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# Transcatheter Thrombolysis with Percutaneous Transluminal Angioplasty Using a Trans-Brachial Approach to Treat Thrombosed Arteriovenous Fistulas

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**Background:** Arteriovenous fistulas (AVFs) are used to provide vascular access for hemodialysis in patients with end-stage renal failure. However, stenosis and thrombosis can compromise long-term AVF patency. The objective of this study was to evaluate catheter thrombolysis with percutaneous transluminal angioplasty (PTA), using a trans-brachial approach, for acutely thrombosed AVFs.

**Material/Methods:** This retrospective study examined 30 cases of AVF thrombosis treated between January 1, 2015 and January 1, 2017. All patients received transcatheter thrombolysis with PTA using a trans-brachial approach. AVF patency was assessed after 6 months.

**Results:** Thrombolysis with PTA was performed at 2 to 72 h after diagnosis of AVF occlusion due to acute thrombosis, and AVF patency was restored in all patients. After 6 months, the primary and secondary patency rates were 76.7% and 93.3%, respectively. For type I stenosis, primary patency was achieved in 10 of 16 patients (62.5%) and secondary patency was achieved in 14 of 16 patients (87.5%). For type II stenosis, primary patency was achieved in 13 of 14 patients (92.9%) and secondary patency was achieved in 14 of 14 patients (100%). Comparing type I and II stenosis, a significant difference was detected in the rates of primary patency (odds ratio=0.909, 95% confidence interval 0.754–1.096, P=0.049), but not secondary patency (P=0.178), after 6 months.

**Conclusions:** Our study provides preliminary evidence that catheter-directed thrombolysis with PTA using a trans-brachial approach can achieve high patency rates when used to treat acutely thrombosed AVFs.

**MeSH Keywords:** **Angioplasty • Arteriovenous Fistula • Hemodialysis Units, Hospital • Thrombolytic Therapy • Thrombosis**

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## Background

The maintenance of hemodialysis (HD) in patients with end-stage renal failure requires sustained vascular access. Upper-extremity arteriovenous fistula (AVF) is most commonly used to provide venous access in these patients [1,2]. However, the long-term patency of AVF is not satisfactory, and thrombosis and vascular stenosis can lead to AVF failure in these patients, with an incidence of 14–36%. A systematic review of 12 383 HD patients found that AVF patency was 71% at 1 year and 64% at 2 years [3,4]. Because the life expectancy of patients with end-stage kidney disease has been considerably extended, some patients receive HD for many years or even decades, and multiple AVFs may be required. In some cases, the loss of vascular access may lead to lack of access for a life-saving HD [5,6]; thus, it is prudent to manage and maintain AVF patency to prolong survival of patients who depend on HD.

Previous methods for restoring AVF patency, such as surgical salvage of an internal fistula or percutaneous embolectomy, have been associated with large trauma areas and serious complications such as bleeding and infection [7,8]. Following the development of interventional radiology, percutaneous methods are now more commonly used to restore AVF patency [9–11]. Pharmacological and/or mechanical thrombolysis can dissolve or remove the thrombus in the failed AVF [12,13] but do not address the AVF stenosis. Angioplasty alone can adequately restore the patency of a stenosed AVF [14], but the fistula thrombus must be treated first. Therefore, combining thrombus management and angioplasty may be effective for acutely thrombosed AVFs [15,16].

There are no uniform guidelines for restoring AVF patency, and the optimal approach remains unknown. The aim of the present study was to assess the utility of catheter thrombolysis combined with percutaneous transluminal angioplasty (PTA) to treat acutely thrombosed AVFs.

## Material and Methods

### Study design and patients

This was a retrospective study of all patients who received treatment for failed AVF at Nanjing First Hospital between January 1, 2015 and January 1, 2017. The patients included in this study were identified in the procedure database for the Department of Interventional Radiology in our hospital by searching the key words “failed AVF”, “thrombolysis”, and “percutaneous transluminal angioplasty”. The patients’ demographic information and clinical data were abstracted from their medical records. This study was approved by the Ethics Committee of Nanjing First Hospital and the committee waived the requirement for

informed consent for this retrospective study. The interventional radiologists, in consultation with the patients’ nephrologists and surgeons, discussed treatment options such as thrombolysis, PTA, surgical revision or AVF re-creation with the patients. If a patient opted for the interventional procedure with thrombolysis and PTA, informed consent was obtained prior to the procedure, as required for clinical management.

All patients included in this study underwent AVF to maintain HD, and the diagnosis of thrombosed AVF was based on clinical examination and Doppler ultrasound results. All AVFs included in this study were created with anastomosis of the radial artery to the cephalic vein. The diagnostic criteria included auscultation indicating lack of blood flow in the AVF, lack of pulse and absence of thrill/fremitus on palpation of the AVF, interruption of AVF blood flow based on Doppler ultrasound findings, and visible thrombosis in the lumen on the ultrasound scan [4]. None of the included patients had any contraindications for thrombolytic therapy, such as active internal bleeding, intracerebral hemorrhage, surgery within the last 3 months, gastrointestinal bleeding within the last 2 weeks, severe trauma, severe hypertension, pregnancy, bacterial endocarditis, left-atrial thrombosis, severe cardio-cerebral disease, severe anemia, or thrombocytopenia [17,18].

We used a combination of ultrasound images and color Doppler parameters (Acuson Antares, Siemens, Erlangen, Germany) to diagnose thrombosed AVFs. All ultrasound studies of AVFs were performed in the vascular laboratory of the Department of Ultrasound in our hospital. Peak systolic velocity (PSV) was used to grade the stenosis. We considered a stenosis to be significant if the PSV was greater than 375 cm/s for an AVF or if 50% or more of the AVF was narrowed in the ultrasound images. The scan reports also contained qualitative descriptions of the scan results such as the cephalic vein near the AVF being stiff, thickened and filled with nonhomogeneous echo patterns, and the blood flow in the AVF being thinned or interrupted. In addition, the ultrasound reports included a depiction of each AVF, indicating the location of the stenosis.

### Treatment

All patients were treated with transcatheter thrombolysis and PTA to restore AVF patency. All treatment procedures were performed by 2 senior interventional radiologists (TW and WL), each with more than 10 years of experience. The patients were divided into 2 groups according to the angiographic results: type I stenosis (at or close to the anastomosis) and type II stenosis (at the puncture site) [19].

For the treatment procedure, each patient was placed in the supine position with the affected upper limb supported. The medial condyle of the humerus was used as the bone mark for

the cubital fossa for all cases, and the puncture was performed along the brachial artery by palpating the 1 to 2 cm before the antecubital fossa skin. After local anesthesia with 1% lidocaine, we used antegrade puncture into the anterior wall and moved the needle along the brachial artery by forming a 30° to 45° angle with the skin. After injection of contrast agent (iodixanol injection, VISIPAQUE, GE Healthcare, Ireland) through the puncture needle to evaluate the shape of the blood vessel, a vascular sheath was placed to allow insertion of a 4-Fr catheter (MPA or H1, Cordis Medical, Fremont, CA, USA) and a 0.035-inch guidewire (Terumo, Tokyo, Japan). The site of AVF occlusion was determined using contrast agent. The average amount of contrast agent used per patient was less than 100 ml. The AVF occlusion was perforated using the catheter and guidewire, and the catheter tip was retained at the start of the occlusion. A urokinase solution (125 000–250 000 IU) was injected for 15 to 20 min.

Balloon dilatation was performed in all patients because more than 50% of the stenosis remained after thrombolysis. The size of the balloon (Sterling SL, Boston Scientific, Natick, MA, USA or Pacific Xtreme, Medtronic, Fridley, MN, USA) was selected according to the diameter of the vessel (diameter: 2 to 4 mm; length: 8 to 12 cm). The balloon was inserted into the stenosis and intermittently expanded 1 to 2 times. Then, a 4-Fr thrombolytic catheter (Uni\*Fuse, AngioDynamics, Latham, NY, USA) was inserted into the stenotic section of the AVF, and the tip was retained in the arterial side of the AVF for examination by angiography. Catheter insertion was followed by continuous infusion of urokinase (25 to 50 million IU/day).

During thrombolysis, the AVF fremitus and vascular murmur were checked frequently. Once the fremitus and murmur were detected, blood flow recovery was confirmed by angiography and thrombolysis was stopped. During the thrombolytic therapy, the patient's vital signs and blood coagulation parameters were monitored closely. If the plasma fibrinogen level fell below 1.0 g/L or if bleeding occurred, thrombolysis was stopped immediately.

After the intervention, the wound was covered with a tight pressure bandage, which allowed normal palpation of the pulse in the radial artery by finger movement. The bandage remained at the puncture site for at least 24 h after the procedure.

### Postoperative observation and follow-up

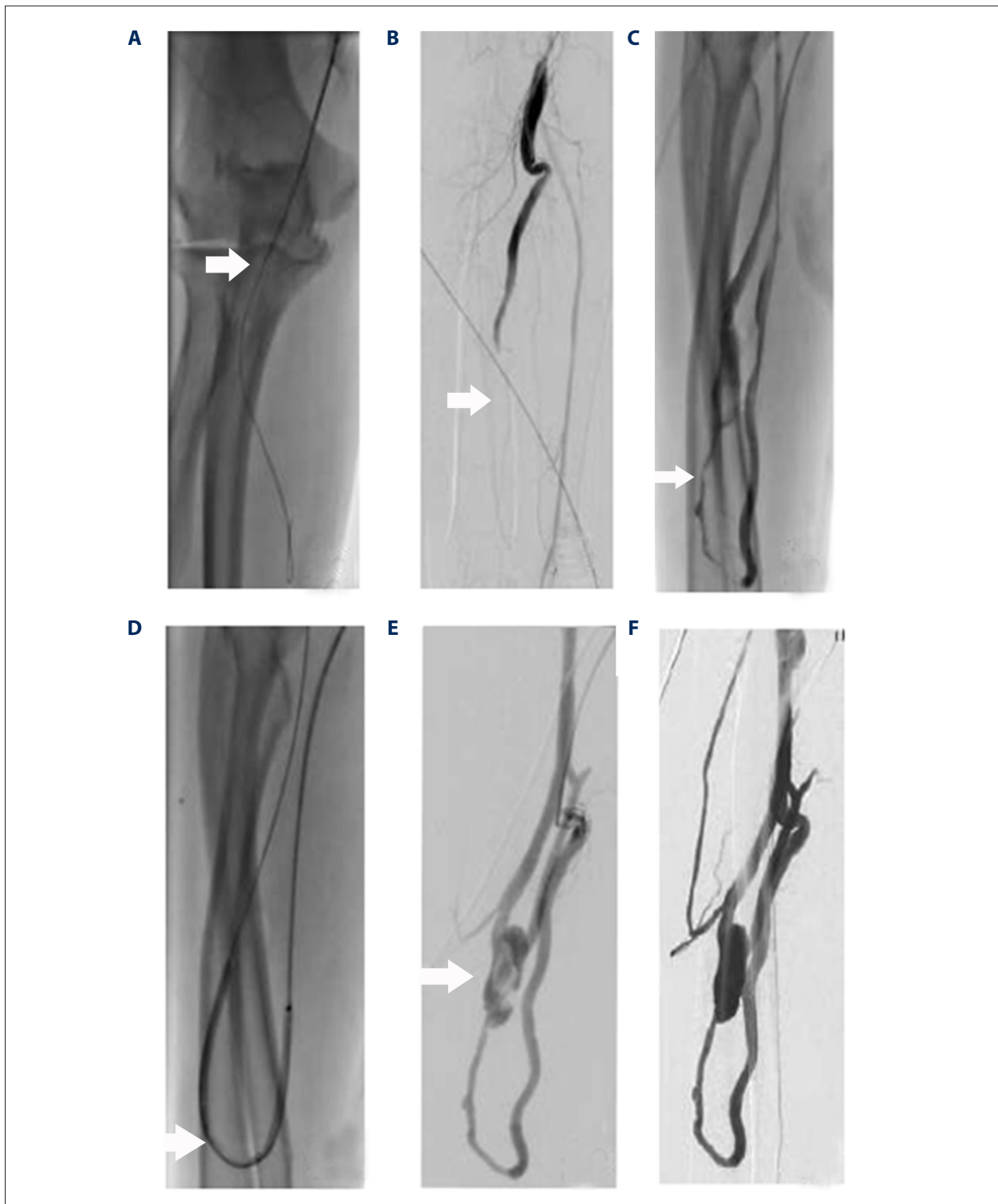
Upon detection of palpable fremitus and vascular murmur, angiography was performed to confirm the return of blood flow. A thrombus clearance rate greater than 90% was considered successful restoration of patency [20,21]. If the blood flow in the AVFs did not recover within 72 h of continuous thrombolytic therapy, the percutaneous treatment was stopped and

**Table 1.** Patient characteristics.

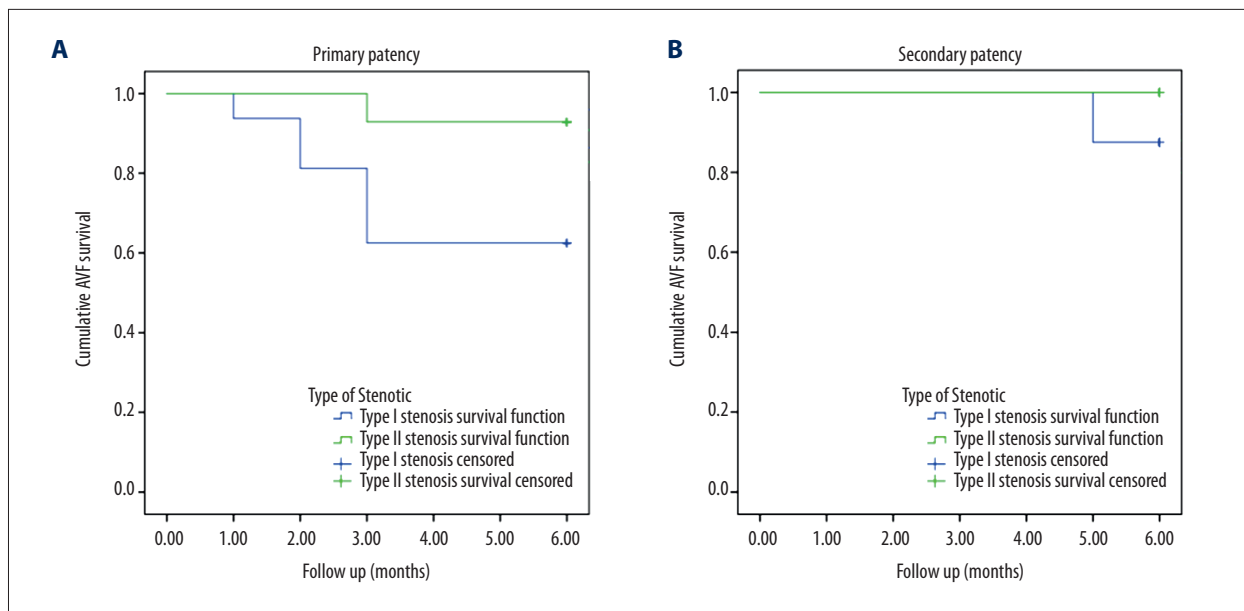
	N (%) or mean ±SD
Sex	
Male	14 (46.7%)
Female	16 (53.3%)
Age (years)	53.8±7.9
Indication for hemodialysis	
Diabetic nephropathy	4 (13.3%)
Hypertensive nephropathy	6 (20.0%)
Primary chronic glomerulonephritis	16 (53.3%)
Chronic interstitial nephritis	3 (10.0%)
Lupus nephritis	1 (3.3%)
Time before occlusion of AVF (months)	23.9±10.1
Occlusion duration before treatment	
<24 h	19 (63.3%)
24-48 h	8 (26.7%)
>48 h	3 (10.0%)
Hemoglobin (g/dL)	13.94±1.50
Serum creatinine (mg/dL)	10.01±2.86
Glomerular filtration rate (mL/min)	6.55±1.78
Type of stenosis	
I	16 (53.3%)
II	14 (46.7%)

the patients were consulted for surgical creation of a new fistula. To reduce the risk of bleeding, we did not use antiplatelet drugs or statins after the intervention.

All patients returned for a follow-up appointment at 6 months after the interventional treatment, and AVF patency was evaluated using ultrasound. The patient was considered to have primary patency if the AVF was patent during the follow-up period without a further need for interventional or surgical treatment. The patient was considered to have secondary patency if stenosis or occlusion was detected during the initial follow-up period and the AVF remained patent during the follow-up after repeated interventional therapy. The primary patency rate was defined as 100%×(patients with primary patency)/(total patients). The secondary patency rate was defined as 100%×(patients with primary patency+patients with secondary patency)/(total patients). The percentage of thrombus clearance was defined as 100%×(pre-operative thrombus



**Figure 1.** Treatment procedure for a patient on hemodialysis who had an acutely thrombosed arteriovenous fistula (AVF) with occlusion in the right forearm. **(A)** Sheath insertion through the distal brachial artery puncture site (arrow). **(B)** Catheter angiography shows a middle-end occlusion (arrow). **(C)** Angiography after puncture of the occlusion shows the arterial fistula with severe type II stenosis and thrombosis (arrow). **(D)** Perfusion with 25 million IU of urokinase along the catheter (arrow), performed prior to balloon dilatation. **(E)** Angiography after balloon dilatation therapy shows improved AVF stenosis and some residual thrombus (arrow). **(F)** Angiography shows AVF patency achieved after 24 h of continuous thrombolysis therapy.



**Figure 2.** Kaplan-Meier survival curves for AVF patency after restoration of blood flow. (A) Primary patency rates for type I and type II stenosis ( $P=0.049$ ). (B) Secondary patency rates for type I and type II stenosis ( $P=0.178$ ).

length-follow-up thrombus length)/(pre-operative thrombus length) [20,21].

### Statistical analysis

Data for continuous variables were assessed using the Kolmogorov-Smirnov test. Normally distributed continuous data are presented as means  $\pm$  standard deviations (SD) and were analyzed using the *t* test. Non-normally distributed continuous data are presented as medians (ranges) and were analyzed using the non-parametric Mann-Whitney U test. Categorical data are presented as frequencies and were analyzed using Fisher's exact test. Kaplan-Meier analysis and the log-rank test were used to analyze AVF patency during the follow-up period. Statistical analysis was performed using SPSS 23.0 (IBM, Armonk, NY, USA). P values below 0.05 were considered statistically significant.

## Results

### Patient characteristics and treatment

Our study cohort consisted of 30 consecutive patients with acutely thrombosed AVFs who underwent thrombolysis and PTA to restore AVF patency (Table 1). In all patients, the AVF occlusion was confirmed using ultrasound, and thrombolysis with PTA was initiated at 2 to 72 h after diagnosis of AVF occlusion. Figure 1 shows the detailed steps for angiographic confirmation of AVF thrombosis and the percutaneous thrombolytic treatment with angioplasty in a representative patient.

### Characteristics of occluded AVFs

Analysis of the stenotic sites indicated that 16 patients (53.3%) had type I stenosis and 14 (46.7%) had type II stenosis.

### Treatment complications

Two patients experienced bleeding at the puncture site during thrombolysis, which was stopped by compression. There were no serious bleeding complications. There were no cases with symptomatic pulmonary embolism.

### Follow-up

Post-procedural follow-up was performed initially shortly after the treatment and then again at 6 months after treatment. Evaluation of clinical signs and vascular ultrasound results indicated that 23 patients (76.7%) had patent AVFs and 7 patients (23.3%) had recurrence of occlusions. Among those with recurrence, 6 had type I stenosis and 1 had type II stenosis. AVF patency was restored in 5 of the 7 patients with recurrence (4 with type I stenosis, 1 with type II stenosis) using repeated transcatheter thrombolysis with PTA. However, AVF patency was not restored in 2 out of 7 patients (both with type I stenosis) using repeated transcatheter thrombolysis with PTA and these 2 patients underwent surgery to create new AVFs.

Primary patency was achieved in 23 of 30 (76.7%) and secondary patency was achieved in 28 of 30 patients (93.3%). For type I stenosis, the primary patency rate was 10 of 16 patients (62.5%) and the secondary patency rate was 14 of 16 (87.5%).



For type II stenosis, the primary patency rate was 13 of 14 patients (92.9%) and the secondary patency rate was 14 of 14 patients (100%). The difference in the primary patency rates between type I and type II stenosis reached significance (odds ratio [OR]=0.909, 95% confidence interval [CI] 0.754–1.096,  $P=0.049$ ), but a significant difference was not detectable in the secondary patency rates between type I and type II stenosis ( $P=0.178$ ) at the 6-month follow-up (Figure 2).

## Discussion

In this study, we evaluated the utility of catheter thrombolysis combined with PTA to treat acutely thrombosed AVF. Our study achieved a primary patency rate of 76.7% and a secondary patency rate of 93.3%, which was similar to or better than other reports in the literature. For example, Cildag et al. evaluated thrombus aspiration followed by PTA, which achieved a technical success rate of 83% and primary and secondary patency rates of 40% to 55% at 6 and 12 months [15]. Kim et al. used mechanical thrombectomy followed by PTA and reported a primary patency rate of 63% at 6 months [16]. Liang et al. used urokinase with PTA and reported primary and secondary patency rates of 80% and 81%, respectively, at 6 months [22]. Our combined use of thrombolysis and PTA is promising in that the AVF patency was sustainable to at least 6 months and there were few complications.

There is no consensus about the optimal approach for treating thrombosed AVFs. Several approaches, such as percutaneous interventional methods and open surgery, have been used to restore AVF patency [7–16]. The current interventional therapies for acutely thrombosed AVFs include local thrombolysis, thrombectomy, percutaneous balloon dilatation, and stent placement [23,24]. Percutaneous interventional therapy, in contrast to open surgery, leads to a smaller area of trauma, fewer complications, increased reproducibility, shorter procedure time, shorter hospital stay, and the ability to use the AVFs for dialysis immediately after the procedure without the need to use a central venous catheter [9–11]. In clinical practice, we commonly perform interventional therapy to treat AVF occlusions because the intervention can rapidly remove the occluding thrombus, restore the dialysis pathway, and retain the length of the available blood vessels [25]. Our study results support continued use of the percutaneous approach.

Most patients with AVF thrombosis also have stenosis of the fistula. Therefore, the simple removal of thrombus without treatment of stenosis will likely lead to short-term treatment failure [12,25]. The use of an arterial thrombectomy device provides rapid recovery of blood flow through the fistula, and requires a low dose of a thrombolytic agent, leading to fewer thrombolysis-related complications. However, this method

requires a target vessel with a large diameter to accommodate the thrombectomy device, which is not always feasible [25,26]. Stent placement is effective for refractory stenosis, but previous studies have reported problems with stent placement, such as the higher cost of the stent and lower patency rates than PTA. In addition, the diameter of the blood vessel affects stent patency, with larger-diameter vessels having higher patency than smaller-diameter vessels. Furthermore, there is an issue with stents placed across joints affecting the joint activity [26–29]. In this study, we used a combined approach with both thrombolysis and PTA to treat thrombosed AVFs, with promising results.

The interventional procedure described here required careful attention to the procedural details, as compression hemostasis is needed to prevent procedure-related complications such as pseudoaneurysm, ischemia, and thrombosis of the upper limb [5]. We used the brachial artery rather than the femoral artery because the brachial approach allows earlier ambulation and participation in daily activities. Furthermore, a trans-brachial approach can overcome the disadvantages of the trans-femoral approach, which sometimes fails to reach the occluded AVF segment due to a limited catheter length. To reduce the incidence of complications from brachial artery puncture, it was important to select an appropriate puncture location. The superficial location of the brachial artery and the nearby medial epicondyle made it effective for postoperative compression. We used a catheter guidewire to perforate the thrombus before initiating thrombolysis. This helped to accelerate lysis because it increased the contact area for the thrombolytic drugs. None of our 30 patients had any signs of symptomatic pulmonary embolism, which could have resulted from a small thrombus load in the AVFs. Our experience was consistent with a previous study indicating a low frequency of embolization of small thrombus fragments into the pulmonary circulation, thus explaining why most patients showed no symptoms of pulmonary embolism [30]. Also, since there were no uniform guidelines regarding long-term anticoagulation or antiplatelet therapy during the perioperative period [31], we did not put all patients on anticoagulation or antiplatelet therapy. Instead, we used a personalized treatment approach, in consultation with the patient's primary physician and nephrologist, to optimize prevention of thrombosis and reduce the bleeding risk for each patient.

We also found that type II stenosis had a higher primary patency rate than type I stenosis, likely because neointimal hyperplasia can occur in and around the thrombosed AVF [32]. Six of the 16 patients with arterial anastomotic stenosis (type I) who received percutaneous balloon dilatation therapy experienced short-term recurrence. Therefore, surgical treatment may be useful for these type I stenosis patients. Type II stenosis is mainly caused by hyperplasia of fibrous tissues due

to repeated punctures, and percutaneous balloon dilatation therapy may be preferred for the stenosis. Nevertheless, the 2 types of stenosis had similar secondary patency rates. Another study reported excellent patency rates using a variety of balloon types, such as a cutting balloon and a drug-eluting balloon, but the long-term efficacy of these approaches has not been confirmed [33].

This study has several limitations. First, our sample size was small, with only 30 patients in the study cohort. This limited our statistical power to detect differences between type I and type II stenosis. Second, we had a short follow-up of 6 months and we did not have information about long-term AVF patency in these patients. Third, this was a single-center study and the results may not be generalizable to other patient populations or treatment centers. Nevertheless, this study also has strengths. It allows us to generate hypotheses that will guide the design of a future large-scale multicenter clinical trial to compare various methods used in the treatment of acutely thrombosed AVFs.

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## Conclusions

This study provides preliminary evidence supporting the use of transcatheter thrombolysis with PTA, using a trans-brachial approach, to treat acutely thrombosed AVFs based on patency rates at 6 months.

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## Conflict of interests

None.

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