Kidney International, Vol. 67 (2005), pp. 1554–1558

DIALYSIS – TRANSPLANTATION

Regular ultrasonographic screening significantly prolongs patency of PTFE grafts

JAN MALIK, MARCELA SLAVIKOVA, JAROSLAVA SVOBODOVA, and VLADIMIR TUKA

Third Department of Internal Medicine; and Department of Cardiovascular Surgery, General University Hospital and First School of Medicine, Charles University, Prague, Czech Republic

Regular ultrasonographic screening significantly prolongs patency of PTFE grafts.

Background. Polytetrafluoroethylene (PTFE) dialysis grafts have considerably shorter patency than native arteriovenous fistulas, despite the use of a complex of screening monitoring methods (venous pressure, access flow). PTFE grafts are used often in subjects with depleted subcutaneous veins after previous abandoned accesses, so keeping the access patent is crucial. We hypothesized that regular duplex Doppler ultrasound screening for access stenoses, together with their sooner treatment, would prolong PTFE graft patency.

Methods. We performed a randomized, prospective study of PTFE grafts' cumulative patency in 192 subjects. In group 1, regular ultrasound examinations performed every 3 months was added to traditional screening (i.e., regular access examination at hemodialysis unit, monitoring of venous pressure and access flow). Group 2 was screened only traditionally (without ultrasound). Interventions of suspected stenoses were indicated by nephrologists, vascular surgeon, and, in group 1, also by ultrasonography. Classic ultrasound criteria for significant stenosis were used, even if the access flow had not been decreased. The mean follow-up lasted 392 ± 430 days.

Results. Groups were similar with respect to age, gender, diabetes status, and number of previous abandoned accesses. Group 1 had significantly longer access patency ($P < 0.001$). Number of interventions per graft was 2.1 ± 1.8 and 1.3 ± 1.0 in group 1 and group 2.

Conclusions. Regular screening duplex Doppler ultrasonography results in significantly longer PTFE graft patency due to early detection of access stenosis and, thus, more frequent elective interventions of access stenoses.

Polytetrafluoroethylene (PTFE) dialysis grafts have shorter longevity than native arteriovenous fistulas [1]. Thrombosis of PTFE grafts continues to be a major source of morbidity in hemodialysis patients [2]. In European countries, implantation of PTFE grafts remains to be a method of second choice. It is used when the creation of native arteriovenous fistula is not possible, especially due to lack of patent subcutaneous veins. The use of PTFE graft is therefore significantly associated with higher risk of cardiovascular disease, as characterized by older age, higher body mass index, diabetes mellitus, and signs of peripheral vascular disease [3]. In the United States, where the use of PTFE grafts is considerably higher, subjects with this type of vascular access have higher mortality than subjects with native arteriovenous fistulas [4].

Failure of vascular access, either with inadequate blood flows or by clotting, results in the need of emergent percutaneous or surgical intervention, which have poorer results than elective procedures. In some cases, placement of a temporary dialysis access is necessary. Failure of vascular access is usually preceded by development of access stenosis. Therefore, several monitoring techniques have been developed to forecast graft failure. These especially include monitoring of dynamic venous pressure, measurement recirculation, and access flow [5]. Best vascular access care is summarized by Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines. These guidelines are followed worldwide in developed countries, including our country.

To compare longevity of vascular accesses between various centers, primary and secondary patency rates are calculated. Primary patency is defined as the functional access patency until any type of intervention; secondary patency is defined as the functional access patency until either final failure or the access is abandoned. In a meta-analysis published recently by Huber et al [1], secondary (cumulative) patency rates of PTFE grafts were as low as 76% at 6 months, and 55% at 18 months. Thus, placement of PTFE graft is not a long-term solution for subjects with lack of patent peripheral veins, and, often with history of repeated closure of previous accesses. More effective screening techniques for in-time detection of imminent closure are needed.

Duplex Doppler ultrasonography has been repeatedly proven as an accurate method for diagnosing access complications in comparison to access angiography [6, 7].

Key words: vascular access, ultrasonography, stenosis, access patency.

Received for publication June 4, 2004
and in revised form August 28, 2004
Accepted for publication October 12, 2004

Although it is a simple, cheap, and accurate method, duplex Doppler ultrasound access monitoring has not been yet widely established. DOQI guidelines [5] support the use of ultrasound only partially (evidence/opinion level) because no clear evidence of prolongation of access patency after ultrasound examinations has been suggested. We hypothesized that regular duplex Doppler ultrasound screening for access stenoses, together with their sooner treatment, would prolong PTFE graft patency. To prove it, we performed a randomized, prospective study of PTFE grafts survival, where 1 group of patients was screened traditionally (without ultrasound), and the other also by regular ultrasound examinations every 3 months, which was added to traditional screening.

METHODS

This randomized prospective study was performed in an unselected population of hemodialysis subjects between the years 1999 and 2004. Patients indicated for creation of vascular access with PTFE graft located in the upper extremity (as judged by the surgeon) were consecutively included into this study. All subjects received 6 mm Gore-tex stretch PTFE grafts in the Department of Cardiovascular Surgery, General University Hospital in Prague. The percentage of access types was as follows: 42% subjects received direct graft originating at the radial artery, 36% had antebrachial loop, in 20%, PTFE started at the brachial artery, and 2% got PTFE loop between subclavian vessels. Before access creation, patients were randomized into 2 groups: subjects in group 1 were regularly examined by duplex Doppler ultrasonography every 3 months, while subjects in group 2 were screened without the use of ultrasound. Age, gender, diabetes status, and number of previous abandoned or nonmaturated accesses were recorded. All subjects in both groups were regularly screened for possible access complications, including dynamic venous pressure, recirculation, and blood flow monitoring, as guided by DOQI guidelines in their hemodialysis units. Patients came from 25 hemodialysis units. Moreover, the vascular surgeon examined both groups at a regular basis 3 to 4 times per year. In both groups, fistulography was indicated either by nephrologist or by vascular surgeon if access dysfunction was suspected. It was the case in the following conditions: abnormal physical findings (conversion of thrill to pulse, intensification of bruit at certain sites, edema of the extremity bearing the vascular access), prolonged bleeding after needle withdrawal, elevation of venous pressure (above 140 mm Hg at 200 mL/min flow or trend to pressure increase), decrease of access flow for more than 25% or values below 600 mL/min, abnormal recirculation measurements, and unexplained decrease in measurement of dialysis dose. Specific indications guided by ultrasonography are listed below. Secondary patency rates were calculated and shown as Kaplan Meier curves. Secondary patency was defined as the time until the graft was abandoned either due to irreversible thrombosis or due to graft infection.

The local Ethical committee approved this study, and all subjects signed informed consent.

Ultrasonography

Examinations were performed directly by an experienced doctor with use of a linear array 7.5 MHz ultrasound probe Hewlett Packard SONOS 2000 device until the year 2002, then by linear ultraband (3–11 MHz) transducer of Phillips SONOS 5500 device. Examinations started at the axillary artery, followed by the brachial and antebrachial arteries. First, careful morphologic and color Doppler examinations of brachial, ulnar, and radial arteries were performed. Then, the feeding artery was assessed by spectral pulse-wave Doppler imaging of the blood flow at suspected sites identified by color Doppler mapping. Detailed examinations of the arteries were followed by inspection of PTFE graft, including calculation of blood flow (mL/min). Blood flow was calculated by the internal software of the ultrasound device according to the following relation: $Qa = \pi .r^2.v_{mean}$, where Qa = access flow, r = access radius, v_{mean} = mean time averaged velocity representing mean velocity of flowing blood layers during cardiac cycle. Mean value of 3 calculations was accepted. We have validated this method against thermodilution measurement [8, 9].

Special attention was given to venous anastomosis and adjacent segment of outflow vein, where stenoses are mostly located. Then we followed the outflow vein up to the subclavian vein. More than doubling of the peak systolic blood flow velocity compared with unaffected segment was used as a criterion of significant stenosis if combined with stenosis in B mode. The exception was in the arterial anastomosis, which was examined only by B mode because high-flow velocity is a normal pattern in this site. Ultrasound access examination is highly sensitive and specific for both identification of stenoses and calculation of blood flow, as shown previously [6, 7]. In our hands, ultrasonography has 85% sensitivity and 94% specificity compared with fistulography [6].

Ultrasound-guided indications to fistulography and/or percutaneous or surgical treatment procedure were the following: (*1*) finding of "significant" stenosis (inflow artery, PTFE, or outflow vein) as defined above, with or without decrease of blood flow; and (*2*) finding of stenoses which did not seem significant, but were associated with >25% decrease of access flow. In case of uncertainty of stenosis significance, an arbitrarily defined residual diameter less than 2.0 mm was the additional indication to fistulography. Subjects with indeterminate findings (i.e., the

Table 1. Characterization of studied groups

	Group 1	Group 2
Age *years*	58.7 ± 14.2	58.3 ± 13.9
% Female	57	55
% Diabetic	53	51
Number of previous failed accesses	1.4 ± 1.6	1.3 ± 1.6

Group 1, subjects screened by ultrasound; group 2, subjects screened only traditionally.

presence of only 1 of the aforementioned criteria) were reexamined after 4 to 6 weeks by ultrasound. Similarly, absolutely normal findings (high flow, no intimal hyperplasia, and no stenosis) were indicated for reexamination after 4 months.

Statistics

All measured values were expressed as mean ± SD. Baseline differences between groups were tested by unpaired *t* test. *P* values < 0.05 were considered as significant. Secondary patency rate between groups are reported by Kaplan-Meier survival curves. Log-rank test was used to compare differences between curves. The association of ultrasound screening with secondary patency rates was examined using univariate Cox regression analysis. To obtain a gross estimate of the influence of access flow on access patency, we performed Kaplan-Meier analysis of access patency in group 1, where the access longevity was compared in the highest and in the quartile of access flow.

RESULTS

We included 192 patients: 97 into group 1 and 92 into group 2. These groups were similar, as shown in Table 1. All subjects continued in the study except those who died. The mean follow-up lasted 392 ± 430 days. Ultrasound screening interval, primarily set to 3 months, varied between 1 and 5 months, depending on findings (defined in **Methods**) and on compliance.

In hemodialysis units, 100% of patients had monitoring of dynamic venous pressure; access flow measurement was performed in 46% of subjects in group 1, and in 49% in group 2 (90% of measurements by thermodilution, 10% by ultrasound dilution), and recirculation was measured in 86% and 85%, respectively.

Ultrasonographically screened subjects (group 1) had significantly higher secondary patency rates ($P < 0.001$ by log-rank test). Significance appeared after 6 months of follow-up (*P* value = 0.09 at 6 months, 0.045 at 12 months, 0.002 at 18 and 24 months, and later $P < 0.001$). Relative risk of access failure in group 2 calculated by Cox univariate regression analysis was 3.75 (95% CI 1.7–8.1). Number of interventions per graft was 2.1 ± 1.8 and 1.3 ± 1.0 in group 1 and group 2, respectively. Radiologic interventions (percutaneous transluminal angioplasty, stent implantations to outflow veins, mechanical thrombolysis) were considerably more frequent than surgical revisions (96% vs. 4%). Twenty-six ultrasound examinations were performed in group 2 subjects; they were indicated by nephrologists in case of allergy to contrast agents, need of examination of extraluminal masses, in patients who refused repeated fistulography, and others.

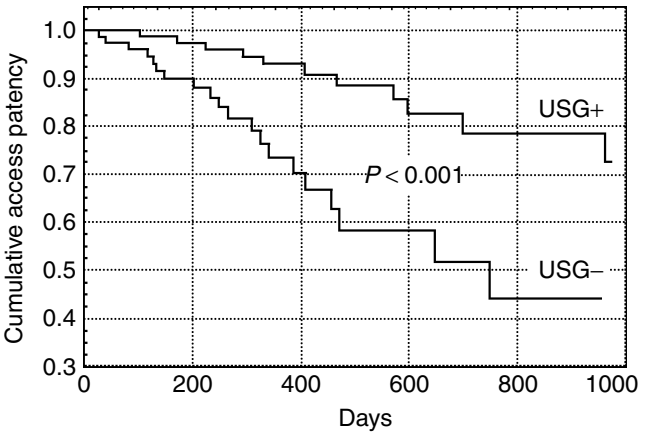

Fig. 1. Cumulative PTFE graft patency in subjects screened only traditionally (USG−) and in subjects screened also by regular ultrasonography (USG+).

In group 1, baseline access flow measured by ultrasonography was 769 ± 303 mL/min (median 718 mL/min). In the absence of access stenosis, access flow remained stable during follow-up, with the variability of ± 10%. We observed significantly higher percentage of access survival within the first year in subjects with baseline access flow values in the highest quartile compared to those in the lowest quartile of access flow ($P = 0.03$), but later this difference disappeared ($P = 0.38$).

DISCUSSION

This study has shown that regular ultrasound screening together with more aggressive approach to the treatment of PTFE graft stenoses results in significant prolongation of secondary patency rate. To the best of our knowledge, it is for the first time that regular use of ultrasound has been proven as a method leading to longer access patency.

Prolonged access patency in subjects screened by ultrasonography might be explained by earlier diagnosis of stenoses by combining flow calculation and morphologic evaluation during ultrasound examinations. It was previously shown that elective treatment of access stenosis prolongs access life when compared to repair after an initial episode of clotting [10]. Our results are in accord with some previous studies, which identified ultrasonography as a predictor of future access thrombosis. Decreased access blood flow, as measured by duplex Doppler ultrasonography, was repeatedly proven to be a significant

predictor of access failure [11, 12]. Stenosis detection per se was a significant predictor of future thrombosis of PTFE graft in the study of Strauch et al [13]. On the contrary, in a larger study that included both PTFE grafts and native fistulas, duplex ultrasonographic detection of access stenosis was not a strong predictor of incipient thrombosis [14].

Surprisingly, our patients had considerably lower access flow than in other studies [15]. It was probably caused by the fact that PTFE graft is a second choice type of hemodialysis access in our country, and by higher proportion of diabetic subjects in our study. Diabetic angiopathy and mediocalcinosis prevents dilatation of the feeding artery after access creation, with subsequent lower access flow. Secondary patency rates were higher in subjects with the highest quartile of access flow in comparison to those having access flow within the lowest quartile of values. However, this difference disappeared during follow-up longer than 1 year. It could be assumed that low-flow access (for example 500 mL/min) is at higher risk of thrombosis in case of significant stenosis than high-flow access (1500 mL/min) because the fall of access flow is percentual, and in the former case, it could reach "critically low" values. Regular visualization of the entire vascular access could determine developing stenoses before they cause hemodynamic changes. We believe that ultrasound screening is particularly important in low-flow accesses, such as in diabetic patients. It is of potential importance also for subjects with congestive heart failure because safer (lower) access flow could be maintained.

Although higher access flow has been linked to lower incidence of access thrombosis, it may lead to heart failure.

Our results of secondary patency rates in subjects who were not regularly screened by ultrasound are comparable with literary data. Sert et al [16] reported 12-month secondary patency of PTFE grafts of 65%. In a meta-analysis, Huber et al reported mean secondary patency of 76% at 6 months and 55% at 18 months. Excellent results were published by Hurlbert et al [17], who compared 2 types of grafts—at 12 months, 87% to 96%, and at 24 months, 78% to 87%, of accesses were patent. The latter results are comparable with our patients screened by regular ultrasonography.

The advantage of ultrasonography is that it is an accurate method (with the exception of central lesions, such as the medial part of subclavian vein/artery), which does not have limitations typical for methods based on the dysfunction hypothesis. This hypothesis states that stenosis causes graft dysfunction, and this dysfunction reliably precedes and accurately predicts thrombosis [18]. Such dysfunction is mirrored by increase of venous pressure, or by decrease of access flow. Unfortunately, in praxis, the dysfunction hypothesis might fail, and traditional monitoring programs may allow disappointingly large proportion of grafts to thrombose [18], for example, in case of thrombophilia or outflow vein branching. Vein branching could partially and temporarily compensate a stenosis of outflow vein. Such patients may have no change of access flow or dynamic venous pressure increase. Therefore, it is evident that the term "hemodynamically significant stenosis" by imaging methods is wider than that based on dysfunction hypothesis. As we have previously shown, clinical diagnosis of access thrombosis with the use of venous pressure and access flow monitoring has a low sensitivity, but high specificity in comparison with duplex Doppler ultrasonography [19].

Future research should be oriented on cost/benefit ratio of this approach. We think that longer access patency compensates higher cost, especially in subjects with depleted sites for future creation of next vascular access.

A possible limitation is the fact that it was a study performed in only 1 vascular access center. Absolute values of secondary patency rates are probably higher than in smaller centers [1]. Another limitation is that patients came from 25 hemodialysis centers, so we did not control both the level and regularity of access monitoring by traditional methods and, thus, it could be not optimal. Advantage of this fact is that our study population more exactly reflects routine care.

CONCLUSION

Regular ultrasonographic screening for access stenoses together with their earlier treatment leads to significant prolongation of cumulative patency. This approach is of highest importance to subjects with depleted sites for next accesses.

ACKNOWLEDGMENTS

This study was supported by the Research Project MSM-0021620807 of Ministry of Education, Czech Republic, and by the Grant Agency of Ministry of Health, Czech Republic No. NR 8334.

Reprint requests to Dr. Jan Malik, Third Department of Internal Medicine, General University Hospital, Unemocnice 1, Prague 2, 128 08, Czech Republic.
E-mail: JMALI@LF1.CUNI.CZ

REFERENCES

1. Huber T, Carter JW, Carter RL, Seeger JM: Patency of autogenous and polytetrafluoroethylene upper extremity arteriovenous hemodialysis accesses: A systematic review. *J Vasc Surg* 38:1005–1011, 2003
2. Hakim R, Himmelfarb J: Hemodialysis ayccess failure: A call to action. *Kidney Int* 54:1029–1040, 1998
3. Pisoni RL, Young EW, Greenwood RN, *et al*: Vascular access use in Europe and the United States: Results from the DOPPS. *Kidney Int* 61:305–316, 2002
4. Dhingra RK, Young EW, Hulbert-Shearon TE, *et al*: Type of vascular access and mortality in U.S. hemodialysis patients. *Kidney Int* 60:1443–1451, 2001
5. Centers for Medicare & Medicaid Services: 2002 Annual Report, End Stage Renal Disease Clinical Performance Measures Project. *Am J Kidney Dis* 42(Suppl 2):S1–S96, 2003

6. Gadallah MF, Paulson WD, Vickers B, Work J: Accuracy of Doppler ultrasound in diagnosing anatomic stenosis of hemodialysis arteriovenous access as compared with fistulography. *Am J Kidney Dis* 32:273–277, 1998
7. Malik J, Slavikova M, Maskova J, Hradec J: Comparison of ultrasound findings of significant dialysis access stenoses with angiography. *Cor Vasa* 44:68–72, 2002
8. Malik J, Slavikova M, Maskova J: Dialysis access-associated steal syndrome: The role of ultrasonography. *J Nephrol* 16:903–907, 2003
9. Lopot F, Nejedly B, Sulkova S, Blaha J: Comparison of different techniques of hemodialysis vascular access flow evaluation. *JVA* 5:25–32, 2004
10. Sands JJ, Miranda CL: Prolongation of hemodialysis access survival with elective revision. *Clin Nephrol* 44:329–333, 1995
11. Bay WH, Henry NL, Lazarus JM, *et al*: Predicting hemodialysis access failure with color flow Doppler ultrasound. *Am J Nephrol* 18:296–304, 1998
12. Shackleton CR, Taylor DC, Buckley AR, *et al*: Predicting failure in polytetrafluoroethylene vascular access grafts for hemodialysis: A pilot study. *Can J Surg* 30:442–444, 1987
13. Strauch BS, O'Conell RS, Geoly KL: Forecasting thrombosis of vascular access with Doppler color flow imaging. *Am J Kidney Dis* 19:554–557, 1992
14. Lok CE, Bhola C, Croxford R, Richardson RM: Reducing vascular access morbidity: A comparative trial of two vascular access monitoring strategies. *Nephrol Dial Transplant* 18:1174–1180, 2003
15. Sands J, Young S, Miranda C. The effect of Doppler flow screening studies and elective revisions on dialysis access failure. *ASAIO J* 38:M524–M527, 1992
16. Sert S, Demirogullari B, Ziya Anadol A, *et al*: Bovine and PTFE vascular graft results in hemodialysis patients. *JVA* 1:148–151, 2000
17. Hurlbert SN, Mattos MA, Henretta JP, *et al*: Long-term patency rates, complications and cost-effectiveness of polytetrafluoroethylene (PTFE) grafts for hemodialysis access: A prospective study that compares Impra versus Gore-tex grafts. *Cardiovasc Surg* 6:652–656, 1998
18. Paulson WD: Prediction of hemodialysis synthetic graft thrombosis: Can we identify factors that impair validity of the dysfunction hypothesis? *Am J Kidney Dis* 35:973–975, 2000
19. Malik J, Slavikova M, Malikova H, Maskova J: Many clinically silent access stenoses can be identified by ultrasonography. *J Nephrol* 15:661–665, 2002