Peripheral Arterial Occlusive Disease – PAOD

Comparison of Minimally Invasive Thrombectomy with Percutaneous Balloon Angioplasty for Organized Thrombi in Hemodialysis Access

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Background: Thrombi are an important challenge when establishing hemodialysis access for hemodialysis. We developed a minimally invasive thrombectomy (MIT) salvage treatment to solve this problem when traditional percutaneous transluminal angioplasty (PTA) fails.

Objectives: The study aimed to investigate the safety and patency rate following MIT as a rescue procedure for traditional PTA with organized thrombi obstructing hemodialysis access.

Methods: This was a prospective study of MIT as a rescue procedure for traditional PTA to remove organized thrombi and establish hemodialysis access. We included patients with (1) stenotic lesions, (2) vascular access thrombi, (3) high venous pressure, (4) vascular collapse and suction. Nephrologists evaluated hemodialysis access immediately post-thrombi removal and patency at 7, 30, 60, 120, and 180 days post-removal, in addition to complications. Kaplan-Meier survival analysis was performed to analyze the primary and secondary patency rates after clinical procedural success.

Results: From June 2014 to May 2015, 746 patients underwent PTA in our hospital, and 425 patients consented to participate in this study. Of these patients, we enrolled 46 who underwent simultaneous PTA and MIT. Immediate clinical success was achieved in 100% of the patients in the MIT group. No complications were observed in any of the 46 patients, including major bleeding, shock, or hospitalization. The primary and secondary patency rates did not differ between MIT and PTA alone (p = 0.93 and p = 0.28, respectively).

Conclusions: MIT can be considered a safe rescue procedure for removing organized thrombi to establish vascular access for hemodialysis when initial and traditional PTA fails.

Key Words: Angioplasty • Hemodialysis • Organized thrombi • Thrombectomy

INTRODUCTION

Hemodialysis vascular access is vital for patients who require dialysis. Due to low infection and good patency rates, autogenous arteriovenous fistula (AVF) is recommended by the National Kidney Foundations’ Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines over other means of establishing hemodialysis access. However, large organized thrombi usually occur with AVF, especially combined with aneurysm formation. Traditionally, large organized thrombi are treated by local thrombolytic therapy, traditional percutaneous transluminal angioplasty (PTA) alone, or surgical intervention. Although catheter interventions have improved and new endovascular devices [e.g., the AngioJet Thrombectomy System, Boston Scientific, Marlborough,
MA, USA or Arrow-Trerotola percutaneous thrombolytic device (PTD) have been developed to treat hemodialysis fistulas and grafts, these devices are expensive. Also, the wound created by surgical interventions is relatively large because of the vascular clamps that are placed at the proximal and distal parts of the fistula. Here, we describe minimally invasive thrombectomy (MIT) as an alternative solution for the treatment of large, organized thrombi. MIT combines the advantages of minor invasive endovascular treatment and the effectiveness of surgical thrombectomy. We also compared the safety, efficacy, and patency rate of MIT with traditional PTA alone. This report describes our single-center experience of using MIT as rescue therapy following PTA for large, organized thrombi.

METHODS

Ethical consideration

This study was approved by the ethics committee of Pingtung Christian Hospital and was conducted according to the guidelines of the International Conference on Harmonization for Good Clinical Practice (ICH-GCP; IRB 442A).

Study design

This was a prospective study of PTA and MIT procedures performed at our cardiovascular laboratory from June 2014 to May 2015. All study patients provided written informed consent, and fulfilled the following inclusion criteria: (1) stenotic lesions, (2) presence of vascular access thrombosis, (3) high venous pressure, and (4) vascular collapse and suction. Patients from our hospital hemodialysis unit and nearby hemodialysis centers with suspected vascular access thrombosis were referred to our cardiovascular laboratory. All patients received traditional PTA initially. If traditional PTA failed, MIT was performed simultaneously (Figure 1). Demographic data, access characteristics, blood pressure, and procedure details were recorded in the cardiovascular laboratory before the procedure (Table 1). Following the procedure, vascular access patency and complications were assessed by nephrologists at 7, 30, 60, 120, and 180 days after the procedure.

Percutaneous transluminal angioplasty techniques

Patients diagnosed with hemodialysis vascular access dysfunction — including vascular access thrombosis, high venous pressure, and vascular collapse and suction — were referred from the hemodialysis unit. A 6 Fr introducer sheath (Terumo, Tokyo, Japan) was inserted anterogradely or retrogradely according to the stenosis site, and diagnostic angiography was performed through the sheath. A hydrophilic-coated, steerable, 0.035” Terumo radifocus wire (Terumo Corp., Tokyo, Japan) was passed through. A balloon catheter was passed over the guidewire and advanced to the most central lesion. Depending on the size of the veins, 4-7 mm balloons (Inva- tec, Medtronic, Inc. Minneapolis, USA) were used. Balloon size was determined based on fistulography findings or known graft diameter. A pressure of 12-14 atm was routinely used. If this was not effective in breaking the lesion, a high-pressure balloon CONQUEST® PTA Dilatation Catheters (Bard, Peripheral Vascular, Tempe, AZ, USA) was sequentially applied at 30 atm. The balloon was inflated for 30-90 seconds each inflation. Multiple inflations were used for resistant lesions. The choice of the appropriate percutaneous approach depended on the size and location of the thrombus, as detected by angiography. A short segment thrombosis could be treated simply with balloon angioplasty alone; however, an extensive thrombosis necessitated the addition of MIT. When the stenotic lesion was fully opened, the balloon was taken out of the sheath to ensure proper blood flow. After a successful procedure, the wire, balloon, and sheath were immediately removed. Hemostasis was achieved by manual compression using gauze and elastic bands around the puncture wound. The patient was monitored for 30 minutes after the procedure for bleeding and discomfort and was then taken out of the laboratory.

![Figure 1. Strategy for group allocation. PTA, percutaneous transluminal angioplasty.](image-url)
Minimally invasive thrombectomy

When a large organized thrombus occupied and burdened a vessel, thrombectomy was performed (Figures 2, 3). This involved inflation of a balloon over the proximal site of the arteriovenous (AV) anastomosis segment and total occlusion of blood flow. Then, after applying a local aseptic and anesthesia, a longitudinal skin incision was made to identify the vessel and to retrieve the thrombi from the vessel by squeezing or using a Fogarty catheter balloon (Edwards Lifesciences Corporation, California, United States). A Fogarty catheter with a collapsed balloon at its end was passed into the vessel.
from the incision site and past the clot. The balloon was then inflated and pulled back to remove the clot. This was repeated from both sides of the incision until the vessel was clear. The wound was sutured layer-by-layer, starting at the vessel then the skin with Prolene 4.0 sutures. The proximal occluded balloon was then deflated, the bleeding was checked, and follow-up angiography was performed. PTA was repeated if there was residual stenosis.

Follow-up after PTA and thrombectomy

Patients enrolled in this study were followed up by nephrologists at our hospital hemodialysis unit and nearby hemodialysis centers at 7, 30, 60, 120, and 180 days following the procedure. At each follow-up visit, we assessed the patency of AV access and complications such as bleeding or infection. Re-intervention and vascular access dysfunction were determined based on the following criteria: total occlusion, hardened aneurysm, decreased or absent thrill, increased pulsation, limb swelling, difficulty in cannulation, prolonged bleeding after hemodialysis, high venous pressure during hemodialysis, or presence of a suction phenomenon at the arterial site. Patients were referred for repeat angiography and intervention if the above criteria were met.

Definitions and statistics

Based on the Society of Interventional Radiology guidelines, we used the following definitions of procedure success and patency rate in this study: Procedure success was defined as restoration of flow in combination with less than 30\% residual stenosis of the target lesion. Clinical success was defined as the ability to resume dialysis at least once after the intervention. Primary patency was determined if the patient exhibited no revascularization of the target lesion during follow-up. Secondary patency was determined based on the patency of the target lesion after treatment of a re-occlusion of the index lesion. Complications were classified as follows: vessel perforation which required surgery, hospital admission, unplanned increase in the level of care, permanent adverse sequelae, or death. In this study, a thrombus was considered to be “large” if the largest diameter was > 3 cm in a fistulagram. AV shunt age referred to the interval between the creation of the AV shunt to intervention. Baseline characteristics are presented as percentages for categorical variables and means and standard deviations for continuous variables. A chi-square test was used for categorical variables and a two-sample Student’s t-test for continuous variables. Kaplan-Meier survival curves were generated for primary patency and secondary patency. For all comparisons, \( p < 0.05 \) was considered to be statistically significant. All data were analyzed using SPSS statistical package version 23.0 (SPSS Inc. Chicago, IL, USA).

RESULTS

From June 2014 to May 2015, 746 patients underwent PTA in our hospital. Of these, 425 consented to participate in the study. Among these patients, 46 who underwent PTA and MIT simultaneously were enrolled and 379 were enrolled as the PTA alone group (Figure 1). The mean age was 63.1 ± 10.5 years, and 40\% were male (Table 1). There were no significant differences between the MIT group and PTA only group in age, sex, BMI, underlying diseases, and use of medications. In the MIT group, 44 patients (95.7\%) had complete blood flow occlusion by thrombi, compared to 166 in the PTA alone group (43.8\%, \( p = 0.01 \)). The mean shunt age of the MIT group (63 ± 5.0 months) was significantly longer than that in the PTA only group (36 ± 3.6 months, \( p = 0.01 \)). Adjuvant pharmacological thrombolysis was achieved with 2500 units of heparin before and after the procedure.

Patency rate

Comparisons of patency rates are shown in Table 2. There were no significant differences in primary patency
rate (Figure 4, p = 0.93) or secondary patency rate (Figure 5, p = 0.28) between the MIT and PTA alone groups at any follow-up point. One hundred and sixty-six patients (43.8%) met the large thrombus criteria and received PTA only. The primary and second patency rates are included as a supplement to this report (Supplement Table 1).

**Immediate outcome**
All patients in the MIT group achieved clinical success. Two patients in the MIT group received MIT following PTA due to residual stenosis. The average procedure time for simultaneous MIT and PTA was 67.4 ± 29.0 minutes compared to 18.3 ± 12.5 minutes for PTA alone.

**Complications**
There were no complications, including vessel perforation requiring surgery, hospital admission, unplanned increase in the level of care, permanent adverse sequelae, or death. A few venous dissections were encountered, but all were resolved with prolonged balloon inflation. There were no arterial embolism events following MIT.

**DISCUSSION**
Vascular access thrombosis, especially for huge and organized thrombi, is a major challenge for interventional physicians. Many hemodialysis centers first refer patients with total occlusion to vascular surgeons after thrombectomy to create blood flow prior to referral back for PTA. If the patient is treated with PTA directly, the fragmented thrombi may be dislodged and travel to the pulmonary artery after blood flow is restored. Large, organized thrombi may not wash away due to marked inflammatory activity.4 Bech et al. reported that residual thrombi are common and demonstrate an irregular sur-

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**Table 2. Comparison of patency rate**

<table>
<thead>
<tr>
<th>Procedure time (min)</th>
<th>Total (N = 425)</th>
<th>MIT (N = 46)</th>
<th>PTA alone (N = 379)</th>
</tr>
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<tbody>
<tr>
<td>Success rate (%)</td>
<td></td>
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<td></td>
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<tr>
<td>Primary patency (%)</td>
<td>7 days</td>
<td>97.12%</td>
<td>95.56%</td>
</tr>
<tr>
<td></td>
<td>30 days</td>
<td>93.20%</td>
<td>93.33%</td>
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<tr>
<td></td>
<td>60 days</td>
<td>86.06%</td>
<td>91.11%</td>
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<tr>
<td></td>
<td>120 days</td>
<td>74.26%</td>
<td>82.22%</td>
</tr>
<tr>
<td></td>
<td>180 days</td>
<td>69.67%</td>
<td>69.77%</td>
</tr>
<tr>
<td>Secondary patency (%)</td>
<td>7 days</td>
<td>97.60%</td>
<td>95.56%</td>
</tr>
<tr>
<td></td>
<td>30 days</td>
<td>95.63%</td>
<td>95.56%</td>
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<td></td>
<td>60 days</td>
<td>93.89%</td>
<td>91.11%</td>
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<td></td>
<td>120 days</td>
<td>92.82%</td>
<td>91.11%</td>
</tr>
<tr>
<td></td>
<td>180 days</td>
<td>92.48%</td>
<td>86.95%</td>
</tr>
</tbody>
</table>

MIT, minimally invasive thrombectomy; PTA, percutaneous transluminal angioplasty.

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**Figure 4.** Kaplan-Meier curves showing the primary patency rate between MIT and PTA alone. MIT, minimally invasive thrombectomy; PTA, percutaneous transluminal angioplasty.

**Figure 5.** Kaplan-Meier curves showing secondary patency rate between MIT and PTA alone. MIT, minimally invasive thrombectomy; PTA, percutaneous transluminal angioplasty.
face. This surface is a source of turbulence and platelet aggregation and may thereby facilitate restenosis.\(^5\) We found that MIT was a rapid, effective, and safe rescue procedure for removing large, organized thrombi to establish hemodialysis vascular access when initial PTA failed. Our primary and secondary patency rates were higher than previously reported. For example, Hung et al. reported overall primary patency rates of 74.1%, 48.1%, and 34.3% and overall secondary patency rates of 95.4%, 93.5%, and 91.7% at 30, 90, and 180 days, respectively, and Trerotola et al. reported a 3-month primary patency rate of 39%.\(^6,7\)

Current percutaneous thrombi removal devices such as the aspiration catheter and PTD have shown unsatisfactory results for the removal of organized thrombi. However, a significant portion of the thrombus may remain within the access site despite the use of these modalities, particularly when aneurysms form during vascular access. Also, the catheters of these devices are relatively small compared to the diameter of vascular access, and firm, organized thrombi are difficult to fragment.

Only two types of endovascular mechanical thrombectomy devices are currently available in our country: the Arrow-Trerotola PTD and the rheolytic thrombectomy device “AngioJet system” (Boston Scientific). The PTD catheter works as a basket that expands and traps the thrombus. After capturing the thrombus, the PTD rotates up to 3,000 rpm, fragments the thrombus, and drags it out. The AngioJet system uses both thrombolytic agent infusion and thrombus aspiration. Philip et al. reviewed the safety and efficacy of the AngioJet system, but the quality of the current evidence is poor.\(^8\) The efficacy of wall-contact devices is supported by an angiographic study that showed that wall-contact devices left less residual thrombus than hydrodynamic devices.\(^9\) Unfortunately, these methods are very expensive and not covered by the Taiwan National Health Insurance Program.

The procedure times in the PTA alone and simultaneous MIT group were 18.3 ± 12.5 mins and 67.4 ± 29.0 mins, respectively; the simultaneous MIT procedure time was shorter than for the AngioJet system but longer than PTD alone.\(^6,10\)

Most clotted AVFs have one or more underlying stenotic lesions. A complete thrombectomy, in conjunction with angioplasty of the stenotic lesion, is usually required to successfully treat an AVF thrombosis and save the previous dialysis access site.\(^11\) MIT has been used to salvage thrombosed AVFs in our institution since June 2000. MIT can feasibly remove thrombi in the surgical field and correct underlying causative lesions, as determined by intra-operative fluoroscopy. MIT had a superior technical success rate (95.56%) and higher primary patency rate than percutaneous mechanical thrombectomy in other reports.\(^12,13\)

To avoid complications, we followed the following principles. 1. We choose an appropriately sized balloon for inflow vessel occlusion to avoid bleeding and vessel rupture during thrombectomy. We did not use traditional vascular clamps at the proximal and distal part of the fistula, since a residual thrombus could accidentally flush to the brachial artery and cause an arterial emboli. 2. We preferred to pass the wire through the lesion into the central vein and conduct a contrast test to evaluate the thrombus burden. This step allowed us to evaluate whether the amount of removed thrombus was adequate. Retaining the wire in the vessel during open thrombectomy also allowed us to complete bailout therapy if necessary. Examples of bailout therapy included covered stent deployment or aspiration thrombectomy. 3. We favored a longitudinal skin incision at the aneurysm, as this facilitates easier removal of the thrombus and allows for partial or reduction aneurysmectomy. A large aneurysm or aneurysmal degeneration is commonly accompanied by a large thrombus burden.

Concerning safety, there are reports of vessel rupture-related complications associated with the AngioJet system\(^10\) and arterial embolism in PTD.\(^6\) Although the possibility of vessel rupture and arterial embolism is minor due to layer-by-layer wound closure and occlusion of blood flow before thrombectomy, there is a risk of blood leakage after wound suture. The results of our study confirm the safety of MIT for the treatment of large, organized thrombi. Another safety concern is the risk of acute pulmonary embolism. Since we occluded blood flow before removing the thrombi, there was a low possibility of acute pulmonary embolism. Another concern regarding long-term effects is suture wound restenosis; however, we observed no suture wound restenosis or infection among our study subjects because the wound was sutured layer-by-layer.
Limitations
The primary limitation of this study was that it was not a head-to-head comparison of the PTA and MIT procedures. All patients in the MIT group received traditional PTA first.

Second, this study was performed in a single hospital, and MIT is a pioneering procedure performed by an internal medicine physician. Third, the number of patients was relatively small, with a short follow-up period. Finally, the telephone interviews and follow-up depended on the cooperation of the patients and hemodialysis centers.

CONCLUSIONS
Large, organized thrombi which impede hemodialysis vascular access are challenging for interventional doctors. There are concerns about the bleeding risk with thrombolytic therapy, and endovascular devices are expensive. MIT is a new alternative salvage technique for large, organized thrombi that impede hemodialysis access when traditional PTA fails.

ACKNOWLEDGMENT
None.

CONFLICT OF INTEREST
All authors have nothing to disclose and declare no conflicts of interest.

REFERENCES
SUPPLEMENT

Supplement Table 1. Primary patency and secondary patency of large thrombus with PTA only

<table>
<thead>
<tr>
<th></th>
<th>7 days</th>
<th>30 days</th>
<th>60 days</th>
<th>120 days</th>
<th>180 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>93.14%</td>
<td>91.26%</td>
<td>82.41%</td>
<td>72.22%</td>
<td>67.1%</td>
</tr>
<tr>
<td>Secondary patency</td>
<td>94.33%</td>
<td>93.45%</td>
<td>90.64%</td>
<td>89.16%</td>
<td>85.26%</td>
</tr>
</tbody>
</table>

PTA, percutaneous transluminal angioplasty.