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Impact of Cuffed, Expanded Polytetrafluoroethylene Dialysis Grafts on Graft Outlet Stenosis

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Abstract
Background:The objective of this study was to determine prospectively the difference between the graft outlet strictures of a polytetrafluoroethylene (ePTFE) graft with a cuff at the graft-vein anastomosis (Venaflo; Bard industries, Tempe, Ariz.) and that of the regular ePTFE graft (Stretch Gore-Tex; Gore, Flagstaff, Ariz.) placed for hemodialysis access.
Methods: Between January and April 2005, 36 consecutive patients (average age: 63.3 years) underwent ePTFE graft implantation (36 implantations) for hemodialysis at the Vascular Surgery Section of Chang Gung Memorial Hospital. The patients of the study cohort were randomly assigned to two groups based on the graft used: cuffed graft group (Venaflo graft) and non-cuffed standard graft group (Gore-Tex graft). Each patient underwent antegrade venography at the 3-month follow-up to demonstrate the graft outlet stricture. Results of the graft outlet angiography analysis were examined, and all medical records were reviewed at end of the study. The degree of the graft outlet stenosis was compared between the two groups.
Results: Average stenosis of the cuffed graft group and non-cuffed (standard) graft group were 22.76 ± 26.37% and 44.95 ± 27.48%, respectively; the difference between the two groups was statistically significant ($P < 0.05$).
Conclusions: The graft outlet stricture of cuffed ePTFE grafts for hemodialysis 3 months after implantation was less severe than that for the standard ePTFE graft. The correlation between the stricture level and dialysis graft patency requires further clarification.

Three treatment modalities exist for the treatment of end-stage renal disease patients: hemodialysis; peritoneal dialysis; kidney transplantation. Vascular access has served as a lifeline for chronic hemodialysis patients, and vascular access-related expenditures are the largest component of all dialysis-related costs. Although dialysis fistula is the optimal approach for vascular access, artificial dialysis grafts are utilized for a remarkable number of cases requiring dialysis access.[1] Dialysis graft thrombosis is the most frequently encountered complication dialysis surgeons face in daily practice.

With venous outflow stenosis identified as a major cause of arteriovenous graft (AVG) thrombosis, various anastomotic strategies have been developed to ameliorate the graft venous outlet stenosis and, thereby, improve the clinical outcome of hemodialysis access.[2] Cuffed expanded polytetrafluoroethylene (ePTFE) hemodialysis grafts were developed to specifically address the problem of stenosis at the graft-vein anastomosis. However, the effect of a cuffed graft on venous outlet stenosis has yet to be elucidated.

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This report presents the results of a randomized, prospective clinical study comparing the graft outlet stricture of cuffed and non-cuffed (standard) ePTFE grafts placed for hemodialysis access. Since angiography is the gold standard for quantitative assessment of vasculature stenosis, this study documented and analyzed the graft venous anastomosis stenosis, calculated from the angiographic study, of two different graft designs 3 months after AVG implantation.

MATERIALS AND METHODS

Study Group

Between January and April 2005, 36 consecutive end-stage renal disease patients who were being placed on chronic hemodialysis and, consequently, requiring the implantation of a prosthetic graft for hemodialysis were prospectively randomized to receive a cuffed ePTFE graft (Venaflo; Bard, Tempa, Ariz.) or standard non-cuffed ePTFE graft (Stretch Gore-Tex; Gore, Flagstaff, Ariz.). The patients were informed of the purpose and methods of this study and signed informed consent forms before the operation. Randomization was carried out according to random numbers created by a computer. There were 17 patients assigned to the cuffed group and 19 patients assigned to the standard group. Each patient underwent a preoperative evaluation, including medical history and physical examination, which ultimately led to the decision of prosthetic graft implantation. Superficial veins of the upper extremities of all patients were cautiously surveyed when applying a tourniquet compression proximally in order to dilate the vessels, and those patients without adequate superficial veins palpable for the creation of dialysis fistula were enrolled in the study. All patients were hemodynamically stable outpatients suitable for graft implantation under local anesthesia.

Graft Placement and Follow-Up

Procedures were conducted under local anesthesia. An ultrasound scanner (SiteRiteIII; Bard) was used to choose the site of graft implantation. Only veins > 3 mm were candidates for a venous outlet of the dialysis grafts. All implanted grafts were 6 mm in diameter, and all procedures were completed by the same surgeon (PJK) using the same suture material (6-0 Gore-Tex suture). The procedures were performed on an outpatient basis. No oral antibiotics and anticoagulants were administered postoperatively.

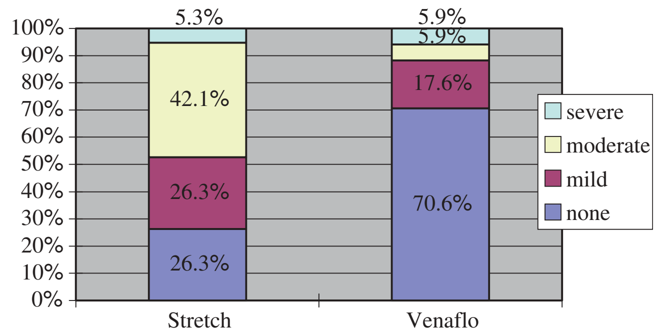

Figure 1. The degree of stenosis (D) was calculated as the diameter at the most narrow section of venous outlet (d1) compared with that of the nearest normal vein size (d2) and expressed as a percentage: D = d1/d2.

All of the grafts were used for dialysis after maturation. No implanted grafts were punctured for dialysis access prior to 3 weeks post-surgery and before limb swelling had subsided. The patency of the ePTFE grafts was repeatedly assessed by the medical staff in the dialysis unit. Surgical thrombectomy was the only technique used to keep the graft recannalized when a graft failed. Three months after implantation of the dialysis graft, each patient underwent fistulographic analysis to determine the condition of the ePTFE graft outlet.

Data and Statistical Analysis

The presence or absence of angiographic stenotic lesions on the graft outlets and lesion lengths were recorded. The degree of stenosis was defined as the diameter at the most narrow section of venous outlet compared with that of the nearest normal vein size (Fig. 1). The degree of stenosis of each lesion was recorded and graded quantitatively as follows: grade 1, no stenosis (< 29%); grade 2, mild stenosis (30–49%); grade 3, moderate stenosis (50–74%); grade 4, severe stenosis (75–99%). Additionally, graft locations, size of outlet vein, and inlet artery were also measured.

The *t*-test and chi-square test were used to compare the demographic data, graft location, and size of the arteries and veins between the two groups. Differences in angiography data, degree of stenosis (as a percentage or as graded), and length of stenosis between the two groups were analyzed using the *t*-test or Spearman correlation. Statistical significance was defined as $P < 0.05$.

RESULTS

Table 1 summarizes the demographic data of the patients of the study cohort. The average age of the patients

Table 1.
Patient demographics

Patient demographics[a]	Standard graft	Cuffed graft	*P* value
Age (years)	62.5 ± 11.5[b]	64.2 ± 13.5	0.684
Sex[a]			0.549
Male	6 (36.84)	7 (41.17)	
Female	13 (63.16)	10 (58.83)	
Comorbidity[a]			
Diabetes mellitus			0.637
Yes	7 (36.8)	5 (29.4)	
No	12 (63.2)	12 (70.6)	
Hypertension[a]			0.709
Yes	10 (52.6)	10 (58.8)	
No	9 (47.4)	7 (41.2)	
Graft location[a]			0.101
Forearm	5 (26.3)	1 (5.9)	
Upper	14 (73.7)	16 (94.1)	
Vein size (mm)	7.26 ± 2.21	6.85 ± 2.03	0.562
Artery size (mm)	4.47 ± 0.92	4.50 ± 0.83	0.929

[a]Values are presented as the number of patients, with the percentage of the study cohort given in parenthesis
[b]Values expressed with (±) are means ± standard deviation.

was 63.3 years (range: 30–86 years). Of the 26 patients, 13 were men and 23 were women. No significant differences were noted between the cuffed and non-cuffed graft groups for age, gender, prevalence of diabetes mellitus (DM), and hypertension. Similarly, no differences were identified in the graft location (upper arm or forearm), size of artery, and size of vein between the two groups. During the observation interval two grafts in the cuffed group and three grafts in the non-cuffed group had developed thrombosis and were all salvaged successfully by surgical thrombectomy. These five grafts were all still patent at 3 months when being put on the venography study. Table 2 presents the analytical results of dialysis graft venous outlet stenosis calculated from the angiography data 3 months after surgery. The mean degree of graft outlet stenosis was significantly different between the cuffed graft group and non-cuffed graft group (22.76 ± 26.37% vs. 44.95 ± 27%; $P = 0.019$). On the basis of a graded scale (1–4) that was used to measure the degrees of stenosis, scale, nearly half (47.4%; 9/19) of the non-cuffed graft's outlet stenosis was assessed to be moderate or severe stenosis; conversely, only 11.8% (2/17) of the cuffed graft group developed moderate or severe outlet stenosis (Fig. 2). The differences in the grade of stenosis between the two groups were significantly different.

However, the mean length of outlet stenosis for the standard graft and cuffed graft groups were1.69 ± 1.59 and 1.13 ± 1.81 mm, respectively, and not significantly different.

DISCUSSION

Most cases of dialysis graft thrombosis result from graft outlet stenosis caused by intimal hyperplasia[3] and, once a graft is occluded, an outlet stricture must be treated by angioplasty[4] or revision. Abnormal hemodynamic shear stress, mismatch of compliance between graft and vessel, and the iatrogenic injuries due to surgical anastomosis may contribute to the graft outlet intimal hyperplasia.[2] Intimal hyperplasia increases with time and eventually compromises a graft-venous anastomosis, leading to the frequently observed graft outlet stenosis. When such stenosis is not addressed, dialysis graft blood flow is likely impeded, and the graft eventually becomes thrombosed.

The optimization of venous anastomosis to enhance the patency of AVG is a principal goal of dialysis access surgery. Several strategies, such as using a venous cuff,[5] cuffed ePTFE dialysis graft, and improved anastomotic methods, have been proposed to minimize dialysis graft outlet stricture. The cuffed dialysis ePTFE graft was designed to improve graft-to-vein configuration and reduce graft outlet stenosis.[6] Computational analysis has shown that the geometric design of cuffed graft-end reduces the wall shear stress gradient, wall shear stress angle gradient, and radial pressure gradient of the graft-vein anastomosis.[7–10] Theoretically, this minimizes or delays the development of dialysis graft outlet intimal hyperplasia. The spacious outlet produced by the cuffed design will likely minimize the extent of stenosis caused by late intimal hyperplasia. Hence, the cuffed graft potentially offer improvements in the development of graft outlet stenosis.

Based on our experience and published reports, some 25–55% of dialysis grafts develop their first thrombosis episode within 6 months following implantation.[11] A certain proportion of the grafts should have developed graft outlet stenosis before thrombosis. Hence angiographic analysis results for the two graft designs at 3 months post-surgery were compared in this study. Our analytical results indicate that the cuffed graft performed substantially better than the non-cuffed graft for mean degree of stenosis (44.95 vs. 22.76%) and incidence of significant stenosis (11.8 vs. 47.4%).

The mean degree of stenosis in the non-cuffed graft group (44.95%) was significantly greater than that of the cuffed graft group (22.76%), indicating that, to some extent, the cuffed design reduces the incidence of graft outlet intimal hyperplasia, leading to fewer obstructed venous outlets. Almost one-half (47.4%, 9/19) of the patients in the non-cuffed group developed significant

Table 2.
Analysis of graft outlet stenosis between Stretch group and Venaflo group

	Standard graft	Cuffed graft	*P* value
Mean stenosis (%)	44.95 ± 27.48	22.76 ± 26.37	0.019*
Grade of stenosis-no. (%)			0.007*
None	5 (26.3%)	12 (70.6%)	
Mild	5 (26.3%)	3 (17.6%)	
Moderate	8 (42.1%)	1 (5.9%)	
Severe	1 (5.3%)	1 (5.9%)	
Length of stenosis (cm)	1.69 ± 1.59	1.13 ± 1.81	0.33

*$P \leq 0.05$

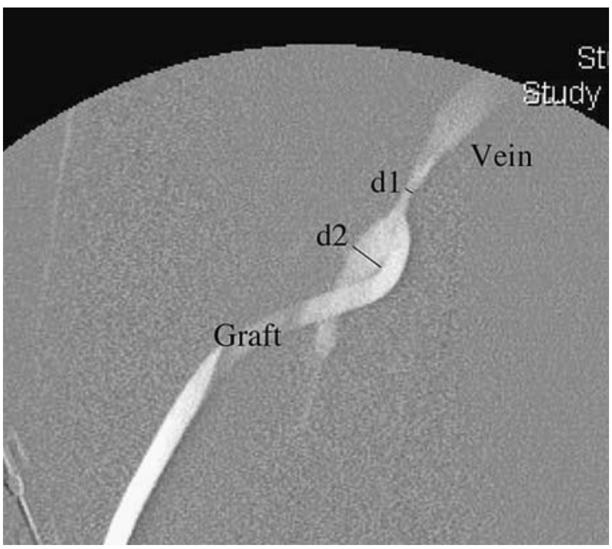

Figure 2. Graded graft outlet stenosis of two different graft groups.

outlet stricture (> 50% stenosis). Conversely, only 11.8% (2/17) of cuffed group patients developed an outlet stenosis of greater than 50%. Most patients in the cuffed graft group (70.6%, 12/17) had no stenosis according to the angiographic study, whereas only 26.3% (5/19) of the non-cuffed group had no stenosis. Since the demographic data were similar in both groups and all the operations were performed by the same surgeon using similar techniques and selection criteria, the differences in outlet stenosis can be attributed to the different hemodynamic characteristics affected by the different graft outlet designs.

Nyberg *et al.*[12] demonstrated that cuffed ePTFE grafts are able to provide stable and adequate blood flow rate for dialysis patients. Other studies successfully demonstrated the cuff design's advantage with respect to dialysis graft outlet. Using duplex measurements Lemson *et al.*[5] showed that a venous cuff at the graft-vein junction can decrease the outlet stenosis and increase graft blood flow.[9] Sorom *et al.*[13] also demonstrated that the cuffed ePTFE graft was associated with increased blood flow rate during hemodialysis.[13] However, no study has demonstrated quantitatively – by means of angiography study – the effect of cuffed design on graft outlet intimal hyperplasia and stenosis. Our data indicates that the cuffed grafts has less of a tendency to develop graft outlet stricture.

The cuffed design of the dialysis graft likely reduced the abnormal hemodynamic shear stress over the outlet. After 3 months of implantation, the cuffed graft had fewer cases of intimal hyperplasia over the graft-venous junction and, consequently, more cases retained wide outlets. However, increased hemodynamic shear stress after the dialysis graft implantation may not be the only cause of intimal hyperplasia-induced stenosis. Even in the cuffed graft group, 12.8% (2/17) of cuffed grafts developed outlet stenosis of greater than 50% (graded as moderate to severe stenosis) 3 months after surgery. Although the cuffed design overall decreased the abnormal hemodynamic shear stress, it did not prevent all graft outlet stenosis. Factors such as endothelial injury induced by suturing and compliance mismatch between vessel and graft likely contributed to graft outlet strictures of the cuffed dialysis grafts.

Vascular surgeons are still searching for an ideal prosthetic graft for dialysis access. An ideal dialysis graft should be easily implanted, easy to maintain, and complication-free. Clearly, the cuffed design is not the perfect graft. The cuff design has merit in terms of outlet morphology. However, in these authors' experience, implanting a cuffed graft is more technically demanding than implanting a standard cuff, requiring more effort to trim the edge of the graft cuff and adjust the anastomosis angle. It is also more time-consuming to implant a cuffed graft as a longer segment of vein must be dissected to create a larger anastomosis than that required for a non-cuffed graft. Perhaps the principal cause of graft outlet stricture in the cuffed graft group is an association with excessive suture injury and not the hemodynamic factors. In addition, it is somewhat more difficult to remove thrombus from the bulbous anastomotic region while carrying out a thrombectomy on a cuffed graft than on a regular graft.

Although the sample size of this study was small and the observation period was short, the difference between two groups was statistically significant. This significant difference may imply that the cuff design does decrease the development of outlet stenosis remarkably in a relative short period of time. In light of graft outlet morphology, our experimental results suggest that the cuffed graft has a beneficial effect for hemodialysis vascular access and if the cuffed graft does have favorable effects on graft outlet stenosis, it may lead to further improvements on clinical patency. However, the long-term patency of the cuffed graft versus standard graft still requires further prospective, large-scale and long-term study.

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