ORIGINAL ARTICLE

Post–angioplasty Intra-access Flow Predicts Survival of Arteriovenous Fistula for Hemodialysis

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Background: Arteriovenous fistula (AVF) stenosis is an important complication in hemodialysis (HD) patients. Prediction of survival after percutaneous transluminal angioplasty (PTA) is also crucial for close-up monitoring and early correction. The impact of post-angioplasty access flow rates on AVF survival was controversial. The authors conducted a prospective study to assess the relationships between post-angioplasty access flow rate and AVF survival.

Materials and Methods: The cohort study in hemodialysis patients undergoing PTA for AVF stenosis at Srinagarind Hospital was performed between January 2012 and September 2022. Intra-access flow rates were measured by an ultrasound dilution technique during 2 weeks after PTA and followed every 3 to 6 months. Comparison of incidence rates and median survival times of AVF between the different access flow groups were conducted. Risk factors of AVF re-stenosis were evaluated by the Cox proportional hazard model.

Results: 62 patients with 94 PTA procedures (1 to 7 procedures/patient) were enrolled. The mean post-angioplasty intra-access flow rate was 726±327 ml/min. The incidence of AVF dysfunction was 1.05 per 1,000 patients-days (95% CI: 0.82 to 1.35) and the median post-angioplasty survival time was 341 days (95% CI: 233 to 802). Multivariable analysis demonstrated that comparisons with <500 ml/min group, hazard ratios (HR) of AVF failure in 501 to 750 and >750 ml/min groups were 0.43 (p=0.003) and 0.29 (p<0.001). The other risk factors were upper arm AVF (HR 2.58), a previous angioplasty procedure (HR 1.86), and body mass index (HR 0.90 for every increase 1 kg/m^2).

Conclusion: Higher intra-access flow was associated with higher post-angioplasty AVF survival rate. The intra-access flow of less than 500 ml/min was associated with unacceptable survival times and a very high risk for AVF failure. Monitoring and surveillance for detection of early AVF re-stenosis are encouraged to strengthen the successful correction with high access flow and extended the usage duration.

Keywords: Arteriovenous fistulae; Percutaneous transluminal angioplasty; Post-angioplasty patency; Intra-access flow; Hemodialysis

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Well-functioning vascular access (VA) is necessary for chronic hemodialysis (HD) patients. There are three main types of VA, i.e., arteriovenous fistulas (AVF), arteriovenous grafts (AVG), and central venous catheters (CVC). From "Fistula First-Catheter Last Initiative" program to improve outcome of prevalent hemodialysis patients, an AVF is recommended as the first line of hemodialysis VA because it has a better patency rate and fewer complications than other types[1-3] while CVC may consider in patients with poor long-term prognoses and limited life expectancy or absence of AV access creation options[4,5]. Loss of VA patency caused inadequate HD and leads to increased mortality and morbidity. The National Kidney Foundation-Kidney disease outcomes quality initiative (NKF-KDOQI) clinical practice guidelines recommend regular physical examination to detect clinical indicators of flow dysfunction of the AVF while surveillance procedures may consider as supplementary to clinical monitoring[5]. Intra-access blood flow (ABF) monitoring is a preferred method in both AVF and AVG surveillance and preemptive treatment of subclinical AVF stenosis reduces thrombosis rate, hospitalization, central venous catheterization and improves AVF survival rate[6-8]. Percutaneous transluminal angioplasty (PTA) is the first-line modality for treatment of

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VA dysfunction because of high success rate, defined as an improvement of anatomic and hemodynamic parameters[5], is safe and minimally invasive[9] but patency after PTA is highly variable that depends on various factors, e.g. age of patient, comorbidities, cause of end stage kidney disease (ESKD), type and location of VA, metabolic and inflammatory markers, length of stenotic lesion, and residual stenosis[9-12]. Prediction of patency of VA after angioplasty is also crucial for further monitoring and early intervention. Results from previous studies, however, indicated that post-angiographic ABF remained inconclusively to be the predictor of secondary patency of VA especially in AVF[7, 13-15]. Therefore, this research was performed to determine whether post–angioplasty ABF predicted AVF patency and to identify the potential factors that effect AVF patency which may help physicians to enhance AVF surveillance and preemptive treatment to improve patient outcomes.

Materials and Methods

Ethical considerations and patient selection

The retro- and prospective cohort study was conducted in the Srinagarind Hospital, Khon Kaen University between January 1st, 2012 and September 30th, 2022. Chronic HD patients included were ≥18 years of age, receiving HD via AVF and who underwent PTA for AVF stenosis or thrombosis. Exclusion criteria were failure of VA correction with PTA, unable to measure an ABF by the ultrasound dilution technique or loss to follow-up. The present study was approved by the Ethics Committee for Human Research, Faculty of Medicine, Khon Kaen University, Thailand (HE581144) and all patients were provided with written informed consents.

Patient management

After patients were enrolled, ABFs were measured by the ultrasound dilution technique within 2 weeks after PTA then serially evaluated every 3 to 6 months until the end of study or until they met the study composite outcomes, i.e., access abandonment, AVF stenosis or thrombosis, or re-PTA from previous AVF failure. The intra-dialytic AVF blood flow measurement was performed during an initial 30 minutes of HD session by the trained HD nurse (BT). The authors measured intra-access flows by using the ultrasound dilution machine [H4FX Flow/Dilution Sensors with HD03 Monitor (Transonic® system Inc.)]. The procedure composed of an injection of 10 ml of isotonic saline via a venous blood line after reversal of dialysis lines and measured blood velocity at arterial line by ultrasound technique which its protein and ion concentrations influenced the velocity. After diluting with saline infusion, a change of ultrasound velocity was proportional to the concentration of blood which blood flow can be calculated by the mathematical analysis[16]. Post-angioplasty patency was defined as an interval from the time of intervention until thrombosis or the time of re-intervention to maintain or reestablish patency[16]. Patient data were terminated when patient was shifted to peritoneal dialysis, received kidney transplantation or death. During the study period, patients with ABF less than 350 to 400 ml/min were suggested for re-PTA. If patients denied or were unsuitable for re-PTA, patients were followed-up and ABF was measured as per study protocol.

Data collection

Baseline characteristics and demographic data, e.g., age, sex, weight, height, body mass index, comorbid diseases, causes of ESKD, history of smoking, site and primary patency of AVF (an interval from the time of access placement until any intervention designed to maintain or reestablish patency)[17] and an episode of previous PTA were collected from the interview, physical examination and review of medical records. AVF failure was diagnosed when the AVF was not successfully used for HD whether it was patent or not[17]. HD adequacy assessed by using a urea kinetic model, Kt/V value, was evaluated monthly during the study period.

Statistical analysis

Sample size was calculated by Rubinstein's formula[18] or survival analysis that compared 2 survival curves with a minimum hazard ratio of 2.87 and median survival times in the control group that was 6 months. The power of the test that was 0.9 and a p-value <0.05 was considered statistically significant. The total samples size should be 49 post-angioplasty procedures.

Continuous data were expressed as mean ± SD or median and 25 and 75 percentiles. Categorical data were expressed as number and percent of total participants. Two groups were compared by using Student's t-test or Mann-Whitney U test for the continuous variables expressed as mean or median differences and a 95% confidence interval (CI), and the Chi-square test or Fisher's exact test for categorical variables. In patients with multiple PTA, the value of each post angioplastic ABF and its number of angioplasty procedure were used for analyses of AVF survival and the potential risk factors. Survival analyses were expressed as Kaplan-Meier curves and compared between groups by Log-rank tests. Cox regression analysis was used to analyze factors that were potentially related to survival of AVFs and expressed as the hazard ratio and 95% CI. HRs that accounted for the effects in univariable analysis with p-value <0.05 and other potential factors related with AVF survival reported in previous studies were entered into a multivariate Cox regression model. Statistical analyses were done using STATA version 17.0 and p-value less than

0.05 was considered to be statistical significance.

Results

62 chronic HD patients, 59.7% and 40.3% of them who had twice and thrice weekly HD, with 94 PTA procedures (range of 1 to 7 procedures/patient) were enrolled. The overall mean age was 62.2±9.7 years, 61.3% male, 77.4% had forearm AVF, median duration of ESKD and AVF ages were 32 (15.4 to 64.1) months, and 21.5 (9.7 to 37.8) months. In 57.5% of all post-angioplasty procedures these were the first PTA procedure (Table 1).

The mean and median ABFs in pre- and 2 weeks post-angioplasty were 147.2±121.1, 150 (0 to 230) ml/min and 725.7±326.8, 690 (460 to 920) ml/min. All patients were received ABF monitoring every 3 to 6 months throughout the entire the present study period. Median follow-up times was 246.5 (152 to 741) days. During the follow-up period of total 94 post-angioplasty procedures, 63 of them met the outcome of AVF stenosis/thrombosis, 31 of them still had patency of AVFs, however, 22 post-angioplasty procedures were censored: 11 from death, 7 from referred to other hospitals, 3 from received kidney transplantation, and 1 from shifted to peritoneal dialysis. Therefore 9 of total 94 AVF post-angioplasty procedures still continuously patented at the end of study.

Survival analysis

The follow-up time of 94 post-angioplasty procedures from 62 chronic HD patients was 59,814 patient-days. The incidence of composite outcomes was 1.05 per 1,000 patients-days (95% CI: 0.82 to 1.35) and the median post-angioplasty survival time was 341 days (95% CI: 233 to 802). The post-angioplasty AVF survival rate was 74.5% and 49.7% at 6 and 12 months.

There was an association between post-angioplasty ABF and survival of AVF; lower ABF was significantly associated with lower survival rate and even the cut point levels were 350, 450, 500, 550, 600, 650, 700, 750, 800 and 850 ml/min but this association was not significant when the cut point value was 900 ml/min.

The patients were classified into 3 groups according to the post-angiographic ABF (≤500, 501 to 750, and >750 ml/min) in which their incident rates of AVF failure were 2.15 (95% CI: 1.47 to 3.16), 1.15 (95% CI: 0.67 to 1.98), and 0.66 (95% CI: 0.44 to 0.98) per 1,000 patient-days and median survival times were 224 (95% CI: 124 to 433), 322 (95% CI: 162, -), and 867 (95% CI: 308 to 2,147) days (p=0.001) as shown in Figure 1. Furhthermore, there was an association between post-angiographic ABF and survival of AVF demonstrated by an increasing of ABF every 50 ml/min reduced the hazard ratio of AVF failure 6.4%, p=0.004 (Table 2) and the positive correlation between post-angiographic ABF and duration of AVF patency (r=0.32, p=0.002, Figure 2).

Table 1. Patient characteristics

	Participants (n=62)
Sex, male, n (%)	38 (61.3)
Age (years), mean ± SD	62.2±9.7
Duration of ESKD (months), median (IQR)	32 (15.4 to 64.1)
Caused of ESKD, n (%)	
Diabetic nephropathy	34 (54.8)
Hypertensive nephropathy	13 (21.0)
Gout	6 (9.7)
Glomerulonephritis	4 (6.5)
ADPKD	2 (3.2)
Nephrolithiasis	1 (1.6)
Unknown	2 (3.2)
Comorbid disease, n (%)	
Dyslipidemia	61 (98.4)
Hypertension	60 (96.8)
Diabetes mellitus	34 (54.8)
Ischemic heart disease	6 (9.7)
Dilated cardiomyopathy	2 (3.2)
Obstructive sleep apnea	2 (3.2)
Cerebrovascular disease	1 (1.6)
Peripheral arterial disease	1 (1.6)
Smoking status, n (%)	
Nonsmoking	45 (72.6)
Former smoking	13 (21.0)
Current smoking	4 (6.5)
Body mass index (kg/m^2), mean ± SD	22.5±3.7
Hemoglobin (g/dL), mean ± SD	10.7±1.6
Hemodialysis adequacy (Kt/V), mean ± SD	1.61±0.25
Age of AVF (months), median (IQR)	21.5 (9.7 to 37.8)
PTA procedure, n (%)	94 (100)
Number of PTA procedures (n=94)	
1st PTA	54 (57.5)
2nd PTA	20 (21.3)
3rd PTA	10 (10.6)
4th PTA	5 (5.3)
5th PTA	3 (3.2)
6th PTA	1 (1.1)
7th PTA	1 (1.1)
Site of AVF (n=94)	
Forearm	63 (67.0)
Upper arm	31 (33.0)
Intra-access flow (ml/min), mean ± SD (n=94)	
Pre PTA	147.2±121.1
Post PTA	725.7±326.8

ESKD=end stage kidney disease; ADPKD=autosomal dominant polycystic kidney disease; AVF=arteriovenous fistula; PTA=percutaneous transluminal angioplasty; SD=standard deviation; IQR=interquartile range

The factors related with AVF survival evaluated by univariate analysis were the ABF and location of AVF, number of PTA procedures, number of HD sessions per week and body mass index (Table 2). The other factors e.g. age, sex, comorbidity diseases of; - diabetes mellitus, hypertension, myocardial infarction, dyslipidemia, and cerebrovascular diseases, smoking status, duration of ESKD, and lifespan of AVF had no significant affect on post-angiographic AVF survival rates (Table 2).

After adjustment for potential factors related with AVF survival by multivariate analysis, post-angioplasty ABF, repeated angioplasty, body mass index and location of AVF had significant effects on AVF failure (Table 3). When compared with patients whose post-angioplasty ABF <500 ml/min group, the adjusted HRs for AVF failure were 0.43, and 0.29 in patients who had post-angioplasty ABF 501 to 750 and >750 ml/min groups. Increase of post-angioplasty ABF every 50 ml/min reduced the adjusted HR of AVF failure 7.3%, p=0.003. Patients with repeated angioplasty had an AVF failure more than patients with the

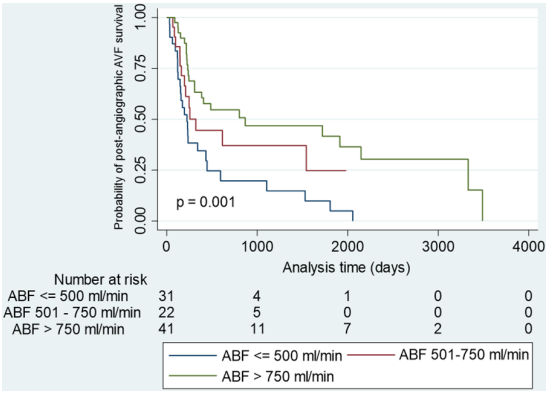

Figure 1. The post-angiographic survival of AVF compared 3 groups categorized by post-angiographic intra-access blood flow (ABF): ≤500, 501 to 750, and >750 ml/min.

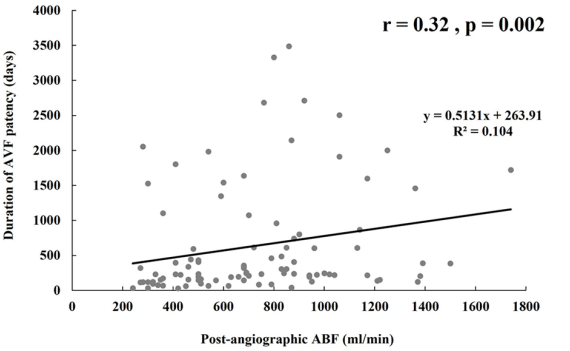

Figure 2. The correlation between post-angiographic intra-access blood flow (ABF) and duration of arteriovenous fistula (AVF) patency.

Table 2. Risk factors for post-angiographic AVF failure assessed by univariate analysis.

Variables	HR (95% CI)	p-value
Intra-access blood flow (every increase 50 ml/min)	0.936 (0.90 to 0.98)	0.004
Location of AVF (upper arm/forearm)	2.54 (1.50 to 4.30)	0.001
Number of PTA treatment (every increase 1 time)	1.15 (1.01 to 1.31)	0.03
Repeated PTA (yes/no)	2.50 (1.43 to 4.39)	0.001
Body mass index (every increase 1 kg/m^2)	0.89 (0.82 to 0.97)	0.007
HD sessions/week (trice/twice)	0.51 (0.30 to 0.88)	0.015
Age (every increase 5 years)	1.03 (0.91 to 1.17)	0.64
Sex (male/female)	1.23 (0.72 to 2.11)	0.44
Duration of ESKD; every increase 100 days	0.99 (0.96 to 1.01)	0.33
Underlying and comorbidity diseases (presence/absence)		
Diabetes mellitus	1.34 (0.81 to 2.23)	0.26
Hypertension	0.88 (0.21 to 3.62)	0.86
Cardiovascular disease	1.26 (0.56 to 2.80)	0.58
Dyslipidemia	0.40 (0.05 to 2.92)	0.37
Smoking status (quit or current/none)	1.13 (0.66 to 1.94)	0.65
Hemoglobin level (every increase 1 g/dL)	0.90 (0.76 to 1.08)	0.25
Post-angioplasty Kt/V (every increase 1 unit)	0.60 (0.23 to 1.60)	0.31
Age of AVF (every increase 50 days)	0.99 (0.98 to 1.01)	0.40
Site of AVF stenosis (anastomosis/non-anastomosis)	1.57 (0.88 to 2.82)	0.13
Percentage of pre-PTA AVF stenosis (every increase 1%)	1.005 (0.98 to 1.03)	0.39
Percentage of residual stenosis ≥30% (yes/no)	1.19 (0.53 to 2.68)	0.67

HR=Hazard ratio; CI=confident interval; AVF=arteriovenous fistula; PTA=percutaneous transluminal angioplasty; HD=hemodialysis; ESKD=end stage kidney disease

Table 3. Risk factors for post-angiographic AVF failure from multivariate analysis*

	Crude HR	Adjusted HR	95% CI	p-value
Intra-access blood flow				
≤500 ml/min	1	1	-	-
501 to 750 ml/min	0.58	0.43	0.20 to 0.92	0.03
>750 ml/min	0.35	0.29	0.15 to 0.56	<0.001
Location of AVF				
Forearm	1	1		
Upper arm	2.54	2.58	1.41 to 4.73	0.002
Number of PTA procedures				
1	1	1		
≥2	2.50	1.86	1.02 to 3.40	0.042
BMI (every increase of 1 kg/m^2)	0.89	0.90	0.80 to 0.997	0.043

* Multivariate analysis adjusted for age, BMI, comorbid disease, smoking status, location of AVF, lifespan of AVF, repeated angioplasty, and frequency of HD per week D adequacy.

PTA=percutaneous transluminal angioplasty; AVF=arteriovenous fistula; BMI=body mass index; HR=hazard ratio; CI=confident interval

first procedure and upper arm AVF location was associated with higher risk of AVF failure than forearm AVF. Patients with high BMI were associated with decreasing risk of AVF failure (11% for every 1 kg/m²), after classified into high (>25 kg/m²), normal (18.5 to 25 kg/m²) and low (<18.5 kg/m²) BMI groups found that the patients in high BMI group had significant lower AVF failure when compared with normal BMI group (HR 0.28, 95% CI 0.10 to 0.78; p=0.016) while patient in low BMI group does not significantly increase risk of AVF failure (p=0.29) (Table 3).

Discussion

In the present study, there were 94 PTA procedures from 62 HD patients; 57.45% were the first time for PTA. Overall survival rate of AVF was 74.5% and 49.7% at 6 and 12 months and median post-angioplasty survival time was 341 days. These results were comparable with previous studies in that survival rate of AVFs ranged from 52 to 85% and 26 to 55% at 6 and 12 months after angioplasty[9,14,19,20], however, high post-angiographic survival rates were reported from studies that only included the patients with first time of PTA.

The NKF-KDOQI guideline recommends that HD patients should be surveilled for AVF dysfunction by regularly physical examination and review of clinical indicators associated with AV access dysfunction[5]. ABF may be also useful for detection of AV access dysfunction, however, there is no validated threshold of ABF that accurately predict further AVF loss. The previous RCT study of AVF surveillance using ultrasound dilution technique demonstrated the trend to detect AVF stenosis earlier, however, benefit on VA patency was inconclusive[21]. Moreover, the present study in patients without clinical of VA dysfunction found that the prophylactic intervention might increase risks for infection and pseudo-aneurysm without benefit on VA survival[22]. Nevertheless, levels of ABF threshold suggesting physicians to perform further investigations and treatment were vary by different guidelines, ranging from <300 to 500 ml/min[23,24]. The post-angioplasty ABF ≤500 ml/min discovered from the authors' study was significantly associated with further AVF failure therefore this value should be considered as threshold for close monitoring or surveillance of AVF re-stenosis after the angioplasty.

Successful angioplasty was defined as residual diameter stenosis less than 30%[5] and flow restoration that exceeded pre-defined threshold values[25]. In this current study, there was a limitation in angiographic evaluation for residual stenosis after angioplasty. This anatomical endpoint with a residual stenosis of less than 30%, however, was unreliable for predicting the long-term patency. A poor correlation between residual stenosis and subsequence patency was reported from a study of 96 interventions in native AVF[19] while Heye et al.[11] found that technical success PTA of a residual stenosis of <30% was associated with higher VA dysfunction from thrombosis (HR 6.15; p=0.013) and trended to increase VA dysfunction (HR 2.59; p=0.107). Heerwagen et al.[14] reported a good correlation between the anatomic endpoint (<30% residual stenosis) and hemodynamic endpoint (post-interventional flow >600 mL/min by endovascular flowmeter) with a discrepancy rate that was 25% (23 of 93 intervention). In the current study, the post-intervention ABF was 686±323 ml/min which was higher than the routine ABF prescription for adequate hemodialysis and the post-PTA 6-month patency rate was 60% more than the threshold of 50% from Kidney Disease Outcomes Quality Initiative (KDOQI) recommendations for clinical success of PTAs.

Post-angiographic ABF may predict long-term patency in AVG[26,27] but these findings in the AVF are still

inconclusive. It was found that post-angiographic ABF can predict survival rate of AVF after PTA. According to post-intervention ABF, the survival rate of AVF was significantly lower in the post-angiographic ABF ≤350 ml/min group by univariate and multivariate analyses, comparable with the recommendation that the functional VA should be able to deliver a flow rate of 350 to 400 mL/min without access recirculation for the entire HD treatment time[17]. These results were supported by the Tessitore et al.[7] study that higher post-intervention ABF was significantly associated with improved access longevity (RR: 0.995, 95% CI 0.990 to 0.999; p=0.044). A non-significant effect of post-angioplasty ABF on AVF patency, however, was also reported from previous studies. Heerwagen et al.[14] reported that post-interventional blood flow more than 600 mL/min did not improve primary patency at 12 months (p=0.35). This finding was similar with the result from Guedes-Marques et al.[15] in that increasing of post-intervention ABF more than 2 times of pre-intervention ABF, did not even have a significant impact on AVF survival (88.9% vs. 68.8% at 12 months; p>0.05). These findings might be explained by higher flow improvement reflects a more vascular sheer stress trauma that causes endothelial cell injury and stimulates inflammation and cell proliferation resulting in early restenosis from intimal hyperplasia[28,29].

The AVF age was previously identified as a factor that affected post-angiographic AVF patency. The study from Heerwagen et al.[14] found that increasing the fistula age every 10 months was associated with a decreasing of patency loss 2.6% (HR 0.974 for a one-month difference, 95% CI 0.950 to 0.998; p=0.038). This finding was confirmed by other 2 studies that shorter AVF age especially, less than 6 months, was associated with a significantly increased risk of patency loss. Heye et al.[11] reported that the older AVF had smaller probability of recurrence stenosis and occlusion and the AVF age less than 6 months was associated with shorter post-intervention patency and from the Maeda et al.[20] study, the age of fistula ≤6 months significantly increased risk of patency loss (RR 4.52; 95% CI 1.5 to 13.6, p=0.007). In the current study, the increasing of AVF age did not significantly increase post-angiographic patency (p=0.570), however, mean AVF age in the present study was relatively longer than previous study (mean 28.8 months vs. 18.95 months[8] and median 20 months[20]) and only about 10% of patients in that AVF age were less than 6 months. This might be mitigating the effect of AVF age on post-angiographic patency.

The association between location of AVF, type of AVF and post-angiographic AVF patency remained inconclusive. A non-significant difference in post-PTA patency between upper arm and forearm AVF was reported from a previous study (HR 1.17; p=0.27)[30] while Rajan et al.[10] reported lower post-PTA patency at 12 months in patients with an upper arm AVF (39% ±7 vs. 62% ±5; p=0.004). The upper arm AVF was associated with a higher risk for post-angiographic AVF failure that was observed in the current study (HR 3.38, 95% CI 1.57 to 7.25; p=0.002) and this may result from a higher flow rate and turbulent flow in the upper arm AVF and some patients had the upper arm AVF due to a limitation in forearm fistula creation from peripheral arterial disease in which peripheral artery disease, coronary artery disease and diabetes mellitus were previously reported as the risk factors of patency loss after intervention[19].

Most studies found that previous intervention and early recurrence of stenosis was a strong risk factor for AVF failure after PTA[11,12,14,31]. The angioplasty procedure itself causes endothelial injuries resulting in cellular proliferation and neo-intimal hyperplasia which are the major predisposing factors of VA dysfunction. In the present study by Chang et al.[28], it was found that the cellular proliferation indices using an antibody to the expression of a proliferating cell nuclear antigen, of both intimal and medial layers, were significantly greater in the post-PTA restenosis group than the primary stenosis group. In the restenosis group, proliferation indices correlated positively with the number of PTAs per lesion (r=0.754; p<0.001) and negatively with the interval from PTA to restenosis (r=-0.741; p<0.001). These results support the findings of the current study that patients with at least one previous PTA had higher risks for AVF failure after PTA.

From previous study of impact of obesity on AVF outcome in 388 HD patients (47.2% fistula first) found that obese patients (BMI ≥30 kg/m²) had poor long-term AVF survival compared with non-obese patients (HR 2.74; 95% CI 1.48 to 7.90; p=0.004)[31]. The Potential explanation of inferior survival of AVF in obese patients were 1) smaller utilized vessels, 2) soft tissue thickening that increase risk for vein transposition and/or infiltration during cannulation, 3) risk for hypercoagulable state, and 4) more aggressive myointimal hyperplasia. Contrast with the authors' study that high BMI and/or obese patients were associated with better post angioplasty AVF survival which may result from high ABF in these patients (mean ABF 686 vs. 789 ml/min in BMI <30 and ≥30 kg/m² respectively). Previous study which found that patients with overweight status (BMI ≥25 kg/m²) was independently associated with higher ABF (mean difference 160 ml/min; p=0.02)[32]. Yang et al.[33] study to determine the ideal body weight (IBW) base access flow threshold to predict AVF patency reported that low ABF/IBW is an independent predictor of AVF functional loss better than low ABF alone and suggested to use normalized ABF with body size for further investigation rather than use single ABF threshold for all patients. The authors analyzed by using normalized ABF with IBW and BMI the results was similar, higher ABF/IBW (ml/min/kg) and ABF/BMI (ml * m²/min/kg) were independently associated with lower

risk of AVF failure (HR 0.93; 95% CI 0.88 to 0.98; p=0.007 and HR 0.97; 95% CI 0.95 to 0.99; p=0.018 respectively).

The present study has several limitations. Because angiographies were not performed in all participants, therefore, some details discovered in angiography and probably related with AVF patency such as severity, length and multiple lesions of stenosis were lacking. These parameters, however, were defined variably among studies and previous study found that location of stenosis (HR 4.11; p=0.25), degree of stenosis (HR 0.44; p=0.51), length of stenosis (HR 3.08; p=0.08) and presence of multiple stenosis lesions (HR 0.18; p=0.67) were not significantly related with post-angioplasty VA dysfunction[11]. However, result from Aktas et al. study shown that grade of stenosis (HR 1.02; p=0.38) and multiple stenosis lesion (HR 0.62; p=0.43) were not significantly associated with secondary patency of AVF after angioplasty while length of stenosis (HR 1.01; p=0.003) associated with poor AVF patency[12].

Conclusion

PTA is an effective and highly successful intervention for AVF dysfunction in HD patients. Multiple factors are potentially related with post-angiographic AVF patency. Prediction of AVF patency is beneficial for close-up monitoring or a suggestion to create new VA in some patients. Post–angioplasty ABF can predict the patency of AVF, i.e., higher ABF flow correlated with longer survival time and a lower risk for AVF failure was reported. HD patients with post-angioplasty ABF <500 ml/min especially in patients with upper arm AVF and who previously received a PTA should be classified as high-risk patients for AVF failure which need more aggressive surveillance and monitoring. Further studies are needed to find out new innovations or medications that can prolong post-angiographic AVF patency especially in the high-risk groups.

What is already known on this topic?

From international guideline of vascular access in hemodialysis patient, supplemented intra-access blood flow (ABF) with clinical monitoring is preferred than clinical examination alone to early detection of vascular access dysfunction especially in patient with history of vascular access stenosis. However, there is no validated threshold of ABF to diagnose vascular access dysfunction or predict of vascular access survival which can be used for further optimal surveillance or preemptive intervention.

What this study adds?

From this study, patient with post angioplasty ABF <500 ml/min should undergo close monitoring for vascular access dysfuction especially in patients with upper arm AVF and previous angioplasty procedure. Post angioplasty ABF >500 ml/min may be one of the parameter of successful angioplasty; however, the benefit from preemptive re-angioplasty in these groups need to be identified in further study.

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Conflicts of interest

The authors declare no conflict of interest.

References

1. Moist LM, Trpeski L, Na Y, Lok CE. Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001-2004. Clin J Am Soc Nephrol 2008;3:1726–32. Available from: https://doi.org/10.2215/CJN.01240308
2. Pisoni RL, Arrington CJ, Albert JM, Ethier J, Kimata N, Krishnan M, et al. Facility hemodialysis vascular access use and mortality in countries participating in DOPPS: an instrumental variable analysis. Am J Kidney Dis 2009;53:475–91. Available from: https://doi.org/10.1053/j.ajkd.2008.10.043
3. Vassalotti JA, Jennings WC, Beathard GA, Neumann M, Caponi S, Fox CH, et al. Fistula First Breakthrough Initiative Community Education Committee: Fistula first breakthrough initiative: targeting catheter last in fistula first. Semin Dial 2012;25:303–10. Available from: https://doi.org/10.1111/j.1525-139X.2012.01069.x
4. Lee T. Fistula First Initiative: Historical Impact on Vascular Access Practice Patterns and Influence on Future Vascular Access Care. Cardiovasc Eng Technol. 2017;8(3):244–54 Available from: https://doi.org/10.1007/s13239-017-0319-9
5. Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. American Journal of Kidney Diseases. 2020;75(4):S1–164. Available from: https://doi.org/10.1053/j.ajkd.2019.12.001
6. Roca-Tey R, Samon Guasch R, Ibrik O, García-Madrid C, Herranz JJ, García-González L, et al. Vascular access surveillance with blood flow monitoring: a prospective study with 65 patients. Nefrologia 2004;24:246–52. Available from: https://pubmed.ncbi.nlm.nih.gov/15283315/

7. Tessitore N, Lipari G, Poli A, Bedogna V, Baggio E, Loschiavo C, et al. Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. Nephrol Dial Transplant 2004;19:2325–33. Available from: https://doi.org/10.1093/ndt/gfh316
8. Tessitore N, Mansueto G, Bedogna V, Lipari G, Poli A, Gammaro L, et al. A prospective controlled trial on effect of percutaneous transluminal angioplasty on functioning arteriovenous fistulae survival. J Am Soc Nephrol 2003;14:1623–27. Available from: https://doi.org/10.1097/01.asn.0000069218.31647.39
9. Haage P, Günther RW. Radiological intervention to maintain vascular access. Eur J Vasc Endovasc Surg 2006;32:84–9. Available from: https://doi.org/10.1016/j.ejvs.2005.10.004
10. Rajan DK, Bunston S, Misra S, Pinto R, Lok CE. Dysfunctional autogenous hemodialysis fistulas: outcomes after angioplasty--are there clinical predictors of patency? Radiology 2004;232:508–15. Available from: https://doi.org/10.1148/radiol.2322030714
11. Heye S, Maleux G, Vaninbroukx J, Claes K, Kuypers D, Oyen R. Factors influencing technical success and outcome of percutaneous balloon angioplasty in de novo native hemodialysis arteriovenous fistulas. Eur J Radiol 2012;81:2298–303. Available from: https://doi.org/10.1016/j.ejrad.2011.09.004
12. Aktas A, Bozkurt A, Aktas B, Kirbas I. Percutaneous transluminal balloon angioplasty in stenosis of native hemodialysis arteriovenous fistulas: technical success and analysis of factors affecting postprocedural fistula patency. Diagn Interv Radiol. 2015;21(2):160–6. Available from: https://doi.org/10.5152/dir.2014.14348
13. Neuen BL, Gunnarsson R, Webster AC, Baer RA, Golledge J, Mantha ML. Predictors of patency after balloon angioplasty in hemodialysis fistulas: a systematic review. J Vasc Interv Radiol 2014;25:917–24. Available from: https://doi.org/10.1016/j.jvir.2014.02.010
14. Heerwagen ST, Hansen MA, Schroeder TV, Ladefoged SD, Lönn L. Endovascular treatment of hemodialysis arteriovenous fistulas: is immediate post-interventional blood flow a predictor of patency. J Vasc Access 2012;13:315–20. Available from: https://doi.org/10.5301/jva.5000046
15. Guedes-Marques M, Maia PA, Neves F, Ferreira A, Cruz J, Carvalho D, et al. Does pre- and post-angioplasty Doppler ultrasound evaluation help in predicting vascular access outcome? J Vasc Access 2016;17:465–70. Available from: https://doi.org/10.5301/jva.5000604
16. Krivitski NM. Novel Method to Measure Access Flow During Hemodialysis by Ultrasound Velocity Dilution Technique. ASAIO Journal 1995;41(3):741-5. https://doi.org/10.1097/00002480-199507000-00111
17. Sidawy AN, Gray R, Besarab A, Henry M, Ascher E, Silva M, et al. Recommended standards for reports dealing with arteriovenous hemodialysis accesses. J Vasc Surg 2002;35:603–10. Available from: https://doi.org/10.1067/mva.2002.122025
18. Rubinstein LV, Gail MH, Santner TJ. Planning the duration of a comparative clinical trial with loss to follow-up and a period of continued observation. J Chronic Dis 1981;34:469-79. Available from: https://doi.org/10.1016/0021-9681(81)90007-2
19. Clark TWI, Hirsch DA, Jindal KJ, Veugelers PJ, LeBlanc J. Outcome and prognostic factors of restenosis after percutaneous treatment of native hemodialysis fistulas. J Vasc Interv Radiol 2002;13:51–9. Available from: https://doi.org/10.1016/s1051-0443(07)60009-8
20. Maeda K, Furukawa A, Yamasaki M, Murata K. Percutaneous transluminal angioplasty for Brescia-Cimino hemodialysis fistula dysfunction: technical success rate, patency rate and factors that influence the results. Eur J Radiol 2005;54:426–30. Available from: https://doi.org/10.1016/j.ejrad.2004.07.011
21. Polkinghorne KR, Lau KK, Saunder A, Atkins RC, Kerr PG. Does monthly native arteriovenous fistula blood-flow surveillance detect significant stenosis–a randomized controlled trial. Nephrol Dial Transplant. 2006;21(9):2498-506. Available from: https://doi.org/10.1093/ndt/gfl242
22. Dember LM, Holmberg EF, Kaufman JS. Randomized controlled trial of prophylactic repair of hemodialysis arteriovenous graft stenosis. Kidney Int 2004;66:390–98. Available from: https://doi.org/10.1111/j.1523-1755.2004.00743.x
23. Tordoir J, Canaud B, Haage P, Konner K, Basci A, Fouque D, et al. EBPG on Vascular Access. Nephrology Dialysis Transplantation. 2007;22(suppl_2):ii88–117. Available from: https://doi.org/10.1093/ndt/gfm021
24. Fluck R, Kumwenda M. Renal association clinical practice guidelines on vascular access for hemodialysis. Nephron Clin Pract, 2011,118(suppl 1):c225-c240 Available from: https://doi.org/10.1159/000328071
25. Gray RJ, Sacks D, Martin LG, Trerotola SO. Society of Interventional Radiology Technology Assessment Committee: Reporting standards for percutaneous interventions in dialysis access. J Vasc Interv Radiol 2003;14:S433–S432. Available from: https://doi.org/10.1097/01.rvi.0000094618.61428.58
26. Itkin M, Trerotola SO, Stavropoulos SW, Kobrin S, Tuite CM, Shlansky-Goldberg RD, et al. Can catheter-based blood flow measurement after hemodialysis access intervention predict long-term patency? J Vasc Interv Radiol 2008;19:S37.
27. Murray BM, Herman A, Mepani B, Rajczak S. Access flow after angioplasty predicts subsequent arteriovenous graft survival. J Vasc Interv Radiol 2006;17:303–8. Available from: https://doi.org/10.1097/01.rvi.0000196337.03227.a1
28. Chang C-J, Ko P-J, Hsu L-A, Ko Y-S, Ko Y-L, Chen C-F, et al. Highly increased cell proliferation activity in the restenotic hemodialysis vascular access after percutaneous transluminal angioplasty: implication in prevention of restenosis. Am J Kidney

Dis 2004;43:74–84. Available from: https://doi.org/10.1053/j.ajkd.2003.09.015
29. Roy-Chaudhury P, Sukhatme VP, Cheung AK. Hemodialysis vascular access dysfunction: a cellular and molecular viewpoint. J Am Soc Nephrol. 2006;17:1112–27. Available from: https://doi.org/10.1681/asn.2005050615
30. Wu C-C, Wen S-C, Yang C-W, Pu S-Y, Tsai K-C, Chen J-W. Plasma ADMA predicts restenosis of arteriovenous fistula. J Am Soc Nephrol 2009;20:213–22. Available from: https://doi.org/10.1681/asn.2008050476
31. Bountouris I, Kristmundsson T, Dias N, Zdanowski Z, Malina M. Is Repeat PTA of a failing hemodialysis fistula durable? Int J Vasc Med 2014;2014:369687. Available from: https://doi.org/10.1155/2014/369687
32. Arhuidese IJ, Holscher CM, Elemuo C, Parkerson GR, Johnson BL, Malas MB. Impact of Body Mass Index on Outcomes of Autogenous Fistulas for Hemodialysis Access. Ann Vasc Surg. 2020;68:192–200. Available from: https://doi.org/10.1016/j.avsg.2020.04.009
33. Yang CY, Wu BS, Wang YF, Lee YHW, Tarng DC. Weight-Based Assessment of Access Flow Threshold to Predict Arteriovenous Fistula Functional Patency. Kidney International Reports. 2022;7(3):507–15. Available from: https://doi.org/10.1016/j.ekir.2021.11.016