

Alteplase Use for Occluded Hemodialysis Catheters

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BC Renal Agency
An agency of the Provincial Health Services Authority

Vascular Access Guideline

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Alteplase Use for Occluded Hemodialysis Catheters

This guideline is intended for adults and for children weighing over 10 kilograms. For children weighing less than or equal to 10 kilograms, the concentration and dosage need to be adjusted.

1.0 Scope of Guideline

This guideline provides recommendations for the use of thrombolytic alteplase (Cathflo^{TM1}) to maintain catheter patency.

A well functioning vascular access is a prerequisite for hemodialysis (HD). To be consistent with national and international standards, the Provincial Vascular Access Service Team (PVA) has identified the preferred form of HD vascular access as the native arterio venous fistula (AVF), followed by the artificial arteriovenous graft (AVG) and lastly the central venous catheter (CVC).

Despite all best efforts for patients undergoing HD to have an AVF (preferred) or AVG (2nd choice), there will always be patients that receive HD by CVC on a temporary or permanent basis. The most common complications of CVCs are thrombosis and infection (Develter, 2005 and Little, 2001). Even with care, fewer than half the catheters placed as “long-term accesses” are in use a year after placement (Ponikvar, 2005) and about a third are removed because they fail to deliver adequate blood flow (K/DOQI 2006).

The initial approach to treatment of a dysfunctional or blocked catheter is conservative – rule out mechanical issues such as machine problems or kinks in the catheter and forcefully flush the lines with normal saline. If conservative measures fail, the administration of thrombolytic agents may be required.

2.0 Summary of the Literature

Use of recombinant tissue plasminogen activators (rTPAs) (alteplase, reteplase or tenecteplase)

Mokrzycki and Lok (2010) reviewed the literature on the use of recombinant TPAs (alteplase, reteplase or tenecteplase) for the treatment of thrombosis in CVCs between 1993 and 2010. The short-term success rate ranged from 40% to 92% in the 18 studies reviewed. None of the trials compared the effects between the three different TPAs.

Mokrzycki and Lok stratified the 18 studies according to method of instillation: push / pause method, dwell (short and long-term) and / or infusion. They noted that:

- None of the trials compared the push / pause method and the short or long dwell method.
- Dwell time did not significantly impact short-term or 2-week patency rates in the two trials where this was studied (Nguyen, 2004 and MacRae, 2005).
- The success rate diminished with each subsequent dose of rTPA.

¹ Alteplase, the generic name, is used throughout the remainder of the document.

Alteplase Use for Occluded HD Catheters

Success rates by method of instillation:

Push / pause method (4 studies):

- Short-term: 59% – 92%.
- Long-term: 60% patency at 30 days

Short dwell (6 clinical trials; dwell time \leq 60 min):

- Short-term: 69% - 97%; 22% - 97% if Tumlin’s tenecteplase study (2010) is included.
- Long-term: median time to next intervention: 12.5 – 30 days.

Long-dwell (7 studies; dwell time 2–72 hrs):

- Short-term: 79%-100%; 22% - 100% if Tumlin’s tenecteplase study (2010) is included.
- Long-term: median patency after rTPA was 14 – 30 days.

Infusion (3 studies):

- Short-term: 84% - 91%
- Long-term: 55% patency at 30 days

Use of Alteplase

Alteplase is used for CVC thrombosis in dialysis centres in BC.

Table 1 provides a summary of the results of 13 clinical trials on the use of alteplase for the treatment of thrombosis in CVCs (details of study design, population, definitions of “success” etc are available in the table in Appendix 2). There have been no new published studies since 2005.

Table 1: Clinical Trials on Alteplase Use, 1999 to 2010

Author	Dose	Method	ST Success	LT Success
Haymond et al (2005)	1 mg / lumen	Long dwell	72% (1st dose) – 83% (2nd dose)	Time to next tx: 14 d (median); \$22,000 cost savings (11 mos)
MacRae et al (2005)	1 mg / ml, dose det’d by lumen vol	Short vs long dwell	77% (short dwell) – 79% (long dwell)	Time to next tx: 14 (short dwell) to 18 days (long dwell)
Nguyen et al (2004)	1.5 mg / lumen	Short & long dwell	84% - 100%, dep on timing of instillation	Not specified \$3,300 cost savings
Dowling et al (2004)	2.5 mg / hr / lumen x 2 hrs (10 mg)	Infusion (2 hrs)	84% (1st dose) – 100% (2nd dose)	54% patency at 30 days
Davies et al (2004)	1 mg / hr (partial occlusion) – 2 mg / hr (full occlusion) x 4 hrs (4 – 8 mg)	Infusion (4 hours)	85% (2mg) – 88% (1 mg)	Not specified

Author	Dose	Method	ST Success	LT Success
O' Mara et al (2003)	1 mg / ml, dose det'd by lumen vol	Short dwell	69%	Time to next tx: 12.5 d (mean)
Zacharias et al (2003)	1 mg / ml, dose det'd by lumen vol	Push / pause	85% (fully occluded) – 92% (partially occluded)	60% patency at 30 days
Little et al (2002)	1 mg / ml, dose det'd by lumen vol	Long dwell	10% of catheters required alteplase	34% patency at 1 yr
Eyrich et al (2002)	1 mg / lumen	Push / pause	86%	Not specified
Savader et al (2001)	2.5 mg / lumen	Infusion (3 hours)	91%	55% patency at 30 days
Spry (2001)	1 mg / ml, dose det'd by lumen vol	Push / pause	59%	Not specified
Daeihagh et al (2000)	2 mg / lumen	Long dwell	88%	Not specified
Meers et al (1999)	1 mg / lumen	Push / pause & / or long dwell	97%	Time to next tx: 30 d (mean)

Success rates:

- Definitions of “success” differed between studies. Common definitions included:
 - Short-term success: blood pump speeds of 250 – 300 mL / min and / or the ability to initiate dialysis.
 - Long-term success: the time from the first course to the next course of alteplase treatment and / or catheter patency and / or survival.
- Short-term success rates ranged from 59% - 100%.
- The time from the first course to the next course of alteplase ranged from 12.5 – 30 days. Patency rates ranged from 54% to 60% at 30 days.

Method of instillation

- There was no obvious correlation between method of instillation and success.
- This finding was similar to that reported in two systematic review articles (Mokrzycki and Lok, 2010 and Lok, 2006).

Dosages:

- For the push / pause and dwell methods, dosages ranged from 1 – 2 mg / lumen. There was no obvious correlation between dosage and success.
- For the infusion methods, the dosage ranged from 4 – 10 mg. Again, there was no obvious correlation between dosage and success.
- The observed lack of correlation between dosages and success was similar to that reported in two systematic review articles (Mokrzycki and Lok, 2010 and Lok, 2006).
- Two studies reported a cost savings from the use of a lower dosage (Hamond, 2005 and Nguyen, 2004).

Prevention of Catheter Lumen Occlusion with recombinant-TPA versus heparin (Pre-Clot) Study

- The Pre-Clot study is a randomized controlled trial evaluating the effectiveness of weekly alteplase lock for the prevention of HD catheter malfunction. Patients from 14 centres across Canada were randomized to the treatment arm received alteplase 1 mg per lumen once per week, with heparin 5,000 units per ml as a catheter locking solution for the remaining two sessions. Patients randomized to the control arm received heparin 5,000 units per ml as a catheter locking solution after each dialysis.
- Preliminary results suggest that patients in the alteplase arm had significantly fewer catheter malfunctions (primary outcome) and bacteremia (secondary outcome). There were no significant differences in bleeding events between arms.
- This is the first large, well-designed trial that has studied the routine prophylactic use of alteplase lock in HD catheters. Until the details have been published, cost effectiveness has been proven and similar results replicated in other trials, the use of rTPA to prevent thrombosis is not recommended.

In summary, alteplase and other rTPA medications appear to be effective as a short-term option for treating thrombosis-related dysfunctional CVCs. Most studies do not support the use of rTPA in preventing thrombosis, nor for use on an ongoing basis unless as a last resort (no other catheter sites, maturing fistula, etc).

3.0 Recommendations & Rationale

Recommendation 1: Prevent and/or reduce incidences of CVC-related thrombosis by:

- ***Regularly assessing dialysis performance and early recognition of problems (see next point for signs of CVC dysfunction).***
- ***Forceful flushing with normal saline pre and post dialysis and capping the CVC pre- and post-dialysis with heparin or citrate.***
- ***Regularly reversing the flows (opinion) (e.g., once per week) if using Palindrome catheters. Not recommended with any other catheter.***
- ***Using of newer catheters that are capable of achieving rates of ≥ 400 mL/min when properly placed.***
- ***Using needle-free connectors for HD lines.***

Signs of CVC dysfunction include (K/DOQI, 2006):

- Blood pump flow rate <300 mL/min
- Arterial pressure (< -250 mm Hg) or Venous pressure (>250 mm Hg)
- Ratio of blood pump flow to the absolute value of pre-pump pressure (conductance) (<1.2)
- Urea reduction ratio (URR) progressively <65% (or Kt/V <1.2)
- Unable to aspirate blood freely (late manifestation)
- Frequent pressure alarms—not responsive to patient repositioning or catheter flushing
- Trend analysis of changes in access flow is the best predictor of access patency and risk for thrombosis.

Recommendation 2: If CVC dysfunction is identified, rule out causes other than thrombosis as the source of the dysfunction.

Causes of CVC dysfunction other than thrombosis include mechanical reasons, kinks (angulation in tunnel), misplaced sutures, catheter migration, drug precipitation (some antibiotic locks or IV IgG), hypovolemia, patient position, catheter integrity, holes and cracks (KDOQI; 2006). Such causes need to be ruled out prior to the use of thrombolytics.

Recommendation 3: If CVC dysfunction is related to thrombosis, administer alteplase as per physician's order, using the algorithm (section 4.0) and pre-printed orders (section 5.0) as a guideline.

After mechanical reasons, thrombotic occlusion (partial or total) is the most common cause of catheter dysfunction and/or occlusion. Common sites of thrombus formation are the catheter lumen, the site where the catheter enters the vein, the catheter tip and along the external surface of the catheter.

Alteplase is the thrombolytic agent of choice for treating occluded HD CVCs. Alteplase works by binding to fibrin in a thrombus, then converting the entrapped plasminogen to plasmin which results in local fibrinolysis (i.e. digests fibrin and dissolves blood clot).

While alteplase has proven to be useful in the management of catheter-related thrombotic occlusions, little published evidence exists addressing the most effective method(s) of administration. Guidelines are provided in this document for the three most commonly used methods: push/pause, dwell (short and long) and infusion (simultaneous infusion method via arterial and venous lumens prior to initiating HD and single lumen method during HD). Selection of the method will depend on individual circumstances including the severity of the occlusion and the timing and urgency of the need for dialysis.

Alteplase is an expensive medication (2 mg = \$65; 4 mg = \$130). It is important that its use and dosage be limited to that which is absolutely necessary. Generally speaking, a graduated dosing scheme is recommended, starting with a lower dose and increasing to a higher dose if the lower dose is not effective. This guideline provides a range of dosages to allow for this practice.

Recommendation 4: Notify the physician if one or both lumens are still "sticky" or blocked after administering alteplase more than twice on two separate occasions in a 2-week period.

Recommendation 5: Chronic use of alteplase is strongly discouraged other than in exceptional circumstances (i.e., resistant CVCs) and:

- **CVC is the last option for HD access AND the patient is unable to tolerate further CVC replacements; OR**
- **A maturing AVF or AVG is imminent.**

4.0 Algorithm for the Use of Alteplase in Occluded HD CVCs

Difficulty instilling or aspirating catheter lumens, blood pump speed <300 mL/min or decrease in blood flow of 20% during HD

- Rule out machine problems
- Check for kinks beneath catheter clamps or at exit site
- Change patient's position
- Confirm the HD catheter has not been used for non-HD uses (e.g., TPN)
- Flush lines forcefully with 20 mL NS into each lumen
- Reverse lumens & increase BPS as high as possible
- If a maturing peripheral access, is it ready to be cannulated?
- If catheter inserted <1 week, obtain order for CXR to rule out catheter position problem

Adequate Flow?

Yes

Adequate blood flow established; proceed with HD; continue to observe & monitor; lock catheter with heparin or sodium citrate (as ordered)

No

Notify physician as per unit protocol

As per MD orders, instill alteplase using 1 of the following instillation methods:

1. If no flow or blood pump speed <200 mL/min, instill 1-2 mg/lumen using:
 - a) Push/pause method; or
 - b) Short dwell method (60 minutes); or
 - c) Long dwell method (overnight); or
 - d) Simultaneous infusion method via arterial & venous lumens prior to initiating HD.
2. If blood pump speed is ≥200 mL/min and <300 mL/min:
 - a) Instill 1-2 mg/lumen using the long dwell method (overnight); or
 - b) Instill 2-4 mg using the single lumen infusion method during HD.

Note re instillation method:

- Little published evidence exists about the effectiveness of one method over another.
- Method selected will depend on individual circumstances including the severity of the occlusion and the timing & urgency of the need for dialysis.

Note re alteplase dosing:

- Alteplase is expensive (2 mg = \$65, 4 mg = \$130).
- Use of alteplase & dosage should be limited to that which is absolutely necessary.
- A graduated dosing scheme is recommended. Start with the lower dose in the range & increase to the higher dose if not effective.

Adequate Flow?

Yes

No

Repeat instillation of alteplase using one of the methods above

Adequate Flow?

Yes

No

Contact MD and MD to investigate and INTERVENE:

- Chest x-ray PA & lateral
- Consider linogram
- CVC exchange
- Creation of AVF or AVG (if feasible)
- Utilizing peritoneal dialysis (if feasible)

Adequate Flow?

Yes

No

Under the exceptional circumstances, MD may consider implementing the protocol for resistant CVCs (alteplase to cap off CVC post-dialysis 1-3 x/wk OR instill alteplase 1-2 x/wk using the push/pause or infusion method).

Adequate blood flow established; proceed with HD; continue to observe & monitor; lock catheter with heparin or sodium citrate (as ordered)

Reconstitution instructions for alteplase

Reconstitute immediately before use as there is no preservative in alteplase vials. The reconstituted solution may be used within 8 hours following reconstitution when stored at 3 to 30°C.

a. Reconstitution instructions for push/pause and dwell instillation methods:

To prepare alteplase to a final concentration of **1 mg/mL**:

1. Using aseptic technique, withdraw 2.2 mL of sterile water for injection. Do **not** use bacteriostatic water for injection for reconstitution.
2. Inject the 2.2 mL of sterile water for injection into the alteplase 2 mg vial, directing the diluent stream into the powder. Slight foaming is not unusual; let the vial stand undisturbed to allow large bubbles to dissipate.
3. Mix by gently swirling until the contents are completely dissolved. **Do not shake.** The reconstituted preparation results in a colorless to pale yellow transparent solution containing alteplase 1 mg/mL.
4. Withdraw prescribed amount of alteplase 1 mg (1 mL) or 2 mg (2 mL) of solution from the reconstituted alteplase vial.

To prepare alteplase to a final concentration of **2 mg/mL (only use this strength for catheter volumes <2 mL)**:

1. Using aseptic technique, withdraw 1.1 mL of sterile water for injection. Do **not** use bacteriostatic water for injection for reconstitution.
2. Inject the 1.1 mL of sterile water for injection into the alteplase 2 mg vial, directing the diluent stream into the powder. Slight foaming is not unusual; let the vial stand undisturbed to allow large bubbles to dissipate.
3. Mix by gently swirling until the contents are completely dissolved. **Do not shake.** The reconstituted preparation results in a colorless to pale yellow transparent solution containing alteplase 2 mg/mL.
4. Withdraw 2 mg (1 mL) of solution from the reconstituted alteplase vial.

b. Reconstitution instructions for infusion methods:

To prepare a **1 mg** dose of alteplase:

1. Using aseptic technique, withdraw 2.2 mL of sterile water for injection. Do **not** use bacteriostatic water for injection for reconstitution.
2. Inject the 2.2 mL of sterile water for injection into the alteplase 2 mg vial, directing the diluent stream into the powder.
Slight foaming is not unusual; let the vial stand undisturbed to allow large bubbles to dissipate.
3. Mix by gently swirling until the contents are completely dissolved. **Do not shake.** The reconstituted preparation results in a colorless to pale yellow transparent solution containing alteplase 1 mg/mL.
4. Withdraw 1 mg (1 mL) of solution from the reconstituted alteplase vial and inject into sodium chloride 0.9% 50 mL as per order.

To prepare a **2 mg** dose of alteplase:

Perform above steps 1 – 3. Withdraw 2mg (2 mL) of solution from the reconstituted alteplase vial and inject into sodium chloride 0.9% 50 mL or 100 mL as per order.

To prepare a **4 mg** dose of alteplase:

Perform above steps 1 – 3. Repeat x 1 to prepare a second reconstituted vial. Withdraw the contents of both reconstituted vials (4 mg) and inject into sodium chloride 0.9% 100 mL as per order.

6.0 References

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7.0 Sponsors

This provincial guideline was developed to support improvements in the quality of vascular access care delivered to patients with chronic kidney disease in BC. Based on the best information available at the time it was published, the guideline relies on evidence and avoids opinion-based statements where possible. When used in conjunction with pertinent clinical data, it is a tool that health authorities and health professionals can use to develop local guidelines.

Developed by a Vascular Access Working Group of multidisciplinary care providers from across BC, the guideline was approved by the Provincial Vascular Access Services Team, the BCPRA Pharmacy and Formulary Committee (Jan 17, 2011) and the BC Provincial Renal Agency Medical Advisory Committee (Jan 21, 2011). It has been adopted by BCPRA as a provincial guideline.

8.0 Effective Date

- March 4, 2011.
- Refer to www.bcrenalagency.ca for most recent version.

9.0 Appendices

Appendix 1: Alteplase Use for Occluded CVCs (Sample Procedure)

Appendix 2: Summary of the Studies on the Use of Alteplase in the Treatment of HD Catheter Thrombosis

Appendix 1: Alteplase Use for Occluded CVCs (Sample Procedure)

1.0 Practice Standard

Skill Level (Nursing): Specialized

Registered nurses who have completed the required hemodialysis (HD) specialty education and who provide care in a BC In-Centre and/or Community Renal Program may perform this procedure, upon the order of a physician.

Need to Know

1. Use of alteplase in occluded hemodialysis central venous catheters (CVCs) requires a physician's order.
2. Blocked or dysfunctional central venous catheters are identified by: difficulty instilling or aspirating catheter lumens, a blood pump speed of <300 mL/min and/or a decrease in blood flow of 20% during hemodialysis.
3. Low-dose alteplase is the thrombolytic of choice for treatment of a blocked or dysfunctional HD catheter.
4. Alteplase may be instilled using one of three methods: push/pause, dwell (short and long) and infusion (single lumen or simultaneous infusion via two lumens).
5. If no flow or blood pump speed <200 mL/min, instill as per orders using one of the following:
 - Push/pause method; or
 - Short dwell method (60 minutes); or
 - Long dwell method (overnight); or
 - Simultaneous infusion method via arterial & venous lumens (prior to initiating HD).
6. If blood pump speed is 200 mL/min or greater and less than 300 mL/min, instill as per orders using one of the following:
 - Long dwell method (overnight); or
 - Single lumen infusion method during HD.
7. Notify the physician if one or both lumens are still "sticky" or blocked after administering alteplase twice on two separate occasions in a two week period.
8. The physician may prescribe an ongoing alteplase order for patients who have problematic HD catheters that repeatedly become occluded or function poorly (resistant catheters).
9. Alteplase is a thrombolytic agent that works by binding to fibrin in a thrombus, then converting the entrapped plasminogen to plasmin which results in local fibrinolysis (i.e. digests fibrin and dissolves blood clot).

10. Alteplase vials need to be protected from light and kept in their original box until needed. Alteplase vials do not contain antibacterial preservatives and should be stored in a refrigerator at a temperature between 2 and 8 degrees C and reconstituted **immediately** before use. The solution must be used within 8 hours following reconstitution when stored between 2 and 30 degrees C.
11. Alteplase must be reconstituted with Sterile Water for injection. Do not shake vial to dissolve.
12. Heparin / sodium citrate and alteplase are incompatible when mixed together; therefore, if heparin is used to lock the catheter, the heparin must be aspirated or flushed from the catheter lumens prior to the instillation of alteplase.
13. Common sites of thrombus formation; catheter lumen, site where catheter enters the vein, catheter tip and along the external surface of the catheter.

2.0 Definitions & Abbreviations

Alteplase	Recombinant tissue plasminogen activator, rtPA, Cathflo™
CVC	Central venous catheter
HD	Hemodialysis

3.0 Equipment

Push/pause and dwell methods:

- 1 or 2 vials alteplase with 2 mg/vial
- 1 or 2 vials of sterile water for injection (do not use bacteriostatic water for injection)
- 4 x 3 mL luer lock syringes with needles (2 for alteplase and 2 for sodium chloride 0.9%)
- 2 x 10 mL luer lock syringes (to withdrawal old anticoagulant and clot from lumens)
- 4 x 10 mL or 2 x 20 mL luer lock syringes with sodium chloride 0.9% (to flush lumens)
- 2 luer lock caps (to cap off lumens)
- 2 medication labels
- Chlorhexidine gluconate 2% aqueous or per unit protocol

IV infusion method:

- 1 or 2 vials alteplase with 2 mg/vial
- 1 or 2 vials of sterile water for injection (do not use bacteriostatic water for injection)
- 2 or 3 x 3 mL luer lock syringes
- 1 or 2 x 18g needles
- Chlorhexidine gluconate 2% aqueous or per unit protocol
- 1 or 2 medication labels
- 1 or 2 minibags containing sodium chloride 0.9% (50 ml or 100 mL)
- 1 or 2 volumetric infusion pumps and tubing
- "Y" luer lock adaptor

4.0 Assessment & Interventions

Separate sub-procedures are identified for each of the three methods of administration:

1. Dwell (short & long);
2. Push/pause; and
3. Infusion (single lumen method during HD & simultaneous infusion method via arterial and venous lumens prior to initiating HD).

4.1 Preparation for All Administration Methods

1. Prior to initiating each dialysis treatment, attempt to aspirate the heparin/sodium citrate from each lumen of the CVC with a 10 mL syringe using aseptic technique.
2. If aspiration is unsuccessful, attempt to forcefully flush each lumen as follows:
 - a. Draw sodium chloride 0.9% in 2 x 10 mL or 1 x 20 mL luer-lock syringe(s) for each CVC lumen.
 - b. Flush each catheter port with a total of 20 mL sodium chloride 0.9% using maximum force.
3. If flush is successful, attempt to aspirate blood and perform 2 – 3 additional forceful flushes with aspirated blood.
4. If flush is unsuccessful, repeat step 2; if still unsuccessful, contact the physician.
5. Prepare alteplase as per physician order, the product monograph and the reconstitution procedure on the reverse side of the pre-printed orders.

4.2 Alteplase Administration

4.2.1 Dwell (Short & Long) Method

1. Follow steps 1 to 5 under “Preparation for All Administration Methods.”
2. Clean stopper with alcohol swab. Using 3 mL syringes with needles, withdraw the alteplase solution.
 - a. If using alteplase **1 mg** per lumen, draw 1 mL of alteplase 1 mg/mL solution into each of two 3 mL syringes (label carefully). Fill two additional 3 mL syringes with sufficient sodium chloride 0.9% to fill the internal volume of each CVC lumen plus 0.1 mL overfill (e.g., if catheter volume is 2.2 mL per lumen, draw 1 mL of alteplase 1 mg/mL and 1.3 mL sodium chloride 0.9% for each lumen).
 - b. If using alteplase 2 mg per lumen and catheter lumen volume is **2 mL or greater**, draw up 2 mL of alteplase 1 mg/mL solution into each of two 3 mL syringes (label carefully). Fill two additional 3 mL syringes with sufficient sodium chloride 0.9% to fill the internal volume of

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each CVC lumen plus 0.1 mL overfill (e.g., if dose is 2 mg alteplase per lumen and catheter volume is 2.2 mL per lumen, draw 2 mL of alteplase 1 mg/mL and 0.3 mL sodium chloride 0.9% for each lumen).

- c. If using alteplase **2 mg** per lumen and catheter lumen volume is **less than 2 mL**, draw up 1 mL of alteplase **2 mg/mL** solution into each of two 3 mL syringes (label carefully). Fill two additional 3 mL syringes with sufficient sodium chloride 0.9% to fill the internal volume of each CVC lumen plus 0.1 mL overfill (e.g., if dose is 2 mg alteplase per lumen and catheter volume is 1.3 mL per lumen, draw 1 mL of alteplase 2 mg/mL and 0.4 mL sodium chloride 0.9% for each lumen).
3. Clamp both lumens and then attach the 3 mL syringe(s) filled with alteplase to the occluded CVC port(s).
4. Instil alteplase as per order into the each of the arterial and venous lumens of the CVC then add sodium chloride 0.9% without preservative to fill the internal volume of each lumen plus 0.1 mL overfill.
5. Clamp both lumens.

For Short (Pre-dialysis) Dwells:

- a. Leave the alteplase solution instilled in the catheter for at least 30 minutes but preferably 60 minutes, unless otherwise ordered by the physician.
- b. Withdraw the alteplase solution and residual clot from both lumens and discard. If unable to withdraw alteplase solution, try to re-position the catheter or patient to aid in the withdrawal.
- c. Attempt to flush the CVC with sodium chloride 0.9% using the forceful flush protocol described under "Preparation for All Administration Methods".
- d. If one or both lumens are still "sticky" or blocked, repeat administration of alteplase. If still "sticky" or blocked after administering alteplase twice on two separate occasions within a two week period, notify the physician for further orders.

For Long (Overnight) Dwells:

- a. Remove the emptied 3 mL alteplase or sodium chloride 0.9% syringe from each lumen and secure a luer lock cap.
- b. When patient returns for the next HD treatment:
 - i. Withdraw the alteplase solution and residual clot from both lumens and discard. If unable to withdraw alteplase solution, try to re-position the catheter or patient to aid in the withdrawal.

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- ii. Attempt to flush the CVC with sodium chloride 0.9% using the forceful flush protocol described under “Preparation for All Administration Methods”.
- iii. If one or both lumens are still “sticky” or blocked, repeat administration of alteplase. If still “sticky” or blocked after administering alteplase twice on two separate occasions within a two week period, notify the physician for further orders.

4.2.2 Push/Pause Method

1. Follow steps 1 to 5 under “Preparation for All Administration Methods” and step 2 under the instructions for dwell (short & long) method for drawing up the syringes.
2. Clamp both lumens and then attach the 3 mL syringe(s) filled with alteplase to the occluded CVC port(s).
3. Instill alteplase as per order into each catheter lumen then add sodium chloride 0.9% without preservative to fill the internal volume of each lumen plus 0.1 mL overflow.
4. Attach a 3 mL syringe filled with sodium chloride 0.9% without preservative to each lumen.
5. Wait 10 minutes, then gently push sodium chloride 0.9% 0.3 mL.
6. Wait another 10 minutes, then repeat sodium chloride 0.9% push as above.
7. Wait another 10 minutes, then use a 10 mL syringe to aspirate any clots and discard; may push remaining alteplase if unable to withdraw. Forcefully flush each catheter lumen as per protocol.
8. If one or both lumens are still “sticky” or blocked, repeat administration of alteplase. If still “sticky” or blocked after administering alteplase twice on two separate occasions within a two week period, notify the physician for further orders.

4.2.3 Infusion Method

For Infusion of Alteplase through a Single Lumen During Hemodialysis

Scenario:

- One catheter lumen provides a minimum blood flow of 200 mL/min.
 - One catheter lumen does not provide adequate blood flow, however, alteplase can be administered through this lumen.
1. Follow steps 1 to 5 under “Preparation for All Administration Methods.”
 2. Prepare alteplase infusion:
 - Add alteplase in the amount ordered by the physician to the 100 mL sodium chloride 0.9% minibag for infusion and label the minibag.

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- Connect the infusion tubing to one limb of the “Y” adapter.
 - Prime the infusion pump tubing and “Y” adapter.
3. Connect arterial blood-line to the catheter lumen that provides adequate blood flow. Prime circuit with blood as per procedure to initiate HD.
 4. Connect the venous blood-line to the “Y” adapter and then connect the male end of the “Y” adapter to the problematic lumen of the catheter. blood-line
 5. Initiate dialysis as per routine.
 6. Commence alteplase infusion to run over 1 hour.
 7. Monitor and document q 15 min: vital signs and signs and symptoms of adverse complications (e.g., bleeding or allergic reaction).
 8. After 30 min of alteplase infusion, consider switching lines to prophylactically administer alteplase through the opposite lumen as follows:
 - Stop blood pump and infusion pump.
 - Using aseptic technique, disconnect and switch arterial blood-line and “Y” adapter with venous blood-line.If lines are not switched, continue infusion into the same line for 60 minutes.
 9. Restart blood pump and infusion pump.
 10. Observe and document blood pump speed and arterial and venous pressures. Continue dialysis treatment.
 - ➔ Key point: A blood pump speed of 300 mL or more per minute with corresponding arterial and venous pressures is an indication of successful fibrinolysis.
 11. In the event that adequate blood pump speeds are not attainable after switching the lines (i.e., more than 300 mL per minute), stop blood pump and infusion pump. Using aseptic technique, switch the arterial blood-line and “Y” adapter with the venous blood-line to resume the alteplase infusion through the problematic lumen. Repeat vital signs. Continue dialysis treatment.
 12. When infusion is complete, if unable to attain blood pump speeds of greater than 300 mL/min, notify the physician.

For Simultaneous Infusion of Alteplase into the Arterial and Venous Lumens Prior to Initiating HD

Scenario:

- One catheter lumen provides a blood flow of less than 200mL/min
 - Unable to initiate hemodialysis due to inadequate blood flow
 - Unable to aspirate from either lumen, however, can administer alteplase through both lumens
1. Follow steps 1 to 5 under “Preparation for All Administration Methods.”

2. Prepare alteplase infusion:
 - a. Add alteplase in the amount ordered by the physician to the 50 mL sodium chloride 0.9% minibag for infusion and label the minibag.
 - b. Prime both infusion pump tubing sets and load onto pumps.
3. Connect pump infusion tubing directly to arterial & venous ports on central line. Open clamps on arterial & venous ports.
4. Commence alteplase infusions to run over 30 minutes (simultaneously infuse alteplase into both ports).
5. Monitor and document q 15 min: vital signs and signs and symptoms of adverse complications (e.g., bleeding or allergic reaction).
6. After completion of alteplase infusion, perform procedure to initiate HD.
7. Observe and document blood pump speed and arterial and venous pressures. Continue dialysis treatment.
8. If unable to aspirate blood from lumens, notify physician.
9. If unable to attain blood pump speed of greater than 300 mL/min, continue treatment and notify physician.
 - ➔ Key point: A blood pump speed of 300 mL or more per minute with corresponding arterial and venous pressures is an indication of successful fibrinolysis.

5.0 Documentation

1. Document according to unit protocol:
 - a. Pre, intra and post assessments of patient and catheter function.
 - b. Interventions: MD notification, additional monitoring and procedures performed.
 - c. Alteplase dose and method of delivery.
2. Enter the dose of alteplase, the method of delivery, and the outcome in the medication record and dialysis access module in PROMIS.

6.0 References

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Appendix 2: Summary of the Studies on the Use of Alteplase in the Treatment of HD Catheter Thrombosis

Study	Design	Dose	Protocol	Pop'n	Defn of Success	Short-term Success	Long-term Success	Author's Conclusions
Haymond, Shalansky & Jastrzebski (2005)	Prospective, nonrandom, open-label, consecutive patients with dysfnl catheters	Alteplase 1 mg / lumen (previously used 2 mg / lumen)	60 min dwell (only 3 pts); repeat once if necessary or overnight dwell between HD sessions (large majority of pts)	50 pts 50 CVCs	Qb \geq 300 mL/min for at least 3/4s of HD & pt had to finish session at or above that rate Reduced costs when compared to costs 11 mos prior to implementation of new protocol	1 st dose 72% (36/50). 2 nd dose: 83%. Financial savings: \$22,000 (compared costs 11 mos prior to & after implementation of new protocol)	62% required a subsequent alteplase tx course with a median time to next course of 14 days. 38% had radiological interventions within 4 mos of initial dose; 8 CVCs were replaced, 7 were stripped.	1 mg / lumen successfully treated CVC occlusions, with a resulting cost reduction.
MacRae et al (2005)	Prospective, randomized, non-blinded	Alteplase 1 mg / 1 ml, vol determined by lumen size	Short (1 hr) vs long (>48 hrs) dwell	60 pts 60 CVCs	Qb >250 mL/min at next HD run & no CVC dysfunction for 2 weeks	Short dwell: <ul style="list-style-type: none"> Next HD: 77% (20/26) 2 wks: 42% (11/26) Long dwell: <ul style="list-style-type: none"> Next HD: 79% (27/34) 2 wks: 53% (18/34) No stat sign dif	Median days to next catheter event: <ul style="list-style-type: none"> Short dwell: 14 Long dwell: 18 	Either short or long alteplase dwell time achieves patency for the next HD run but neither is reliable for LT patency. Use of alteplase for catheter dysfunction is temporary & provides a 2

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Study	Design	Dose	Protocol	Pop'n	Defn of Success	Short-term Success	Long-term Success	Author's Conclusions
						in patency in short vs long dwell groups at subsequent HD run or at 2 weeks.		week window to employ more definitive therapies.
Nguyen & Dikun (2004)	Non-randomized case series	Alteplase 1.5 mg / lumen	Gp A: 1.5 mg/lumen x 30 min if unable to initiate HD. Gp B: 1.5 mg/lumen x 30 min at start of HD if last session Qb<300 mL/min Gp C: 1.5 mg/lumen as 48 hr dwell if last session Qb<300 mL/min	# pts not specified 52 episodes	Qb>300 mL / min	Overall success: 94% <ul style="list-style-type: none"> Gp A: 97% (22/23) Gp B: 84% (18/21) Gp C: 100% (8/8) Cost savings: \$45 for 1.5 mg vs \$77 for 2 mg alteplase (\$3,354 over 6 mos)	Not specified	1.5 mg alteplase effective in treating occluded HD catheters with lumen volumes ranging from 1 – 2.5 mL. Cost savings also realized.
Dowling et al (2004)	Retrospective case studies	Alteplase 2.5 mg / hr / lumen (total 10 mg)	Infusion over 2 hrs while pts were off dialysis.	25 pts 25 CVCs	Qb \geq 250 mL / min Catheter patency (blood speed \geq 250 mL/min), tested immediately after the	Immediately after infusion: 100%, with 84% after 1st dose & 100% after the 2 nd dose	54% at 30 days 33% at 45 days	Alteplase is a safe & effective means of clearing blocked tunnelled catheters.

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Study	Design	Dose	Protocol	Pop'n	Defn of Success	Short-term Success	Long-term Success	Author's Conclusions
					infusion & at 30 days & 45 days.			
Davies et al (2004)	Retrospective case studies	Alteplase 1 or 2 mg / hr x 4 hrs (1 mg if partial obstruction & 2 mg if total).	Infusion over 4 hrs	20 pts 57 alteplase infusions	Blood speed ≥ 250 mL/min for >4 hrs after infusion.	Completely blocked lines: 85% with 2 mg infusion. Partially blocked: 88% with 1 mg infusion.	Not specified	Alteplase 2 mg /hr for blocked lines & 1 mg/hr for sluggish lines effectively restores HD CVC patency.
O'Mara et al (2003)	Prospective, non-randomized consecutive catheters	Alteplase 1 mg / 1 ml , vol determined by lumen size	Dwell 30 min + an add'l 30 min if needed (2 nd dose if needed)	25 pts 30 CVCs 62 episodes	Success: Qb ≥ 300 mL/min Partial: Qb ≥ 200 - <300 mL/min (min 50 mL/min increase req'd)	Complete or partial responses combined: 69% (43/62)	15/30 (50%) received more than 1 dose: mean time from 1 st to 2 nd dose was 12.5 days	Alteplase 1mg/mL was effective for restoring patency in CV dialysis catheters
Zacharias et al (2003)	Prospective, nonrandomized case series	Alteplase 1 mg/mL to fill catheter volume	Push protocol of 0.3 mL NS at 2 x 10 min intervals; aspirate catheter at 30 min mark (30 min dwell)	30 pts 66 catheters 116 doses	Qb >200 mL/min for remainder of HD session	92% for partially occluded catheters & 85% for completely occluded catheters.	60% patency rate 30 days after 1 alteplase treatment.	Unable to access original article
Little & Walshe (2002)	Prospective study, all consecutive catheters inserted over a 3 year period	Alteplase 1 mg/mL, dose det'd by lumen vol	Dwell: left in 2 – 8 hrs Alteplase used if Qb <250 mL/min & likely related to thrombosis	Total #'s: 336 pts 570 CVCs Alteplase: 196 CVCs 614 doses	Catheter survival	Alteplase req'd in 2.77 catheters/100 HD sessions 10% (62) catheters req'd alteplase in	34% 1 yr primary patency rate (insertion to 1 st episode of thrombosis/catheter failure) Median survival	Very little benefit to repetitive alteplase treatments

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Study	Design	Dose	Protocol	Pop'n	Defn of Success	Short-term Success	Long-term Success	Author's Conclusions
						>10% of HD sessions; this subgp accounted for 47% of alteplase use	to 2 nd intervention: 27 days; decreased to <20 days for each additional episode.	
Eyrich et al (2002)	Retrospective review	Alteplase 1 mg or 5000 IU urokinase in each port, then filled with NS to catheter volume	Push protocol of 0.2 mL NS at 20 min intervals. Duration: 60 min.	Alteplase: 27 pts received 43 doses Urokinase: 10 pts received 20 doses	Qb>300 mL/min maintained for at least 30 min during HD session	Alteplase: avg Qb increased from 110 to 291 mL/min. 70% achieved Qb>300 mL/min. Urokinase: avg Qb increased from 63 to 203 mL/min. 35% achieved Qb>300 mL/min.	Alteplase: 86% functioned at next HD session. Urokinase: 65% functioned at next HD treatment.	HD blood flow rates increased after either alteplase or urokinase. Alteplase was more likely than urokinase to result in a HD blood flow rate of >300 mL/min.
Savader (2001)	Prospective, non-randomized	Alteplase 2.5 mg / lumen infused over 3 hrs	Infusion over 3 hrs	55 pts 55 CVCs	Effortless manual aspiration & infusion capability from both ports followed by at least one successful HD session.	91%.	1 ^o patency: 55% at 30 days 36% at 60 days 25% at 90 days 15% at 120 days 2 ^o patency: 70% at 60 days 46% at 120 days 30% at 180 days 27% at 240 days	Alteplase 2.5 mg infusion safe & effective. Immediate return of catheter function is achieved in most patients. 1 ^o patency rates are relatively short, but catheters

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Study	Design	Dose	Protocol	Pop'n	Defn of Success	Short-term Success	Long-term Success	Author's Conclusions
								that fail can be retreated, resulting in 2 ⁰ rates that are significantly improved.
Spry (2001)	Prospective, non-randomized, open label	Alteplase 1 mg/mL, dose det'd by lumen vol	Push 0.3 mL of alteplase q10 min to exhaust syringe volume.	44 pts 117 episodes (113 evaluable)	Qb>300 mL/min during next attempted HD session	59% achieved Qb>300 mL/min (91% of pts could "resume HD")	Not specified	Unable to access original article
Daeiagh, P et al (2000)	Prospective, consecutive patients with non-functional catheters	Alteplase 2 mg / lumen	Dwell time 2 – 96 hrs	22 pts 56 episodes	Qb \geq 200 mL/min during the next attempted HD session	87.5%		Alteplase is as effective as urokinase
Meers et al (1999)	Non-randomized case series	Alteplase 1 mg per lumen; filled to catheter volume with NS	0.2 mL NS pushed into lumen at midpoint (20 min or 40 min) in 14 cases or a 48 hr dwell post HD in 26 cases	17 pts 21 catheters 40 doses	Ability to dialyze pts at current or next session who previously had catheter malfunction causing frequent alarms	Results combined for the push and dwell protocols: 39/40 with "restored function" Average Qb=148.5 increased to 238.7 mL/min	Primary patency (time from tx to next intervention required) was a mean of 29.7 days +/- 27 days	Unable to access original article