# Guidelines for the management of patients undergoing intra-venous and intra-arterial thrombolysis with Alteplase

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## Background

Thrombolytic therapy is a useful tool in the management of acute arterial/venous thrombosis. This most frequently involves the lower limbs and extremities. The principal objective of thrombolytic therapy is to remove pathological thromboemboli and to facilitate restoration of vascular patency.

## Clinical characteristics of acute occlusion

The onset of clinical characteristics can often be rapid. They include severe pain, pallor (pale), absent or diminished pulse, paraesthesia, paralysis and polar sensation (cold limb).

## Treatment

Alteplase (Recombinant tissue plasminogen activator (r-TPA) is the treatment of choice for intra-arterial thrombolysis, with a heparin co-infusion. This is an unlicensed indication of Alteplase but there is an extensive evidence base for this. An arterial catheter is placed in Interventional Radiology, through which bolus Alteplase doses are delivered to the thrombus, followed by a continuous infusion of Alteplase. Treatment duration will be determined by repeat angiogram at 6-8hours.

**Contraindications to thrombolysis with Alteplase**

| **Absolute** |
| --- |
| • Established cerebrovascular event (including transient ischemic attacks) within the last 3 months<br>• Active bleeding diathesis<br>• Recent gastrointestinal bleeding (<10 days)<br>• Neurosurgery (intracranial, spinal) within last 3 months<br>• Intracranial trauma within last 3 months<br>• Recent thoracic or abdominal surgery (within 2-4weeks) |
| **Relative contraindications** |
| • Age > 80 years<br>• Confused patient who is unable to tolerate lying flat<br>• Cardiopulmonary resuscitation within last 10 days<br>• Major nonvascular surgery or trauma within last 10 days<br>• Uncontrolled hypertension (>180 mmHg systolic or >110 mmHg diastolic)<br>• Puncture of noncompressible vessel<br>• Intracranial tumour<br>• Recent eye surgery or Diabetic haemorrhagic retinopathy<br>• Hepatic failure, particularly those with coagulopathy<br>• Bacterial endocarditis<br>• Pregnancy |

These contraindications come mainly from trials relating to systemic thrombolysis, and the bleeding risk from catheter-directed thrombolysis is thought to be less due to the lower doses and targeted therapy used; any treatment should be based on a risk:benefit decision for the individual patient.

The process for a patient to receive Alteplase for catheter-directed thrombolysis is as follows:

1. Patient assessed by vascular team and discussed with IR.
2. HDU bed booked as patient needs monitoring
3. Groin sheath placed and angiogram/venogram of limb performed.
4. An infusion catheter is placed via the sheath for Alteplase infusion and heparin is infused via side arm of sheath
5. The prescription for the heparin and Alteplase will be prescribed on the drug chart by the IR team as per protocol.
6. Patient transferred to HDU with a protocol for monitoring
7. After 6-8 hours patient needs a repeat angiogram and further treatment
8. Patient may need further thrombolysis; if not the sheath will be removed either in IR or on HDU.
9. If there are any concerns then please follow the algorithm below to escalate the matter.

## Dose and Administration

Bolus Alteplase Doses
In Radiology: Documentation of Alteplase and heparin boluses given via catheter on the drug chart

## Continuous infusions

Continuous infusions of Alteplase and Heparin to be started prior to transfer to HDU and continued until re-check angiogram.

### Alteplase

1. Reconstitute a 10mg vial of Alteplase with 10mls of Water for Injections. Agitate gently until dissolved. This Alteplase solution is 1mg/ml.
2. Take 2.5mls (2.5mg) of this reconstituted 1mg/ml solution and dilute to 50mls with sodium chloride. This Alteplase solution is 50micrograms/ml
3. Administer the 50microgram/ml solution using a syringe pump via arterial catheter at 10ml-20ml (0.5mg-1.0mg) per hour.
4. Infusion to be continued until re-check angiogram performed and duration of treatment confirmed

### Storage and Expiry

Reconstituted Alteplase has an in use expiry of 8 hours at room temperature. Any unused contents of the vial from step 1 above can be stored in a refrigerator at 2-8°C for 24 hours.

### Heparin

1. Dilute 2,500 units Heparin to 50ml with 0.9% Sodium chloride
2. Administer using a syringe pump via catheter sheath side arm at initial rate of 10ml (500units) per hour
3. Infusion to be continued until re-check angiogram performed and duration of treatment confirmed

### Storage and Expiry

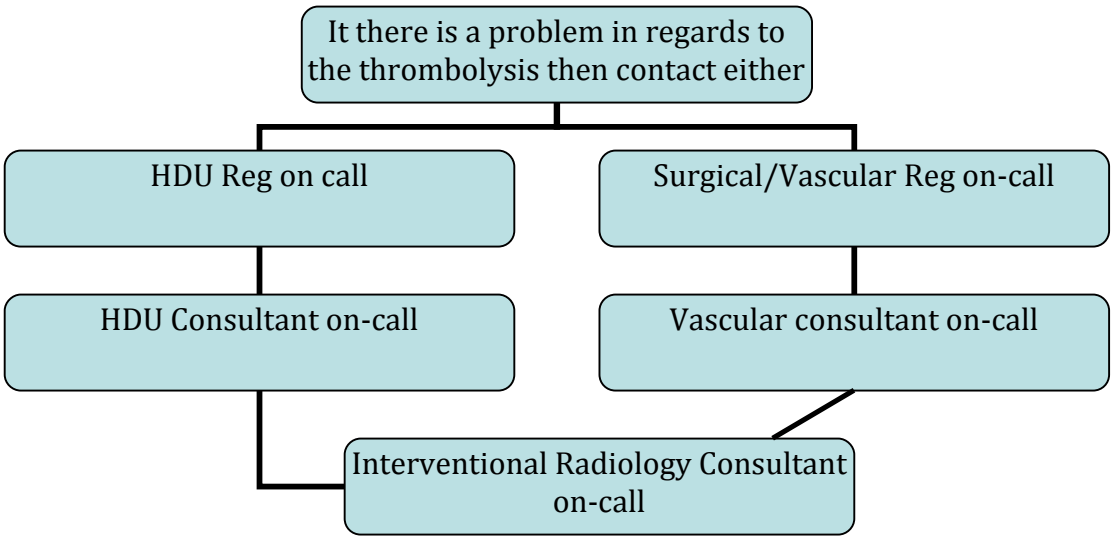
Heparin infusions have an in use expiry of 24hours at room temperature.

## Monitoring and Adverse Events

### Complications of Alteplase

- Haemorrhage – can be minor e.g. from around the catheter site (approx 40%) or major e.g. a retroperitoneal haematoma (approx. 9% and requiring blood transfusion).
- Cerebral Vascular Accident CVA – (1-2% risk of intra-cranial haemorrhage)
- Allergy/anaphylaxis
- Renal Failure
- Distal emboli (approx 4 % - these may break off from the dispersing thrombus and shower down the limb causing ischaemic pain. Small clots will be dissolved by the continuation of lysis)
- Reperfusion injury (2% - restoring blood flow to ischaemic tissues may lead to systemic inflammatory response and multi-organ dysfunction)

If any adverse events are suspected, escalate the matter as per the algorithm below. IR consultant to be contacted once patient has been assessed by the HDU/Vascular team if any concerns regarding the thrombolysis.



| PATIENT'S TRANSFER TO HDU | |
|---|---|
| **Action** | **Rationale** |
| On collecting the patient from IR, the HDU Nurse & IR Nurse should check the following:<br>• Catheter site<br>• Labelling of the arterial/ venous catheter and sheath<br>• That both Volumetric pumps are working and the drug administered, solution, rate etc<br>• All documentation has been completed<br>• Any specific instructions noted | To ensure safe hand-over of patient to HDU staff |
| **CARE OF THE PATIENT RECEIVING ALTEPLASE** | |
| **Action** | **Rationale** |
| 1.Assess cardio-vascular ½ hourly for 4hours then hourly if stable. | To enable deviations (i.e. tachycardia, hypotension, bleeding, allergic reaction or shock) to be established quickly and complications to be treated promptly |
| 2.Observe arterial catheter insertion site hourly for peri-catheter bleeding, haematoma, line disconnection | Bleeding may be visible or concealed causing e.g. retro-peritoneal haematoma, and occur at any time during the period of lysis |
| 3.Monitor patient for abdominal pain, restlessness, back pain | Distant haemorrhagic complications may occur due to altered anti-coagulant status. |
| 4.Monitor patient for other potential bleeding complications, e.g.intra-cranial (causing strokes), renal tract (causing haematuria) and GI Tract (causing oral and/or rectal bleeding). | Haemorrhage may be due to lysis of pre-existing blood clots acting as "plugs" |
| 5.If severe systemic or intra-cranial bleeding occurs, discontinue peripheral arterial/venous thrombolysis and seek urgent medical assistance | To assess effectiveness of rt-PA, level of action, worsening of ischaemia or compartment syndrome |
| 6.Lower limb vascular observations hourly. | Lysis is contra-indicated if there is total limb anaesthesia, paralysis, swollen or tense muscles<br>or persistent skin discolouration |
| 7.Monitor clotting profile and platelets daily. If APTTr >2, consider reducing Heparin infusion to 200units per hour | The heparin doses used are lower than doses used in systemic anticoagulation but could still affect the clotting profile. A drop in platelets could indicate the onset of heparin induced thrombocytopenia |

## References

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