**Evidence base of policy:**

These guidelines have been derived using the following evidence base.

7. SPC for Urokinase (Syner-kinase®)

**Audit Plans:**

The following items are suggested for audit:

1. Number of catheter dysfunctions severe enough to delay or prolong dialysis therapy (per patient treatment months)
2. Number and type of catheter interventions e.g. thrombolytic drugs, referrals to interventional radiology.

**Training and implementation:**

The guidelines are available on the Trust intranet and via the NUH clinical guidelines app. New members of staff will be made aware of the guidelines as part of their induction programme.

**Limitations of evidence base:**

There is little published evidence comparing the effectiveness of one method of administration of catheter thrombolytic versus another. The KDOQI guidelines support the use of high dose urokinase infusions although the evidence base for this is relatively weak.
INTRODUCTION
Tunnelled cuffed catheters are widely used, often while waiting for permanent vascular access to be created or mature. Increasingly they are also used as the sole form of vascular access for patients who have exhausted other access options. Catheter dysfunction is defined as failure to attain and maintain an extracorporeal blood flow sufficient to perform haemodialysis without significantly lengthening the dialysis treatment. **Dysfunction is defined as failure to attain and maintain an extracorporeal blood flow of 300 mL/min or greater at a pre-pump arterial pressure more negative than –250 mm Hg.** Other signs of CVD dysfunction are described below. A dysfunctional catheter is usually easier to salvage than a non-functional catheter. Early treatment also reduces the likelihood of inadequate dialysis caused by catheter dysfunction.

<table>
<thead>
<tr>
<th>Table 1: Signs of CVC dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pump flow rates &lt;300ml/min</td>
</tr>
<tr>
<td>High arterial pressures (&lt;-250mmHg)</td>
</tr>
<tr>
<td>High venous pressures (&gt;250mmHg)</td>
</tr>
<tr>
<td>URR progressively &lt;65% (or delivered KT/V &lt;1.2)</td>
</tr>
<tr>
<td>Unable to aspirate blood freely (late manifestation)</td>
</tr>
<tr>
<td>Frequent pressure alarms – not responsive to patient repositioning or catheter flushing</td>
</tr>
<tr>
<td>Recurrent need to reverse lines</td>
</tr>
<tr>
<td>Trend analysis of changes in access flow is the best predictor of access patency and risk of thrombosis</td>
</tr>
</tbody>
</table>

Early flow problems are often related to technical problems at the time of insertion. Common causes of early flow problems include: kinked catheter (usually at apex of catheter’s curve), tip malposition (too high or too low), tip malorientation (catheter tip abutting against vessel wall) or catheter located in the wrong vessel. These early technical problems can often be identified using a Chest X-ray. The catheter should be repositioned (usually by exchanging the catheter over a guide wire).

Delayed malfunction (defined as a catheter that previously functioned well, but then develops impaired flow) usually reflects thrombus either within the catheter or around the catheter tip. Thrombus may progress on to form fibrinous tissue surrounding the catheter - a fibrin sheath. The fibrin sheath often acts as a one-way valve, permitting infusion of fluid, but not aspiration of blood.

MANAGEMENT OF DYSFUNCTIONAL CATHETER
1. Check for mechanical obstruction – kink in line, catheter migration, narrowing of tubing proximal to the catheter hub due to clamp indentation. Check for machine problems.
2. Change patient’s position to see if this improves flow.
3. Consider volume depletion as a cause of catheter dysfunction. Undertake a fluid assessment. Consider infusion of 500mls 0.9% sodium chloride over 15 minutes to assess whether this improves catheter function. If catheter flow is improved continue dialysis and reset target weight.
4. Provided the citrate lock can be removed from the catheter lumens, flush lines forcefully with saline. NB Do not use this technique if unable to aspirate the citrate lock as it would lead to rapid system administration of a concentrated citrate solution. The syringe should be filled with 10mls 0.9% sodium chloride, attached firmly to the catheter, and flushed into the catheter with as much force as can be generated with the hand. Once done, an attempt to aspirate blood should be made. If no blood can be aspirated, the saline flush can be repeated several times. If blood can be aspirated, the procedure should be repeated multiple times using blood until flow seems to be free and easy.
   The saline flush technique has the advantages of being easily performed, economical, safe, and frequently effective. Although a successful saline flush means that the thrombus that occluded the catheter has embolised, this does not appear to be a problem clinically since the thrombus is very small. Thrombi of this type and size are frequently embolised in catheter-dialyzed patients without being recognized.
5. A dysfunctional catheter that does not respond to the above interventions should be treated within...
the dialysis unit using low dose intraluminal urokinase (see urokinase section). Low dose urokinase should be attempted as the first procedure to resolve thrombosis as it is the least invasive, easiest to administer and least costly of all the catheter salvage techniques.

6. High dose urokinase has also been used successfully when low dose fails. This may avoid a radiological procedure and manipulation of the catheter, although whilst controlled studies have shown reasonable short term patency rates, medium term patency rates are relatively poor. This may be a reasonable technique to consider in patients who will only need a catheter for a short time (ie. due to maturing vascular access).

7. A radiological catheter exchange should be requested:
   - If lytic therapy is unable to restore blood flow to a level that is adequate for dialysis,
   - The duration of effect of lytic therapy is short lived (requirement for further intraluminal lytic therapy within 2 weeks).
   Catheter imaging at the time of line change will identify other correctable problems (residual lumen thrombosis, fibrin sheath, malpositioned catheter tip). In general the dysfunctional catheter is exchanged over a guide wire.

**Low Dose Urokinase Push Protocol (generally used pre-dialysis)**

It is important to ensure that this protocol is followed correctly to ensure urokinase is used in the most effective way. The licensed formulation of urokinase is significantly more expensive at £46/ 25,000 unit vial.

1. Based on the catheter type determine the appropriate priming volume for urokinase. Table 1 lists all catheters currently in use in the unit and the appropriate filling volume to be used.
2. For Permcaths, reconstitute 25,000 units of urokinase (SynerKinase®) with twice the filling volume of normal saline plus an additional 3 mls (0.5mls for each “push”). This produces two 12,500 unit solutions, one for each lumen.
3. Attempt to aspirate the occluded catheter lumen to remove citrate lock. If it is not possible to remove the citrate lock test to see if the catheter has infusion function. Draw up 10 mls 0.9% sodium chloride into a 10ml syringe and slowly inject into the catheter lumen over 30 seconds. Patients should be informed of possible side effects, including a metallic taste in the mouth and tingling in the fingers. These side effects disappear within 1 minute. If neither lumen can be aspirated, then flush each lumen separately as above but ENSURE AT LEAST 5 MINUTES GAP between the first and second injection.
4. If sodium chloride can be infused without significant resistance then urokinase can be administered. A doctor should be contacted if sodium chloride cannot be infused into the catheter.
5. Steadily inject urokinase with a 5ml or other small syringe into the occluded catheter lumen. The first push consists of the priming volume + 0.5mls. The whole catheter lumen will be filled with urokinase. Clamp the catheter.
6. After 10 minutes push an additional 0.5mls of solution into the catheter lumen. Repeat the process after a further 10 minutes.
7. Attempt to aspirate catheter after a further 10 minutes.
8. May be repeated as needed.
9. The use of intra-luminal urokinase should be recorded on the dialysis assessment sheet and the Renal IT system.
Low Dose Urokinase Lock

Additional methods of administering a low dose urokinase lock include:

1. Short dwell method (lines locked with urokinase for 60 minutes)
2. Long dwell method (lines locked with urokinase overnight). Used for patients who are able to hold dialysis overnight.
3. Intra-dialytic lock (lines locked with urokinase between dialysis sessions). Often used prophylactically at the end of a dialysis session for patients with sluggish flow or where lytic therapy has been needed at the start of the dialysis session.

In these circumstances the urokinase should be administered as a standard lock. Reconstitute urokinase 25,000 units with the correct amount of 0.9% sodium chloride ensuring that the urokinase solution is made up to the priming volume + 0.1 mls to ensure that the urokinase solution completely fills the catheter lumen.

High Dose Urokinase Protocol

High dose urokinase involves the systemic administration of urokinase. Although in published studies adverse events are very rare, high dose urokinase should not be used without careful consideration of the benefits, risks and costs (between £113 and £226 per infusion). Treatment should not be started without discussion with a Renal SpR or Consultant. Treatment should be clearly documented in the patient’s medical notes.

Contra-indications to high dose systemic urokinase

**Absolute Contra-indications**
- Active internal bleeding
- Recent cerebrovascular accident, intracranial or intraspinal surgery (within 2 months)
- Recent severe trauma including cardiopulmonary resuscitation
- Intracranial neoplasm, arteriovenous malformation, or aneurysm
- Severe uncontrolled hypertension
Precautions

- Recent (within 10 days) major surgery, organ biopsy, previous puncture of non-compressible vessels or obstetric delivery
- Intra-arterial diagnostic procedure within 10 days
- Recent (within 10 days) serious gastrointestinal bleed
- Subacute bacterial endocarditis
- Uncontrolled hypocoagulable state
- Cerebrovascular disease
- Haemorrhagic diabetic retinopathy
- Concurrent use of anticoagulants
- Left heart thrombus
- Pregnancy

A. No blood flow or Intermittent Flow Insufficient to Maintain Dialysis

1. If patient is on dialysis, discontinue treatment.
2. Reconstitute 100,000 units urokinase in 2ml 0.9% sodium chloride and add to 50mls of 0.9% sodium chloride. Repeat the procedure to reconstitute a second 100,000 units infusion.
3. Each lumen can be treated concurrently or separately. If treating separately treat arterial lumen first, then venous lumen.
4. Each 100,000 units infusion should run over 90 minutes.
5. Dialysis may be started immediately or electively on the next shift.

B. Poor blood flow, but >100 mls/min and able to continue dialysis

1. Doses between 100,000 units and 200,000 units should be used depending on the severity of the catheter dysfunction.
2. Reconstitute 100,000 units to 200,000 units urokinase with 0.9% sodium chloride (2mls 0.9% sodium chloride for each 100,000 units vial of urokinase). Add to 100mls 0.9% sodium chloride and infuse slowly to the venous chamber over 3 hours (rate of infusion is 34mls/hour).
3. Gradually increase the patient’s blood pump speed to their normal blood flow rate.

Monitoring of Adverse Reactions

Vital signs (pulse, blood pressure) should be monitored every 15 to 30 minutes during the infusion. Patients should be observed for bleeding and possible allergic reactions (skin rashes and bronchospasm).

Catheter exchange over guide wire

Persisting dysfunction requires the replacement of the catheter. Catheter exchange may be performed over a guide wire under fluoroscopic guidance. If there is any sign of infection at the old exit site, the catheter should be placed via a new venotomy site and tunnel or a new system placed on the contralateral side.
PREVENTION OF CATHETER THROMBOSIS

Routine management following dialysis

- As soon as the bloodline is disconnected from each side of the catheter, the catheter should be flushed with 10 mls 0.9% sodium chloride to remove any blood. The catheter must be clamped before the syringe is removed to prevent blood from entering at the tip while the catheter is open.
- Each catheter lumen is filled with a trisodium citrate 46.7% solution (see Guidelines for the commencement and termination of Extra-corporeal therapies via a central venous catheter (tunnelled and non-tunnelled) using trisodium citrate 46.7% locking solution).

Systemic Anticoagulation

It remains unclear whether there is a reliably effective way of preventing catheter thrombosis using systemic anticoagulation.

- Studies using fixed low dose warfarin (1mg/day) have proved this to be an effective technique in preventing catheter related thrombosis in oncology patients. A randomised trial in dialysis patients found this approach not to be efficacious.
- Some centres have reported a stepwise dosing of warfarin. With this method, patients are commenced on low dose warfarin (1mg) after their first clotting episode. With each subsequent episode, the dose of warfarin is increased aiming to raise the INR by 0.5 until clotting episodes do not recur. In selected patients INRs of between 3.0 and 4.0 have been needed using this technique.
- There is anecdotal evidence that formal anticoagulation with a target INR of 2.0-2.5 is effective in preventing catheter thrombosis. Webb et al reported the success of such a protocol in patients who had failed to respond to simple locking with urokinase. They noted a significant risk of catheter dysfunction in patients whose INR became sub-therapeutic.

Based on the available evidence it seems that fixed low dose (1mg) warfarin is unlikely to be effective. Whether it is necessary to achieve a therapeutic INR (2.0-2.5) or whether the stepwise dosing strategy can achieve the same results is unclear. Decisions should be made on an individual basis weighing the risks of catheter dysfunction against the additional need for monitoring and the inherent risks of anticoagulant therapy in the dialysis population (including the risk of promotion of vascular calcification/ calciphylaxis).

Relapsing catheter dysfunction may indicate a prothrombotic state caused by inflammation, latent infection, hyperfibrinogenaemia, high platelet count or other abnormalities of the clotting cascade.

ROLES AND RESPONSIBILITIES

Nursing staff are able to undertake the initial management of a dysfunctional catheter (steps 1 to 5 page 3 above). This includes the use of low dose urokinase using the push protocol and short dwell methods described above. If these interventions are successful dialysis should be initiated/ continued as prescribed and the intervention recorded on the renal IT system.

If these interventions are unsuccessful (including if the dialysis session is suboptimal with effective treatment time <50% prescribed time) nursing staff should seek further advice from renal medical staff (either SpR or consultant – arrangements may vary dependent on the time of day/site). This guideline describes the potential approaches to managing a dysfunctional catheter in these circumstances but the approach needs to be individualised and is a medical decision. An up-to-date U+E/ venous bicarbonate and an assessment of the patient’s fluid balance status are important factors in determining management. For example an overnight urokinase dwell and rescheduling dialysis for the next day may be appropriate in a patient with a safe potassium and minimal fluid overload; whereas a patient with hyperkalaemia and/or significant fluid overload is likely to need admission for urgent intervention/ temporary vascular access. Management plans should be clearly documented on the renal IT system.
Patients with recurrent episodes of catheter dysfunction should be discussed in monthly quality assurance meetings so that the overall vascular access plan can be reviewed.
# Intra-luminal Filling Volumes for Dialysis Catheters – Nottingham Renal Unit

## Non- tunnelled Catheters

### Non-tunnelled Dual Lumen Catheters

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Site</th>
<th>Number of lumens</th>
<th>Catheter length (cm)</th>
<th>Arterial volume (ml)</th>
<th>Venous volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimal Pre-curved</td>
<td>Jugular (R)</td>
<td>2</td>
<td>15</td>
<td>1.0</td>
<td>1.0</td>
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<td>Kimal Pre-curved</td>
<td>Jugular (L)</td>
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<td>1.0</td>
<td>1.0</td>
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<tr>
<td>Kimal Straight</td>
<td>Femoral</td>
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<td>15</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Kimal Straight</td>
<td>Femoral</td>
<td>2</td>
<td>20</td>
<td>1.1</td>
<td>1.2</td>
</tr>
</tbody>
</table>

### Non-tunnelled Triple Lumen Catheters (Trialysis lines)

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Site</th>
<th>Number of lumens</th>
<th>Catheter length (cm)</th>
<th>Arterial volume (ml)</th>
<th>Venous volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimal Pre-curved</td>
<td>Femoral / Jugular</td>
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<td>15</td>
<td>0.8</td>
<td>0.9</td>
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<tr>
<td>Kimal Pre-curved</td>
<td>Femoral / Jugular</td>
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<td>20</td>
<td>0.89</td>
<td>1.0</td>
</tr>
</tbody>
</table>

## Tunnelled Catheters

### Tunnelled Dual Lumen Catheters (Permcaths)

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Site</th>
<th>Number of lumens</th>
<th>Catheter length (cm)</th>
<th>Arterial volume (ml)</th>
<th>Venous volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimal Split</td>
<td>Jugular (R)</td>
<td>2</td>
<td>23</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>Kimal Split</td>
<td>Jugular (L)</td>
<td>2</td>
<td>27</td>
<td>1.7</td>
<td>1.8</td>
</tr>
<tr>
<td>Kimal Split</td>
<td>Femoral / Jugular</td>
<td>2</td>
<td>50</td>
<td>2.5</td>
<td>2.6</td>
</tr>
<tr>
<td>Covidien Palindrome¹</td>
<td>Jugular (R)</td>
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<td>23</td>
<td>1.9</td>
<td>1.9</td>
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<tr>
<td>Covidien Palindrome¹</td>
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<td>28</td>
<td>2.1</td>
<td>2.1</td>
</tr>
<tr>
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<td>33</td>
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</table>

¹ For use in interventional radiology
MANAGEMENT OF TUNNELED CUFFED CENTRAL VENOUS CATHETER DYSFUNCTION IN HAEMODIALYSIS PATIENTS

Guidelines for the management of tunnelled CVC dysfunction. Reviewed January 2017, next review January 2022