Prognostic Factors of Patency Loss of Arteriovenous Fistula After Percutaneous Transluminal Angioplasty

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Abstract

Introduction: Arteriovenous fistula (AVF) is recommended as 1st choice of vascular access for hemodialysis (HD). Percutaneous transluminal angioplasty (PTA) helps increase the patency of AVF, which enhances HD adequacy. However, a slow decline in blood flow rate over time after PTA is common. The present study examined factors associated with patency loss at 6 months after PTA.

Method: This is a single-center prospective cohort study of 54 HD patients using AVF as dialysis access. Demographic data and characteristics of AVF were collected at baseline. The changes in blood flow rates after PTA were recorded immediately and at 3- and 6-month after the procedure. Factors associated with patency loss at 6 months after PTA were evaluated.

Results: The average age of AVF was 77.1 ± 68.4 months. Sixty-three percent of the fistula were in the upper arm. Central vein stenosis was present in 15.3%. Forty-six percent had previous interventions to the fistula. The most common type of intervention was plain balloon angioplasty (90.7%). The access blood flow rate (ABF) rate improved significantly immediately after the PTA. However, a slow but significant decline in ABF rate was observed at 3 and 6 months. The patency rates of the fistula at 3 and 6 months were 94.4% and 75.9 %, respectively. Independent predictors for patency loss at 6 months were ABF <500 ml/min immediately after the procedure, multiple stenotic lesions, and higher PTH level. Higher hemoglobin and lower ABF rate immediately after the PTA were independently correlated with >25% decline in the ABF at follow-up

Conclusion: Low ABF rate immediately after PTA, higher number of stenotic lesions, and higher PTH level predicted patency loss of AVF after PTA. These findings could help identify patients at high risk of AVF failure who might benefit from close monitoring.

Keywords: AV access; stenosis; thrombosis; dialysis; kidney failure; ESKD; ESRD

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ปัจจัยที่พยากรณ์การตันของเส้นฟอกเลือดชนิด arteriovenous fistula หลังจากการขยายเส้นเลือดด้วยบอลลูน

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บทคัดย่อ

บทนำ: เส้นฟอกเลือดชนิด arteriovenous fistula (AVF) ถูกแนะนำให้เป็นทางเลือกแรกของเส้นฟอกเลือดในผู้ป่วยที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียม การขยายเส้นฟอกเลือดด้วยบอลลูนสามารถช่วยให้ AVF ที่ตีบหรือตันกลับมาใช้งานได้นานขึ้น จึงช่วยเพิ่มประสิทธิภาพของการฟอกเลือด การลดลงของอัตราการไหลเวียนของเลือดหลังจากการขยายเส้นเลือดด้วยบอลลูนไปแล้วนั้นพบได้บ่อย จึงเป็นที่มาของการศึกษานี้ว่ามีปัจจัยอะไรบ้างที่สามารถพยากรณ์การตันของ AVF หลังจากได้รับการขยายด้วยบอลลูน

ระเบียบวิธีวิจัย: การศึกษานี้เป็นการศึกษาไปข้างหน้าในสถาบันเดียวในผู้ป่วยที่ได้รับการฟอกเลือดโดยใช้ AVF จำนวน 54 คน มีการเก็บข้อมูลพื้นฐานของผู้ป่วยและข้อมูลของ AVF ณ.จุดเริ่มการศึกษา และเก็บข้อมูลการเปลี่ยนแปลงของอัตราการไหลเวียนของเลือดในเส้นฟอกเลือด ทันทีหลังจากการขยายด้วยบอลลลูน และที่ 3 เดือน และ 6 เดือน และวิเคราะห์ปัจจัยที่สามารถพยากรณ์การตันของ AVF ที่ 6 เดือน

ผลการศึกษา: อายุเฉลี่ยของ AVF คือ 77.1 ± 68.4 เดือน ร้อยละ 63 ของ AVF อยู่บริเวณต้นแขนส่วนบน พบ central vein stenosis ร้อยละ 15.3 และร้อยละ 46 เคยได้รับการแก้ไข AVF มาก่อน หัตถการที่ทำมากที่สุดคือ plain balloon angioplasty (ร้อยละ 90.7) ทันทีหลังการขยายเส้นเลือดพบว่ามีการเพิ่มขึ้นของอัตราการไหลเวียนของเลือดอย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามอัตราการไหลเวียนของเลือดค่อยๆ ลดลงเรื่อยๆ ที่ 3 และ 6 เดือนหลังการขยายเส้น อัตราการอยู่รอดของ AVF ที่ 3 และ 6 เดือน คือ ร้อยละ 94.4 และร้อยละ 75.9 ตามลำดับ ปัจจัยที่พบว่ามีความสัมพันธ์อย่างอิสระกับการตันของ AVF ที่ 6 เดือน ได้แก่ อัตราการไหลเวียนของเลือดทันทีหลังการขยาย <500 มิลลิลิตร/นาที เส้นที่มีการตีบหลายแห่ง และระดับฮอร์โมนพาราไทรอยด์ที่สูง นอกจากนี้ฮีโมโกลบินที่สูง และอัตราการไหลเวียนของเลือดทันทีหลังการขยายต่ำ มีความสัมพันธ์อย่างเป็นอิสระกับการลดลงของอัตราการไหลของเลือดมากกว่าร้อยละ 25

สรุป: อัตราการไหลเวียนของเลือดที่ต่ำหลังจากการขยายหลอดเลือดด้วยบอลลูน เส้นที่มีบริเวณของการตีบหลายแห่ง และระดับฮอร์โมนพาราไทรอยด์ที่สูง สามารถพยากรณ์การตันของ AVF ที่ 6 เดือนหลังได้รับการขยายหลอดเลือด ปัจจัยเหล่านี้อาจสามารถนำไปใช้ในการคัดกรองผู้ป่วยที่มีความเสี่ยงสูงต่อการตันของ AVF ซึ่งอาจได้รับประโยชน์จากการเฝ้าระวังอย่างใกล้ชิด

คำสำคัญ: เส้นฟอกเลือด; ไตวายเรื้อรังระยะสุดท้าย; การบำบัดทดแทนไต; เส้นตีบ; เส้นตัน

Introduction

The vascular access that provides adequate blood flow is important for the adequacy of hemodialysis (HD).[1] Arteriovenous fistula (AVF) has advantages in its ability to provide high access blood flow (ABF) rate, having long lifespan and lower risk of complications such as infection and thrombosis. Thus, current KDOQI guideline recommends AVF as the first choice of vascular access for HD.[2] Nevertheless, stenosis or even thrombosis of AVF can still occur requiring percutaneous balloon

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angioplasty (PTA) or even surgical revision.[3] AVF stenosis and thrombosis remain the leading causes of AVF failure.[4] According to KDOQI guideline, it is reasonable to use balloon angioplasty as a primary treatment for significant AVF stenosis (>50% stenosis). A previous study form Thailand confirmed the safety and efficacy of PTA with a success rate of 83% and 1-year primary assisted patency rate of 68.7%.[5] Unfortunately, despite the high success rate of PTA, approximately 30% of the fistula lost the patency within 1 year. The previous study showed that vascular access flow rate after PTA could predict future AVF thrombosis.[6] A retrospective study by Henricus et al reported that patients with diabetes had lower rate of patency which could be improved with tight control of the blood sugar.[7] Another study by Romann et al. showed a significant risk of AVF failure up to 1.8 times after intervention in patients with diabetes, compared with those without diabetes.[8] Outflow stenosis and ≥2 cm stenotic lesion were also associated with patency loss. Another study by Manou et al showed that previous history of AVF thrombosis, history of previous intervention, non-white ethnicity, longer length of stenotic lesion, >65 years old, and outflow stenosis were risk factors of patency loss after PTA.[9] A systematic review from Neuen et al showed that the age of AVF <6 months and length of stenosis >2 cm were associated with reduced patency after intervention.[10] The present study explored risk factors associated with patency loss after PTA among HD patients with AVF stenosis.

Materials and Methods

Patients

This is a prospective cohort study conducted at Rajavithi hospital between August 1, 2021 to August 30, 2022. Patients with AVF who received regular HD from Rajvithi hospital and those who were referred from other hospitals to see the interventional nephrologists at Rajvithi hospital were screened. The inclusion criteria were age >18 years old and having been using AVF for at least 3 months. The exclusion criteria were failed angioplasty and switching to peritoneal dialysis or receiving a kidney transplantation during the 6-month follow-up period. The study protocol was reviewed and approved by the Ethical committee of Rajavithi hospital (Approval number 64128) and was performed in accordance with the Helsinki Declaration. Informed consent was obtained from all participants.

Percutaneous Transluminal Balloon Angioplasty

Two interventional nephrologists at Rajvithi hospital performed the procedure. The indications for PTA were clinically or hemodynamically significant stenosis, access blood flow rate <400 ml/min without significant stenosis, and clinical indicator of AVF stenosis. The procedures performed were plain balloon, drug-eluting balloon, bare-stent, or covered-stent (stent graft). The decision on the type of the procedure was made by the interventional nephrologist.

Data Collection

Baseline patient characteristics and laboratory data were collected. The ABF and brachial artery blood flow rates were obtained from Doppler ultrasound before, immediately after, and at 3 and 6 months after the procedure.

Outcome

The outcomes were changes in the ABF rate and predictive factors of patency loss at 6 months after PTA

Definitions

Arteriovenous fistula (AVF): vascular access which connects vein and artery for HD

Primary patency after PTA: an interval between the time of PTA until any intervention to maintain the patency or access abandonment.

Percutaneous transluminal angioplasty (PTA): a procedure to open the blocked blood vessel using a small, flexible plastic tube, or catheter with a balloon, a drug eluting balloon, a bare stent, or stent graft.

Access blood flow rate (ABF): a velocity of the blood that passes through the AVF measuring at the level of brachial artery by duplex doppler ultrasound.

Clinical indicator of significant AVF stenosis: a presence of at least one of the following:

difficulty placing needles; low pump speed; prolonged bleeding after removal of needles; low KT/V; decreased thrill; pulsatile AVF; ipsilateral extremity edema

Pre-emptive criteria for PTA: a decrease in ABF rate to <400 ml/min

Percent stenosis: the percent stenosis was calculated from the formula (1– ABF rate at the stenotic area/ABF rate at the normal area) × 100%

Location of AVF stenosis: peripheral lesion included Juxta-anastomotic vein, drainage vein, and cephalic arch vein; central lesion included subclavian vein and brachiocephalic vein.

Statistical analyses:

Data were presented as number (%), median (minimum-maximum) or mean ± standard deviation. Chi-square or fisher's exact test was used to compare categorical data. Factors associated with primary patency after PTA were analyzed by binary logistic regression. Repeated measures ANOVA was used to compare multiple means of the same group. The survival of AVF was analyzed by Kaplan-Meier survival curve. Univariate and multivariate Cox proportional hazard models were used to determine factors associated with AVF survival at 6 months. P-value <0.05 was considered statistically significant.

Results

A total of 77 patients were screened. Twenty-three patients were excluded due to failed angioplasty (2 patients), kidney transplantation (1 patient), switching to peritoneal dialysis (1 patient) and loss to follow-up (19 patients). Fifty-four patients were included in the final analysis. **Tables 1 and 2** show baseline demographic and laboratory data, and characteristics of AVF.

Table 1 Baseline characteristics and laboratory data of all patients

Parameters	N=54
Age (years)	56 ± 15
Male (n/%)	29 (54)
Body mass index (kg/m^2)	22.9 ± 0.4
Underlying disease (n/%) • Hypertension • Dyslipidemia • Diabetes mellitus • Ischemic heart disease • Cerebrovascular disease • Peripheral vascular disease	 34 (63) 36 (66.7) 22 (40.7) 9 (16.7) 6 (11.1) 1 (1.9)
Medications (n/%) • Erythropoietin • Antiplatelets • Anticoagulants • Statins	 41 (75.9) 20 (37.0) 3 (5.6) 37 (68.5)
Systolic Blood pressure (mmHg)	140.2 ± 29
Laboratory data	
Hemoglobin (g/dl)	10.6 ± 1.6
Platelets x 100 (UL)	205.7 ± 63.6
Partial thromboplastin time (seconds)	33.1 ± 25.9
International normalized ratio (seconds)	1.2 ± 0.7
Hemoglobin A1c (%)	5.7 ± 1.6
Intact parathyroid hormone (pg/mL)	489.5 (16.3-2,403)
Calcium (mg/dl)	9.4 ± 0.9
Phosphate (mg/dl)	4.6 ± 1.7
Arteriovenous fistula Location (n/%) • Upper arm (brachiocephalic or brachiobasilic) • Lower arm (radiocephalic)	 34 (63) 20 (38)
Age (months)	77.1 ± 68.3
Previous intervention (n/%)	25 (46)

Table 2 Characteristics of arteriovenous fistula

Parameters	
ABF rate prior to PTA (ml/min)	551 (0-2416)
Total number of stenotic lesions (n)	83
Median number of stenotic lesions per one fistula	1 (1-3)
Single stenotic lesion (n/%)	28 (51.9)
Location of stenosis (n/%) Peripheral lesion • Juxta-anastomotic vein • Drainage vein • Cephalic arch vein Central • Subclavian vein • Brachiocephalic vein Combined	 72 (84.7) 23 (27.1) 34 (40.0) 15 (17.6) 13 (15.3) 5 (5.9) 8 (9.4) 9 (10.6)
Location of stenotic length ≥2cm (n/%) • Juxta-anastomotic vein • Drainage vein • Cephalic arch vein • Subclavian vein • Brachiocephalic vein	27 (73) 5 (8) 11 (44) 5 (20) 1 (4) 5 (24)
Thrombosis (n/%)	1 (2%)
Types of PTA (n/%) • plain balloon • drug eluting balloon • bare stent • stent graft	 49 (90.7) 2 (3.7) 1 (1.9) 2 (3.7)
ABF rate after PTA (ml/min) Increase in ABF rate immediately after PTA (ml/min) <20% increase in ABF rate (n/%) ≥20% increase in ABF rate (n/%)	945 (218-5,392) 113.5 ± 144.1 12 (22) 42 (78)
% Stenosis prior to PTA	66.7 ± 19.9
% Stenosis after PTA 50-75% (n/%) 76-90% (n/%) >90% (n/%)	36.4 ± 17.9 56 (67.0) 17 (20) 10 (13)
% Residual stenosis immediately after PTA <30 % (n/%) ≥30 % (n/%)	36.4 ± 17.9 32 (39) 51 (61)

ABF, access blood flow; PTA, percutaneous transluminal angioplasty

The patency rates at 3 and 6 months were 94.4% (51 patients) and 75.9% (41 patients), respectively **(Figure 1)**. The ABF rates at 3 and 6 months were 1,109.06 ± 725.74 and 1061.51 ± 742.74 ml/min, respectively.

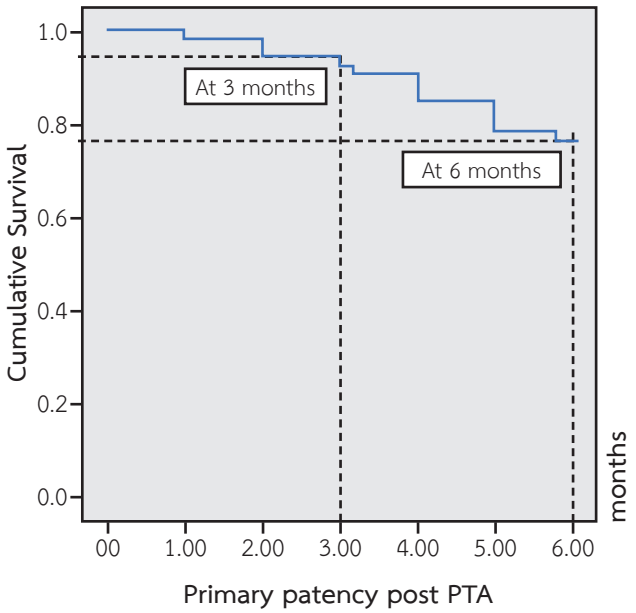

Figure 1. Patency of arteriovenous fistula after percutaneous transluminal angioplasty

Repeated Measures ANOVA revealed a significant increase in the mean ABF rates at 3 and 6 months after PTA (P=0.013). Pairwise comparisons revealed a significant difference between the ABF rate before PTA and 3 months after PTA (p=0.038). The difference between the ABF rate before PTA and 6 months after PTA did not reach statistical significance. The number of patients who had ABF rate ≥400 or ≥500 ml/min continued to decrease at 3 and 6 months **(Table 3)**. When using the cut-off ABF rate of 500 ml/min, there was no statistical difference in the number of patients with ABF rate ≥500 or <500 ml/min between prior to PTA and 6 months after PTA.

Factors associated with the loss of patency at 6 months are shown in **Table 4**. ABF rate <500 ml/min immediately after PTA, location of stenosis at the cephalic arch vein, higher number of stenotic lesions, and higher PTH level, were associated with the loss of patency at 6 months. In the multivariate Cox proportional hazard regression analysis, ABF rate <500 ml/min immediately after PTA,

multiple stenotic lesions, and higher PTH level were independently associated with the loss of patency at 6 months. Moreover, higher hemoglobin level and lower ABF immediately after PTA were independently correlated with >25% decrease in the ABF rate at follow-up **(Table 5)**

Table 3 Access blood flow rate before and after percutaneous transluminal angioplasty

Parameters	Before PTA	After PTA			P-value
		Immediately	3 months	6 months	
No of patients (n/%)	54 (100)	54 (100)	51 (94.74)	41 (76)	
ABF rate (ml/min)	710 ± 573	1,080 ± 743	1,109 ± 726	1,016 ± 742	0.013
Patients with ABF rate (n/%)					
≥400ml/min	36 (66.7)	50 (92.6) *	47 (92.2) **	36 (90) ***	0.01* 0.001** <0.001***
<400ml/min	18 (33.3)	4 (7.4) *	4 (7.8) **	5 (10) ***	
≥500ml/min	30 (55)	50 (93) *	45 (88) **	30 (73)	<0.001* <0.001**
<500ml/min	24 (45)	4 (7) *	6 (12) **	11 (27)	

*Before PTA vs. *immediately after PTA; **3 months after PTA; ***6 months after PTA*
PTA, percutaneous transluminal angioplasty; ABF, access blood flow

Table 4 Univariate and multivariate Cox proportional hazard regression analyses of factors associated with patency loss at 6 months

Parameters	Crude HR (95%CI)	p-value	Adjusted HR (95%CI)	p-value
Cephalic arch vein stenosis (Y/N)	3.69 (1.24-11.02)	0.001	1.59 (0.34-6.32)	0.513
Number of stenotic lesions	2.56 (1.16-5.66)	0.020	4.01 (1.41-11.36)	0.009
ABF rate immediately after PTA <500 ml/min (Y/N)	9.08 (2.42-33.97)	0.001	18.17 (3.61-91.40)	0.001
Intact PTH level (1 pg/mL)	1.00 (1.01-1.02)	0.012	1.002 (1.001-1.003)	0.008

HR, hazard ratio; CI, confidence interval; ABF, access blood flow; PTA, percutaneous transluminal angioplasty; PTH, parathyroid hormone level

Table 5 Univariate and multivariate logistic regression analyses of factors associated with >25% decrease in the access blood flow rate

Parameters	Crude OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Hemoglobin level	2.03 (1.30-3.16)	0.002	2.09 (1.29-3.38)	0.003
ABF immediately after PTA	0.98 (0.97-0.99)	0.039	0.98 (0.97-0.99)	0.034

OR, odds ratio; CI, confidence interval; ABF, access blood flow rate; PTA, percutaneous transluminal angioplasty

Discussion

The present study showed that the ABF rate improved significantly immediately after PTA. However, a slow but significant decline in ABF rate was observed at 3 and 6 months. The patency rates of the fistula at 3 and 6 months were 94.4% and 75.9 %, respectively. Independent predictors of patency loss at 6 months were ABF rate <500 ml/min immediately after the procedure, multiple stenotic lesions, and higher PTH level. Higher hemoglobin and lower ABF rate immediately after PTA were also independently correlated with >25% decline in the ABF at follow-up.

The result on the 6-month patency rate of AVF after PTA from the present study was comparable with the previous report.[5] However, diabetes was not associated with patency loss in the present study, whereas the previous study reported diabetes as a risk factor for decreased AVF survival after PTA.[9] This may be explained by the lower prevalence of diabetes and peripheral vascular disease in the present study.

The present study also observed the relationship between increased Intact parathyroid hormone level and patency loss after PTA. The risk increased by 0.2% for every 1 pg/mL increase in parathyroid hormone level. A study by Gardezi, Ali L et al. found similar correlation between parathyroid hormone level and AVF failure.[12]. This may be related to an increase in vascular calcification among patients with increased parathyroid hormone level or other unknown mechanism.

Similar to the recent study in Chinese population, multiple stenotic lesions were associated with several folds increase in the risk of AVF failure after PTA.[13] Others have also observed the relationship between the length of stenosis and the location of stenosis at the outflow vein with patency loss.[8,10] Cephalic arch vein stenosis tended to loss patency after PTA.[13] The previous study by Kim et al reported the patency rate of 40.5% at 6 months after PTA.[14]

Limitations of the present study were small sample size, higher rate of loss to follow-up and short follow-up time.

In conclusion, predictive factors for patency loss of AVF at 6 months after PTA were ABF rate <500 ml/min immediately after the procedure, multiple stenotic lesions, and higher PTH level. These findings could help identify patients at high risk of AVF failure who might benefit from close monitoring.

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