Prevalence of true vein graft aneurysms: Implications for aneurysm pathogenesis

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Background: **Circumstantial evidence suggests that arterial aneurysms have a different cause than atherosclerosis and may form part of a generalized dilating diathesis. The aim of this study was to compare the rates of spontaneous aneurysm formation in vein grafts performed either for popliteal aneurysms or for occlusive disease. The hypothesis was that if arterial aneurysms form a part of a systemic process, then the rates of vein graft aneurysms should be higher for patients with popliteal aneurysms than for patients with lower limb ischemia caused by atherosclerosis.**

Methods: **Infrainguinal vein grafting procedures performed from 1990 to 1995 were entered into a prospective audit and graft surveillance program.** ***Aneurysmal change*** **was defined as a focal increase in the graft diameter of 1.5 cm or greater, excluding false aneurysms and dilatations after graft angioplasty.**

Results: **During the study period, 221 grafting procedures were performed in 200 patients with occlusive disease and 24 grafting procedures were performed in 21 patients with popliteal aneurysms. Graft surveillance revealed spontaneous aneurysm formation in 10 of the 24 bypass grafts (42%) for popliteal aneurysms but in only 4 of the 221 grafting procedures (2%) that were performed for chronic lower limb ischemia.**

Conclusion: **This study provides further evidence that aneurysmal disease is a systemic process, and this finding has clinical implications for the treatment of popliteal aneurysms. (J Vasc Surg 1999;29:403-8.)**

The disease of arterial aneurysms is now well documented. An analysis of the established abdominal aneurysmal tissue has shown that the aortic wall is characterized by a derangement of the extracellular matrix with a reduction in elastin concentration.[1-4] These structural changes within the aorta are associated with increased levels of matrix metalloproteinases,[5-8] a diffuse white cell infiltrate,[9,10] and the expression of auto-antigenic proteins in the aortic adventitia.[11,12] However, despite the extensive characterization of the abnormalities within the aortic wall, the cause of arterial aneurysms remains undefined.

This failure to elucidate the initiating factors in aneurysmal disease reflects the emphasis of previous research on the characterization of the pathophysiology of established aneurysmal tissue. Unfortunately, the analysis of the tissue at the end of a disease process will not differentiate causal factors from degenerative effects. To overcome these difficulties, a source of tissue at the beginning of the aneurysmal process is necessary, but this tissue has been practically impossible to obtain.

Despite the difficulties in determining the cause of abdominal aneurysms, several investigators have suggested that the patients with arterial aneurysms have a systemic disease.[13] Ward[14] observed that the mean diameters for all the peripheral arteries were significantly greater in the patients with aortic aneurysms than in the control groups, and Baxter et al[15] demonstrated that the extracellular matrix abnormalities that were present in the aneurysmal wall were also identifiable in the aortic tissue proximal to the aneurysmal site. Both of these studies suggested that localized aneurysmal disease may be a manifestation of a systemic dilating process.

True aneurysms may affect virtually any part of the circulation, and several contemporary reports have observed that aneurysmal dilatation may complicate both coronary and infrainguinal vein grafts.[16-20] The aim of the present study was to determine the prevalence of true infrainguinal vein graft aneurysms

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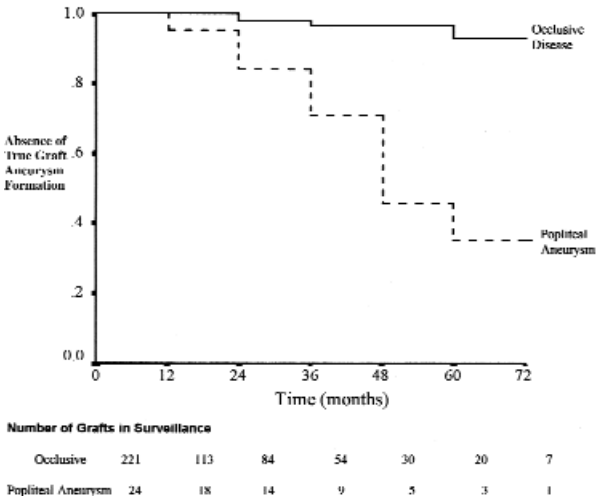

Fig 1. Cumulative 5-year life-table analysis shows the proportion of vein grafts without true aneurysm formation at 12 monthly intervals. Figures in the table represent total number of grafts under surveillance for up to 6 years.

in two groups of patients—those who underwent bypass grafting for chronic lower limb ischemia as a result of atherosclerotic occlusive disease and those who underwent bypass grafting and ligation of a popliteal aneurysm. The hypothesis of the investigation was that if the arterial aneurysms were a part of a systemic dilating disease, then the prevalence of true vein graft aneurysms should be higher for the patients with popliteal aneurysms.

METHODS

Patients. All patients who underwent infragenicular bypass grafting for lower limb arterial occlusive disease or for popliteal aneurysm between January 1990 and December 1995 were entered into the study. The demographic data, the vascular risk factors, and the clinical findings were prospectively recorded. The technique used in our center of femoropopliteal-crural bypass grafting for patients with occlusive disease has been described previously.[21-23] Our operative strategy for the treatment of elective popliteal aneurysms involved a medial approach with a long saphenous vein bypass graft from the superficial femoral artery to the most proximal patent run-off vessel, which was combined with proximal and distal aneurysm ligation. No patient in the study underwent a posterior approach with inlay grafting.

Surveillance. After surgery, all the patent vein grafts were entered into a graft surveillance program as previously described.[24,25] Duplex scans were performed at 1, 3, 6, and 12 months after surgery and then every 6 months thereafter. All the data were entered into a computerized audit database. *True vein graft aneurysm formation* was defined as a focal increase in the graft diameter in excess of 1.5 cm. Aneurysm formation after transluminal or patch angioplasty was classified as false, rather than true.

Statistical analysis. The prevalence of true vein graft aneurysm formation in patients who underwent bypass grafting for occlusive disease or for popliteal aneurysm was calculated with life-table analysis. The differences between the two groups were compared by means of Kaplan-Meier method and with the χ^2 test. Multiple logistic regression analysis was performed to establish the role of the independent risk factors in vein graft aneurysm formation. For the comparison of the demographic factors between the two patient groups, the Mann-Whitney test for continuous variables and the χ^2 test for discrete variables were used.

RESULTS

During the study period, a total of 245 infrainguinal vein grafting procedures were performed in 221 patients. In 200 patients, 221 grafting procedures were performed for arterial occlusive disease, and in 21 patients, 24 procedures were performed for bypass grafting of popliteal aneurysms. The demographic data and the individual vascular risk factors for these two groups of patients are tabulated in Table I. None of the demographic factors were significantly different between the two patient groups (Mann-Whitney and χ^2 tests).

The median follow-up period for the patients with occlusive disease was 19 months (range, 1 to 91 months) as compared with 24 months (range, 1 to 84 months) for the group with popliteal aneurysms ($P > .05$, Mann-Whitney test). Overall, the prevalence of true vein graft aneurysms for the patients with occlusive arterial disease was 4 from a total of 221 grafts (1.8%). Correspondingly, the prevalence of graft aneurysms in those bypass grafting procedures for popliteal aneurysms was 10 of the 24 grafts (41.6.%). This difference was highly significant ($P < .001$, Kaplan-Meier method), as shown by the life-table analysis illustrated in Fig 1.

Of those aneurysms that were detected in the vein grafting procedures for popliteal aneurysms, three were in the proximal third of the graft, one was found at mid graft, and four were within the distal third. The remaining three aneurysms exhibited multiple aneurysmal areas throughout the graft. In the occlusive group, two of the vein graft aneurysms

Table I. Demographic data and incidence rates of individual risk factors in the group of 200 patients with occlusive disease and in the 21 patients with popliteal aneurysms

	Occlusive disease	*Aneurysmal disease*	*P value*
Median age (years)	72 (range, 31 to 97)	67 (range, 40 to 85)	.18
Sex (% male)	68	90	.47
IHD (%)	22	24	.82
CVD (%)	14	24	.59
Smoking (%)	77	85	.71
Hypertension (%)	35	24	.95
Diabetes (%)	31	15	.61

IHD, Ischemic heart disease; *CVD,* cerebrovascular disease.
Statistical analysis was performed with the Mann-Whitney and χ^2 tests.

Table II. Life-table analysis

Interval (months)	*No. patients entering this interval*		*No. grafts withdrawn during this interval*		*No. of graft aneurysms detected*		*Interval aneurysm detection rate*		*Cumulative proportion of vein grafts without aneurysm at end of interval*		*Standard error*	
	A	B	A	B	A	B	A	B	A	B	A	B
0 to 12	221	24	108	5	0	1	0.000	0.046	100	95.3	0.00	4.54
12 to 24	113	18	27	2	2	2	0.020	0.118	98.0	84.1	1.41	8.46
24 to 36	84	14	29	3	1	2	0.014	0.160	96.6	70.7	1.97	11.2
36 to 48	54	9	9	1	0	3	0.000	0.353	96.6	45.7	1.97	13.7
48 to 60	30	5	13	1	1	1	0.039	0.222	92.8	35.6	4.17	13.9
60 to 72	20	3	5	2	0	0	0.000	0.000	92.8	35.6	4.17	13.9
72 to 84	7	1	5	0	0	0	0.000	0.000	92.8	35.6	4.17	13.9

A, Column A represents patients with occlusive disease; *B,* column B represents patients with popliteal aneurysms.

were in the proximal third, one was at mid graft, and one was in the distal third.

The aneurysms that were detected in those grafting procedures for occlusive disease were detected marginally earlier (median, 18 months; range, 6 to 48 months) than those procedures for popliteal aneurysms (median, 24 months; range, 6 to 84 months), although this difference was not significant. Six of the aneurysms that were detected in the bypass grafts for popliteal aneurysms were larger than 2 cm, and only one of the aneurysms that were detected in the occlusive group reached this size. There was no difference in the follow-up period between the group of patients with vein graft aneurysms as compared with the group without.

Multiple logistic regression analysis was performed to evaluate the contribution of each of the individual vascular risk factors to the development of true vein graft aneurysms. Only one factor, the presence of a popliteal aneurysm, had a significant effect on the development of vein graft aneurysms, with a relative risk of vein graft aneurysm formation in patients with popliteal aneurysms of 22.7 times that of patients with occlusive disease.

To date, three patients with true vein graft aneurysms have undergone segmental surgical revision (Fig 2). All three patients had their original operation for popliteal aneurysm and had vein graft dilatation in excess of 3 cm. None of these patients were seen with acute complications, and none of the procedures were revised on the basis of the scan results. All the other aneurysms continued in the surveillance program. Four of the patients with popliteal aneurysms had aortic aneurysms of greater than 4 cm in diameter—two patients in the group had true vein graft aneurysm, and three have been repaired to date. The graft type and the anastomosis sites for the group with popliteal aneurysms are shown in Table III.

DISCUSSION

The existence of aneurysms that complicate vein grafts is relatively well documented.[20,26] Szilagyi et al[27] reported aneurysmal degeneration in 4% of the infrainguinal vein grafts, whereas coronary and renal grafts appear to be similarly affected.[20] The present study has revealed similar findings for the development of aneurysmal changes in 1.8% of the infrain-

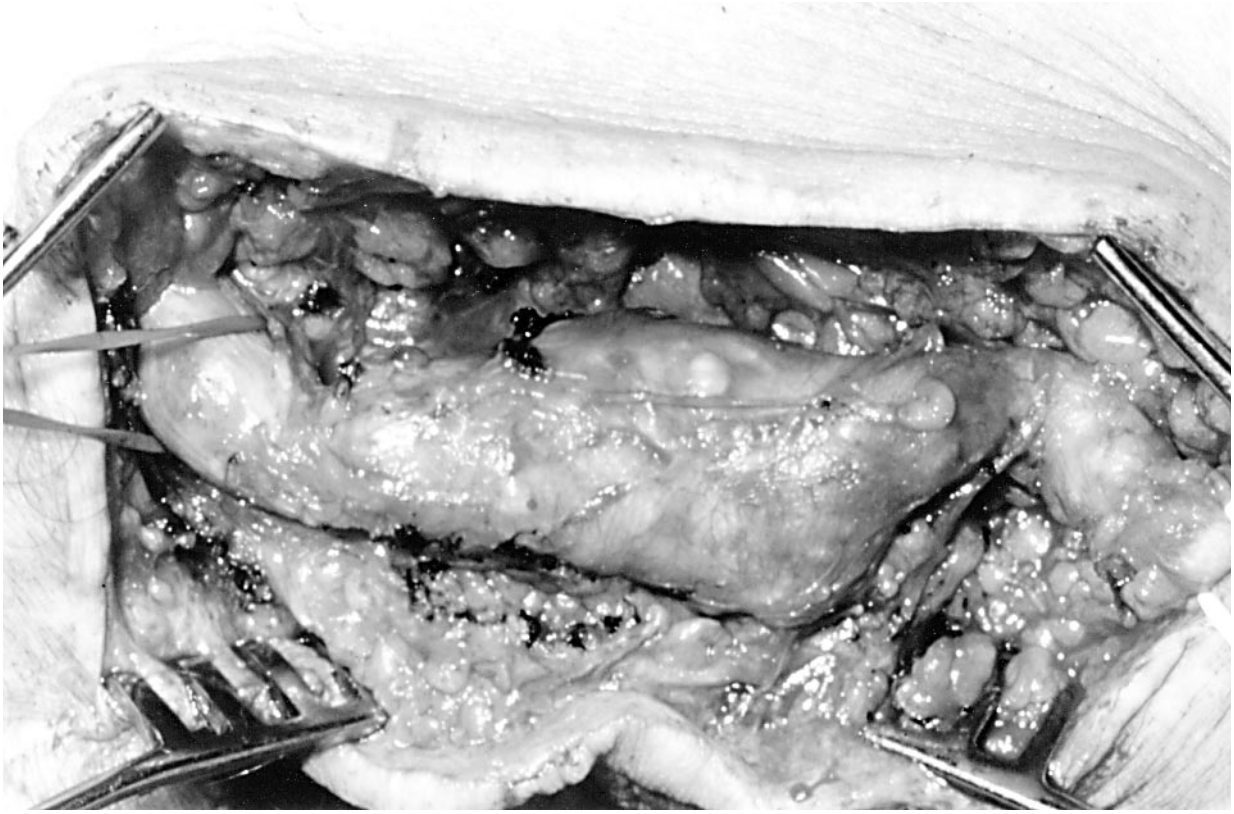

Fig 2. Intraoperative photograph of above-knee true vein graft aneurysm undergoing formal repair after dilatation to diameter of greater than 3 cm. Both loops surround nondilated vein graft.

guinal grafting procedures that were performed for occlusive disease.

The cause of vein graft aneurysms has not received a great deal of attention presumably because of their rarity. Several authors have suggested that vein graft aneurysms may be associated with arterial aneurysms elsewhere,[28-30] and Alexander and Liu[18] suggested that these aneurysms developed as a result of atherosclerosis. The present study has shown conclusively that the only factor significantly associated with the development of vein graft aneurysms is the presence of a popliteal aneurysm with a relative risk of 23. These data strongly support the observations of Tilson[31] who suggested that the patients with vein graft aneurysms have a systemic dilating diathesis that may affect the veins and the arteries. This observation may have important clinical and scientific implications.

Previous series that reported the results of surgery for popliteal aneurysm have not shown a high incidence rate of vein graft aneurysms,[32-34] which may reflect the time to develop graft dilatation (median, 24 months) or the intensive graft surveillance protocol used in this study. One of the flaws in this study is the low number of patients with long follow-up periods in the popliteal aneurysm group. However, this is true of all the investigations into this condition, and reviews suggest that major vascular centers will only encounter four to five cases per year.[35] Similarly, no data are available regarding preoperative vein diameter, and it may be that the patients with popliteal aneurysms had larger long saphenous veins than did the control population. However, because obviously varicosed veins would not have been used for the bypass grafts, the magnitude of the relative risk of vein graft aneurysm formation, which is attributable to the presence of popliteal aneurysm, cannot be explained by this factor alone. The definition of vein graft aneurysms at a diameter of 1.5 cm is obviously arbitrary, but it is interesting to note that if a larger diameter had been used (eg, 2 cm), only one vein graft aneurysm would have been shown in the atherosclerotic group.

Traditionally, the autologous vein has been the preferred conduit for bypass grafting of popliteal aneurysms. However, the tendency to aneurysm formation may lead to a high incidence rate of revision

Table III. Details of the graft types and the anastomosis sites for those patients in the popliteal aneurysm group with and without true vein graft aneurysm formation

A. Graft type	*Reversed vein (n = 19)*	*In situ vein (n = 4)*	*Composite vein (n = 1)*
Graft aneurysm (n = 10)	9	0	1
No graft aneurysm (n = 14)	10	4	0
B. Proximal anastomosis site	*Common femoral (n = 4)*	*Superficial femoral (n = 17)*	*AK popliteal (n = 3)*
Graft aneurysm (n = 10)	1	7	2
No graft aneurysm (n = 14)	3	10	1
C. Distal anastomosis site	*BK popliteal (n = 15)*	*Tibioperoneal trunk (n = 2)*	*Calf vessel (n = 7)*
Graft aneurysm (n = 10)	7	0	3
No graft aneurysm (n = 14)	8	2	4

AK, Above knee; *BK,* Below knee.

surgery, with its attendant risks. Interestingly, Sarcina et al[32] have reported that expanded polytetrafluoroethylene and autologous venous conduits have similar patency rates during popliteal aneurysm bypass grafting, and they have suggested that expanded polytetrafluoroethylene be the conduit of choice. Further studies clearly are necessary to confirm these findings, but they do have implications for the traditional management of popliteal aneurysms in view of the high rate of degeneration of autologous venous bypass grafts.

The association between popliteal aneurysms and vein graft aneurysm formation appears to be shown strongly in this study. Of all the vascular risk factors that were analyzed, the presence of arterial aneurysmal disease was the only significant predictor of vein graft dilatation. This has important scientific implications because the data strongly support the concept of aneurysmal disease as a systemic disorder, with differing risk factors to atherosclerosis.[13] The idea that the patients with popliteal aneurysms have a localized manifestation of a dilating diathesis that affects their veins when implanted into the arterial circulation is attractive scientifically. Perhaps more significantly, the findings from this study suggest a novel approach to the investigation of the cause of arterial aneurysms. For the first time, a preaneurysmal tissue has been identified. The long saphenous vein from a patient with a popliteal aneurysm has a 40% likelihood of aneurysmal degeneration when used as a bypass graft conduit as compared with a 2% chance in the control tissue from patients with occlusive disease. A biochemical and molecular comparison of the long saphenous vein from these two groups of patients may help elucidate the initiating factors that are responsible for aneurysmal disease.

The biochemical changes within the wall of the abdominal aortic aneurysm are well documented, including the loss of elastin, medial degeneration, inflammatory infiltration, and increased levels of matrix metalloproteinase.[36] Such changes may be involved in the aneurysmal change identified in these vein grafts. However, the number of grafts that are revised remains small, and we are currently investigating both the histologic and the biochemical changes within the long saphenous vein in patients with aneurysmal and occlusive disease.

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