Pharmacomechanical Thrombolysis of Dialysis Access Grafts Using the MTI Castañeda Over-the-Wire Brush Catheter and Reteplase

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ABSTRACT

Pharmacomechanical thrombolysis (PMT) has emerged as an alternate treatment used in most patients presenting with a thrombosed hemodialysis graft. Although the gold standard, surgical revision of thrombosed hemodialysis grafts is reserved for those cases of recurrent thrombosis despite the use of percutaneous techniques and for complicated cases after PMT. Nevertheless, as for every other procedure, PMT has its own set of limitations and cost issues. New mechanical devices have begun to emerge on the market to help accelerate clot dissolution with or without thrombolytic medications. These devices have decreased the time required to lyse clot and decrease the overall cost of percutaneous treatment. This article describes the use of the Microtherapeutics, Inc. (MTI) Castañeda over-the-wire brush and our experience with this device in the treatment of the clotted hemodialysis graft.

KEYWORDS: Dialysis, thrombolysis, intervention

There are ~155,000 individuals receiving chronic hemodialysis in the United States.¹ Vascular access complications are the single largest cause of morbidity, accounting for ~15% of all hospitalizations in the hemodialysis population.² These complications add up to an annual cost to the Medicare program of between \$700 and \$900 million.³ Because of the rapid increase of patients with end-stage renal disease (ESRD) in the United States, dialysis access has become a commonly performed procedure at many hospitals. More than 80% of vascular accesses in the United States are expanded polytetrafluoroethylene (ePTFE) grafts.⁴ The 1-year patency rate for ePTFE hemodialysis grafts has been reported to be ~5%.^{5,6} An estimated 60% of individuals with an ePTFE graft will need to undergo at least one revision per year.⁷ The most

common cause of graft failure is thrombosis secondary to stenosis.⁸⁻¹⁴

Initial surgical therapy traditionally has involved either the use of the Fogarty balloon catheter to remove occlusive in situ thrombi or emboli with or without surgical revision of the graft, or complete replacement of the graft. However, these surgical interventions have been associated with acute complications including vascular damage and delayed complications of accelerated atherosclerosis and intimal/medial hyperplasia. Percutaneous thrombolytic interventions have the advantage of direct visualization of possible underlying etiologies for graft failure. The arterial and venous anastomoses, as well as the arterial inflow vessel and venous outflow veins, including the central veins, can be more accurately assessed under fluoroscopy.

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In the last 10 years, alternative methods for treatment of thrombosed dialysis grafts have emerged. Pharmacological thrombolysis (PMT) never became the standard percutaneous treatment for thrombosed arteriovenous (AV) dialysis grafts due mainly to repeated imaging, intensive care monitoring, and the expense required by pharmacological thrombolysis. Recently, however, there has been a resurgence in efforts to find a faster, more efficient method to eradicate clot from the graft. Consequently, new mechanical devices have begun to emerge on the market to help accelerate clot dissolution with or without thrombolytic medications. These devices have decreased the time required to lyse clot and decrease the overall cost of percutaneous treatment. The Microtherapeutics, Inc. (MTI) Castañeda over-the-wire brush (Fig. 1) is one such mechanical device.

The use of a mechanical device in conjunction with infusion of a thrombolytic agent to treat the thrombosed hemodialysis graft has been named PMT. This article describes our technique and experience using the MTI over-the-wire catheter and adjuvant reteplase infusion.

PHARMACHOMECHANICAL THROMBOLYSIS

The Castañeda over-the-wire thrombolytic brush is a soft nylon, 1.5-cm-long, 7-mm-diameter brush loaded in a 6-French catheter attached to a motor drive (Fig. 1) capable to be advanced over a 0.035 in guidewire. The brush is exposed outside its external catheter once the motor drive is connected to the catheter.

Patients are prepared and draped in the standard aseptic fashion for the procedure. The graft is punctured near the arterial and venous anastomoses. Two short 6-French vascular sheaths are inserted in a criss-cross fashion using the standard Seldinger technique (Fig. 2). At this point, a 5-French multipurpose catheter is

Figure 2 Short, 6-French vascular sheaths inserted into the venous and arterial limbs of the hemodialysis graft in a criss-cross fashion.

advanced over a guidewire through the vascular sheath placed in the arterial limb of the graft to place the guidewire across the venous anastomosis and selectively catheterize the venous outflow. A venogram is obtained from the venous anastomosis to the right atrium. Lesions identified in the venous outflow are treated using the indicated percutaneous intervention.

Once the venous outflow is cleared, the diagnostic angiographic catheter is removed leaving the guidewire across the venous anastomosis. The MTI Castañeda over-the-wire thrombolytic catheter is advanced into the graft, with the brush within the external catheter, over the guidewire, placing the tip just proximal to the venous anastomosis, within the distal graft (Fig. 3). The thrombolytic agent we use consists of a mixture of 50:50 (14.5/14.5 cm³) normal saline/intravenous contrast medium and a 1-cm³ aliquot of reteplase (1 U/cm³) in a 30-cm³ syringe. This syringe is attached to the side port of the MTI Castañeda over-the-wire catheter. The motor drive is then attached to the catheter, exposing the brush outside the external catheter. PMT is

Figure 1 The MTI Castañeda brush consists of a soft nylon, 1.5-cm-long, 7-mm-diameter brush, which comes loaded in a 6-French catheter body attached to a motor drive.

Figure 3 Diagram depicting the location of the MTI Castañeda over-the-wire thrombolytic brush catheter at start of pharmacomechanical thrombolysis just proximal to the venous anastomosis within the synthetic graft. Notice the brush is not advanced into the native vein.

Figure 4 The catheter is pulled back with a continuous slow motion macerating the thrombus and cleaning nearly the entire hemodialysis graft with the exception of the arterial plug (arrow) proximal to the arterial sheath puncture site.

performed under direct intermittent fluoroscopic visualization during continuous infusion of the thrombolytic mixture while the brush is activated. Special attention should be paid to prevent the brush from going into the native venous outflow and excessive brushing of the venous anastomosis should be avoided to prevent intimal damage. The catheter is pulled back with a continuous slow motion, moving intermittently back-and-forth as needed, to macerate the thrombus (Fig. 4). Systemic heparin (2000 to 4000 U) is administered intravenously prior to initiation of the PMT.

Once the first pass with the MTI Castañeda over-the-wire catheter through the graft is completed, the brush is pulled within the catheter by detaching the motor drive and the entire catheter is pulled outside the diaphragm of the arterial sheath, leaving the guide-wire in place and across the venous anastomosis, well into the venous outflow. A Fogarty catheter is advanced through the venous sheath and manipulated across the arterial anastomosis. The balloon is inflated within the proximal native artery and pulled in one motion through the arterial anastomosis, bringing any residual thrombus left within the proximal segment of the arterial limb,

between the arterial anastomosis and the puncture site (arterial “plug”) back into the venous limb of the graft (Fig. 5A and B). This maneuver is performed at least twice. Finally, the brush is reinserted and lysis of the arterial plug and any residual thrombus is completed (Fig. 6A and B). A follow-up shuntogram is obtained to assess the overall results and to rule out potential complications.

After successful PMT, the hemodialysis access in most cases can be used immediately.

RESULTS

In our experience with 100 patients, technical success was achieved in 97% of cases, and clinical success was achieved in 87% of cases.

The mean reteplase dose administered was 1.27 U (range, 0.5 to 3.67 U). The mean heparin dose administered was 2663.29 U. The mean time to thrombolysis was 3.60 minutes (range, 1 to 21 minutes).

Complications occurred in 5% ($n=5$) of the cases; 4% ($n=4$) were minor, 1% ($n=1$) were major. The minor complications included two cases of venous extravasation following percutaneous transluminal angioplasty, which were successfully treated with non-covered, endovascular, self-expanding stents. A small, distal embolus, lodged in the interosseus artery, was noted in one case; this patient was asymptomatic and required no further therapy. A hematoma developed at a previous puncture site and resolved without treatment. The only major complication, which required surgical intervention, involved an intragraft rupture following PTA. Surprisingly, this graft was more than 10 years old and had developed mural calcification throughout its course. The patient was transferred to the operating room for a new graft, which was performed successfully.

With the exception of the distal, arterial emboli, all other complications were not related to the thrombolysis portion of the procedure, but to the required intervention to fix the underlying problem (PTA).

Figure 5 The Fogarty catheter is passed across the arterial anastomosis (A) and then pulled back into the venous limb of the graft (B) to remove the arterial plug and residual thrombus.

Figure 6 Once the arterial plug is in the venous limb of the graft the MTI Castañeda over-the-wire brush is advanced into the graft (A) and thrombolysis is completed by activating the brush one last time and until the graft is completely free of thrombus (B).

DISCUSSION

Vascular access complications are the single largest cause of morbidity, accounting for ~15% of all hospitalizations in the hemodialysis population.² These complications add up to an annual cost to the Medicare program of between \$700 and \$900 million.³ Because of the rapid increase of patients with ESRD in the United States, dialysis access has become a commonly performed procedure at many hospitals. The majority of vascular hemodialysis access procedures use ePTFE with a 1-year patency of ~65%.⁴⁻⁶ Although the gold standard treatment for an occluded dialysis graft is Fogarty balloon embolectomy, pharmacological thrombolysis has emerged as the standard percutaneous treatment for thrombosed AV grafts. However, because of shortcomings of extended intensive care unit stay and expense, alternate methods have been developed such as PMT, thus eliminating the above-mentioned drawbacks.

In our experience, the clinical success rate of 87% achieved with PMT reflects the Dialysis Outcomes Quality Initiatives (DOQI) guidelines that recommend rates of immediate patency to the next dialysis session of 85% for both percutaneous thrombolysis with PTA, and surgical thrombectomy and revision.¹⁵ It has been suggested that in dialysis graft studies, comparisons of pulse spray pharmacomechanical thrombolysis (PSPMT) and infusion methods might be difficult because of the varying methods of infusion as well as the various criteria for success.^{16,17}

Keeping such limitations in mind, a review of thrombolytics and the pharmacomechanical method of PSPMT revealed that 59% to 100% (weighted average, 66%) success was achieved with thrombolytics, whereas outcomes with PSPMT were 95%.¹⁶

Dolmatch noted an 80 to 95% range of success with any mechanical method. Patients in a study that compared the Cragg thrombolytic brush catheter with PSPMT had 85% and 88% success rates, respectively.¹⁸ Similarly, a comparison by Beathard¹⁹ found a 92.8%

mechanical and 93.8% pharmacomechanical success rate, with no statistically significant difference.

One of the controversial issues related to mechanical methods of thrombolysis has been the potential risk for pulmonary emboli. In our experience, we have not had such complications. We preferred a pharmacomechanical technique to improve efficacy as well as to reduce the risk of thrombus-related complications. Previous studies using mechanical thrombolysis have suggested that pulmonary embolism did not present a significant problem.^{18,20,21} Authors of these and other studies^{19,22} have noted that graft clots or clot fragments, although small and released into the circulation, are too small to result in symptomatic pulmonary embolism. In a recent study, all pulmonary embolisms were asymptomatic during PSMT, but treatment with urokinase reduced the rate of pulmonary embolism and tended to result in smaller defects in lung scan results.²³ In our study, reteplase in combination with the Castañeda brush proved to be fast and effective, with few complications. This combination should result in minimal disruption of angiographic suite schedule and optimize prompt return of the patient to dialysis.

A previous study²⁴ performed to compare the endothelial damage caused by the three most commonly used wall-contact mechanical thrombus removal devices (Fogarty embolectomy, Arrow-Trerotola, and the MTI-brush catheter), showed that throughout the entire vessel, the depth of the lesions produced by the Fogarty embolectomy catheter extended into the tunica media, a 4.4 value in the scale used (Table 1), with 80% involving three fourths of the whole depth of this layer.

The Arrow-Trerotola device followed with a 3.9 value in the scale used, and statistical analysis showed no difference in the amount of vessel wall injury seen between this device and the Fogarty embolectomy catheter ($p > 0.05$). This correlates well with findings of a previous study²⁵ in which the Arrow-Trerotola device and Fogarty embolectomy catheter were compared in a rabbit model; venous injury was similar to both devices.

Table 1 Histologic Grades of Arterial Damage in the Device Groups

Grade	Involvement	Fogarty Catheter	Arrow-Trerotola Device	Castañeda Brush
0	None	0 (0)	0 (0)	0 (0)
I	Endothelium with or without internal elastic lamina	0 (0)	0 (0)	2 (20)
II	Inner 1/4 of media	0 (0)	0 (0)	3 (30)
III	Inner 1/2 of media	2 (20)	3 (30)	4 (40)
IV	Inner 3/4 of media	2 (20)	5 (50)	1 (10)
V	Whole media	6 (60)	2 (20)	0 (0)
Mean	Not applicable	4.4	3.9	2.4

Note: Data are the number of arteries. Data in parentheses are percentages. Results of the Kruskal-Wallis test were $\chi^2 = 14.9$, degrees of freedom = 2, $p < 0.001$.

The vascular damage compares well with the results of our study.

The Castañeda brush produced the least damage, with a mean of 2.4 on the scale used. When compared with other two devices, the results were statistically significant (Table 2).²⁴

Studies^{27,28} have shown that large areas of endothelial denudation without significant medial trauma cause only mild intimal thickening, whereas focal endothelial denudation with significant medial trauma produces marked intimal thickening. These results are also substantiated by other studies²⁹ that have shown that smooth muscle cells are normally quiescent with respect to proliferation but that deep injuries result in the expression of a proliferative phenotype of vascular smooth muscle cells that exhibits a high proliferative response to other mitogens. Although both motorized devices are only approved for use within synthetic hemodialysis grafts, there is always the potential for inadvertent protrusion into the native vascular segments close to the anastomotic regions. In this circumstance, endothelial damage can occur. If the conclusions of these studies are correct, there might be some benefit in using the least damaging device even when mechanical thrombolysis in a synthetic graft is performed.

Cost has been a major factor in the evolution of graft clearance techniques. According to the U.S. Renal Data System, spending for ESRD in 1997 totaled 15.64 billion dollars.³⁰ The majority of these patients use hemodialysis as their treatment modality,³⁰ with 85% attending sessions three times per week.³¹

Table 2 Comparison of Arterial Damage Grades in the Device Groups

Device	D Value of Nemenyi Test	
	Arrow-Trerotola Device	Castañeda Brush
Fogarty catheter	40.5*	142.5†
Arrow-Trerotola device	Not applicable	102‡

* $p > 0.05$.

† $p < 0.01$.

‡ $p < 0.05$.

When thrombolytic therapies, such as alteplase and urokinase, were emerging, cost was often judged to be prohibitive,³² and data showed mixed results and questionable cost-benefit ratios. With time, more drug and storage/aliquot options have decreased the overall cost required for thrombolytic use. At our institution, the cost for 1/10 of the reteplase vial (1 U) did not place an undue burden on the financial management of these cases, and our team believed the potential benefit derived from adjunctive pharmacological treatment was substantial.

SUMMARY

In summary, PMT has emerged as an alternate treatment used in most patients presenting with a thrombosed hemodialysis graft. Although it is the gold standard, surgical revision of thrombosed hemodialysis grafts is reserved for those cases of recurrent thrombosis despite the use of percutaneous techniques and for complicated cases after PMT. Nevertheless, as in every other procedure, PMT has its own set of limitations and cost issues. Although early results are encouraging, further prospective randomized trials are necessary to establish the true efficacy of this technique. In the meantime, PMT is an excellent alternative therapy for the thrombosed hemodialysis graft.

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