Effects of ultrasound-guided percutaneous transluminal angioplasty for stenosis of arteriovenous fistula used for hemodialysis and related factors influencing patency

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AIM: *To evaluate the effects of ultrasound-guided percutaneous transluminal angioplasty (PTA) on the arteriovenous fistula (AVF) stenosis of hemodialysis graft.*
MATERIALS AND METHODS: *A total of 189 patients with AVF dysfunction who underwent ultrasound-guided PTA were enrolled. Their baseline data were collected. The Log-rank test, Kaplan-Meier survival analysis and univariate Cox proportional risk regression analysis were performed to compare the primary and secondary patency rates and to explore the related influencing factors.*
RESULTS: *A total of 256 sites of stenosis were found by ultrasonography, including 80 sites in anastomotic segment, 28 in supply artery segment, 60 in drainage vein segment and 88 in proximal segment of the internal fistula vein. The mean length of stenosis was 22.4 mm, and the mean degree was 93.4%. The success rate of surgery was 96.09%, with the postoperative residual stenosis of >30% in 3.91% of patients. The clinical success rate was 97.66% and complications occurred in 2.34% of patients. The mean follow-up time was 30.2 months, and vascular patency was observed in 25.93% of patients. The primary patency rates in 1st, 2nd and 3rd years after surgery were 84.66%, 60.85% and 21.69%, respectively, and the patients with diabetes (P=0.002) and old age (P<0.001) had lower rates. The secondary patency rates in 1st, 2nd and 3rd years after surgery were 91.00%, 74.07% and 32.80%, respectively, and a lower secondary patency rate was significantly correlated with diabetes (P=0.019), old age (P<0.001), long stenosis segment (P<0.001) and high degree of residual stenosis (P=0.012).*
CONCLUSIONS: *Vascular patency can be maintained in hemodialysis patients with AVF dysfunction through repeated intervention, and there is no need to shorten the venous segment by surgery. Ultrasound-guided PTA is a promising substitute for traditional surgery.*

KEY WORDS: Arteriovenous Fistula, Hemodialysis, Ultrasound, Percutaneous Transluminal Angioplasty

Introduction

End stage renal disease (ESRD) is the terminal stage of chronic kidney disease. It is the irreversible change of renal structure and function caused by multiple factors, which eventually leads to the complete loss of renal function. According to the World Health Organization, the global mortality rate of ESRD patients in 2012 was 1.5%, ranking the 14th among those of the major causes for death. Therefore, ESRD patients have become a heavy burden on public health resources [1]. In 2012, a Chinese epidemiological study reported that the number of adults with chronic kidney disease in China was 120 million, and the number of patients receiving renal replacement therapy grew at a rate of over 11% annually [2].

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As one of the main methods of renal replacement therapy, hemodialysis is a process in which blood is led outside and then returned to the body through the vascular access (VA), so the life expectancy and quality of lift of patients receiving maintenance hemodialysis (MHD) are largely determined by the quality of VA. About 15%-20% of patients receiving hemodialysis are hospitalized because of VA-related complications, and 14%-20% of the total medical expenses are spent on the establishment and maintenance of VA [3].

The hemodialysis for ESRD and its VA are now crucial for MHD patients, and the establishment of arteriovenous fistula (AVF) access is the first choice [4]. The National Kidney Foundation and the National Kidney Foundation Kidney Disease Outcomes Quality Initiative have used the service life of AVF and low infection rate as the criteria to select VA of early hemodialysis for ESRD patients at various stages [5]. The thrombosis rate of artificial polytetrafluoroethylene (PTFE) access was 10 times that of AVF [6,7]. Even though it is well-documented that AVF has advantages over artificial PTFE access, they both eventually lose functions, and then patients have to receive interventional therapy and surgery, and even suffer from chronic hemodialysis-related complications. Significantly stenosed access is the most common complication which induces AVF dysfunction during hemodialysis, also requiring repeated percutaneous transluminal angioplasty (PTA) to keep the patency. However, the effect is limited, with the patency rate of 26%-62% in the 1st year. Besides, the rate is affected by many factors [8-10]. Thus, we herein retrospectively assessed the effects of ultrasound-guided PTA on the AVF stenosis of hemodialysis graft, and analyzed the factors influencing the success rate and patency rate of AVF.

Materials and Methods

Baseline Clinical Data

This study has been approved by the ethics committee of our hospital, and written informed consent has been obtained from all patients. This study enrolled 189 patients with AVF dysfunction who underwent ultrasound-guided PTA in our hospital from January 2016 to October 2019. Their baseline data were collected from electronic medical and hospitalization records. The patients included 110 males and 79 females with the mean age of (59.5±12.1) years old. All enrolled patients received ultrasound-guided PTA for the first time. Inclusion criteria: AVF dysfunction was confirmed by physical examination and color Doppler ultrasonography; without history of stenosis or thrombosis, or other complications. Exclusion criteria: Patients receiving comprehensive dialysis, o having PTFE or AVF thrombosis.

Apparatus

EDGE color Doppler ultrasound system was purchased from SonoSite (USA), using an HFL38x/13-6 MHz transducer probe. the Mustang high-pressure balloon catheter (Boston Scientific, USA; push rod length: 40 cm, balloon diameter: 4~7 mm) was utilized for peripheral blood vessels, accompanied by 5F sheath canal, 0.89 mm hydrophilic coated guidewire and balloon expansion pressure pump.

Surgical Methods

Selection of surgical approach: Surgical approach was selected based on the site of stenosis and local anatomical characteristics. For AVF, if stenosis occurred in the anastomotic region, the approach was selected at the proximal end, and the sheath was reversely placed. If stenosis occurred in the puncture region, the approach was selected at the distal end, and the sheath was placed in the forward direction.

Selection of balloon: The balloon length was generally determined by the range, location and shape of stenosis. For non-anastomotic stenosis, a balloon with a length of 4 cm was usually selected. If the range of stenosis was small and the blood vessel was curved (e.g. anastomotic stenosis), a balloon of 2 cm in length was selected. The diameter of balloon was determined according to the inner diameter of normal blood vessel adjacent to the stenotic vessel. Generally, the balloon with a diameter of 1.1-fold that of the normal blood vessel adjacent to the stenotic vessel was selected for expansion. In most cases, balloons with the inner diameters of 5 mm, 6 mm and 7 mm were employed.

Surgical procedure: First, the expansion path was established. After intravenous heparinization using 0.5 mg/kg unfractionated heparin, a guide wire was introduced through the sheath under real-time ultrasound guidance. Then a balloon catheter was placed along the guide wire into the site of stenosis, and gradually pressurized to expand the balloon as much as possible. Afterwards, stenosis was eliminated and kept for 60 s, and the balloon was thereafter slowly retracted. The procedure could be repeated once when necessary to further expand the stenosis site.

Related Influencing Factors and Criteria for Successful Surgery

Anatomic factors: Position, length and degree of stenosis, and multiple stenoses. AVF stenosis consisted of 4 segments: Supply artery segment, anastomotic segment, proximal segment of the internal fistula vein, and drainage vein segment.

Clinical factors: Age, gender, type and location of fistula (in left or right arm), and complication with diabe-

tes and primary diseases. Criterion for operational success: With a residual stenosis of <30% confirmed by postoperative ultrasonography. Criterion for clinical success: Dialysis can be effectively conducted.
Primary patency rate: AVF is kept unobstructed between the first and next interventions. Secondary patency rate: AVF is unobstructed after PTA until restenosis/occlusion occurs, requiring surgical embolization, repair or even discarding. According to the standards formulated by the Society of Cardiovascular and Interventional Radiology, complications are classified into primary and secondary ones [11]. Early recurrence refers to the loss of AVF function within 6 months after surgery.

Statistical Analysis

All data were statistically analyzed by SPSS 16.0 software. The normal distribution of measurement data was analyzed by the Shapiro-Wilk test, and they were expressed as mean ± standard deviation (x ± s) or median (range). Means were compared by the t test, and medians were compared with the Mann-Whitney U test. The numerical data were subjected to the Chi-square or Fisher's exact test to calculate the odds ratio (OR) and 95% confidence interval (CI) of each variable. The Log-rank test, Kaplan-Meier survival analysis and univariate Cox proportional risk regression analysis were carried out to compare the primary and secondary patency rates and to explore the related influencing factors. P<0.05 was considered statistically significant.

Results

Baseline Clinical Data

A total of 256 sites of stenosis were found in 189 AVF patients by ultrasonography, including 80 sites located in the anastomotic segment, 28 in the supply artery segment, 60 in the drainage vein segment and 88 in the proximal segment of the internal fistula vein. The mean length of stenosis was 22.4 mm (median: 14 mm, 1-124 mm), and the mean degree of stenosis was 93.4% (median: 91.4%, 47%-98%) (Table I).

Treatment Outcomes of Ultrasound-Guided Pta

The success rate of ultrasound-guided PTA was 96.09% (246/256), with the postoperative residual stenosis of >30% in 3.91% (10/256) of patients. The clinical success rate was 97.66% (250/256) and the complications occurred in 2.34% (6/256) of patients. The mild complications included 3 cases of vasospasm and 1 case of hematoma, and the serious complications included 1 case of vascular rupture and 1 case of thrombogenesis.

Table I - *Baseline clinical data.*

Data	N (%)
Age (year)	59.5±12.1
GENDER (MALE/FEMALE)	110/79
CAUSE FOR ESRD	
ADPKD	25 (13.23)
Diabetes	106 (56.08)
Glomerular disease	8 (4.23)
Hypertension	25 (13.23)
Unknown	25 (13.23)
AVF type	
Brachial artery-basilic vein	9 (4.76)
Brachial artery-median cubital vein	1 (0.53)
Brachial artery-cephalic vein	15 (7.94)
Radial artery-basilic vein	1 (0.53)
Radial artery-cephalic vein	163 (86.24)
AVF site	
Right	41 (21.69)
Left	147 (78.31)
Complication with diabetes	117 (61.90)
STENOSIS SITE	
Anastomotic segment	41 (21.69)
Supply artery segment	20 (10.58)
Drainage vein segment	43 (22.75)
Proximal segment	85 (44.97)

ADPKD: Autosomal dominant polycystic kidney disease.

Factors Affecting Primary and Secondary Patency Rates

The mean follow-up time was 30.2 (1-58) months, and vascular patency was observed in 25.93% (49/189) of AVF patients. The primary patency rates in the 1st, 2nd and 3rd years after surgery were 84.66%, 60.85% and 21.69%, respectively, and the patients with diabetes (P=0.002) and old age (P<0.001) had lower rates (Table II, Table III and Fig. 1). The secondary patency rates in the 1st, 2nd and 3rd years after surgery were 91.00%, 74.07% and 32.80%, respectively, and a lower secondary patency rate was significantly correlated with diabetes (P=0.019), old age (P<0.001), long stenosis segment (P<0.001) and high degree of residual stenosis (P=0.012) (Table III and Fig. 2).

Discussion

ESRD patients require high-quality temporary or permanent vascular channels for hemodialysis treatment [12]. Due to its good patency and low incidence of complications, AVF channels have become the first choice in relevant guidelines in Europe and the United States [13]. Vascular channel complications are one of the leading causes of death in ESRD patients. Venous stenosis is the most common cause of AVF dysfunction, with complicated pathogenesis, but its mechanism has not been fully

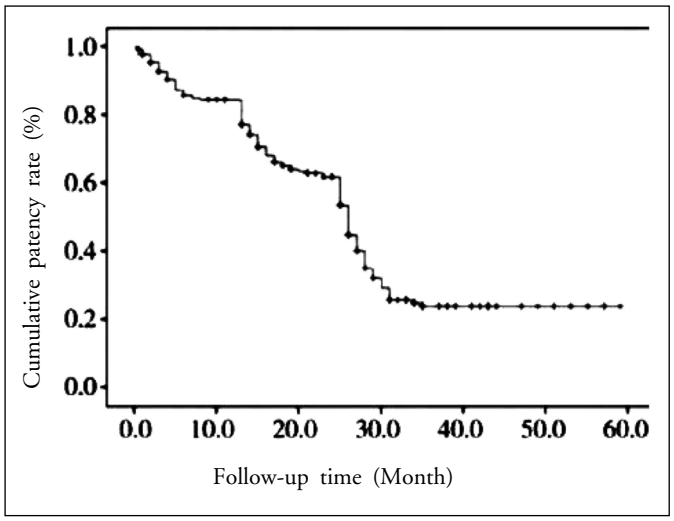

Fig. 1: Kaplan-Meier curve of postoperative primary patency rate.

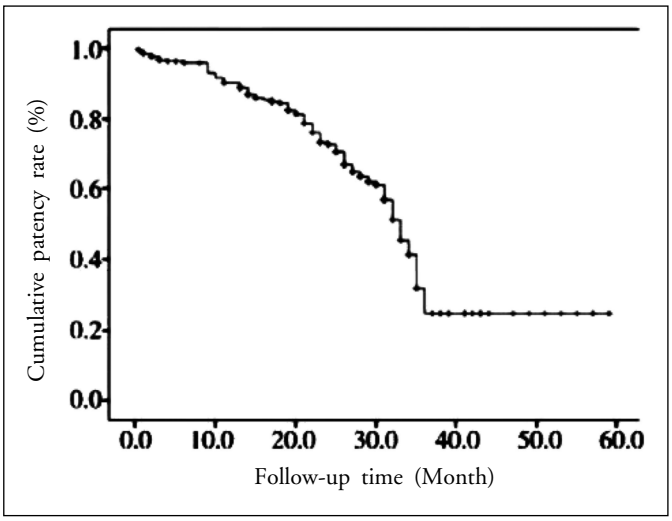

Fig. 2: Kaplan-Meier curve of postoperative secondary patency rate.

TABLE II - *Factors affecting primary patency rate.*

Data	Primary patency rate (%)					
	1 year (160)	2 years (115)	3 years (41)	Duration of patency	Log-rank	P
GENDER					0.218	0.804
Female (79)	83.54	60.76	21.52	28.2 (23.4-33.0)		
Male (110)	85.45	60.00	21.82	29.6 (24.1-33.0)		
CAUSE FOR ESRD					32.287	<0.001
ADPKD (25)	100.00	92.00	44.00	40.8 (31.2-49.6)		
Diabetes (106)	82.08	56.60	14.15	24.2 (20.7-28.8)		
Glomerular disease (8)	100.00	100.00	62.50	39.7 (29.8-49.6)		
Hypertension (25)	72.00	32.00	12.00	19.3 (14.1-24.2)		
Unknown (25)	88.00	64.00	28.00	38.2 (29.7-47.3)		
AVF type					1.879	0.765
Brachial artery-basilic vein (9)	100.00	77.78	44.44	36.6 (21.6-54.2)		
Brachial artery-median cubital vein (1)	100.00	100.00	0.00	33.4 (32.1-35.1)		
Brachial artery-cephalic vein (15)	86.67	80.00	33.33	27.2 (21.4-36.3)		
Radial artery-basilic vein (1)	100.00	100.00	0.00	33.1 (33.1-33.1)		
Radial artery-cephalic vein (163)	83.44	57.67	19.63	27.5 (23.0-33.3)		
AVF site					0.214	0.785
Right (41)	87.80	65.85	24.39	28.6 (23.7-33.4)		
Left (147)	84.35	59.86	21.09	28.2 (24.9-32.5)		
Complication with diabetes					8.287	0.008
No (72)	94.44	72.22	30.56	33.7 (29.5-37.7)		
Yes (117)	78.63	53.85	16.24	24.8 (21.7-29.4)		
Anastomotic segment					0.156	0.638
No (148)	83.78	60.81	22.97	28.7 (25.1-32.0)		
Yes (41)	87.80	60.98	17.07	28.1 (23.7-32.5)		
Supply artery segment					0.223	0.646
No (169)	85.21	60.36	21.89	28.6 (25.5-31.3)		
Yes (20)	80.00	65.00	20.00	26.7 (22.0-31.3)		
DRAINAGE VEIN SEGMENT					0.123	0.796
No (146)	84.93	60.27	20.55	27.5 (24.2-31.5)		
Yes (43)	83.72	62.79	25.58	29.4 (25.6-34.5)		
PROXIMAL SEGMENT					0.945	0.256
No (104)	87.50	67.31	22.12	31.5 (27.0-36.6)		
Yes (85)	81.18	52.94	21.18	25.7 (23.6-29.6)		
Multiple					0.354	0.685
No (126)	84.92	57.94	16.67	28.7 (25.6-31.5)		
Yes (63)	84.13	66.67	31.75	27.2 (18.6-35.9)		
Total	84.66	60.85	21.69	—	—	—

ADPKD: Autosomal dominant polycystic kidney disease

Table III - *Factors affecting primary and secondary patency rates.*

Parameter	RR	95%CI	P
PRIMARY PATENCY RATE			
Age	1.062	1.043-1.079	<0.001
Complication with diabetes	1.021	1.004-1.031	0.002
Degree of stenosis	0.994	0.978-1.032	0.768
Length of stenosis	1.005	1.001-1.022	0.059
Degree of residual stenosis	1.022	0.994-1.035	0.115
SECONDARY PATENCY RATE			
Age	1.049	1.034-1.081	<0.001
Complication with diabetes	1.047	1.004-1.061	0.019
Degree of stenosis	1.019	0.976-1.045	0.487
Length of stenosis	1.017	1.002-1.026	0.001
Degree of residual stenosis	1.030	1.003-1.043	0.012

elucidated. Pathophysiology suggests that cytokines initiate the activation and proliferation of smooth muscle cells, endothelial cells and macrophages, leading to intimal hyperplasia [14]. When the stenosis is >50% (hemodynamics is significantly weakened), the dialysis efficiency is reduced. If not treated, it may lead to thrombosis. Therefore, early diagnosis and treatment of AVF stenosis is very important. The principles for treatment of internal fistula stenosis are as follows. First, limited vascular resources should be protected as much as possible. Second, the surgical method should be as simple as possible to reduce trauma and retain the dialysis puncture point. Dialysis can be performed after surgery to avoid deep vein catheterization. Due to its simple and easy-to-use characteristics, precise treatment effect, and repeatability, PTA can keep internal fistula vessels and dialysis puncture points to the greatest extent. In recent years, it has gradually replaced surgery and become the first choice for the treatment of AVF stenosis.

The repair of AVF dysfunction is usually more difficult than vascular transplantation, which may be due to the thin and unfixed vein walls, the difficulty in clinical and imaging identification for abnormal anatomy of the anastomosis, potential stenosis between the blood supply artery and the superior vena cava, difficult passing due to the severe degree of stenosis, the difficulty in identifying the anatomy of internal fistula when there is collateral vein, and the excessive angulation of the anastomotic level. The anatomic distribution of internal fistula stenosis also affects the treatment and results of percutaneous approach.

This study found that 42.33% of AVF stenosis was located near the anastomosis area, and the length of the stenosis was mostly less than 2 cm (median length: 14 mm, 1-124 mm), which was similar to previous studies [15]. Heye et al. included 162 patients with a total of 167 malfunctioning AVFs, all of whom underwent the first PTA, with the success rate of 87.1%12. Manninen et al. reported that the success rate of surgical technology for 74 patients with nonfunctional AVF was 98% [14]. The average stenosis degree of the patients in this study was 93.4%, and the success rate of surgical technique was 96.09%. Heye et al. reported 48.5%, 31.4%, and 22.5%, respectively [12]. Manninen et al. evaluated the long-term effects of endovascular treatment in 51 patients with fistula stenosis or occlusion of the wrist [14]. The patency rates of the first, second and third year were 44%, 40%, and 32%, respectively. Turmel-Rodrigues et al. reported that the primary patency rates for the first and second years were 53% and 46%, respectively [13]. Kim et al. reported the similar or even lower efficacy data of PTA in the treatment of AVF and transplanted intravascular fistula with or without thrombosis [15]. In this study, the primary patency rates after surgery in the first, second, and third years were 84.66%, 60.85% and 21.69%, respectively, higher than those reported in the literature; Mantha et al. evaluated 100 patients with percutaneously treated AVF and graft endovascular fistula dysfunction [16], and the results showed the primary patency rates at 12 and 18 months were 55% and 47%, respectively. In the study of Heye et al., the secondary patency rates in the first, second, and third years were 83.6%, 68.4%, and 60.8%, respectively [12]. In the literature of Manninen et al., the data were 85%, 79% and 79%, respectively14. Herein, the secondary patency rates for the first, second, and third years were 91.00%, 74.07% and 32.80%, respectively; in this study, there was no significant relationship between the type of AVF and the primary and secondary patency.

In this study, there was no significant relationship between AVF position and postoperative patency rate, which was consistent with reports in other literatures [15]. There was no significant relationship between stenosis sites and primary and secondary patency rates, which was also consistent with other literatures [17-20]. However, Turmel-Rodrigues et al. reported that the primary higher patency rates in patients with stenosis of the supplying arterial segment [13]. Herein, the age of patients with diabetes had a significant effect on the primary patency rate; with the increase of patients' age, the duration of the primary patency rate was shortened ($P < 0.001$); the average patency time of the first stage of the patients with diabetes was 24.8 months, and that of non-diabetic patients were 33.7 months ($P = 0.002$). Heye et al. showed a correlation between age and primary patency rate [12], while Rajan et al. showed a correlation between age and type of internal fistula [9]. In this study, patients' age, accompanied by diabetes, length of stenosis, early restenosis development, and residual stenosis were closely related to the secondary patency rate. Heye et al. found that only age and the existence time of AVF were closely related to the secondary patency rate [12]. Rajan et al. did not find any factors related to the secondary patency rate [9]. The incidence rate of complications in this group was 3%, which was consistent with most of the studies [15,18].

Conclusions

In summary, AVF dysfunction in hemodialysis can be kept unobstructed through continuous follow-up and repeated intervention, without the need to shorten the venous segment by surgery. Ultrasound-guided PTA is an effective alternative to traditional surgery for AVF dysfunction.

Riassunto

Studio per valutare gli effetti dell'angioplastica percutanea transluminale (PTA) guidata da ultrasuoni sulla stenosi della fistola artero-venosa (AVF) dell'innesto per emodialisi. A questo scopo sono stati arruolati un totale di 189 pazienti con disfunzione di AVF sottoposti a PTA ecoguidata. Sono stati raccolti i loro dati di base. Sono stati eseguiti il test Log-rank, l'analisi di sopravvivenza Kaplan-Meier e l'analisi univariata di regressione proporzionale del rischio Cox per confrontare i tassi di pervietà primaria e secondaria ed esplorare i relativi fattori di influenza.

RISULTATI: L'ecografia ha rilevato un totale di 256 siti di stenosi, inclusi 80 siti nel segmento anastomotico, 28 nel segmento dell'arteria di alimentazione, 60 nel segmento della vena di drenaggio e 88 nel segmento prossimale della vena interna della fistola. La lunghezza media della stenosi era di 22,4 mm e il grado medio era del 93,4%. Il tasso di successo dell'intervento è stato del 96,09%, con stenosi residua postoperatoria> 30% nel 3,91% dei pazienti. Il tasso di successo clinico è stato del 97,66% e si sono verificate complicanze nel 2,34% dei pazienti. Il tempo medio di follow-up è stato di 30,2 mesi e la pervietà vascolare è stata osservata nel 25,93% dei pazienti. I tassi di pervietà primaria nel 1°, 2° e 3° anno dopo l'intervento erano rispettivamente dell'84,66%, del 60,85% e del 21,69%, e i pazienti con diabete (P = 0,002) e vecchiaia (P <0,001) avevano tassi più bassi. I tassi di pervietà secondaria nel 1°, 2° e 3° anno dopo l'intervento erano rispettivamente del 91,00%, del 74,07% e del 32,80% e un tasso di pervietà secondaria inferiore era significativamente correlato al diabete (P = 0,019), vecchiaia (P <0,001), segmento di stenosi lunga (P <0,001) e alto grado di stenosi residua (P = 0,012).

CONCLUSIONE: La pervietà vascolare può essere restaurata nei pazienti in emodialisi con disfunzione AVF mediante interventi ripetuti e non è necessario abbreviare il segmento venoso con un intervento chirurgico. La PTA a ultrasuoni è un promettente sostituto della chirurgia tradizionale.

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