Diagn Interv Radiol 2015; 21:160–166

INTERVENTIONAL RADIOLOGY
ORIGINAL ARTICLE

Percutaneous transluminal balloon angioplasty in stenosis of native hemodialysis arteriovenous fistulas: technical success and analysis of factors affecting postprocedural fistula patency

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PURPOSE
We aimed to determine the predictors of technical success and patency after percutaneous transluminal angioplasty (PTA) of *de novo* dysfunctional hemodialysis arteriovenous fistulas (AVF).

METHODS
We performed a retrospective analysis of first time PTA in 228 patients (129 men, 99 women; mean age, 56.8±14.6 years). Anatomical (location, length, grade, and number of stenoses) and clinical variables (sex, age, prior AVF, diabetes mellitus, AVF age, side, and location) were reviewed.

RESULTS
A total of 330 stenoses were found in 228 patients. PTA was technically successful in 96.3% of the stenoses (n=319). Clinical success was achieved in 97.2% (n=321). Early dysfunction (within six months) was positively correlated with patient age ($P < 0.001$) and diabetes ($P < 0.005$). Older age ($P < 0.001$) and diabetes ($P = 0.002$) were associated with a lower primary patency rate. Patient age ($P < 0.001$), presence of diabetes ($P = 0.023$), length of stenosis ($P = 0.003$), early recurrence ($P = 0.003$) and presence of residual stenosis ($P = 0.014$) were associated with a lower secondary patency rate.

CONCLUSION
Patency of dysfunctional hemodialysis fistulas can be maintained safely with continuous follow-up and repeated interventions without shortening the venous segment by surgical revision. Percutaneous approach to hemodialysis access stenosis is an alternative to the conventional surgical approach and PTA is an effective treatment method for dysfunctional AVF.

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Received 4 August 2014, accepted 11 September 2014.

Published online 16 February 2015.
DOI 10.5152/dir.2014.14348

Hemodialysis, and therefore patent hemodialysis access, is of great importance to patients with end-stage renal disease (ESRD). The preferred type of access in patients undergoing hemodialysis is an arteriovenous fistula (AVF) (1). The Kidney Disease Outcomes Quality Initiative provides evidence-based clinical practice guidelines for all stages of ESRD and reports autogenous AVF as the reference standard for primary vascular access, due to their longevity and low infection rates (2, 3). Sands et al. (4) and Schwab et al. (5) demonstrated a 10-fold increase in thrombosis rate of synthetic polytetrafluoroethylene (PTFE) accesses when compared to AVFs. Despite proven advantages of AVF over PTFE, both types of access eventually fail and contribute to multiple hospital admissions, radiological and surgical interventions, and overall morbidity associated with chronic hemodialysis. Significant stenosis causing access dysfunction is a frequent complication in hemodialysis and requires repeated percutaneous transluminal balloon angioplasty (PTA) to maintain patency (6–9). The patency of PTA is limited, however, with first year primary patency rates ranging between 26% and 62% (6–8). Many factors influencing the patency rate have been studied in previously reported series (7, 8). Our study is the first to investigate the effect of early recurrence on secondary patency.

Methods

The records of 228 patients (129 men, 99 women; mean age, 56.8±14.6 years) who underwent first time PTA for a dysfunctional native AVF between January 2007 and January 2011 were retrospectively reviewed. Inclusion criteria were presence of a dysfunctional native AVF referred for fistulography and treatment, no previous history of stenosis or thrombosis, and only stenosis of the AVFs on fistulography. Patients who had synthetic dialysis, composite grafts, or autogenous fistulas that were already thrombosed were excluded from our study. Indications for fistulography included decreased flow rate, difficult cannulation, increased venous pressure, edema of the upper extremity, or pain during dialysis.

Pretreatment fistulography and PTA

Initially, all patients were examined by color Doppler ultrasound (HD 11 XE, Philips Healthcare). For fistulography, access to fistula was obtained through a brachial arterial puncture with a 21-gauge needle. Injection of 30 mL contrast agent was used for diagnostic fistulography. The feeding artery, arteriovenous anastomosis, draining vein(s) and central veins up to the right atrium were visualized. After identification of the stenoses, angioplasty was performed using a standard technique (10, 11).

Prilocaine (Citanest, Zenica medical) was administered to the puncture site for local anesthesia. No patient sedation was requested or used in this series.

For endovascular treatments, a 5 F or 7 F vascular sheath was inserted with the aid of digital road mapping control, and 2000–5000 units of heparin (Clexane, Sanofi Winthrop Industrie) was administered to all patients. The stenosed segments were traversed using a 4 F or 5 F vascular sheath (Terumo) with a 0.0035-inch hydrophilic guidewire (Terumo and Cook Medical), and balloon angioplasty was performed using standard (Cook Medical) or high-pressure noncompliant balloons (Conquest, Bard) up to 25 atm.

Balloon size (range, 3–12 mm) was chosen by visual estimation of the diameter of a normal vessel segment adjacent to the stenosis. Balloon inflation was maintained for 1–3 min by an inflation device.

At the end of the procedure, a fistulogram was performed to visualize the flow from the arteriovenous anastomosis to the superior vena cava. The vascular sheaths were removed and hemostasis was achieved by manual compression or using a purse-string suture (12).

Variables and definitions

Anatomical variables were location, length, and grade of stenosis and presence of more than one stenosis. In terms of location of the stenosis, the AVF was divided into four segments: the feeding artery, the arteriovenous anastomosis, the juxta-anastomotic segment of the fistula vein defined as the first 3 cm of the vein distal to the anastomosis, and the draining vein.

Clinical variables were age and sex of the patient, AVF type, AVF side (right or left arm), presence of diabetes mellitus, and the cause of ESRD.

Technical success was described as residual stenosis of less than 30% after the procedure. Clinical success was defined as the ability to provide adequate dialysis. Primary patency was defined as uninterrupted patency after intervention until the next intervention. Secondary patency was defined as patency after PTA until the AVF was surgically declotted, revised, or abandoned. Complications were classified as major or minor according to the criteria of the Society of Cardiovascular and Interventional Radiology (13).

Statistical analysis

Data were analyzed using the SPSS for Windows 11.5 package software (SPSS Inc.). Shapiro-Wilk test was used to determine whether continuous variables were normally distributed. Descriptive statistics were presented as mean±standard deviation or median (range) while categorical variables were presented as number of cases and percentages. Group means were compared using Student t test and group medians were compared using Mann-Whitney U test. Categorical changes were evaluated using chi-square or Fisher's exact tests. Odds ratio and 95% confidence interval were calculated for each variable. Log-rank test and Kaplan-Meier survival analysis were used to investigate the correlation between the cumulative primary and secondary patency rates and the mean patency duration according to categorical variables. First, second, and third-year patency rates, mean patency duration, and the relevant 95% confidence intervals were calculated for each variable. Univariate Cox proportional hazard regression analysis was used to determine whether continuous variables have a statistically significant effect on patency rate. Relative risk and 95% confidence interval were calculated for each variable. Multivariate backward elimination logistic regression analysis was conducted with factors found to affect early recurrence in univariate analysis and clinical risk factors thought to be possibly effective. Candidate risk factors with $P < 0.25$ in the univariate analysis were included in the multivariate model. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics are summarized in Table 1. A total of 330 stenoses were found. Fistulography revealed 73 stenoses located at the anastomotic segment, 25 at the feeding artery, 78 at the draining vein and 149 at the juxta-anastomotic segment. The mean length of stenosis was 21.5 mm (median, 11 mm; range, 1–127 mm), and mean degree of stenosis was 91.5% (median, 92.5%; range, 52%–98%).

PTA was technically successful in 96.3% of stenoses (n=319). The residual stenosis was greater than 30% in 11 cases (3.7%). The degree of residual stenosis ranged between 31% and 57%. None of the anatomical or clinical variables were significantly related to the technical success at AVF level. The initial grade of stenosis was inversely proportional to the technical success ($P = 0.039$).

PTA was clinically successful in 97.2% of cases (n=321). Complications occurred in seven procedures and consisted of five minor complications (four vasospasms, one hematoma) and two major complications (one rupture and one hyperacute segmental thrombosis).

The mean follow-up time was 28.7 months (range, 1–59 months). AVF remained patent in 60 patients (26.3%) during the entire follow-up.

Early recurrence was defined as recurrence of dysfunction within six months. During the follow-up, early recurrence was seen in 53 cases (23.2%). The only variables with a significant effect on early dysfunction were the age of the patient and diabetes mellitus as the cause of the ESRD. Probability of early recurrence was higher in older patients ($P < 0.001$) and in patients with diabetes mellitus ($P < 0.005$). Univariate analysis revealed a significant relationship between stenosis location at the juxta-anastomotic segment and early recurrence ($P = 0.043$). However, multivariate logistic regression analysis showed no significant relationship between these variables ($P > 0.05$). None of the other anatomical or clinical variables were significantly related to early recurrence.

Primary patency at first, second, and third years was 84.7%, 62.2%, and 23.7%, respectively (Fig. 1). Older age ($P < 0.001$) and the presence of diabetes mellitus ($P = 0.002$) resulted in lower primary patency (Tables 2 and 3).

Secondary patency at first, second, and third years was 90.5%, 72.7%, and 32.1%, respectively, (Fig. 2). Older age ($P < 0.001$), presence of diabetes ($P = 0.023$), longer segment with stenosis ($P = 0.003$), early recurrence ($P = 0.003$),

Table 1. Patient and fistula characteristics

Variables	n=228
Patient age (years), mean±SD	56.8±14.6
Sex (M/F)	129/99 (56.6/43.4)
Cause of ESRD	
ADPKD	19 (8.3)
Diabetes	136 (59.6)
Glomerular disease	10 (4.4)
Hypertension	32 (14)
Unknown	31 (13.6)
AVF type	
Brachiobasilic	9 (3.9)
Brachiobrachial	1 (0.4)
Brachiocephalic	19 (8.3)
Radiobasilic	1 (0.4)
Radiocephalic	198 (86.8)
AVF side	
Right	47 (20.6)
Left	181 (79.4)
Diabetes mellitus	142 (62.3)
Location of stenosis	
Anastomotic segment	73 (32)
Feeding artery	25 (11)
Draining fistula vein	78 (34.2)
Juxta-anastomotic segment	149 (65.4)

Unless otherwise noted, data are presented as n (%).
SD, standard deviation; M, male; F, female; ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease; AVF, arteriovenous fistula.

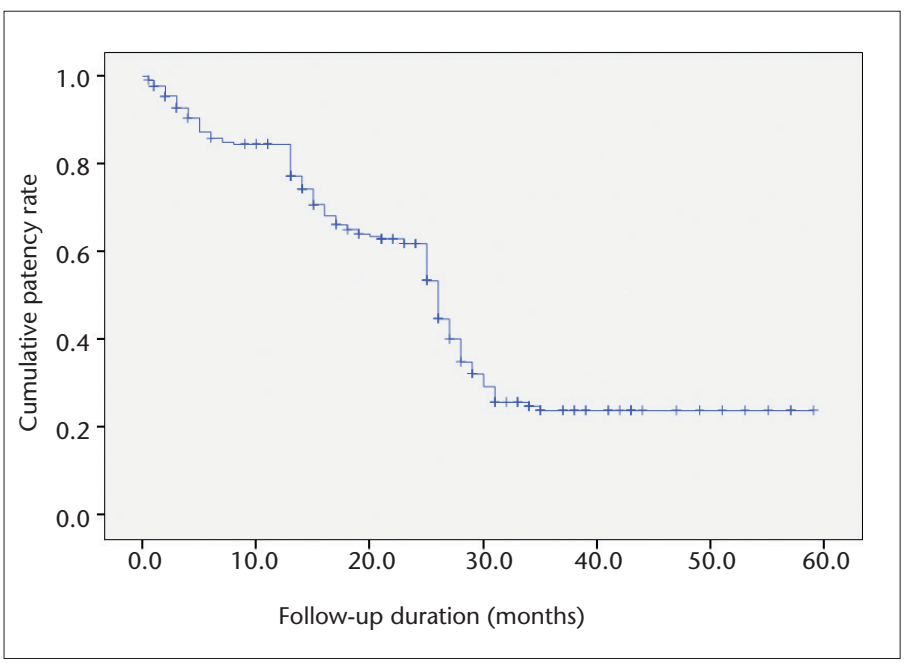

Figure 1. Kaplan-Meier curve of estimated primary patency after angioplasty.

and higher percentage of residual stenosis (P = 0.014) were correlated with lower secondary patency (Tables 3, 4, and Fig. 3).

Discussion

In this study we retrospectively analyzed predictors of long-term patency after first time PTA in patients with dysfunctional AVF. Overall, we found PTA to be technically and clinically highly successful. Age and diabetes were significant predictors for early recurrence of stenosis, as well as primary and secondary patency. Early recurrence, stenosis length, and presence of residual stenosis were additional predictors of secondary patency.

ESRD patients need high-quality temporary or permanent vascular access for hemodialysis treatment (14). AVF is the preferred vascular access route for hemodialysis in both North American and European guidelines, as it provides good patency and a low complication rate (1, 15). Vascular access complications are one of the main reasons related to morbidity and mortality in ESRD. The most common cause of a dysfunctional fistula is venous stenosis. The pathogenesis of venous stenosis has not been fully explained and is a complex process. Cellular proliferation, microvessel formation, and cytokines released by macrophages, endothelial cells, and smooth muscle cells are held responsible for the pathophysiology. Cytokines initiate the activation and proliferation of smooth cell, endothelial cells, and macrophages and result in neointimal hyperplasia (16). When stenosis is >50% (hemodynamically significant), dialysis efficiency is reduced, and access thrombosis may develop if not treated. Therefore, early diagnosis and treatment of AVF stenosis is important (1).

As previously reported, the approach to dysfunctional AVFs is more difficult than grafts (6). The reasons can be listed as follows: a thin and moving venous wall, anatomical irregularities that make the clinical and radiological identification of the anastomosis difficult, an underlying stenosis located between the feeding artery and superior vena cava, a stenosis that is tight and makes passage difficult, the presence of venous collaterals that make anatomic

Table 2. Effect of demographic and clinical factors on primary patency

Variables	Primary patency rate (%)			Patency duration[a] (months)	Log-rank	*P*
	1-year	2-year	3-year			
Sex					0.121	0.728
Female	83.5	63.0	22.3	27.7 (23.5–31.8)		
Male	85.6	61.7	24.5	29.1 (25.5–32.7)		
Cause of ESRD					30.490	<0.001
ADPKD	100.0	93.8	46.2	41.6 (33.6–49.5)		
Diabetes	81.9	58.5	17.0	25.5 (22.3–28.7)		
Glomerular disease	100.0	100.0	60.0	39.8 (29.9–49.7)		
Hypertension	74.2	32.5	9.6	18.5 (13.2–23.8)		
Unknown	93.5	76.3	43.1	37.6 (29.8–45.4)		
AVF type					2.285	0.684
Brachiobasilic	100.0	83.3	44.4	37.2 (21.7–52.7)		
Brachiobrachial	100.0	-	-	-		
Brachiocephalic	84.2	78.2	32.0	28.2 (21.5–34.9)		
Radiobasilic	100.0	100.0	0.0	33.0 (33.0–33.0)		
Radiocephalic	84.0	60.2	22.7	28.0 (25.1–30.9)		
AVF side					0.109	0.741
Right	87.0	68.3	26.0	28.5 (23.6–33.5)		
Left	84.1	60.6	22.9	28.3 (25.2–31.5)		
Diabetes					9.170	0.002
No	94.0	72.3	33.7	34.2 (29.6–38.8)		
Yes	79.1	56.0	17.6	25.0 (21.8–28.2)		
Anastomotic segment					0.110	0.744
No	82.7	61.5	25.9	28.6 (25.2–31.9)		
Yes	88.9	64.1	19.0	28.0 (23.6–32.4)		
Feeding artery					0.210	0.648
No	84.8	61.7	23.1	28.5 (25.6–31.4)		
Yes	84.0	66.4	29.9	25.6 (20.0–31.2)		
Draining vein					0.130	0.720
No	84.3	62.8	22.9	27.4 (24.4–30.5)		
Yes	85.5	62.7	25.0	29.3 (24.5–34.1)		
Juxta-anastomotic segment					0.950	0.331
No	88.2	66.9	27.7	30.8 (25.9–35.7)		
Yes	82.8	59.9	21.8	26.8 (23.7–29.8)		
Multiple stenoses					0.390	0.532
No	84.9	62.0	23.5	28.6 (25.7–31.4)		
Yes	80.0	66.7	33.3	26.4 (17.9–34.8)		
General[b]	84.7	62.2	23.7	28.7 (25.9–31.5)	-	-

ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease; AVF, arteriovenous fistula.
[a]Patency duration is given as mean (95% confidence interval).
[b]All demographic variables are evaluated together.

identification of the fistula difficult, and acute angulation that makes passage at the anastomotic level difficult. The anatomical distribution of fistula stenoses also affects the percutaneous approach and its results.

Similar to other reports, a large percentage (65.4%) of the stenoses identified in our study were in the juxta-anastomotic region (6–8). The majority of AVF stenoses were shorter than 2 cm (median, 11 mm; mean, 21.5 mm), similar to previous reports (6, 7, 17). The median stenosis degree in our study was 92.5% and the mean value was 91.5% compared with 71% and 72.2%, respectively, in the study of Heye et al. (17), which investigated first time PTA of 167 AVF in 162 patients.

While PTA was 87.1% successful in the study of Heye et al. (17), this rate was 98% for percutaneous dilatation of the radial artery in nonmature autogenous radiocephalic fistulas in the Turmel-Rodrigues et al. (18) study consisting of 74 patients. Our rate was similar at 96.3%.

Heye et al. (17) determined early recurrence rate as 54.6%, and identified AVF age (P = 0.033) and diabetes

Table 3. Effect of patient age, grade and length of the stenosis, and degree of residual stenosis on primary and secondary patency

Variables	Relative risk	95% CI	*P*
Primary patency			
Age	1.063	1.047–1.080	<0.001
Grade of stenosis	0.995	0.965–1.027	0.771
Length of stenosis	1.008	1.000–1.016	0.062
Residual stenosis	1.014	0.997–1.031	0.112
Secondary patency			
Age	1.057	1.040–1.075	<0.001
Grade of stenosis	1.020	0.975–1.067	0.385
Length of stenosis	1.011	1.004–1.019	0.003
Residual stenosis	1.021	1.004–1.037	0.014

CI, confidence interval.

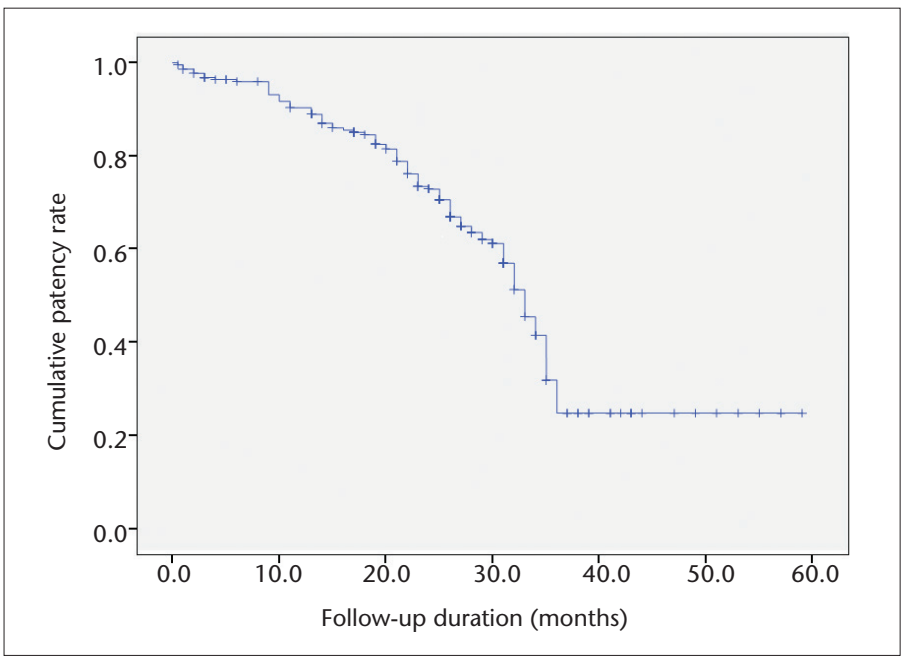

Figure 2. Kaplan-Meier curve of estimated secondary patency after angioplasty.

($P < 0.05$) as factors significantly associated with early recurrence. The early recurrence rate in our study was 23.2%. Although we did not evaluate the age of AVF in our study, patient age ($P < 0.001$) and diabetes mellitus ($P < 0.005$) were found to be associated with early recurrence. Juxta-anastomotic localization of the stenosis was significantly associated with early recurrence in univariate analysis ($P = 0.043$), but its significance did not persist in logistic regression.

Our primary patency rate was 84.7%, 62.2%, and 23.7% for the first, second, and third years, respectively. Heye et al. (17) determined primary patency rate as 48.5%, 31.4%, and 22.5% in the first, second, and third years, with lower first and second year patency than our study. Similar yearly primary patency rates (44%, 40%, and 32%) were also reported by Manninen et al. (19) who studied 51 patients undergoing endovascular treatment of occluded or stenotic antebrachial Brescia-Cimino fistulas to evaluate long-term results of the treatment. Even lower rates were reported by Kim et al. (20), as their series included PTA treatment of thrombosed and nonthrombosed AVF and grafts. Turmel-Rodrigues et al. (18) reported primary patency rate as 53% for the first year and 46% for the second year. Mantha et al. (21) evaluated patency following percutaneous treatment of dysfunctional AVF and grafts in 100 patients and found primary patency rate as 55% in the first year and 47% in the 18th month. Secondary patency rate in our study was 90.5%, 72.7%, and 32.1% for the first, second, third years, respectively. These rates were determined as 83.6%, 68.4%, 60.8% in Heye et al. (17) and 85%, 79%, 79% in Manninen et al. (19), respectively. In other studies secondary patency rates were 96% and 94% for the first and second years (18) and 93% and 90% for the first year and 18 months (21). Rajan et al. (8) reported significantly better primary patency in radiocephalic fistulas compared with the brachiocephalic type. In contrast, there was no significant relationship between fistula type and primary or secondary patency in our study. We found no significant relationship between the AVF location and the patency rate, consistent with other studies (8, 17). In addition, no significant relationship was found between the stenosis location and the primary and secondary patency rates in many studies, including ours (17, 19, 22). However, Turmel-Rodrigues et al. (18) reported a higher primary patency rate in cases with feeding artery stenosis.

In our study the age of the patient and the presence of diabetes had a significant effect on primary patency. As the age of the patient increased, the duration of primary patency became shorter ($P < 0.001$). While the mean primary patency duration was 25 months in patients with diabetes, it was 34.2 months in patients without diabetes ($P = 0.02$). Correlates of primary patency were determined as age in Heye et al. (17) and fistula type in Rajan et al. (8).

Age, presence of diabetes, length of stenosis, early recurrence development, and presence of residual stenosis were found to be significantly associated with secondary patency in our study. Heye et al. (17) found only the patient age and the AVF age to be significantly associated with secondary patency.

Table 4. Effect of demographic and clinical factors on secondary patency

Variables	Rate of secondary patency (%)			Patency duration[a] (months)	Log-rank	*P*
	1-year	2-year	3-year			
Sex					0.774	0.379
Female	90.6	71.0	22.3	32.5 (28.6–36.5)		
Male	90.4	74.1	26.8	35.0 (31.3–38.5)		
Cause of ESRD					22.523	<0.001
ADPKD	100.0	100.0	63.3	47.7 (38.9–56.4)		
Diabetes	88.7	69.6	16.3	30.9 (28.0–33.8)		
Glomerular disease	90.0	90.0	54.0	38.0 (27.9–48.1)		
Hypertension	85.7	46.7	13.6	26.5 (20.8–32.3)		
Unknown	96.7	89.1	56.4	45.2 (36.6–53.9)		
AVF type					8.266	0.082
Brachiobasilic	66.7	55.6	18.5	27.0 (14.0–39.9)		
Brachiobrachial	100.0	0.0	-	14.0 (14.0–14.0)		
Brachiocephalic	89.5	89.5	40.9	33.7 (28.0–39.5)		
Radiobasilic	100.0	100.0	-	-		
Radiocephalic	91.6	72.0	30.5	33.8 (31.0–36.7)		
AVF side					0.261	0.609
Right	89.2	77.6	27.4	33.8 (29.1–38.5)		
Left	90.8	71.3	24.1	33.7 (30.6–36.8)		
Diabetes					5.165	0.023
No	94.0	80.6	37.1	38.7 (33.9–43.5)		
Yes	88.3	67.9	18.8	31.2 (28.1–34.2)		
Anastomotic segment					0.030	0.863
No	89.3	71.8	24.7	33.2 (30.1–36.4)		
Yes	93.0	74.6	25.0	34.7 (29.9–39.4)		
Feeding artery					2.330	0.127
No	89.3	71.9	22.5	33.2 (30.5–36.0)		
Yes	100.0	79.5	53.5	33.4 (29.0–37.9)		
Draining vein					0.110	0.743
No	91.7	73.2	25.3	33.4 (30.4–36.4)		
Yes	88.0	71.9	24.2	33.4 (28.8–38.0)		
Juxta-anastomotic segment					0.260	0.608
No	86.9	71.7	31.8	35.6 (30.4–40.8)		
Yes	92.3	73.3	22.0	32.7 (29.9–35.5)		
Multiple stenoses					0.616	0.432
No	91.4	73.8	24.7	34.3 (31.5–37.0)		
Yes	72.7	53.0	35.4	25.4 (17.3–33.4)		
Early recurrence					8.884	0.003
No	89.7	74.2	29.3	35.6 (32.5–38.7)		
Yes	93.2	66.4	0.0	25.9 (23.3–28.4)		
General[b]	90.5	72.7	25.0	34.1 (31.4–36.8)	-	-

ESRD, end-stage renal disease; ADPKD, autosomal dominant polycystic kidney disease; AVF, arteriovenous fistula.
[a]Patency duration is given as mean (95% confidence interval).
[b]All demographic variables are evaluated together.

Rajan et al. (8) found no variables associated with secondary patency.

One limitation of our study was its retrospective design. Patients were referred from various centers, making follow-up difficult. However, as far as we are aware, ours is the largest series investigating the technical success of PTA in dysfunctional AVF due to stenosis and the clinical and anatomical variables influencing patency after angioplasty. We also did not find any other articles on the relationship between the secondary patency rate and early recurrence in the literature. Our complication rate was 3%, consistent with complication rates reported in most studies (8, 17, 20, 23).

In conclusion, the patency of dysfunctional hemodialysis fistulas can be maintained safely with continuous

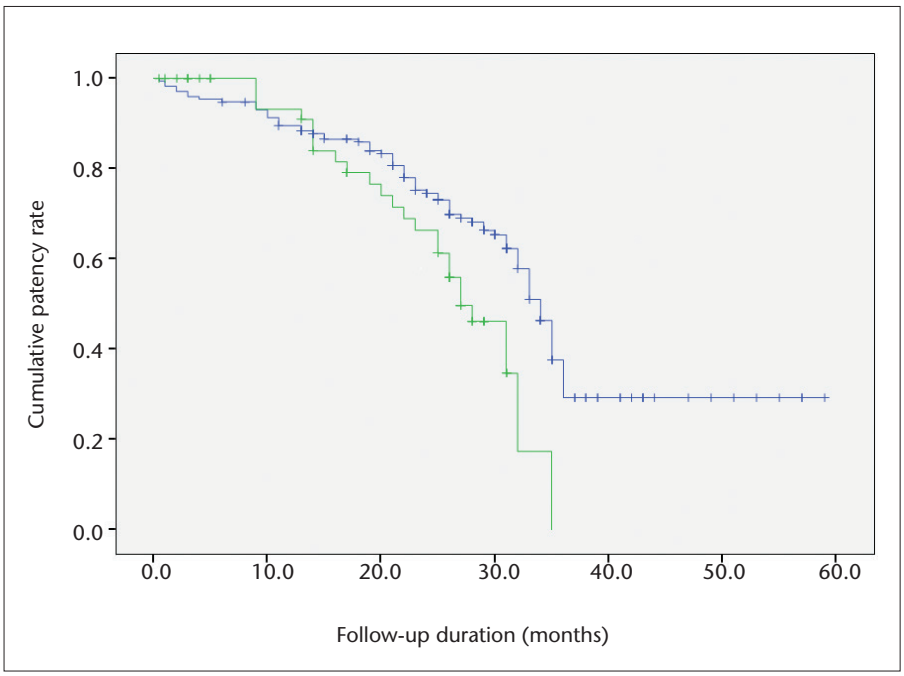

Figure 3. Kaplan-Meier curve of estimated secondary patency with or without early recurrence. Blue line, cumulative patency rate of the group without early recurrence; green line, cumulative patency rate of the group with early recurrence.

follow-up and repeated interventions without need to shorten the venous segment by surgical revision. The percutaneous approach to hemodialysis access stenosis is an alternative to the conventional surgical approach, and PTA is an effective treatment method for dysfunctional AVF.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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