195-204.
5. Szilagyi DE, Elliott JP, Hageman JH, Smith RF, Dall'olmo CA. Biologic fate of autologous vein implants as arterial substitutes. Ann Surg 1973;178:232-46.
6. Davies MG, Hagen P-O. Pathophysiology of vein graft failure: a review. Eur J Vasc Endovasc Surg 1995;9:7-18.
7. Sayers RD, Jones L, Varty K, Allen K, Morgan JD, Bell PR, et al. The histopathology of infrainguinal vein graft stenoses. Eur J Vasc Surg 1993;7:16-20.
8. Veith FJ, Weiser RK, Gupta SK, Ascer E, Scher LA, Samson RH, et al. Diagnosis and management of failing lower extremity arterial reconstructions prior to graft occlusion. J Cardiovasc Surg 1984;5:381-4.
9. Nehler MR, Moneta GL, Yeager RA, Edwards JM, Taylor LM, Porter JM. Surgical treatment of threatened reversed infrainguinal vein grafts. J Vasc Surg 1994;20:558-65.
10. Bandyk DF, Schmitt DD, Seabrook GR, Adams MB, Towne JB. Monitoring functional patency of in situ saphenous vein bypasses: the impact of a surveillance protocol and elective revision. J Vasc Surg 1989;9:286-96.
11. Mills JL, Harris EJ, Taylor LM, Beckett WC, Porter JM. The importance of routine surveillance of distal bypass grafts with duplex scanning: a study of 379 reversed vein grafts. J Vasc Surg 1990;12:379-89.
12. Idu MM, Blankenstein JD, de Gier P, Truyen E, Buth J. Impact of a color-flow duplex surveillance program on infrainguinal vein graft patency: a five-year experience. J Vasc Surg 1993;17:42-53.
13. Berguer R, Higgins RF, Reddy DJ. Intimal hyperplasia: an experimental study. Arch Surg 1980;115:332-5.
14. Dobrin PB, Littooy FN, Endean ED. Mechanical factors predisposing to intimal hyperplasia and medial thickening in autogenous vein grafts. Surgery 1989;105:393-400.
15. Cambria RA, Lowell RC, Glovicki P, Miller VM. Chronic changes in blood flow alter endothelium-dependent responses in autogenous vein grafts in dogs. J Vasc Surg 1994;20:765-73.
16. Mattsson EJ, Kohler TR, Vergel SM, Clowes AW. Increased blood flow induces regression of intimal hyperplasia. Arterioscler Thromb Vasc Biol 1997;17:2245-9.
17. Faulkner SL, Fisher RD, Conkle DM, Page DL, Bender HW Jr. Effect of blood flow rate on subendothelial proliferation in venous autografts used as arterial substitutes. Circulation 1975;52:163-72.
18. Morinaga K, Eguchi H, Miyazaki T, Okadome K, Sugimachi K. Development and regression of intimal thickening of arterially transplanted autologous vein grafts in dogs. J Vasc Surg 1987;5:19-30.
19. Lundell A, Bergqvist D, Mattsson E, Nilsson B. Volume flow measurements with a transit time flowmeter – an in vivo and in vitro variability and validation study. Clin Physiol 1993;13:547-57.
20. Albäck A, Mäkisalo H, Nordin A, Lepäntalo M. Validity and reproducibility of transit time flowmetry. Ann Chir Gynaecol 1996;85:325-31.
21. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, et al. Recommended standards for reporting with lower extremity ischemia: revised version. J Vasc Surg 1997;26:517-38.
22. Mattos MA, van Bemmelen PS, Hodgson KJ, Ramsey DE, Barkmeier LD, Sumner DS. Does correction of stenoses identified with color duplex scanning improve infrainguinal graft patency? J Vasc Surg 1993;17:54-66.
23. Buth J, Disselhoff B, Sommeling C, Stam L. Color-flow duplex criteria for grading stenosis in infrainguinal vein grafts. J Vasc Surg 1991;14:716-28.
24. Ihlberg L, Albäck A, Roth W-D, Edgren J, Lepäntalo M. Interobserever agreement in duplex scanning for vein grafts. Eur J Vasc Endovasc Surg 2000;19:504-8.
25. Cheshire NJ, Wolfe JH, Barradas MA, Chambler AW, Mikhailidis DP. Smoking and plasma fibrinogen, lipoprotein (a) and serotonin are markers for postoperative infrainguinal graft stenosis. Eur J Vasc Endovasc Surg 1996;11:479-86.
26. Beattie DK, Sian M, Greenhalgh RM, Davies AH. Influence on systemic factors on pre-existing intimal hyperplasia and their effect on the outcome of infrainguinal arterial reconstruction with vein. Br J Surg 1999;86:1441-7.
27. Irvine C, Wilson YG, Currie IC, McGrath C, Scott J, Day A, et al. Hyperhomocysteinaemia is a risk factor for vein graft stenosis. Eur J Vasc Endovasc Surg 1996;12:304-9.
28. Nielsen TG, Nordestgaard BG, von Jessen F, Andreasen JJ, Wiik A, Heegaard NHH, et al. Antibodies to cardiolipin may increase the risk of failure of peripheral vein bypasses. Eur J Vasc Endovasc Surg 1997;14:177-84.
29. Marin ML, Veith FJ, Panetta TF, Gordon RE, Wengerter KR, Suggs WD, et al. Saphenous vein biopsy: a predictor of vein graft failure. J Vasc Surg 1993;18:407-15.
30. Davies AH, Magee TR, Baird RN, Sheffield E, Horrocks M. Prebypass morphological changes in vein grafts. Eur J Vasc Surg 1993;7:642-7.
31. Varty K, Porter K, Bell PR, London NJ. Vein morphology and bypass graft stenosis. Br J Surg 1996;83:1375-9.
32. Idu MM, Buth J, Hop WCJ, Cuypers PH, van de Pavoordt WM, Tordoir JMH. Factors influencing the development of vein-graft stenosis and their significance for clinical management. Eur J Vasc Endovasc Surg 1999;17:15-21.
33. Davies AH, Magee TR, Sheffield E, Baird RN, Horrocks M. The etiology of vein graft stenoses. Eur J Vasc Surg 1994;8:389-94.
34. Watson HR, Buth J, Schroeder TV, Simms MH, Horrocks M. Incidence of stenoses in femorodistal bypass vein grafts in a multicenter study. Eur J Vasc Endovasc Surg 2000;20:67-711.
35. Laurikka J, Sisto T, Auvinen O, Tarkka M, Laara E, Hakama M. Varicose veins in a Finnish population aged 40-60. J Epidemiol Community Health 1997;14:125-33.
36. Bandyk DF, Johnson BL, Gupta AK, Esses GE. Nature and management of duplex abnormalities encountered during infrainguinal vein bypass grafting. J Vasc Surg 24:430-8.
37. Wilson YG, Davies AH, Currie IC, McGrath C, Morgan M, Baird RN, et al. The value of pre-discharge duplex scanning in infrainguinal graft surveillance. Eur J Vasc Endovasc Surg 1995;10:237-42.
38. Olojugba DH, Varty K, Hartsthorne T, Naylor AR, Bell PRF, London NJM. Predischarge duplex imaging of infrainguinal vein grafts does not predict the development of stenoses. Br J Surg 1998;85:1225-7.
39. Laustsen J, Pedersen EM, Terp K, Steinbruchel D, Kure HH, Pauls PK, et al. Validation of a new transit time flowmeter in man. Eur J Vasc Endovasc Surg 1996;12:91-6.
40. Blankenstein JD, Gertler JP, Brewster DC, Gambria RP, LaMuraglia GM, Abbott WM. Intraoperative determinants of infrainguinal graft patency: A prospective study. Eur J Vasc Endovasc Surg 1995;9:375-82.
41. Grigg MJ, Wolfe JH, Tovar AN, Nicolaides AN. The reliability of duplex-derived haemodynamic measurements in the assessment of femoro-distal grafts. Eur J Vasc Surg 1988;2:177-81.
42. Lundell A, Bergqvist D. Prediction of early graft occlusion in femoropoliteal and femorodistal reconstruction by measurement of volume flow with a transit time flowmeter and calculation of peripheral resistance. Eur J Vasc Surg 1993;7:704-8.
43. 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 grafts. Eur J Vasc Endovasc Surg 2000;20:447-53.

44. Gimbrone MA, Anderson KR, Topper JN. The critical role of mechanical forces in blood vessel development, physiology and pathology. J Vasc Surg 1999;29:1104-6.
45. Langille BL. Arterial remodeling: relation to hemodynamics. Can J Physiol Pharmacol 1996;74:834-41.
46. Fillinger MF, Cronenwett JL, Besso S, Walsh DB, Zwolak RM. Vein adaptation to the hemodynamic environment of infrainguinal grafts. J Vasc Surg 1996;19:970-9.
47. Mattsson EJ, Kohler TR, Vergel SM, Clowes AW. Increased blood flow induces regression of intimal hyperplasia. Arterioscler Thromb Vasc Biol 1997;17:2245-9.
48. Mattsson EJR, Geary RL, Kraiss LW, Vergel S, Liao JK, Corspn MA, et al. Is smooth muscle growth in primate arteries regulated by endothelial nitric oxide synthase? J Vasc Surg 1998;28:514-21.
49. Diamond SL, Eskin SG, McIntire LV. Fluid flow stimulates tissue plasminogen activator secretion by cultured human endothelial cells. Science 1989;243:1483-5.
50. Carmeliet P, Collin D. Role of the plasminogen/plasmin system in thrombosis, hemostasis, restenosis and atherosclerosis. Trends Cardiovasc Med 1995;5:117-22.
51. Kauhanen P, Carpen O, Vaheri A, Lepäntalo M, Lassila R. Plasminogen activator inhibitor-1 in neointima of vein grafts. Its role in reduced fibrinolytic potential and graft failure. Circulation 1997;96:1783-9.
52. Faulkner SL, Fisher RD, Conkle DM, Page DL, Bender HW Jr. Effect of blood flow rate on subendothelial proliferation in venous autografts used as arterial substitutes. Circulation 1975;52(2 Suppl):I163-72.
53. Hamsho A, Nott D, Harris PL. Prospective randomised trial of distal arteriovenous fistula as an adjunct to femoro-infrapopliteal bypass. Eur J Vasc Endovasc Surg 1999;17:197-201.
54. Eagleton MJ, Ouriel K, Shortell C, Green M. Femoral-infrapopliteal bypass with prosthetic grafts. Surgery 1999;126:759-64.

Submitted Jul 10, 2000; accepted Jan 19, 2001.

Receive table of contents by e-mail

To receive the tables of contents by e-mail, sign up through our Web site at:
http://www.mosby.com/jvs

Choose E-mail Notification
Simply type your e-mail address in the box and click the Subscribe button
Alternatively, you may send an e-mail message to majordomo@mosby.com
Leave the subject line blank and type the following as the body of your message:
subscribe jvs_toc

You will receive an e-mail to confirm that you have been added to the mailing list.
Note that TOC e-mails will be sent out when a new issue is posted to the Web site.