Prophylactic balloon angioplasty fails to prolong the patency of expanded polytetrafluoroethylene arteriovenous grafts: Results of a prospective randomized study

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Purpose: **Maintenance of hemodialysis access grafts represents an enormous social and clinical problem. Current grafts and graft salvage techniques are inadequate. Consequently, there has been increasing interest in the use of minimally invasive catheter techniques to prophylactically treat stenoses in functioning arteriovenous grafts. Prophylactic balloon angioplasty has been widely suggested as prolonging assisted primary patency. We have performed a prospective randomized trial to compare patients who underwent percutaneous transluminal angioplasty (PTA) for graft stenoses >50% with a control group that received no intervention. Our hypothesis was that to be efficacious a minimal benefit of 20% prolongation in patency would be necessary.**

Methods: **Color flow duplex scanning was used to detect >50% stenoses in functioning expanded polytetrafluoroethylene grafts. Patients were then subjected to confirmatory angiographic evaluation. Those who had angiographic stenoses >50% were randomized to balloon angioplasty or observation. Patients were followed-up with duplex scanning every 2 months. Statistical analysis was performed using the Kaplan-Meier technique. Although demographically the patient groups were well matched, there were more prior interventions and concurrent central stenoses in the treatment group. Outcomes were graft thrombosis, graft dysfunction that precluded dialysis, and six or more PTA procedures within 18 months.**

Results: **In the treatment and observation groups, the 6-month patency rates were 69% ± 7% and 70% ± 7%, respectively. The 12-month patency rates for the treatment and observation groups were 51% ± 6% and 47% ± 4%, respectively. There was no significant difference between these two groups ($p = 0.97$), with an 80% confidence limit for detection of a difference greater than 20%.**

Conclusions: **This study demonstrates that a generic approach of PTA to treat all polytetrafluoroethylene grafts with stenoses >50% does not prolong patency and cannot be supported. (J Vasc Surg 1997;26:382-92.)**

The hemodialysis population in the United States continues to grow at approximately 10% per year.[1] Polytetrafluoroethylene grafts are the dialysis mode in 80% of this patient group and represent the most frequently implanted vascular grafts in the nation. Indeed, in 1990 alone there were 22,000 fistula-related hospital admissions for Medicare-insured patients, not including those treated as outpatients.[2]

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Supported in part by NIH Grant # P50DK45215-03 and Clinical Research Center # 324.

Presented at the Twenty-first Annual Meeting of The Southern Association for Vascular Surgery, Coronado, Calif., Jan. 22-25, 1997.

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0741-5214/97/$5.00 + 0 **24/6/83496**

Dialysis is required for some 120,000 Americans with end-stage renal disease.[3]

Unfortunately, expanded polytetrafluoroethylene (ePTFE) bridge grafts are fraught with complications and their durability is limited, with the average duration of patency being only 18 months.[4-7] Failure occurs predominantly from stenoses that develop at the venous anastomosis as a consequence of aggressive neointimal hyperplasia.[8-9] Although this lesion is notoriously difficult to dilate, there has been an increasing number of reports that suggest that angioplasty is both important in prolonging graft patency as well as being an adjunctive measure in opening the thrombosed graft.[10-12] Schwab,[10] in a landmark 1989 report, suggested that early detection and treatment of fistula stenoses would prolong graft patency, preserve alternate sites, and reduce the number of central venous cannulations for acute dialysis. Most studies that have supported prophylactic intervention, although retrospective in design, have suggested a statistically significant benefit and have had a profound effect on the approach to management of the failing graft. Consequently, endovascular techniques are being increasingly advocated as a method of improving secondary patency rates. Angioplasty, stenting, and thrombolysis have all been reported as providing efficacy and have been widely adopted as the new gold standard for the management of arteriovenous grafts.[11-15] Indeed, the concept of prophylactic intervention has been born as a consequence of the development of these minimally invasive interventions and has led to the proliferation of graft surveillance protocols to detect early stenoses.[10,16-26] Although this concept initially appears reasonable, it is predicated on the belief that an intervention exists that is effective in prolonging graft patency. This study was initiated to test the assumption that balloon angioplasty of hemodialysis-related stenoses (>50% diameter) would improve patency rates when compared with untreated, similarly stenotic ePTFE arteriovenous grafts.

PATIENTS AND METHODS

During the period December 1993 to November 1996, all chronic hemodialysis patients with ePTFE grafts in a single inner-city dialysis unit were screened as candidates for enrollment in this trial. By virtue of the location of the unit, this was a preselected group of patients, largely representing an inner-city population, whose demographics are provided in Table I. Reasons for nonenrollment included patient refusal, a contrast dye allergy, or a nonfunctioning ePTFE graft. Data on demographics, comorbidities, and dialysis access history were obtained from review of the clinic dialysis records. Other forms of access not evaluated in this study included Brescia-Cimino fistulas and bovine carotid artery heterografts. The design of the study is demonstrated in Fig. 1. Approval for this study was obtained from the Human Investigations Committee at Emory University. A full, informed consent was obtained from each patient. All patients in the study underwent color flow duplex imaging (CDI) of the entire graft (arterial anastomosis, midgraft, venous anastomosis, outflow to the limits of visualization). Those patients who had a stenosis ≥50% (at any location) by CDI were subjected to angiographic study that included the arterial inflow, entire graft, and entire outflow from the venous anastomosis to the right atrium. It was thought that patients with stenoses <50% by CDI could not ethically be subjected to angiographic evaluation. Therefore, the false-negative rate by CDI cannot be determined.

Table I. Patient demographics and comorbidities

	Observation	*PTA*
Men	14	17
Women	18	15
Age (mean ± SD)	58 ± 11	56 ± 13
Age (range)	35 to 74	34 to 72
Race		
Black (%)	91	94
White (%)	3	6
Oriental (%)	3	0
Hispanic (%)	3	0
Comorbidities		
Diabetes (%)	38	41
Hypertension (%)	91	82
PVD (%)	9	19
CASHD (%)	19	28
Smoking (%)	38	25

PVD, Peripheral vascular disease; *CASHD,* coronary arteriosclerotic heart disease.

CDI. Grafts were examined with a Quantum QAD 1 color flow duplex scanner, using a 7.5-MHz transducer and 18-degree stand-off wedge. Patients were positioned on an examination table with the extremity abducted and externally rotated. The percent stenosis was determined by measuring the diameter of the stenotic flow channel (s) versus the diameter of the normal graft (n) using the following formula: $[1 - (s/n)] \times 100$ = percent stenosis of the graft. Assessment of flow throughout the graft was measured by Doppler interrogation. Mean peak systolic and end diastolic velocities (cm/sec) were measured over four cardiac cycles and averaged. The diameter (d) of a nonstenotic, nondilated midpor-

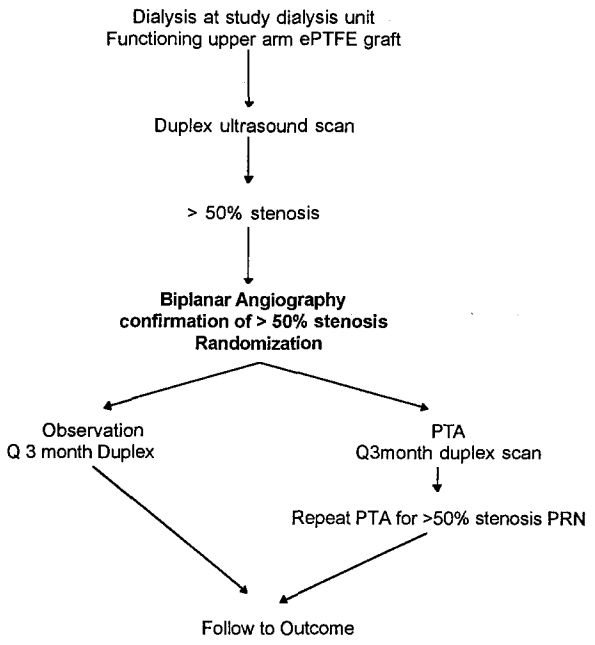

Fig. 1. Study design.

tion of flow channel was measured for the purpose of calculating "normal" flow rates. The peak systolic and end diastolic flow rates (ml/min) were calculated using the following formula: $(\pi d^2) \div 4 \times$ average velocity $\times$ 60.

Patients were eligible for CDI imaging regardless of whether they exhibited any signs or symptoms of graft dysfunction. However, for the purposes of this trial, potential graft dysfunction included an elevated recirculation ratio (>15%) or elevated venous dialysis pressure (>240 mm Hg). To compare graft function in both treatment and control groups, we used a panel of functional tests: venous pressure during dialysis at 400 ml/min flow rate, urea recirculation, and duplex measurement of flow volumes. Measurements of recirculation levels were performed on the same day as the routine CDI, as previously described.[8]

Fistulography. Digital angiographic images of the graft, arterial inflow, and venous outflow to the right atrium were recorded using the Phillips DVI-S system. Using a 5F micropuncture set (Cook Inc., Bloomington, Ind.), the fistula was punctured 5 cm from the arterial end, and a 5F catheter was inserted. Radiographic contrast medium was then injected, and digital subtraction angiograms of the fistula and the venous drainage to the right atrium were recorded on a 512 digital matrix (DVI-S system, Phillips Medical Systems, NA, Eindhoven, The Netherlands). Angiograms involving the arterial anastomosis of the fistula were obtained either by compressing the graft during injection of the contrast medium or by direct injection of contrast medium into the brachial artery through a 3F catheter. The digital angiograms were recorded on x-ray film, and the stenosis within the fistula or veins was measured using an electronic caliper (Sandhill Scientific Inc., Littleton, Colo.). The longitudinal diameter at the point of greatest stenosis was compared with that of the closest normal adjacent lumen.

The percent stenosis by fistulography was defined as:

$$\frac{\text{Longitudinal diameter of the stenosed segment}}{\text{Longitudinal diameter of an adjacent nonstenosed segment}} \times 100$$

Randomization procedure. All patients confirmed by angiographic evaluation to have a stenosis >50% within the graft or at the anastomoses were randomized by drawing cards to either no intervention or to percutaneous transluminal angioplasty (PTA).

Angioplasty procedure. If a stenosis >50% was identified, the 5F catheter was exchanged for a 6F or 7F introducer sheath (Pinnacle sheath, Meditech, Watertown, Mass.) and a 0.035-inch angled tip glide wire (Meditech) was inserted through the sheath and advanced under direct vision across the stenosis into the distal venous or arterial system. An appropriately sized angioplasty balloon (Ultra-thin or Blue Max, Meditech) was selected (generally oversizing by 1 to 2 mm). High-pressure balloons were used because they are frequently required to dilate resistant stenoses. The balloon was inflated until all waisting was eliminated or to the maximum pressure recommended by the manufacturer (17 atm for the Ultra-thin and 25 atm for the Blue Max).

Follow-up. All of the patients were evaluated three times a week at the dialysis center. Estimates of patency were therefore accurate to within approximately 3 days. CDI was performed every 2 months on all grafts. Patients randomized to the treatment arm in whom >50% diameter restenosis developed as determined by duplex scanning were subjected to repeat angiography and repeat angioplasty if >50% stenosis was confirmed. Patients who required more than six PTA procedures in less than 18 months were deemed to be treatment failures and were considered to have had a primary outcome event.

Statistical analysis. Statistical analysis was performed using Kaplan-Meier analysis. A p value less than 0.05 was considered significant.

Table II. Background data—graft type, location, and prior revisions

	Observation	*PTA*	*p*
Upper-arm graft	22	23	
Upper-arm loop	1	0	
Forearm loop	8	7	
Forearm straight	1	1	
Groin loop grafts	0	1	
4-7 mm ePTFE	30	29	
6 mm ePTFE	2	3	
No. of prior revisions			
Surgical	1.06 ± 1.48	1.6 ± 1.7	0.11
PTA	0.52 ± 1.02	0.5 ± 0.8	0.53

Table III. Severity and distribution of angiographically documented stenoses

	Observation	*PTA*
Average % venous stenosis	67 ± 10 (30 stenoses)	66 ± 12 (24 stenoses)
Average % midgraft stenosis	57 ± 8 (16 stenoses)	60 ± 10 (17 stenoses)
Average % arterial stenosis	90 (1 stenosis)	52 (1 stenosis)
Average % central stenosis	64 ± 14 (7 stenoses)	67 ± 15 (17 stenoses)

Table IV. Graft function by venous pressure measurements, recirculation, and duplex determined flow volume

	Observation	*PTA*
Mean venous pressure (mm Hg)	240 ± 45	251.0 ± 56
Mean urea recirculation	10.2 ± 5	9.8 ± 6
Mean volume flow (ml/min)		
Peak systolic	2557	2300
End diastolic	1550	1424
Time to Outcome (days)	234 ± 271	246 ± 270

Outcomes. The primary outcome event was functional graft failure defined as thrombosis or impaired flow such that dialysis was not feasible. During the course of the study, a third outcome was established, namely, of a patient requiring more than six PTA procedures in less than 18 months to maintain luminal dimension >50% diameter.

RESULTS

Of 170 patients screened for the study, 136 (80%) had ePTFE grafts. Sixty-five patients were identified by CDI to have >50% stenoses and were referred for angiography. Of these, 64 patients were confirmed to have eligible stenoses and were randomized—32 into the treatment arm (PTA) and 32 into the nontreatment arm. Thirty-one of the patients were men, and 33 were women. Fifty-nine of the patients were black, three were white, one was Asian, and one was Hispanic. Demographics and comorbidities for each group are provided in Table I. Of the 64 grafts, 36 of the ePTFE grafts were located in the left upper arm, 12 were in the right upper arm, 12 were in the left forearm, three were in the right forearm, and one was in the right thigh. Eight of the grafts had a loop configuration, whereas the majority, 56, were straight (Table II). Both groups were well matched for age, distribution, and type of graft. There were more prior surgical revisions in the PTA group and fewer prior angioplasty procedures in the PTA group than in the observation group (Table II). The degree of stenosis and distribution of the stenoses were similar (Table III), with the exception of a greater number of concurrent central venous stenoses in the PTA group compared with the observation group (17 stenoses versus seven stenoses).

Only eight of the 64 patients (13%) had elevated urea recirculation ratios. Two of these patients were in the treatment group and five were in the observation group. Twenty-nine of the 64 patients (45%) had elevated venous dialysis pressures, all measured at blood flow rates greater than or equal to 400 ml/min. Seventeen of these patients were in the treatment group and 12 were in the observation group, as seen in Table IV.

In the treatment group, four patients died during the course of the study and two were lost to follow-up. One patient received a cadaveric renal transplant. In the observation group, two patients died and one was lost to follow-up. For all patients, the mean duration of follow-up in the treatment group was 462.1 ± 68.4 days and was 463.6 ± 69 days in the nontreatment group.

The average number of transluminal angioplasty procedures performed per patient was 1.94 ± 1.31 (range, 1 to 6). Eight patients required greater than two PTA procedures, with two patients requiring six PTA procedures each (Fig. 2).

The mean duration of patency of those grafts treated with balloon angioplasty was 246 ± 270 days. In the observation group, the mean duration of patency was 234 ± 271 days. Life table analysis demonstrated a 6-month patency rate of 67% ± 8% in the nontreatment group and 63% ± 9% in the treatment group (Table V). The 12-month patency rate was 48% ± 9% in the nontreatment group and 51% ± 9% in the treatment group. There was no

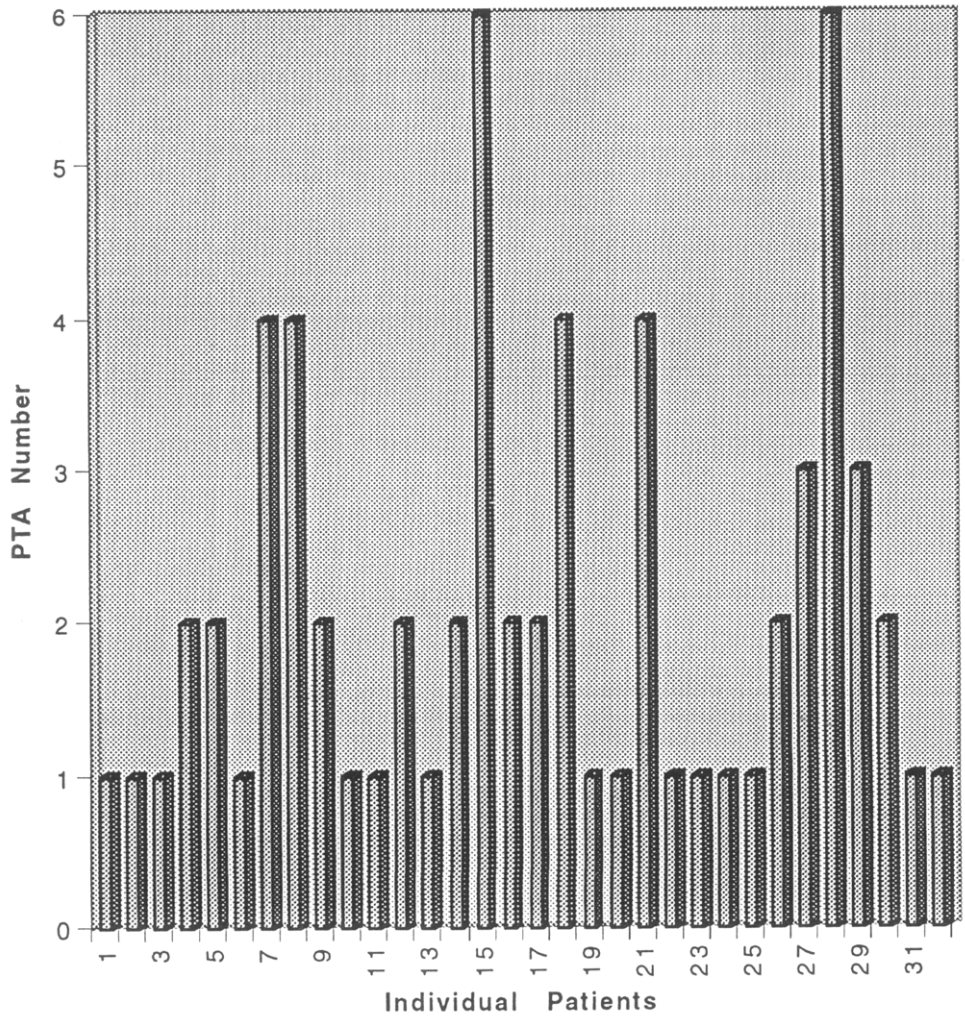

Fig. 2. Number of PTA procedures performed per individual patient during the course of the trial.

Table V, A. Life table patency data—observation

Months	*Patency rate*	*Failure rate*	*Survival standard error*	*Median residual lifetime*	*Median standard error*
0 to 3	1.0000	0	0	11.3509	2.2904
3 to 6	0.8033	0.1967	0.0720	16.5434	4.3230
6 to 9	0.7007	0.2993	0.0837	—	—
9 to 12	0.5929	0.4071	0.0911	—	—
12 to 15	0.4743	0.5257	0.0952	—	—
15 to 18	0.4312	0.5688	0.0958	—	—
18 to 21	0.4312	0.5688	0.0958	—	—
21 to 24	0.3737	0.6263	0.0988	—	—
24+	0.3737	0.6263	0.0988	—	—

significant difference in patency rates between these two groups by life table analysis ($p = 0.97$). This is an 80% confidence limit for detection of greater than 20% difference between the two groups (Fig. 3).

There were three complications of the angioplasty procedure. One patient had dye extravasation at the angioplasty site. Acute graft thrombosis developed in one patient during angioplasty, which was

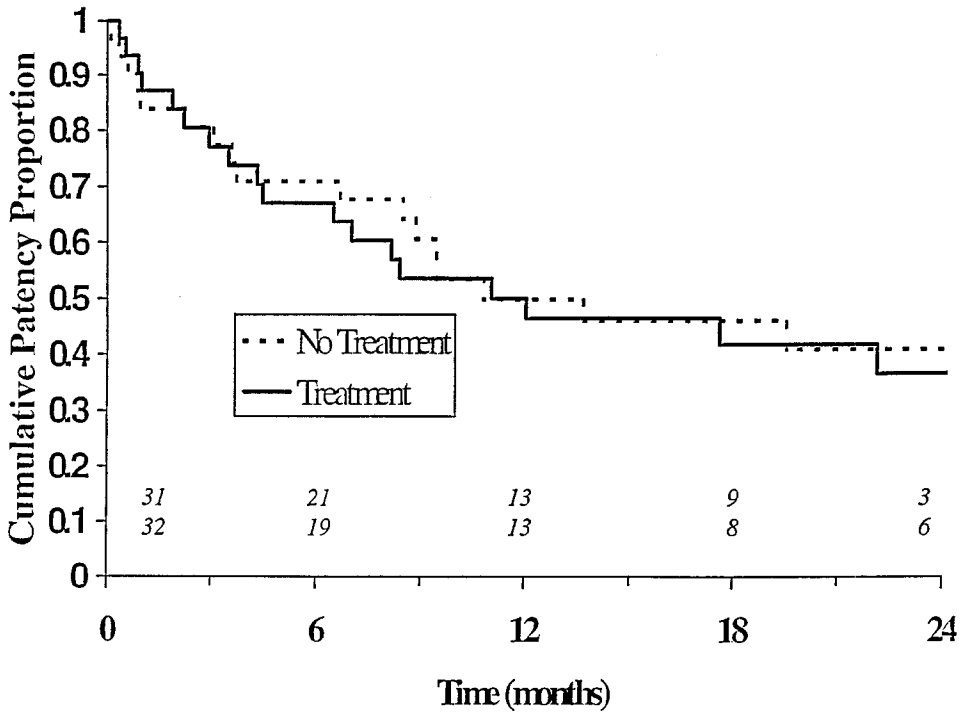

Fig. 3. Life table analysis of graft patency data.

Table V, B. Life table patency data—angioplasty

Months	*Patency rate*	*Failure rate*	*Survival standard error*	*Median residual lifetime*	*Median standard error*
0 to 3	1.0000	0	0	13.1024	6.3714
3 to 6	0.7667	0.2333	0.0772	19.6896	3.4774
6 to 9	0.6970	0.3030	0.0845	—	—
9 to 12	0.5540	0.4460	0.0926	—	—
12 to 15	0.5158	0.4842	0.0937	—	—
15 to 18	0.4728	0.5272	0.0953	—	—
18 to 21	0.4230	0.5770	0.0974	—	—
21 to 24	0.4230	0.5770	0.0974	—	—
24+	0.3525	0.6475	0.1036	—	—

successfully reopened with urokinase during the same procedure. Another patient had intraprocedure chest pain, which was relieved by nitroglycerin. There were no procedure-related complications in the observation group.

A total of 42 lesions were located with CDI in the 32 treated patients. Fifty-nine lesions were identified with angiography in this same group. This averages to 1.35 ± 0.55 lesions per patient studied found by CDI and 1.83 ± 0.76 lesions per graft demonstrated with angiography. A total of 44 lesions were identified with CDI in 32 patients who were not treated. There were 54 lesions identified with angiography in the observation group. This averages to 1.33 ± 0.81 lesions per graft studied with CDI and 1.69 ± 0.85 lesions per graft demonstrated by angiography.

Using both the χ^2 and unpaired t test, there was no significant difference in the number or distribution of stenoses between the PTA and observation groups. There were slightly more prior surgical ($p = 0.11$) and PTA ($p = 0.53$) procedures in the treatment group than in the observation group (Table II).

DISCUSSION

Modern hemodialysis became feasible when Quinton et al. introduced the external arteriovenous shunt in 1960.[27] Recurrent thromboses, infections,

and occasional major bleeding episodes, however, prompted development of the subcutaneous arteriovenous fistula by Brescia et al. in 1966.[28] ePTFE grafts were first used as bridge conduits in 1976 and are currently the most popular method of establishing hemodialysis access in the United States.[4] Despite their widespread use, there has been no improvement in their durability since they were introduced clinically in 1976.[4] The mean duration of primary patency of these grafts is only 18 months, resulting in frequent hospital admissions for thrombectomy, PTA, revision of the venous anastomosis, or new graft placement.[5-7] Most grafts come to clinical attention at the time of graft thrombosis. However, some functioning grafts are evaluated because of recurrent thromboses or fistula dysfunction (high venous pressures, elevated urea recirculation, poor flow rates) that results in impaired dialysis.[10,11,18-26] Unfortunately, surgical salvage of these grafts, typically thrombectomy and patch angioplasty, results in only an additional 3 months of patency.[5-7] Indeed, surgical results are so dismal that others have suggested that the failed graft should be abandoned and that replacement rather than revision should be advocated.[29] Such an approach, however, particularly in the young patient, could result in rapid exhaustion of access sites. Nevertheless, after grafts thrombose, there is no doubt that durability is significantly compromised and new access placement is frequently necessary. Consequently, a reasonable approach would appear to be prophylactic intervention: repair stenoses before graft failure. A variety of techniques have been developed to evaluate graft function or, more specifically, to detect graft dysfunction: venous outflow pressure measurement, urea recirculation, and outflow resistance.[18-20] With the advent of duplex scanning, noninvasive imaging of the graft became feasible and stenoses could be directly measured.[8,16,21] This technique is currently the gold standard for noninvasive evaluation of the arteriovenous access grafts, and its accuracy has been previously reported.[8] Clearly, an effective method for stenosis detection within the graft is now available, although remote stenoses, particularly within the subclavian vein, cannot be demonstrated by CDI. However, graft surveillance can only be justified if an effective intervention is available that provides meaningful prolongation of graft patency. The null hypothesis in this study was that balloon angioplasty would provide such a benefit. We believed that stenoses present in functioning grafts would likely be of lesser severity than those in occluded grafts and that stenoses detected by screening may represent a population that is more amenable to catheter-based intervention (i.e., they may represent a group in which we believed PTA would have the best chance of success). Our hypothesis, therefore, was that early intervention and "prophylactic" angioplasty would prolong the patency of these functioning, but compromised, arteriovenous grafts.

Meaningful prolongation in graft patency was defined in this study for statistical purposes as an increase in patency of more than 20% in the treatment group compared with the control group. No statistically significant improvement was detected. Indeed, there was most likely no improvement in patency associated with prophylactic PTA. This occurred despite an average of 1.94 angioplasty procedures per patient during the study period. Clearly a significant cost, for no observed benefit. In examining the two study populations, they were closely matched in age, sex, comorbidities, and type and location of the graft. There was a difference in the number of concurrent central venous stenoses, with six stenoses in the observation group and 11 in the PTA group. There were no significant differences in the functional graft parameters measured: mean venous pressure, mean urea recirculation, and peak systolic and end diastolic volume flow (Table IV). The latter would suggest that the additional central venous stenoses in the PTA group had little functional impact on the arteriovenous graft.

Perhaps the most important question that arises is why angioplasty of venous stenoses works poorly. Davidson et al.[30] examined the immediate results of PTA in venous stenoses using intravascular ultrasound. However, there was rapid recoil, which reflects the elasticity of the lesion and may be one of the principal physical factors that limits the efficacy of angioplasty. In this respect, these lesions behave very differently from the more rigid, brittle, atherosclerotic arterial lesions. Another source of error when evaluating the efficacy of angioplasty is the variability of stenotic lesions. Only Beathard[31] has attempted to classify these lesions, and further attempts at classification are clearly necessary. It may well be that PTA, as in the arterial system, is most efficacious for selected, short, focal lesions.

Although this study casts some doubt on the role of PTA in treatment of these grafts, vascular surgeons cannot be proud of the patency rates of surgically implanted and revised grafts. Indeed, it is precisely because of the poor surgical results that much of the focus has been placed on catheter-based salvage.[32-37]

Traditional surgical therapy for occluded access grafts consists of thrombectomy with selective graft

revision.[4] Identification of a stenosis is based on tactile feedback from an embolectomy catheter, as well as the lack of brisk prograde and retrograde bleeding. Usually, only one lesion is detected per exploration. This approach prolongs graft patency by an average of only 3 months. The inherent limitations of such an approach are demonstrated by a recent prospective duplex and angiographic study in which we demonstrated that there is an average of 1.3 stenoses in each graft by CDI and 1.6 stenoses in each graft when studied with angiography.[16] Indeed, similar results are noted in this report, where an average of 1.84 and 1.69 lesions were noted in the observation and treatment groups, respectively. It should come, therefore, as little surprise that identifying and treating only one lesion results in poor secondary patency. Angiography alone at the time of thrombectomy identifies lesions in the entire system: arterial inflow to right atrium.[8,38] These lesions are generally not detected or treated during standard surgical thrombectomy. We believe that given the frequency of synchronous lesions, angiography should be a component of graft revision. We believe that a combined surgical and catheter-based approach is necessary. Given the findings in this manuscript, in which PTA of predominantly venous anastomotic stenoses is ineffective, we would continue to advocate surgical revision of that anastomosis. However, angiography and catheter-based approaches may be the only method by which remote lesions can be detected and addressed. This approach is appealing for several reasons: (1) it is an objective, quantitative method to determine the frequency and severity of critical stenoses within the failed access graft; (2) remote and perigraft stenoses can be treated at the same sitting; (3) it avoids repeated violation of planes until surgical revision is necessary; (4) the current approach is inadequate; and (5) the described approach permits complementary use of endovascular and traditional surgical techniques.

The intervention selected should be based on which is the most efficacious for each lesion, as well as which will provide the greatest durability of each access site. There may well be subsets of stenoses that can be treated by PTA. One potential weakness in the study is that there is a greater number of prior interventions and central stenoses in the treatment group. This potentially could adversely affect the outcome. This study, however, demonstrates that a generic approach of PTA to treat all PTFE grafts with stenoses >50% cannot be supported.

A larger study to evaluate patients on the basis of prior interventions and central stenoses may be necessary to definitely address other potential variables.

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Submitted Jan. 29, 1997; accepted May 20, 1997.

DISCUSSION

Dr. S. Timothy String (Mobile, Ala.). This was a very nice presentation and a very timely subject. The authors certainly are to be congratulated in trying to quantify the precursors of failure in the arteriovenous shunt and their potential treatment with endovascular methods. Too, the program committee is to be commended for having several papers on a not-so-popular subject but a very necessary subject on this program for those of us involved in the patient population put before. Furthermore, Dr. Lumsden and his associates have helped confirm in a prospective manner our bias of experience that angioplasty or stent placement in the graft or venous outflow system is very much ineffective. This paper begins to dismiss the myth that is being purported of endovascular success.

Several questions come to mind. First, what are the physiologic data in an arteriovenous fistula that suggest a >50% stenosis, a hemodynamically significant lesion? Were these grafts really, as you quoted in the paper, compromised arteriovenous fistulas, and if so, on what basis? Was the flow in ml/min or any other parameters, such as recirculation time or increased venous pressure, useful as a predictor of failure? Finally, if you used failure of a single PTA procedure as your endpoint and not six as used in the paper, what would have been the failure rate? Certainly six procedures in 18 months, translated to six surgical procedures in that period of time, would have necessitated replacement of the graft.

Again, the authors are to be commended for helping to further define the ongoing problems associated with the arteriovenous fistulas and their attendant problems. Thank you for the privilege of discussion.

Dr. Alan B. Lumsden. You raised some very important points. First of all, none of these were in fact fistulas. We confined ourselves to PTFE grafts. We excluded bo-

vine grafts, and we excluded all the autogenous fistulas. Your first question may be the most important. Why 50%? We chose 50% because if you look, the evolution of this concept basically begins with Schwab, who became interested in maintenance of hemodialysis access grafts. At that point, he used 50% because he equated it with venous outflow pressure. That has essentially been perpetuated down the line. Almost all of the studies have then used 50%. I certainly think you can argue with it. I am not sure, if we had used 80%, for example, whether we would have seen any efficacy from prophylactic intervention. I really don't know what the answer to that question is. The rationale for using 50% is because that was what all the nephrology data have used, and we wanted something that could be directly applied to the nephrology literature and that could equate with their previous studies.

Another question was about the functional parameters. There are a whole variety of different ways in which nephrologists attempt to use noninvasive methods for detecting the failing hemodialysis graft, measurement of venous outflow pressure and urea recirculation, to name but two. You measure the pressure through the venous cannula at set dialysis flow rates. The ones we used were all measured at greater than 400 ml/min. You measure the fraction of blood that is recirculating between the venous canula and the arterial canula, and it is supposed to imply downstream resistance causing recirculation of the blood; greater than 15% is usually considered to be abnormal. More recently, people have just been using venous outflow pressures at slightly lower flow rates. We actually looked at all of these and really could not find any good association between the duplex-identified >50% stenoses and any of these physiologic pressures.

Your final question concerned what the result would have been if we had simply used one angioplasty instead of six as an end point. The average number of angioplasty procedures performed was close to two, it was 1.94. Eight of these patients underwent more than two angioplasty procedures. The majority actually only underwent one angioplasty procedure. I don't know what the answer to your question is. It is a very relevant one, and I think it is one that is worthwhile for us to go back and pull the data and look at it. I really cannot tell you what one angioplasty may or may not have achieved in this group.

Dr. Daniel F. Fisher, Jr. (Chattanooga, Tenn.). You said that the majority of these grafts were 4-to-7 mm tapered grafts. Did you have enough of the 6 mm grafts to look at the patency of 6 mm versus 4-to-7 mm tapered grafts?

Dr. Lumsden. No, we really didn't. The vast majority of them were 4-to-7 mm taper grafts.

Dr. Fisher. How did you revise the venous anastomosis when you had to operate on the group that had surgery? Did you use an interposition graft, or did you patch the venous anastomosis open? And do you think it makes any difference?

Dr. Lumsden. Well, we did not actually operate on any of these patients. The endpoint of the trial was when the graft occluded. At that point, we would operate on them, but not under the basis of a trial. Then, it really ended up depending on an individual surgeon preference. What I do typically is cut down on the venous anastomosis and perform a thrombectomy, but then I routinely obtain on-table arteriograms and venograms. I started one time performing angioplasty in these venous anastomoses, and it really does not work. Having said that, I do think there is a role for endovascular techniques. I think the problem with the way that we tackle these is that we focus on the venous anastomosis and we ignore everything else. You would never dream of doing that in a failed femoropopliteal graft. For some reason or another, we treat these grafts differently. I think you should study the entire graft. I think the advantage of the potential endovascular application is to extend your reach to areas that you can't get to and to the arterial end flow or into that central venous circulation. I think one problem is that addressing one lesion in a graft that clearly has multiple lesions is inadequate.

Dr. Samuel P. Martin (Orlando, Fla.). I also very much enjoyed your paper. We have been concerned with this problem for some time. I was just wondering several things. First, when you performed your duplex scan, did you have a means of getting volume flow measurements with that? I was also concerned that, as you pointed out, there was a significant increased incidence of graft revisions in your group that underwent balloon angioplasty. I think that is a very significant number, 1 as opposed to 1.6 in that group.

Second, on another point, I would like to know about your technique for balloon angioplasty. Some are performing balloon angioplasty where the time of balloon dilatation is only a short time. They are doing this for less than a minute and point out that it is very important that this not be a sustained balloon inflation. They believe there can be injury with that, and they believe that just breaking cicatrix. I was wondering how you are performing your balloon angioplasty procedures, because certainly your results do significantly differ from some of these other observers.

Dr. Lumsden. Your first question was in regards to volume flow. We measured volume flow. There are formulas for calculating this off the duplex data. It is a derived number, and I am not impressed that it is something that is particularly reliable. In looking at it, we really could not predict from the calculated volume flow whether it was >50% stenosis. As regards the number of revisions, that is a major concern, and in fact has led to a fairly contentious argument amongst the coauthors here. This was a prospective randomized study. We did not select these patients, and that may be a criticism. It is not easy to get all of this data in terms of number of graft revisions up front, and we did not stratify. As the chips fall in a prospective randomized study, when we went back and looked at the number of revisions, that is one of the outcomes. That is going to be a criticism. I have absolutely no doubt when this gets

published that that is the nail that the interventional radiology group is probably going to hang their hat on. How to defend that? You know, it is difficult to defend. There are actually more stenoses, if you total them all up, in the observation group than there are in the angioplasty group. In that respect, it is a little weighted in terms of observation, and in all of the function measurements that we did there is not really any difference. I agree, that is still a potential weakness in the interpretation of the study.

Dr. Clifford J. Buckley (Temple, Tex.). One of the things that we have noticed in our own population of dialysis patients is that in recent years the blood flow rate at which they are dialyzed has increased from 250 or 300 ml/min to approximately 500 ml/min. We are observing increasing stenoses in the veins distal to the area of the outflow anastomosis between the fistula graft and the vein. Did you see this in your study group? It is important that you evaluate the outflow vein beyond the anastomotic area, because not uncommonly there may be a stenosis further up the vein. I personally believe that this may be related to the high-volume flow and jet effect associated with it that results in injury to the vein wall.

Dr. Lumsden. I really have no idea whether it is related to higher-volume flow. We defined central venous stenosis as the distal axillary vein and the subclavian vein. As you can see, there was a fairly significant number of those central venous stenoses in this particular group. I think you have touched on something that really only Beathard has tried to do and that is to try and classify these stenoses. We talk here about all stenoses as if they are equal, but they are clearly not equal; there are clearly some lesions that may be much more amenable to angioplasty than others, we just don't know what those are at the moment.