Morphological Lesion Types Are Associated with Primary and Secondary Patency Rates after High-Pressure Balloon Angioplasty for Dysfunctional Arteriovenous Fistulas

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Keywords

Hemodialysis · Arteriovenous fistula dysfunction · Neointimal hyperplasia · Morphological type · Patency rate

Abstract

Background: Neointimal hyperplasia (NIH) is believed to be the main reason for arteriovenous fistula (AVF) dysfunction, but other mechanisms are also recognized to be involved in the pathophysiological process. This study investigated whether different morphological types of AVF lesions are associated with the patency rate after percutaneous transluminal angioplasty (PTA). **Methods:** This retrospective study included 120 patients who underwent PTA for autogenous AVF dysfunction. All the cases were evaluated under Doppler ultrasound (DU) before intervention and divided into 3 types: Type I (NIH type), Type II (non-NIH type), and Type III (mixed type). Prognostic and clinical data were analyzed by Kaplan-Meier analysis and the Cox proportional hazards model. **Results:** There was no statistical difference in baseline variables among groups, except for lumen diameter. The primary patency rates in Type I, Type II, and Type III groups were 78.4, 93.2, and 83.2% at 6 months and 59.5, 84.7, and 75.5% at 1 year, respectively. The secondary patency rates in

Type I, Type II, and Type III groups were 94.4, 97.1, and 100% at 6 months and 90.5, 97.1, and 94.7% at 1 year, respectively. The Kaplan-Meier curve showed that the primary and secondary patency rates of Type I group were lower than those of Type II group. Multivariable Cox regression analysis demonstrated that postoperative primary patency was correlated with end-to-end anastomosis (hazard ratio [HR] = 2.997, $p = 0.008$, 95% confidence interval [CI]: 1.328–6.764) and Type I lesion (HR = 5.395, $p = 0.004$, 95% CI: 1.730–16.824). **Conclusions:** NIH-dominant lesions of AVF evaluated by DU preoperatively were a risk factor for poor primary and secondary patency rate after PTA in hemodialysis patients.

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Introduction

In China, over 500,000 patients with end-stage renal disease (ESRD) rely on hemodialysis treatment, and 80.5–88.3% of those patients use an autogenous arteriovenous fistula (AVF) [1, 2]. However, AVF stenosis is

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common and may lead to a series of problems, such as inadequate dialysis volume, difficulties in cannulation, and ultimately thrombotic events. Endovascular therapy has become a first-line treatment to correct stenosis of dysfunctional AVFs, but it needs to be repeated frequently to maintain AVF patency [3].

Neointimal hyperplasia (NIH) is the major reason for AVF stenosis; however, new evidence shows that besides NIH, other mechanisms, such as adventitia constriction, valve-related stenosis, and inflow artery atherosclerosis, also participates in the pathological process [4–9]. Lesion features can be detected by Doppler ultrasound (DU), which is often undertaken before interventions for dysfunctional AVFs, but it is unclear whether certain morphological lesion types have a unique response to angioplasty treatment. As a consequence, physicians have difficulties selecting an individualized therapeutic strategy for these particular patients.

In this study, cases receiving endovascular repair for dysfunctional AVFs were classified into 3 types according to the preoperative DU imaging. We evaluated the primary and secondary patency rates after percutaneous transluminal angioplasty (PTA) with a high-pressure balloon to determine whether the morphological types of dysfunctional AVFs with clinical indicators are associated with the results of interventional repair.

Materials and Methods

Patients and Data Collection

This is a retrospective study conducted in a tertiary academic referral center and approved by the Ethics Committee on Human Research at Huashan Hospital, Fudan University, Shanghai (KY2017-429). From January 2015 to December 2018, 192 consecutive ESRD patients who received PTA for a dysfunctional AVF were reviewed (online suppl. Fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000516883). The indication for PTA was an AVF with >50% stenosis in conjunction with at least one clinical or physiological abnormality, such as inadequate dialysis flow and abnormal physical findings according to 2006 Kidney Disease Outcomes Quality Initiative guidelines [10]. In this cohort, we only performed PTA for patients who had been receiving hemodialysis for at least 1 month. PTA for immature AVFs was excluded. Hybrid procedures, adjacent drug-eluted balloon angioplasty, or stent implantation was also excluded, leaving 120 cases treated by standard high-pressure angioplasty to analyze. All patients provided written informed consent. The preoperative demographic data, procedure information, and follow-up details were all collected by electronic medical records.

Ultrasound Assessment and Stenosis Classification

Before the operation, each patient underwent preoperative measurements and vein mapping. The inflow arteries, anastomot-

ic sites, and outflow veins were all scanned, and the intimal thickness, flow volume, and inner and outer diameters at the stenosis sites were recorded to identify the morphological patterns. The typical sonograms are shown in Figure 1. All the lesions were categorized as Types I, II, or III. In Type I group, stenosis was >50%, and the intimal thickness measured >0.6 mm at the stenosis lesion site without concomitant inflow artery or distal vein stenosis, which can cause flow limitation. Type I is thought to be initially caused by NIH. In Type II group, the stenosis was >50%, and intimal thickness measured ≤ 0.6 mm at the stenosis lesion site without concomitant inflow artery or distal vein stenosis. NIH is not thought to be the initial cause of stenosis in Type II lesions. In Type III group, the stenosis was >50% combined with tandem lesions, such as inflow artery, anastomosis, and outflow vein stenosis on preoperative ultrasonogram evaluation, regardless of the presence of intimal hyperplasia. This is thought to be a mixed type with an uncertain etiology but not rare in the real world. All the preoperative and follow-up ultrasonography were measured by linear transducer on DU scanners (including HITACHI HI VISION Preirus with a 5–13-MHz linear transducer EUP-L74, Philips IU-22 with a 5–17-MHz linear transducer L17-5, and Philips EPIQ5 with a 5–18-MHz linear transducer L18-5) and reviewed by an independent ultrasound specialist.

Interventional Procedures

All procedures were performed under guided DU. Under local anesthesia, a 5-F or 6-F vascular sheath (Terumo Inc., Japan) was inserted in the outflow vein toward the stenosis, and then semi-heparinization was performed with 40–50 U/kg unfractionated heparin. A 0.035-in. guidewire (Terumo Inc., Japan) was introduced through the sheath and traversed the lesion under ultrasound guidance. In most cases, the tip of guidewire was delivered to the level of the proximal arteries (e.g., brachial artery) to ensure the stability of the working guidewire. According to the diameter of the veins and the length of the lesion, a noncompliant high-pressure balloon (Mustang, Boston Scientific Inc., USA) with a diameter 1 mm greater than the normal diameter of the venous segment was introduced over the guidewire; the size of the balloons ranged from 4 to 7 mm in diameter, and they were 40 mm in length. During dilatation, the lesion was covered by the middle part of the balloon. The balloon was inflated to its rated burst pressure and maintained for at least 1 min until the balloon waist disappeared under the monitor of the DU. Remeasurement of the diameter and flow volume at the lesion site and the brachial artery were routinely performed prior to removal of the sheath. Technical success was defined as <30% residual stenosis, >500 mL/min flow volume in the brachial artery, and perception of a continuous palpable thrill. For residual stenosis >30%, repeated angioplasty or dilation by a larger balloon would be performed; an adjunctive stent was used in the upper arm, while the flow-limiting recoil persisted.

Pathologic Studies of Vascular Specimens

The vascular lesion specimens were obtained from open fistula reconstruction surgery cases to confirm the consistency between ultrasonographic and pathological studies. The indication for open surgery repair was failed reintervention by endovascular procedure or restenosis/occlusion in <3 months. Cross sections of AVF samples were fixed in 4% neutral-buffered paraformaldehyde and processed for light microscopy. All tissue samples were stained

Fig. 1. Ultrasonograms of typical AVF lesions. **a** Type I, intimal hyperplasia at the proximal vein: distance 1 shows the thickness of intima (1.5 mm); the residual lumen is 0.8 mm. **b** Type II, conduit constriction at the vein: distance 1 and 2, respectively, represent the normal (4.4 mm) and constricted lumen (1.7 mm); the intima

(*) is <0.3 mm. **c** Type III, plaque at the artery: distance 1 and 2 represent the bypass (2.0 mm) and the thickness of plaque (2.0 mm), respectively. The borders between intima and lumen are shown on the figure as dotted lines. + measure; * intima; A, artery; V, vein; AVF, arteriovenous fistula.

with hematoxylin and eosin and Masson's trichrome stain to identify the relative thickness of the intima and media [8, 11]. All histologic evaluations were performed by a single pathologist without clinical characteristics of the study patients and AVF outcomes.

Follow-Up and Outcome Definitions

After the procedure, patients were transferred to a dialysis center and followed up by the attending nephrologists before each dialysis session and evaluated by vascular surgeons at 3, 6, 12, 18, and 24 months after the initial operation. During the follow-up vintage, primary patency was defined as the interval that a patent fistula maintained continued success and efficient dialysis sessions without the need for repeat endovascular therapy or surgical revision, while secondary patency was defined as the time from the repairing operation until access abandonment, which was not ter-

minated by interventional procedures to maintain or restore patency.

Statistical Analysis

Quantitative variables of patients' characteristics are expressed as mean $\pm$ standard deviation or as median (interquartile range), while categorical variables are expressed as percentages or ratios. Differences were evaluated using χ^2 test and independent t test. The patency rate was estimated using the Kaplan-Meier method, while intergroup comparisons were assessed with the log-rank test. A Cox proportional hazards model was used to identify independent factors associated with primary and secondary patency after adjustment for confounders. Statistical analysis was performed using SPSS version 19 (Chicago, IL, USA). A p value <0.05 was considered statistically significant.

Table 1. Baseline characteristics of patients of overall, Type I, Type II, and Type III

Characteristics	Overall (N = 120)	Type I (N = 45)	Type II (N = 35)	Type III (N = 40)	p value
Age, year	61.24±12.12	64.60±11.50	59.16±13.28	59.28±11.14	0.061
Male	58 (48.3)	20 (44.4)	16 (45.7)	22 (55.0)	0.583
Dialysis vintage, month	47.13 (10.52, 114.31)	61.27 (13.77, 108.53)	73.08 (9.73, 141.43)	24.53 (6.18, 85.79)	0.324
Primary disease					
Chronic glomerulonephritis	42 (35.0)	17 (37.8)	11 (31.4)	14 (35.0)	0.383
Diabetic nephropathy	23 (19.2)	8 (17.8)	8 (22.9)	7 (17.5)	
Hypertension	14 (11.7)	4 (8.9)	6 (17.0)	4 (10.0)	
Polycystic kidney	16 (13.3)	10 (22.2)	2 (5.7)	4 (10.0)	
Others	25 (20.8)	6 (13.3)	8 (22.9)	11 (27.5)	
Diabetes	32 (26.7)	14 (31.1)	8 (22.9)	10 (25.0)	0.68
History of PAD	11 (9.2)	4 (8.9)	2 (5.7)	5 (12.5)	0.589
History of AVF dysfunction	30 (25.0)	7 (15.6)	10 (28.6)	13 (32.5)	0.167
History of CAC	42 (35.0)	13 (28.9)	13 (37.1)	16 (40.0)	0.536
Blood vessel (radial-cephalic)	88 (73.3)	31 (68.9)	26 (86.7)	31 (86.1)	0.261
Anastomosis (end to side)	71 (59.2)	29 (64.4)	18 (51.4)	24 (60.0)	0.562
Lesion length, cm	3.62±2.30	3.65±1.96	3.47±3.93	3.67±1.39	0.334
Lumen diameter, mm	1.69±0.97	1.49±0.82	1.43±0.78	2.52±1.13	0.001

IH, intimal hyperplasia; AVF, arteriovenous fistula; PAD, peripheral arteria disease; CAC, central venous catheterization; Type I, IH-dominant lesion type; Type II, non-IH lesion type; Type III, partial-IH lesion type; SD, standard deviation; IQR, interquartile range. Data are expressed as mean ± SD or median (IQR) or number (percentage).

Results

Table 1 describes the demographic, clinical, and vascular access characteristics of the 3 groups and of the full cohort of 120 patients. The mean age of the entire patient cohort was 61.2 ± 12.1 year, and 48.3% were male. The median dialysis vintage was 47.1 months. The primary causes of ESRD included chronic glomerulonephritis (35.0%), diabetic nephropathy (19.2%), hypertension (11.7%), polycystic kidney disease (13.3%), and other diseases (20.8%). Fistulas served a median vintage of 24.6 months before intervention, and 74.2% of AVFs were created on the left arm. Type I lesions were observed in 45 (37.5%) patients, while Types II and III included 35 (29.2%) and 40 (33.3%) patients, respectively. There was no significant difference among the 3 groups in baseline characteristics, except for the lumen diameter, which was the largest in Type III group.

A total of 26 patients in this cohort underwent open fistula reconstruction surgery during the follow-up. Vascular samples obtained during the procedure underwent pathological examination (Fig. 2); 8 cases diagnosed as Type I lesions were characterized by neointimal proliferation and 6 diagnosed as Type II featured adventitia constriction (no valve-related lesions in these cases). All pathological diagnoses were consistent with the morphological evaluation by ultrasonography.

In this study, the primary patency rates in Type I, Type II, and Type III groups were 78.4, 93.2, and 83.2% at 6 months and 59.5, 84.7, and 75.5% at 1 year, respectively. The association between AVF stenosis type and AVF primary patency was analyzed using a Kaplan-Meier curve (Fig. 3) and Cox regression (Table 2). The Kaplan-Meier curve showed that the non-IIH group had the highest primary patency among 3 groups ($p = 0.001$). In detail, the primary patency was higher in Type II group than in Type III group ($p = 0.015$), but there was no significant difference between Type I and Type III groups ($p = 0.216$). Multiple Cox regression analysis demonstrated that the postoperative AVF primary patency was correlated with end-to-end anastomosis (hazard ratio [HR] = 2.997, $p = 0.008$, and 95% confidence interval [CI]: 1.328–6.764) and AVF lesion type ($p = 0.012$).

The secondary patency rate was 97.0% of the whole cohort at 6 months and 94.2% at 12 months. Per group, the 6-month and 1-year secondary patency rates were 94.4 and 90.5% in Type I group, 97.1 and 97.1% in Type II group, and 100 and 94.7% in Type III group. Univariable and multivariable analysis results of the association between AVF stenosis type and AVF secondary patency are shown in Figure 3 and Table 3. The Kaplan-Meier curve showed that the secondary patency of Type I group was less than that of Type II and Type III groups ($p = 0.003$), while there was no

Fig. 2. Ultrasonic and histopathological images of AVF lesions. Ultrasonic images show an AVF with significant Type I lesion (**a**) and an AVF with significant Type II lesion (**b**). HE stain (**c, d**) and Masson's trichrome stain (**e, f**) of these samples show their respective histopathology. L, lumen; I, intima; M, media; A, adventitia; AVF, arteriovenous fistula; HE, hematoxylin and eosin.

Table 2. Cox regression analysis of primary patency after PTA of AVF reconstruction

Characteristics	Univariable Cox regression		Multivariable Cox regression		
	HR	<i>p</i> value	HR	<i>p</i> value	95% CI
Age, year	1.015	0.277	1.007	0.659	0.975–1.041
Male	0.7	0.297	0.473	0.062	0.215–1.039
Dialysis vintage, month	1.001	0.956			
Primary disease	–	0.72			
Diabetes	1.79	0.101			
History of PAD	2.095	0.126			
History of AVF dysfunction	1.096	0.796			
History of CAC	0.849	0.635			
Blood vessel (radial-cephalic)	0.486	0.069			
Anastomosis (end to end)	3.022	0.007	2.997	0.008	1.328–6.764
Lesion type	–	0.003	–	0.012	–
Type I	4.932	0.002	5.395	0.004	1.730–16.824
Type II	–	Ref	–	Ref	–
Type III	2.083	0.175	3.135	0.073	0.900–10.916
Lesion length, cm	1.005	0.961			
Lumen diameter, mm	0.885	0.556			

PTA, percutaneous angioplasty; AVF, arteriovenous fistula; PAD, peripheral arterial disease; CAC, central venous catheterization; HR, hazard ratio; 95% CI, 95% confidence interval; Ref, reference; HR = 1.0; Type I, IH-dominant lesion type; Type II, non-IH lesion type; Type III, partial-IH lesion type.

Fig. 3. Kaplan-Meier curve of primary (a) and secondary patency (b) of patients with Type I, Type II, and Type III lesions.

significant difference between Type II and Type III groups ($p = 0.868$). Multiple Cox regression analysis demonstrated that the postoperative AVF secondary patency was correlated with the history of AVF dysfunction ($HR = 16.741$, $p = 0.009$, and 95% CI: 2.009–139.525), end-to-end anastomosis ($HR = 16.117$, $p = 0.006$, and 95% CI: 3.214–114.193), and AVF lesion type ($p = 0.017$).

Discussion

Our study demonstrated that morphological features in dysfunctional AVFs are associated with the primary and secondary patency rate after PTA with a high-pressure balloon. In the 2019 update of Kidney Disease Outcomes Quality Initiative guidelines for vascular access,

Table 3. Cox regression analysis of secondary patency after PTA of AVF reconstruction

Characteristics	Univariable Cox regression		Multivariable Cox regression		
	HR	<i>p</i> value	HR	<i>p</i> value	95% CI
Age, year	0.999	0.958	0.946	0.234	0.864–1.036
Male	0.52	0.343	0.254	0.134	0.042–1.526
Dialysis vintage, month	0.998	0.805			
Primary disease	–	0.474			
Diabetes	1.641	0.474			
History of PAD	3.404	0.222			
History of AVF dysfunction	4.447	0.068	16.741	0.009	2.009–139.525
History of CAC	0.577	0.428			
Blood vessel (radial-cephalic)	0.166	0.25			
Anastomosis (end to end)	9.873	0.032	16.117	0.006	3.214–114.193
Lesion type	–	0.021	–	0.017	–
Type I	8.354	0.046	34.67	0.013	2.130–65.406
Type II	–	Ref	–	Ref	–
Type III	0.838	0.901	2.844	0.51	0.127–36.726
Lesion length, cm	0.948	0.815			
Lumen diameter, mm	0.805	0.584			

PTA, percutaneous angioplasty; AVF, arteriovenous fistula; PAD, peripheral arteria disease; CAC, central venous catheterization; HR, hazard ratio; 95% CI, 95% confidence interval; Ref, reference; HR = 1.0; Type I, IH-dominant lesion type; Type II, non-IH lesion type; Type III, partial-IH lesion type.

endovascular angioplasty (with a high-pressure balloon as needed) was considered a reasonable primary treatment for AVF stenotic lesions with clinical indicators [3]. PTA could immediately restore the flow for hemodialysis while conserving vascular resource for patients, but the high restenosis and reintervention rate remains a significant challenge [12, 13].

Neointimal proliferation is considered to be the main reason for AVF dysfunction by the authoritative textbooks of both nephrology and vascular surgery [14, 15]. However, recent studies have demonstrated that pathological types other than NIH result in dysfunctional AVFs, such as vascular constriction caused by adventitia fibroblasts proliferation, arterial negative remodeling, or atherosclerosis. In 2014, Simone et al. [9] showed that adventitial remodeling played an important role in AVF stenosis and that an increase of adventitial fibrosis and myofibroblast activation was associated with AVF failure. Tabbara et al. [16] investigated biopsy specimens from a prospective cohort undergoing two-stage AVF creation and transportation, and they found that postoperative NIH was not linked to AVF failure or to the loss of primary unassisted patency and revealed no occlusive NIH from the AVF tissue obtained at surgery [7]. Rothuizen et al. [4] postulated that the balance between intimal hyperplasia and vascular outward remodeling may ultimately determine fistula

flow and patency. Therefore, it is recognized that intimal hyperplasia does not account for all the stenosis lesions, and an effective method to evaluate and distinguish different patterns of lesions before treatment is warranted.

In this study, the NIH type accounted for 37.5% of all the dysfunctional AVFs. The primary patency rates in this group were 78.4, 59.5, and 36.4% at 6, 12, and 24 months, respectively; when compared with the non-NIH group's (29.2% of all dysfunctional AVFs) rates of 93.2, 84.7, and 77.1% ($p = 0.001$), these values reflect the discrepant prognosis between these 2 groups featured by differing severity of neointimal proliferation. The criteria of classification were identified by preoperative DU. The advantage of DU is its ability to detect the properties of the structure inside stenosis lesions, whereas digital subtraction angiography can only demonstrate intraluminal fluid information by contrast. The morphological features were significantly different between NIH-dominant and non-NIH lesions. In our experience, the histopathology observation of stenosis lesion specimens taken from fistula repair surgery was highly consistent with the morphologic characteristics evaluated by DU.

To date, few studies have evaluated the impact of different types of AVF/arteriovenous graft (AVG) lesions on the patency rates after intervention. Yamamoto et al. [17] described a cohort of 46 AVG outflow stenosis cases

whose lesions were divided into 3 groups by DU evaluation: vascular constriction types (13/46, 28.3%), neointimal proliferation types (12/46, 26.1%), and mixed types (21/46, 45.7%); the vascular constriction type in their study displayed excellent primary patency rates after stent treatment. Suemitsu et al. [18] investigated 158 AVF venous lesions and divided them into 3 stenosis patterns by ultrasonography: intimal hyperplasia stenosis (110/158, 69.6%), shrinking lumen stenosis (32/158, 20.3%), and venous valve-related stenosis (16/158, 10.1%). In their analysis, the AVF stenosis pattern affected the outcome after PTA; the shrinking lumen morphology had a negative impact on primary patency (HR 2.05, 95% CI 1.25–3.36, and $p = 0.005$), while the venous valve-related stenosis had a positive impact (HR 0.19, 95% CI 0.04–0.79, and $p = 0.023$). To the authors' knowledge, there are yet to be recognized classification criteria for dysfunctional AVF stenosis lesions. Therefore, we adopted an intimal thickness of 0.6 mm on the stenotic site as the cutoff value according to previous research. The intimal thickness of human saphenous veins obtained during coronary artery bypass surgery was found to range from 18.80 to 241.3 μm [19], and Hozumi et al. [20], using intravascular ultrasound in the great saphenous vein for aortocoronary bypass graft, showed a mean intimal thickness of 0.31 ± 0.09 mm 1 month after the operation and 0.65 ± 0.08 mm 1 year after the operation.

Under this method of classification, the primary patency rate at 6 and 12 months in the NIH group (Type I) in our cohort was lower than the results reported in the previous studies using drug-coated balloons (DCBs) but better than using standard PTA. Patane et al. [21] reported 2 types of DCBs compared with the standard PTA in the treatment of juxta-anastomotic stenosis of mature but dysfunctional AVFs; the primary patency rates were 81.8 and 84.1% in the DCB groups and 54.5% in the standard PTA group after 12 months. Irani et al. [22] reported in their randomized controlled trial (RCT) comparing DCB PTA (IN.PACT Admiral DCB, Invatec Medtronic) with conventional PTA for dysfunctional AVFs and AVGs that the primary patency in the DCB group was 81 and 51% after 6 and 12 months, while it was 61 and 34% in the standard PTA group. These reports indicate that dysfunctional AVFs and AVGs caused by lesions of intimal hyperplasia could benefit from the antiproliferative therapy by DCBs, rather than plain balloon angioplasty.

As for the non-NIH group, the 6-month and 1-year primary patency rates were not worse than those reports of the DCBs from previous RCTs [23–25]. Although it is less persuasive to compare the results from different tri-

als, it indicated that PTA by high-pressure balloons alone without DCB may be enough for lesions not initiated by intimal hyperplasia. The univariable/multivariable Cox regression analysis also showed that the lesion type ($p = 0.012$) and anastomosis style (end-to-end anastomosis, HR = 3.022, $p = 0.007$, CI: 1.328–6.764) were risk factors for lower primary and secondary patency after intervention of failed AVFs. In addition, previous PTA history was associated with lower secondary patency.

To some extent, our result explained why some RCTs were unable to show the superiority of DCB over plain old balloon angioplasty [23, 24, 26]. Whether the different pathological patterns are considered before comparing interventional treatments for dysfunction AVFs or not may affect the outcome. To improve the patency of intimal hyperplasia dominant lesions, routine balloon angioplasty is not as effective as DCBs. However, for non-NIH lesions, such as venous valve-related lesions, high-pressure balloons may be a first choice instead of DCBs, considering the current controversies about the safety of the latter. For lesions with instant elastic recoil that result in flow limitations after angioplasty or recurrent constriction by adventitia fibrosis, mechanical scaffolds (bare-metal stent or covered stent) may be required. From this point of view, subgroup analysis based on preoperative lesion characteristics needs to be further investigated prospectively, rather than randomizing them without discrimination, which probably could better embody the advantage of different appliances.

This study has some limitations. First, this is a single-center study; due to its retrospective nature and relatively small number of patients, it is difficult to establish a cause and effect relationship and to generalize the findings to all dysfunctional AVF patients. It should also be mentioned that there is yet to be a consensus regarding the methodology of morphological classification of stenosis lesions under DU or digital subtraction angiography. The present criteria are conducive to classify the dysfunctional AVFs with clinical indicators, but further studies are warranted for the clinical validation and optimization of classification. Besides morphology patterns, other factors, such as the position of the AVFs (brachial or wrist), preoperative proximal flow volume, and the absolute area of the residual lesion, may also account for the patency rate after angioplasty. Some of the factors above were ascribed to Type III group, which caused a confounding bias, and thus need to be stratified and analyzed with a larger sample in the future.

In conclusion, our data indicated that the morphological patterns of dysfunctional AVF stenotic lesions are as-

sociated with the outcome after interventional angioplasty. Non-NIH lesions tend to have a better prognosis, while the NIH-dominant type is a predictor of lower primary patency after high-pressure balloon dilatation. This study supports the concept that the morphological characteristics of stenotic lesions evaluated by DU need to be considered before treatment and individualized intervention strategy should be based on the histological properties of dysfunctional AVFs.

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Statement of Ethics

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by Ethics Committee of Huashan Hospital. Written informed consent was taken from the participants.

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Conflict of Interest Statement

The authors declare that they have no relevant financial interests.

Author Contributions

Research idea and study design: J.T., L.C., and W.Z.; data acquisition: W.Z. and L.C.; preoperative Doppler ultrasound: L.C. and Y.W.; PTA intervention: J.T., M.H., W.S., and B.Y.; statistical analysis: W.Z. and M.Z.; supervision or mentorship: J.T. and J.C.

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