Signature: © Pol J Radiol, 2014; 79: 363-367
DOI: 10.12659/PJR.890801

Polish Journal of Radiology
www.PolRadiol.com
ORIGINAL ARTICLE

Received: 2014.04.03
Accepted: 2014.05.05
Published: 2014.10.18

Pharmacomechanical Thrombolysis for the Treatment of Thrombosed Native Arteriovenous Fistula: A Single-Center Experience

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Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Summary

Background: Native arteriovenous fistula is one of the important routes for hemodialysis patients because of increased long-term survival and preservation of quality of life. We reported on a single-center experience with using pharmacomechanical thrombolysis for the treatment of thrombosed native arteriovenous fistula.

Material/Methods: This was a retrospective study of 12 hemodialysis patients (8 males and 4 females) with 14 thrombosed distal forearm Brescia-Cimino radiocephalic fistulas who were referred for pharmacomechanical thrombolytic treatment in the intervention unit of the Radiology Department, from 1 January 2010 to 30 December 2011. Demographic data, technical success rates, clinical success rates and complications were evaluated. The patency was evaluated by Kaplan-Meier analysis.

Results: The technical and clinical success was found in 12 thrombosed fistulas. Only 3 procedures had minor complications including small amounts of adjacent soft tissue hematoma. There were no procedure-related major complications. The primary patency rates at 6 and 12 months were 67% and 50%. The secondary patency rates at 6 and 12 months were 75% and 67%.

Conclusions: Pharmacomechanical thrombolysis is a minimally invasive, effective, durable, and safe procedure for the treatment of thrombosed native arteriovenous fistula. This procedure can be considered as an alternative treatment for thrombosed dialysis fistulas.

MeSH Keywords: Arteriovenous Fistula • Thrombolytic Therapy • Thrombosis

PDF file: http://www.polradiol.com/abstract/index/idArt/890801

Background

Vascular access is one of the important routes for hemodialysis patients because it helps to increase long-term survival and preserve their quality of life. There are normally two forms of dialysis vascular access: native arteriovenous fistula (AVF) and prosthetic arteriovenous graft (AVG). There are several superior benefits of AVFs compared with AVGs including better patency, fewer infections, lower incidence rates of vascular steal syndrome, and lower morbidity related to shunt creation [1–3]. However, AVFs have also disadvantages compared with AVGs, such as lower rates of functioning accesses due to immaturity or longer time to become a mature access. In the past, the clinical practice guidelines of the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-DOQI) recommended that ultimately 40% of patients undergoing hemodialysis should have an AVF [4]. However, after revision of the clinical practice guidelines to improve patient survival and quality of life and increase the rate of native fistula placement, the rate of fistulas by 2009 was set at 65% [5]. Thus, to increase the number of native AVFs, the maintenance and repair of these dialysis accesses should be optimized [3].

Thrombosed native AVFs are considered an emergency condition for hemodialysis patients because this condition

causes a decrease in the quality of life and results in sequelae such as pulmonary edema or hyperkalemia. The keys to treat thrombosed native AVFs are restoration and maintenance of function as long as possible. The standard treatment is surgical thrombectomy. However, surgical thrombectomy with revision has a poor outcome with reported success rates ranging from 28% to 73% [6–8]. Recently, percutaneous treatment for salvage of thrombosed native AVFs is performed which includes thromboaspiration, balloon maceration of the clot and mechanical thrombectomy. Reported technical success rates of these techniques vary in a range from 73% to 100% [9–13]. Percutaneous pharmacomechanical thrombolysis is another minimally invasive method using thrombolytic drugs and a balloon catheter for treatment of thrombosed native dialysis fistulas. The most common thrombolytic drugs used are urokinase and recombinant tissue plasminogen activator (rt-PA). The objective of this study was to report on our experience with percutaneous transluminal thrombolysis with angioplasty in thrombosed native AVFs.

Material and Methods

Patients

This was a retrospective study of all patients with thrombosed distal forearm Brescia-Cimino radiocephalic fistulas who underwent treatment by pharmacomechanical thrombolysis in the intervention unit of the Radiology Department from 1 January 2010 to 31 December 2011. The patients had no contraindications to thrombolytic agents (i.e., allergy to rt-PA, shunt infection, bleeding diathesis, recent gastrointestinal bleeding, significant stroke including hemorrhage or large infarction within the previous 6 months, prior ocular hemorrhage or prior major surgery within the previous 3 months), and no history of contrast reaction. Written informed consent explaining the procedure was obtained from all patients before intervention. The present study was approved by the Ethics Committee of our institute.

Salvage procedure

A 6 French (F) vascular sheath was introduced retrograde into the patent cephalic vein under ultrasound guidance. A small amount of nonionic contrast medium was injected using the road-mapping technique to clearly define the occluded segment and to evaluate the patency of the venous drainage pathway to the right atrium. An antegrade puncture of the brachial artery was also performed with a 20-gauge cannula sheath for fistulography. A total dose of 3000 IU of heparin was injected via the vascular sheath. Then, a 4 F multiside-hole infusion catheter (Cragg-Mcnamara, EV3, California, USA) was placed in the thrombosed segment of the cephalic vein with its tip nearly at the arteriovenous anastomosis. Catheter-directed thrombolysis was performed by the pulse-spray technique by injection of rt-PA via the multiside-hole infusion catheter (Cragg-Mcnamara, EV3, California, USA). A total dose of 5–7 mg of rt-PA (1mg/mL in a sterile water solution) was administered: 2 mg of loading dose and forceful injections of 0.2 mg of rt-PA every 30 seconds with a 1-mL tuberculin syringe. Then, angioplasty was performed using 5–6 mm balloon catheter (ConQuest, Bard, AZ, USA) to macerate residual clots and treat all underlying stenoses including arteriovenous anastomosis. After balloon angioplasty, complete fistulography was performed from arteriovenous anastomosis to the right atrium. If residual thrombi were detected, additional suction aspirations with a 6 F guiding catheter (Vistabrite tip, Cordis, FL, USA) with infusion of 1–2 mg of rt-PA were performed. The course of the procedure was shown in Figure 1. After the procedure, the vascular sheath was removed and manual compression was performed for hemostasis.

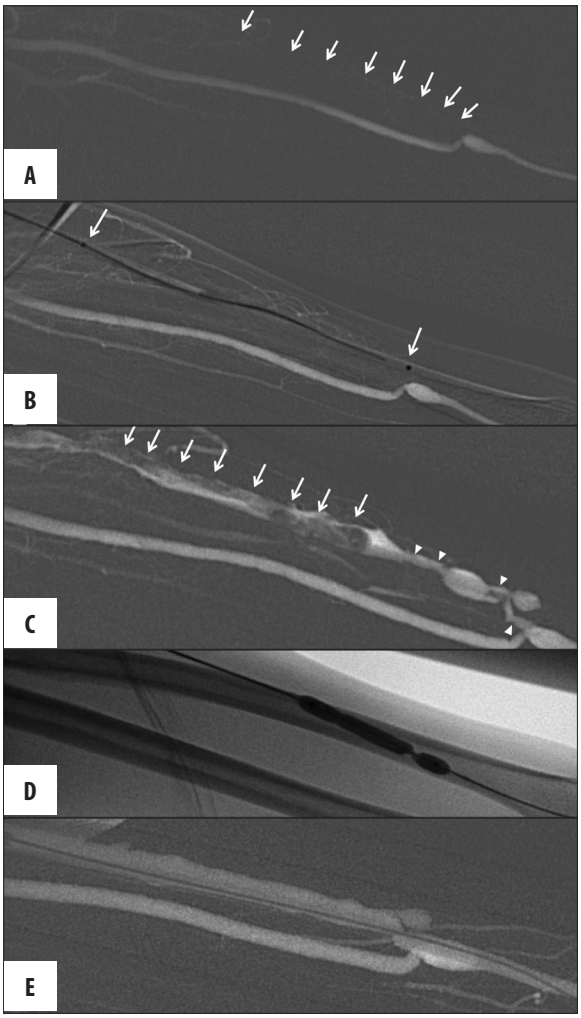

Figure 1. Thrombosed left forearm radio-cephalic dialysis fistula. (**A**) Antegrade fistulogram via left brachial artery showed non-opacity of the cephalic vein (arrows) representing total thrombosis. (**B**) A multiside-hole infusion catheter was placed into the intraluminal thrombus via retrograde left cephalic vein approach. Note proximal and distal markers of the catheter (arrows). (**C**) Fistulogram after thrombolysis showed residual intraluminal thrombi (arrows) with underlying stenoses of cephalic vein (arrow heads). (**D**) Balloon angioplasty was performed to macerate the clot and dilate underlying stenoses. (**E**) The final fistulogram demonstrated patency of the fistula without residual thrombi or segmental stenosis.

Definition

According to the standard practice guidelines published by the Society of Interventional Radiology [14], technical

success was defined as restoration of flow combined with less than 30% residual luminal diameter stenosis. Clinical success was defined as resumption of normal dialysis for at least one session. Primary patency rate was defined as the percentage of patent fistulas after intervention until the next access thrombosis or re-intervention. Secondary patency rate was defined as the percentage of patent fistulas after intervention until the access was surgically declotted, revised or abandoned. Major complications were defined as complications that required additional treatment, permanent sequelae or death. Minor complications were defined as problems requiring no or nominal therapy and no sequelae.

Statistical analysis

The information on patients and fistulas was retrospectively reviewed. The outcomes including techniques and clinical success rates and complications were determined by frequency. Primary and secondary patency rates were calculated by using the Kaplan-Meier test.

Results

Twelve patients with 14 thrombosed dialysis fistulas were enrolled in the study. There were 8 males and 4 females. The mean age of the patients was 55.3±6.4 years (range, 45 to 69 years). The underlying cause of end-stage renal disease requiring hemodialysis included diabetes mellitus (n=8), chronic glomerulonephritis (n=3) and IgA nephropathy (n=1). All thrombosed dialysis fistulas were distal forearm Brescia-Cimino radiocephalic fistula. Two patients had two episodes of thrombosed fistula. The average time of fistula function after creation was 28.2±7.5 months (range, 12 to 36 months). The mean length of thrombosed segment was 10.3±2.6 cm (range, 6.5 to 13 cm). Ten thrombosed fistulas were recanalized within 24 hours and 4 were performed within 48 hours.

The technical success was found in 12 thrombosed AVFs. Technical failure occurred in 2 thrombosed AVFs due to the impossibility of traversing a guide-wire through the stenotic segment of the cephalic vein and stenotic AV anastomosis. In those 2 thrombosed AVFs, open revisions were performed. Twelve thrombosed AVFs with successful thrombolysis with angioplasty was routinely used to carry out dialysis. The mean time of rethrombosis of the primary and secondary patency was 7.4 and 10.5 months, respectively.

One episode of venous rupture occurred, but it was successfully managed by prolonged inflation of the balloon catheter. In another three procedures there were small amounts of perivenous hematoma due to extravasation of the previous recent puncture site for dialysis. However, the leakage was managed by manual compression. None of the patients had clinical respiratory distress during or immediately after the procedure that would represent pulmonary embolism. Moreover, no clinical signs of hemorrhagic stroke occurred. There were no other procedural-related major complications.

The primary patency rates at 6 and 12 months were 67% and 50%. The secondary patency rates at 6 and 12 months were 75% and 67% (Figure 2). One patient underwent kidney transplantation at 12 months after the procedure. Another patient died from myocardial infarction at 16 months after the procedure.

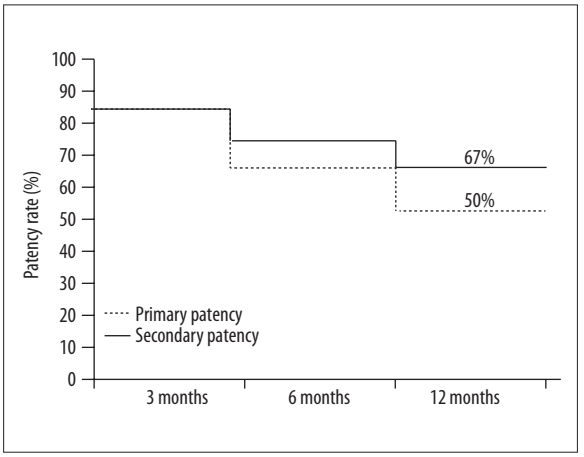

Figure 2. Kaplan-Meier curve for primary and secondary patency rates after restoration of dialysis fistula.

Discussion

The goal to treat thrombosed dialysis fistula is restoration and maintenance of the access function as long as possible. However, endovascular declotting of thrombosed dialysis fistula is a more difficult procedure than correction of the thrombosed dialysis graft for the following reasons: 1) thin-walled native veins are more prone to rupture, 2) the anatomy of native veins is more complex with multiple sites of stenosis, 3) the acute angle of radio-cephalic anastomosis and an underlying tight stenosis make it difficult to pass the guide wire and catheter, and 4) the aneurysmal dilatation of native veins makes the clearance of thrombi more difficult [10]. Today, percutaneous endovascular correction of the thrombosed native fistula is another option for treatment. The two favorite methods include purely mechanical thrombectomy and pharmacomechanical thrombolysis, but it is still unclear which one is better [15]. The advantage of mechanical thrombectomy is shorter time of the operation. However, the disadvantage of this method includes expensive thrombectomy devices and potential damage to the venous wall [16]. While thrombolysis is the procedure that uses a thrombolytic agent to lyse the thrombus, the thrombolytic agent causes clot degeneration by conversion of plasminogen to plasmin and then change of fibrin into fibrin degradation products that help to reduce the clot burden in the fistula. We used rt-PA in our study because it is available in our country. In addition, it is a fibrin-specific thrombolytic agent and has a short half-life; therefore, the risk of systemic bleeding is low [17]. However, urokinase is another thrombolytic agent that is widely used [3,10,15].

Two techniques of thrombolysis that are used include local infusion and pulse-spray techniques. For the local infusion technique, some authors used percutaneous directed puncture into the thrombus and waited 2 to 8 hours for clot lysis before thrombo-aspiration and balloon angioplasty [3,10]. In our opinion, this technique consumes too much

time, is connected with increased risk of local bleeding and need for close monitoring to avoid systemic dysfunction. The pulse-spray technique is a method that injects a thrombolytic drug for lysis of the thrombus in the form of periodic forceful injections (every 30 seconds in our study) after an injection of a loading dose. When this technique is used with multiside-hole infusion catheter being placed along the whole thrombus, it increases the effectiveness of thrombolysis due to the full injection force of the thrombolytic agent as a spray which in turn increases the interactive surface area of the thrombus resulting in effective thrombus maceration. Moreover, the lysis-resistant surface membrane of the thrombus can be penetrated easily [17].

This study showed an 85.7% technical and clinical success rates. The primary and secondary patency rates were 67% and 75% at 6 months and 50% and 67% at 12 months, respectively. Usually, a technical failure is due to the impossibility of traversing a guide wire through the occluded segment or a tight anastomotic stenosis as in our study and in previous studies [3,15,18,19]. A study by Cho et al. [15] used the pulse-spray technique with injection of urokinase for thrombolysis of the thrombosed AVF as in our study. The results showed 75% technical and clinical success rates with primary and secondary patency rates of 64% and 71% at 6 months and 55% and 63% rates at 12 months, respectively. Another study by Rajan et al. [18], who also used a similar technique, reported a 77% technical success rate with primary and secondary patency rates of 28% and 44% at 6 months and 24% and 44% rates at 12 months, respectively. When compared with other studies, the recanalization of thrombosed AVFs using the infusion technique followed by balloon angioplasty such as in the study by Zaleski et al. [19] showed an 82% technical success rate with primary and secondary patency rates at 6 months and 12 months of 71% and 100%, and 64% and 100%, respectively. Our results included a higher technical success rate than in those three studies [15,18,19] possibly because most of the thrombosed dialysis fistulas in this study received an early treatment within 24 hours. We think that early thrombolysis of a fresh thrombus has a higher chance of procedural success because of the reduced risk of permanent endothelial damage and thrombus propagation. As for patency, our results were similar to the study by Cho et al. [15] and better than in the study by Rajan et al. [18]. In contrast, the infusion technique of Zaleski et al. [19] resulted in higher primary and secondary patency rates at 6 months and 12 months than in our study, because that study excluded the results of initial treatment failure. However, there were no data to support whether pulse-spray or infusion technique was better. The goal of 40% of primary patency rates at 3 months was recommended by NKF-DOQI guidelines for the treatment of thrombosed fistulas [5]. However, our results and those in previous studies [3,9,10,15,19] had a higher patency rate than in the standard guideline [5]. The interventional radiologist, interventional nephrologist or vascular surgeon should attempt to perform this procedure as an alternative for treatment of thrombosed dialysis fistulas.

Localized hematoma at the perivenous or perigraft region is the most common complication of the thrombolysis procedure, particularly in cases which use the infusion technique. In our series, we found this complication in three procedures. Other less common complications included puncture site hematoma, venous rupture or dissection and arterial embolism [14]. However, these complications can be managed by conservative or endovascular treatment. Serious complications of pharmacomechanical thrombolysis are uncommon. Major hemorrhage requiring additional treatment was reported in 1% to 7% of the cases [20]. Clinically significant pulmonary embolism is a rare complication of the pharmacomechanical thrombolytic procedure of which the incidence ranges from 0% to 1% [21]. Shah et al. [22] reported a case of cardiac arrest from bilateral pulmonary emboli following thrombolysis of an arteriovenous fistula. However, usually pulmonary emboli after thrombolysis are clinically asymptomatic and these asymptomatic clots can be dissolved by internal autolysis. There was no major bleeding or clinically significant pulmonary emboli in our study.

There are some limitations to our study. Firstly, that was a retrospective study with a small number of enrolled patients. Secondly, the decision on thrombolysis was dependent on a consultation with a clinician which might have been the cause of selection bias. Last but not least, there was no statistical comparison between different techniques.

Conclusions

Pharmacomechanical thrombolysis is a minimally invasive procedure. Our results showed a high procedural success rate, good patency rate, and no major complications. We think that this procedure should be performed as the alternative treatment method in patients with thrombosed native fistula.

Acknowledgment

The authors would like to thank Mr. Glenn Shingledecker of the International Affairs Office, Faculty of Medicine, Prince of Songkla University for editing the English.

References:

1. Beathard GA, Settle SM, Shields MW: Salvage of the nonfunctioning arteriovenous fistula. Am J kidney Dis, 1999; 33: 910–16
2. Chazan JA, London MR, Pono LM: Long-term survival of vascular accesses in a large chronic hemodialysis population. Nephron, 1995; 69: 228–33
3. Liang HL, Pan HB, Chung HM et al: Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. Radiology, 2002; 223: 339–44
4. NKF-K/DOQI Clinical practice guidelines for hemodialysis adequacy: update 2000 [editorial]. Am J Kidney Dis, 2001; 37: S7–64
5. NKF-K/DOQI Clinical practice guidelines for vascular access 2006 [editorial]. Am J Kidney Dis, 2006; 48: S176–247
6. Burger H, Kluchert BA, Kootstra G, Kitslaar PJ, Ubbink DT: Survival of arteriovenous fistulas and shunts for haemodialysis. Eur J Surg, 1995; 161: 327–34
7. Riordan S, Frawley J, Gray L, Niesche J: Primary access surgery for long-term haemodialysis. Aust N Z J Surg, 1994; 64: 763–67

8. Schwab SJ, Raymond JR, Saeed M et al: Prevention of hemodialysis fistula thrombosis: early detection of venous stenosis. Kidney Int, 1989; 36: 701–11
9. Turmel-Rodriques L, Sapoval M, Penqloan J et al: Manual thromboaspiration and dilation of thrombosed dialysis access: mid-term results of a simple concept. J Vasc Interv Radiol, 1997; 8: 813–24
10. Turmel-Rodriques L, Penqloan J, Rodrique H et al: Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. Kidney Int, 2000; 57: 1124–40
11. Wen SC, Pu SY, Tsai KC et al: Angiojet thrombectomy to salvage thrombosed native dialysis fistula. Acta cardiol Sin, 2011; 27: 101–8
12. Jain G, Maya ID, Allon M: Outcome of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. Semin Dial, 2008; 21: 581–83
13. Hyun JH, Lee JH, Park SI: Hybrid surgery versus percutaneous mechanical thrombectomy for the thrombosed hemodialysis autogenous arteriovenous fistulas. J Korean Surg Soc, 2011; 81: 43–49
14. Aruny JE, Lewis CA, Cardella JF et al: Quality improvement guidelines for percutaneous management of the thrombosed or dysfunctional dialysis access. J Vasc Interv Radiol, 2003; 14: S247–53
15. Cho SK, Han H, Kim SS et al: Percutaneous treatment of failed native dialysis fistulas: use of pulse-spray pharmacomechanical thrombolysis as the primary mode of therapy. Korean J Radiol, 2006; 7: 180–86
16. Sofocleous CT, Cooper SG, Schur I et al: Retrospective comparison of the Amplatz thrombectomy device with modified pulse-spray pharmacomechanical thrombolysis in the treatment of thrombosed hemodialysis access grafts. Radiology, 1999; 231: 561–67
17. Roberts A. Thrombolysis: clinical applications. In: Baum S, Pentecost MJ, editor. Abrams' Angiography: Interventional Radiology. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006; 233–56
18. Rajan DK, Clark TW, Simons ME et al: Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. J Vasc Interv Radiol, 2002; 13: 1211–18
19. Zaleski GX, Funaki B, Kenney S et al: Angioplasty and bolus urokinase infusion for the restoration of function in thrombosed Brescia-Cimino dialysis fistulas. J vas Interv Radiol, 1999; 10: 129–36
20. Valji K: Transcatheter treatment of thrombosed hemodialysis access graft. Am J Roentgenol, 1995; 164: 823–29
21. Weng FL, Berns JS: Complication of percutaneous treatment of thrombosed hemodialysis access grafts. Semin Dial, 2003; 16: 257–62
22. Shah A, Ansari N, Hameded Z: Cardiac arrest secondary to bilateral pulmonary emboli following arteriovenous fistula thrombectomy: A case report with review of the literature. Case Rep Nephrol, 2012; 2012: 831726