Low-Flow Polytetrafluoroethylene Accesses: Ultrasound Surveillance and Preemptive Interventions Ensure Long-Term Patency

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Key Words

Hemodialysis • Stenosis • Vascular access • Ultrasonography

Abstract

Background: Vascular accesses (especially polytetrafluoroethylene grafts) with a permanently low flow ($Q_a < 600$ ml/min) are prone to thrombosis and thus have short patency. The reason for a permanently low flow is usually medial calcinosis of the inflow artery in diabetics. We retrospectively studied the long-term patency of low-flow grafts with careful ultrasound surveillance and preemptive interventions. **Methods:** Twenty subjects with Q_a permanently < 600 ml/min were included. Ultrasound surveillance was performed every 3 months in addition to classical monitoring techniques. Significant stenosis was strictly defined as the combination of B-mode narrowing $> 50\%$ + > 2 -fold peak systolic velocity increase + 1 additional criterion (residual diameter < 2.0 mm or flow volume decrease by $> 20\%$). Such stenoses were treated by preemptive percutaneous intervention. Primary and secondary patencies were calculated. **Results:** The primary patency was 357 ± 316 days and the secondary (cu-

mulative) patency was 996 ± 702 days. The number of interventions was 2.09/patient year, but > 10 in 6 (33%) subjects. 93 and 80% of grafts were patent 1 and 2 years after access creation, respectively. **Conclusion:** Low-flow accesses undergoing ultrasound surveillance with strict diagnostic criteria and preemptive interventions had patencies similar to accesses with normal Q_a in our study. This was enabled by a relatively high rate of interventions.

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Introduction

Vascular access is a 'lifeline' for end-stage renal disease patients. Especially in Europe, vascular accesses with polytetrafluoroethylene (PTFE) grafts are created in subjects with no suitable veins for regular dialysis cannulations. Therefore, patients with PTFE accesses are generally more ill and have limited possible sites for the next accesses. Moreover, the hemodialysis population has changed during last years – there are more elderly patients, diabetics, and patients with congestive heart fail-

ure. These factors are responsible for the more frequent access complications, namely medial calcinosis caused by diabetes mellitus and by kidney failure which per se leads to limited inflow. Medial calcinosis, severe atherosclerosis of the feeding arteries or severe congestive heart failure are responsible for chronically low access flow ($Q_a < 600$ ml/min). Patients with permanently low Q_a are at the highest risk of access thrombosis. This situation must be differentiated from a sudden Q_a decrease in a patient with an otherwise normal Q_a . That is usually due to outflow stenosis, which is reversible mainly by percutaneous angioplasty. A number of monitoring and surveillance techniques have been tested to prolong PTFE graft patency, but they still fail to keep PTFE grafts patent for a period longer than 1.5 years [1]. The surveillance techniques include a complex of methods, such as dynamic and static venous pressure measurements [2, 3], duplex Doppler ultrasonography, and Q_a measurement. The latter is emphasized as the most reliable method in the last European [4] and American [5] guidelines: $Q_a < 600$ ml/min and/or reduction of flow by $>20\%$ /month or $>25\%/4$ months are indications for angiography and preemptive intervention. The precise timing of intervention, especially of percutaneous transluminal angioplasty (PTA), is crucial because stenosis after angioplasty develops faster than de novo stenosis, suggesting that the vascular injury produced by angioplasty accelerates the underlying process of neointimal hyperplasia [6]. Unnecessary PTAs also increase the patient's pain and medical expenses.

Duplex Doppler ultrasonography surveillance combines anatomical imaging and measuring of Q_a . However, this method has been criticized for high inter-observer variability. Several randomized clinical trials [7–9] also failed to document a prolongation of secondary patency (i.e. functional patency until either final failure or the abandonment of the access).

In fact, our randomized trial [10] was the only one which documented prolonged secondary patency of grafts by regular ultrasonography surveillance. Similar results were published by Martin et al. [11] in a subset analysis of a prospective randomized study. Dossabhoy et al. [12] reported reduced hospitalization rates and costs by duplex ultrasound surveillance, but not by sole flow surveillance.

Since our aforementioned randomized study [10], we perform regular ultrasound surveillance on all our patients with PTFE grafts in our center. We hypothesized that this surveillance would help to keep even accesses with a permanently low flow (<600 ml/min) patent, i.e. the group at the highest risk of graft failure. Therefore,

the aim of this retrospective study was to describe the outcomes of low-flow PTFE grafts with the help of ultrasound surveillance and preemptive interventions in a large university hospital-based vascular access center.

Methods

Patients with low-flow PTFE grafts (defined as mean Q_a of all measurements of <600 ml/min and $<10\%$ of Q_a measurements of >600 ml/min but <900 ml/min) were searched for in our database of 450 patients (between the years 2001 and 2009). Patients were included in this study only when their access was patent for a period of at least 3 months after creation and was suitable for hemodialysis. All of them underwent regular access ultrasonography every 3 months following the creation of the access. This period was shortened if a borderline stenosis was detected (see below). Low Q_a grafts are known to have a shorter lifespan than grafts with normal Q_a , so we decided not to create a group of normal Q_a for comparison. Similarly, there was no classical 'control' group of low Q_a grafts without ultrasound screening in this study – we found this idea unethical because it was at our center where the benefit of surveillance was proved [10] (opposed to others [7–9]). Besides ultrasonography, all patients were examined clinically on a regular basis and dynamic venous pressure was recorded during all hemodialysis sessions according to the guidelines [4, 5].

Grafts were examined using duplex Doppler ultrasound (broad-band linear array 3–11 MHz probe of SONOS 5500 device (Philips, USA)) as described earlier [10]. In brief, B-mode images and color-coded images were obtained from the feeding artery, arterial anastomosis, the whole graft, the venous anastomosis and the outflow vein. Centerline systolic velocities were obtained from the feeding artery and from the venous anastomosis in all grafts. Q_a was measured in the venous part of the graft at least 2 cm distal to the venous anastomosis as a mean of 3 calculations. The peak systolic velocity ratio (PSR) was defined as the ratio of the peak velocities inside the stenosis and in an adjacent unaffected pre-stenotic segment. Stenoses were considered significant if there was a combination of $>50\%$ lumen reduction in B mode and $PSR > 2$, together with at least one of the following additional criteria: (1) residual diameter of <2.0 mm, and/or (2) blood flow reduction of $>25\%$. Stenosis was considered borderline in the absence of any of the additional criteria. Patients with significant stenosis were referred to PTA, while those with borderline stenosis were advised to come for reexamination after 6–8 weeks. Within this period, the watch-and-wait strategy was maintained, i.e. direct referral to PTA in any suspicion of stenosis progression or other doubts in the hemodialysis unit (i.e. rise in venous pressure, changes in regular physical examination of the access, etc.).

Percutaneous balloon angioplasty or other interventions were indicated by: (1) dialysis staff; (2) vascular surgeon, and (3) access ultrasonography findings. Dialysis units indicated access angiography directly when access dysfunction was suspected. The following conditions were considered grounds for suspicion of access dysfunction: (1) abnormal physical findings (conversion of thrill to pulse, intensification of bruit at certain sites, edema of the extremity bearing the vascular access); (2) prolonged bleeding after needle withdrawal; (3) elevation of dynamic venous pressure; (4) decrease in Q_a by $>25\%$; (5) abnormal recirculation measure-

ments, and (6) unexplained decreases in measurement of dialysis dose. All other angiographies and therapeutic interventions were performed as a result of hemodynamically significant stenosis occurrence on ultrasonography (see above for definition).

Primary patency (from graft placement until any type of intervention) and secondary patency (cumulative, until the final abandoning of the access) of the included grafts were recorded together with the number and types of interventions. Raw data of the included subjects and a Kaplan-Meier graph are used to present the results. Values are presented as mean $\pm$ SD.

Results

We found 20 subjects aged 62.5 ± 15.6 years (6 males) in our database. Fourteen subjects (70%) were diabetics, 90% of patients suffered from hypertension, 30% had coronary artery disease, 30% were current or ex-smokers, and 1 patient had congestive heart failure. Insufficient feeding artery dilatation after access creation caused by medial calcinosis untreatable by angioplasty (due to a length of >10 cm) was responsible for all included cases with low Qa. Nineteen subjects were on single anti-aggregation therapy (aspirin) throughout the study and 1 patient (case 8) was on warfarin. Eighty percent of the PTAs were indicated by duplex Doppler ultrasonography screening, i.e. there was no clear clinical suspicion of access stenosis.

Primary patency was 357 ± 316 days and secondary patency was 996 ± 702 days (range 89–2,550 days; fig. 1). The difference between primary and secondary patency was 640 ± 540 days. Detailed results are presented in table 1.

The high secondary patency (80% at 2 years) was enabled by the relatively high number of preemptive access interventions: 2.09 PTAs/patient year.

Discussion

This retrospective study shows that the secondary patency of low-flow grafts could be long enough when such grafts undergo regular ultrasound surveillance with preemptive interventions. The results in this small series of low-flow accesses are comparable to grafts with normal flow [1, 13].

Patients with permanently low Qa de facto fulfill one of the indications for angiography and preemptive intervention according to the guidelines (Qa <600 ml/min) [4, 5]. We have not found any study specifically investigating the efficacy of Qa monitoring in low-flow accesses. How-

Fig. 1. Kaplan-Meier graph of the secondary (cumulative) patency of grafts.

ever, we can assume that because only the flow decline could be used as the indication for intervention, it would be even less specific than in the general access population. Patients are known to have wide hemodynamic variation during hemodialysis; therefore, the reproducibility of flow measurements from session to session is poor [14]. Flow and change in flow have been identified as inaccurate predictors of thrombosis in an interesting recent study when Qa was assessed every month [15]. Two randomized trials published to date failed to improve graft survival with the use of flow surveillance [16, 17]. The reason for low Qa in this study was primarily diffuse medial calcinosis of the feeding artery. However, an unusually high number of graft stenoses caused by dialysis cannulations and their healing (table 1) probably also played a role. PTFE grafts with permanently low Qa (<600 ml/min) are uncommon – they represent 3% of our database. Qa is known to be negatively correlated with the risk of access thrombosis [14], but we still do not have criteria for individual risk of access thrombosis with sufficient sensitivity and specificity. In our opinion, this study shows that ultrasound screening is able to keep the accesses patent for a long time even in this high-risk group. It is another argument for the currently debated ultrasound surveillance [17–19]. Conversely, in the future we may be able to identify the low-risk group and choose not to perform surveillance in these patients. In other words, there is a need for risk stratification similar to that used in cardiovascular disease prevention. An alternative

Table 1. Characteristics of included subjects and accesses

Patient number	Age years	Access type	Number of previous accesses	Diabetes	Primary patency	First procedure	Number of PTA sessions	Site of stenosis	Number of TL	Number of reoper.	Secondary patency days	Patent at last control?
1	84	FS	0	Yes	169	–	0	–	0	0	169	Yes
2 ¹	83	FS	0	No	110	–	0	–	0	0	110	Yes
3	79	FL	0	Yes	5	TL	12	12 OV	2	2	1,466	Yes
4	78	FS	0	Yes	233	TL	15	14 G, 2 AA, 2 VA	1	1	1,339	Yes
5	76	FS	0	Yes	179	PTA	5	5 VA	1	0	1,731	Yes
6	74	FL	3	Yes	662	PTA	3	3 G	0	0	1,075	Yes
7 ¹	69	FS	0	Yes	89	–	0	–	0	0	89	Yes
8 ¹	65	FL	6	No	311	TL	5	4 VA, 1 OV	1	0	719	Yes
9	64	FS	1	No	143	PTA	11	11 G, 3 VA	1	0	1,353	Yes
10 ¹	61	FS	0	Yes	221	PTA	1	1 VA	0	0	408	Yes
11 ¹	61	FS	0	Yes	96	TL	2	1 G	1	0	180	Yes
12	61	FS	3	Yes	157	PTA	4	4 OV	0	0	602	No
13	43	BA	6	No	1,102	TL	10	6 OV, 4 VA, 2 AA	2	0	2,550	No
14	55	FL	3	Yes	974	PTA	4	4 OV, 3 VA, 1 G	0	0	1,821	Yes
15	54	FS	1	No	381	PTA	14	10 VA, 4 OV	0	1	1,479	No
16	53	FS	0	Yes	458	PTA	14	8 G, 7 VA, 2 FA, 1 VA	1	0	1,437	Yes
17	41	FS	2	Yes	301	PTA	1	1 VA	2	0	587	No
18	23	FS	0	No	934	PTA	7	6 G, 3 VA	0	0	1,744	Yes
19	62	FS	0	Yes	347	PTA	6	5 G, 1 VA, 1 OV	0	0	799	No
20	63	FS	1	Yes	261	TL	0	–	1	0	269	No

Access type: FS = forearm straight; FL = forearm loop; BA = brachial-axillary. Therapy: TL = thrombolysis; PTA = percutaneous transluminal angioplasty. Sites of access stenoses: FA = feeding artery; AA = arterial anastomosis; G = PTFE graft; VA = venous anastomosis; OV = outflow vein.

The type of the first procedure is presented – it determines the primary access patency. Notice that thrombolysis was the first

procedure in 30% of patients, which documents the high risk of thrombosis in this group of patients. Sites of access stenoses treated by PTA are shown. During some sessions more than 1 site was treated. Notice that there are more than usual graft PTAs and the vast majority of PTAs treated re-stenoses.

¹ Patients who died during follow-up, all with patent access.

explanation of the long access patency in this study is that low Qa does not possess an increased risk of graft thrombosis. We have found this idea not likely due to the impact of Qa documented in other studies [14] and also mentioned in the guidelines [4, 5].

Duplex Doppler ultrasonography revealed many significant but clinically ‘silent’ stenoses in this study, including 9 of 17 representing primary patency. Therefore, this study further supports ultrasound graft surveillance which is advocated by some [10, 12] but not all [7–9, 18]. There could be several reasons explaining the different outcomes of ultrasound surveillance in our and other studies [19, 20]. They include differences in sample size, access age at inclusion, organization of access care, and also various criteria of stenosis significance definition. Some centers [8, 21] use the >50% diameter narrowing in B mode as the only criterion of significant stenosis. We

think that this approach is not precise enough because various technical and anatomical irregularities might influence the result. Others [9], including us [10], combine the findings in B mode with a peak systolic velocity increase, which is similar to the examination of peripheral arteries. Our definition of significant stenoses also includes additional criteria (see Methods) which differentiate significant and borderline stenoses. The delaying of PTA is safe in borderline stenoses of PTFE grafts with normal flow [22] and we also used this approach in this study. In other words, precise definition of significant stenosis would not only help us to avoid unnecessary interventions, but also to prevent access thrombosis. A highly experienced ultrasound operator is a must. In our center, access ultrasonography is performed directly by doctors and all of them have the experience of at least 1,000 vascular examinations.

The grafts in this study were kept patent at the price of 2.09 PTAs/patient year, but by more than 10 PTAs in 6 (33%) patients. The higher cost of this approach was, according to us, balanced by the long secondary patency in these seriously ill patients. Percutaneous interventions included only PTAs in this study – no stent was inserted. Implantation of stents could theoretically lower the number of procedures. However, the available data on stent usage in vascular accesses is still controversial [23], despite some newer studies reporting longer graft patency after stenting [24].

The main limitations of this study are the relatively low sample size and the lack of a control group. However, grafts with Qa permanently <600 ml/min are infrequent. This is also the reason why this study was retrospective. We decided not to form a control group with normal Qa because it is well known that low Qa is associated with a higher risk of graft thrombosis.

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