University Hospitals Birmingham NHS
NHS Foundation Trust

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Thrombolysis and Thrombectomy Guidelines for Use in Acute Ischaemic Stroke

CATEGORY:	Clinical Guidelines
CLASSIFICATION:	Clinical
Controlled Document Number:	CG009
Version Number:	3.1
Controlled Document Sponsor:	Clinical Guidelines Group
Controlled Document Lead (Author):	Dr Don Sims (Clinical Lead for Stroke)
Approved By:	Clinical Guidelines Group
On:	August 2017
Review Date:	November 2018

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DEFINITIONS

STROKE is defined as a clinical syndrome, of presumed vascular origin, typified by rapidly developing signs of focal or global disturbance of cerebral functions lasting more than 24 hours or leading to death.

THROMBOLYSIS is a treatment with a thrombolytic agent such as alteplase, usually administered intravenously, in order to dissolve an occlusive thrombus and to allow recanalisation of a blocked blood vessel.

THROMBECTOMY is a treatment to remove the occlusive thrombus blocking a blood vessel endovascularly usually via an arterial puncture and, in stroke, by using a stent-retriever device.

IDENTIFICATION OF APPROPRIATE PATIENTS

It is important to recognise that patients may be suitable for either thrombolysis; or thrombectomy; or both interventions; or neither, depending on their characteristics and the time from stroke onset to presentation.

All patients should be considered for both interventions and if they meet the criteria should receive them promptly to restore perfusion to the ischaemic brain with as little delay as possible.

THROMBOLYSIS CRITERIA

Indications

- Clinical diagnosis of ischaemic stroke causing a measurable neurological deficit
- Onset of symptoms within 4.5 hours prior to initiation of thrombolysis
- Intracerebral haemorrhage has been clearly excluded by brain imaging

Potential Contraindications

- Symptoms strongly suggestive of subarachnoid haemorrhage, even if the CT scan is normal
- Patients currently receiving oral anticoagulants, e.g. warfarin with an INR >1.7
- Administration of heparin at therapeutic dose within the previous 48 hours
- Platelet count of below 100,000/mm^3 (wait for result only if suspected)
- Seizure (only if clinical diagnosis of stroke is then in doubt)
- Systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg
- Known significant coagulopathy or recent, severe or dangerous bleeding
- Significant central nervous system damage (i.e. neoplasm, intracranial or spinal surgery)
- Haemorrhagic retinopathy (unless stroke severity outweighs the risk of visual loss)
- Recent (less than 10 days) traumatic external heart massage, obstetrical delivery or recent puncture of a non-compressible blood-vessel (e.g. subclavian or jugular vein puncture)
- Bacterial endocarditis, or pericarditis
- Acute pancreatitis
- Neoplasm with increased bleeding risk (especially if uncompressible location)
- Severe liver disease, including hepatic failure, cirrhosis, portal hypertension, oesophageal varices and active hepatitis.
- Previous history of intracranial haemorrhage
- Prior stroke within the last 3 months
- Documented ulcerative gastrointestinal disease during the last 3 months
- Major surgery or significant trauma in past 3 months.

The potential morbidity / mortality from an untreated ischaemic stroke is significant so this should be a consideration before treatment is ruled out. The mortality of an untreated total anterior circulation stroke for example exceeds 40% at 30 days.

However, breaching these contraindications should still only occur with the agreement of the on-call stroke consultant and, if possible, following a discussion of the risks with the patient.

THROMBECTOMY CRITERIA

Indications

- Proximal intracranial large vessel occlusion on CT-A
- Disabling acute stroke (NIHSS ≥ 6)
- Procedure can begin within 5 hours (to groin puncture)

Potential Contraindications / Considerations

- Pre-stroke **modified Rankin Score** (mRS) of ≥ 2
- Accessibility of clot on CT-A
- Extensive early infarction changes visible on CT (greater than 1/3 MCA area or ASPECTS <6)
- Poor collateral supply

Patients may still be suitable for thrombectomy with an onset-to-arterial puncture time of over 5 hours if:

- The large artery occlusion is in the posterior circulation, in which case treatment up to 24 hours after onset may be appropriate;
- A favourable profile on salvageable brain tissue imaging has been proven, in which case treatment up to 12 hours after onset may be appropriate.

Thrombectomy for acute ischaemic stroke is always done via the on-call stroke consultant in discussion with the on-call interventional neuroradiologist and neuroanaesthetist.

Thrombectomy is currently available during working hours with the expectation of a full 24 hour service in 2017, however some patients have been treated out-of-hours on a case-by-case basis so if in doubt please call the stroke team.

The modified Rankin Scale (mRS)

The scale runs from 0-6, running from perfect health without symptoms to death.

0: No symptoms.
1: No significant disability. Able to carry out all usual activities, despite some symptoms.
2: Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.

3: Moderate disability. Requires some help, but able to walk unassisted.
4: Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5: Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6: Dead.

THROMBOLYSIS TREATMENT

Alteplase Dosage and Treatment Schedule

The recombinant tissue plasminogen activator (rt-PA/ alteplase/ Actilyse®) is administrated as an intravenous infusion: 0.9 mg/kg (maximum alteplase dose 90 mg), 10% of the total daily dose given as bolus over 1 minute, the remainder given as an infusion over 1 hour.

Treatment must be started within 4.5 hours after symptom onset. The treatment has to be performed in accordance with contraindications, precautions and warnings as described in the inclusion and exclusion criteria and the SPC provided by the manufacturer (see http://www.medicines.org.uk/)

Body weight (stone)	Body weight (kg)	Total rTPA dose (mg)	10% as bolus (ml)	90% as IV infusion (ml/hr)
6st 4	40	36	4	32
6st 8	42	38	4	34
7st	44	40	4	36
7st 3	46	41	4	37
7st 7	48	43	4	39
7st 12	50	45	5	40
8st 2	52	47	5	42
8st 6	54	49	5	44
8st 12	56	50	5	45
9st 1	58	52	5	47
9st 6	60	54	5	49
9st 10	62	56	6	50
10st	64	58	6	52
10st 5	66	59	6	53
10st 9	68	61	6	55
11st	70	63	6	57
11st 4	72	65	6	59
11st 9	74	67	7	60
12st	76	68	7	61
12st 3	78	70	7	63
12st 8	80	72	7	65
12st 12	82	74	7	67
13st 3	84	76	8	68
13st 7	86	77	8	69
13st 12	88	79	8	71
14st	90	81	8	73
14st 6	92	83	8	75
14st 11	94	85	8	77
15st 2	96	86	9	77
15st 7	98	88	9	79
15st 10	100	90	9	81

PATIENTS MUST BE CONTINUOUSLY MONITORED PRIOR TO AND DURING DRUG ADMINISTRATION

And for at least 24 hours following administration.

1. Total dose: 0.9mg/kg **MAXIMUM DOSE IS 90 MG** (See body weight/dose chart)
2. **Should be prescribed by, and administration supervised by, a doctor from the stroke team**
3. 10% of total dose given as an IV bolus over 1 minute by a doctor from the stroke team
4. Give remaining 90% of dose IV over 60 minutes via infusion pump
5. Observe patient for any deterioration during infusion following guidelines for vital signs

It is advised that when 10% of the dose is drawn up, the remaining 90% is left in the vial for later use to prevent accidental administration of 100% as a bolus.

MANAGEMENT OF COMPLICATIONS OF THROMBOLYSIS

Severe Hypertension

Treatment of increased blood pressure should be considered if two readings 5-10 minutes apart reveal a **systolic BP > 180 mmHg** or a **diastolic BP > 105 mmHg**.

Pre-thrombolysis to allow treatment with alteplase

- **Labetalol 10 - 20 mg IV** over 1 - 2 min
- Can be repeated

During / after thrombolysis

- **Labetalol 10 mg IV** for 1 - 2 min
- **GTN infusion 20mg in 50mls** to run at between 2-10ml/hr
- Sodium nitroprusside 0.5 microgram/kg/min IV infusion (ITU only)

May repeat or double labetalol every 10 min to maximum dose of 200 mg, or give initial stat labetalol dose, then start labetalol infusion at 2 - 8 mg/min

Titrate rate of infusions to achieve appropriate blood pressure as desired; if blood pressure is not controlled by labetalol or GTN, consider sodium nitroprusside (ITU only)

Neurological Deterioration (including cerebral haemorrhage)

Senior medical review with a view to considering

- Immediate CT head
- Neurosurgical review

If significant cerebral haemorrhage is present seek advice from stroke consultant on-call and consider the following

- Stop alteplase infusion if still running
- Check FBC, PT, PTT, platelets and fibrinogen
- Give FFP 2 units every 6 hours for 24 hours after dose
- Give cryoprecipitate 20 units. If fibrinogen level < 200 mg/dL at 1 hr, repeat cryoprecipitate dose
- Give platelets 4 adult units

It is worth noting that most deterioration in the first 24 hours is often due to oedema rather than a significant intracranial haemorrhage. Neurosurgical intervention may of course still be required for consideration of decompressive craniectomy.

Orolingual angiooedema

This is a rare complication characterised by swollen lips and tongue and, if worsening, dyspnoea. Tongue swelling may be unilateral initially and prompt action including involvement of ITU to manage the airway may be lifesaving.

- Stop alteplase infusion
- Chlorpheniramine 10 mg iv stat
- Hydrocortisone 200 mg iv stat
- Prednisolone 40mg oral stat

Observe for signs of progression, dyspnoea, anaphylactic shock.
If symptoms are mild and non-progressive, alteplase can be restarted under close observation.

Anaphylaxis

This is a very rare complication which as it becomes increasingly severe is characterised by rash, urticaria, dyspnoea, bronchospasm, angiooedema, hypotension and shock. Early involvement of anaesthetic/ITU staff is essential.

- Stop alteplase infusion
- Urgent medical assessment: **A**irway, **B**reathing, **C**irculation
- Adrenaline 0.5 -1 ml 1:1000 im or sc (**not iv)**
- Chlorpheniramine 10 mg iv
- Hydrocortisone 200 mg iv
- Salbutamol nebulizer 5 mg

If shocked administer intravenous 0.9% sodium chloride and consider repeated doses of adrenaline.

Reperfusion cerebral oedema

This is difficult to distinguish from deterioration secondary to a severe ischaemic stroke but the presence of agitation and / or seizures should raise the suspicion. Other symptoms include clouding of consciousness as in delirium. The neurological deterioration occurs within 24-48 hrs of alteplase infusion and there is no haemorrhage on CT head scan.

- Elevate the head to 30 degrees if not already
- Correct hyperthermia, hypoxia, hyperglycaemia & hypotension
- Mannitol 0.25-0.5 mg/kg over 20 min iv, repeat 6-8 hrly, if necessary
- Consider dexamethasone 4 mg iv qds & frusemide 20-40 mg iv
- Avoid antihypertensives, especially vasodilators
- Consider decompressive hemicraniectomy (once clotting correct / corrected)

If symptoms improve with mannitol reduce dose & frequency gradually.

MANAGEMENT OF COMPLICATIONS OF THROMBECTOMY

Neurological Deterioration

Senior medical review with a view to considering

- Immediate CT head
- Neurosurgical review if needed

If significant cerebral haemorrhage is present seek advice from stroke consultant on-call.

It is worth noting that most deterioration in the first 24 hours is often due to oedema as a result of a completed stroke rather than a significant intracranial haemorrhage. Neurosurgical intervention may of course still be required for consideration of decompressive craniectomy.

Contrast uptake in ischaemic brain tissue post-thrombectomy can resemble intracranial haemorrhage and advice should be sought from a neuroradiologist and the stroke consultant.

Other complications

Other complications of thrombectomy often occur at the time of the procedure and remain rare. These include arterial dissection; distal embolization of the plaque / thrombus; detachment of any stent; formation of a caroticocavernous fistula and reocclusion.

As with other vascular access procedures complications can occur at the site of puncture (usually at the femoral artery) such as haemorrhage, local infection and formation of pseudo-aneurysms.

Rarely, there can be significant sclera oedema on the treated side likely secondary to preferential / diverted flow down the ophthalmic artery. This is usually self-limiting but monitor for redness or painful swelling which may reflect more serious damage to the corneal surface.

Other medical events such as poor blood sugar control, seizures and for general stroke management please refer to the respective guidelines covering these areas.

ONGOING MANAGEMENT POST-THROMBOLYSIS / THROMBECTOMY

- Admit patient to the Hyper-acute Stroke Unit (HASU) on Ward 514 (unless ITU required)

- Continuous cardiac monitoring for 24 hours (telemetry)

- Pulse, BP, RR, oxygen saturations and neurological observations
    - **Every 15 min for 2 hours then,**
    - **Every 30 minutes for 6 hours then,**
    - **Every 60 minutes for 16 then,**
    - **Every 4 hours for the next 72 hours**

- Notify medical staff if systolic BP >175mmHg or <120mmHg, or diastolic>100 or <70mmHg for two readings 5 – 10 minutes apart

- Notify medical staff if change in neurological status, (deteriorating conscious level or new/worsening motor weakness, speech disturbance), or bleeding, (e.g. this could be bruising, haematuria or bleeding from a cannula site)

- Bed-rest for 24 hours, patient to be positioned with their head up to a 30-degree angle to promote cerebral perfusion and reduce intra-cranial pressure

- Ensure patients receive adequate hydration, determine with medical staff intra-venous fluid regime. Normal saline (sodium chloride) at 12 hourly rate is recommended for the first 24 hours, unless the patient is hypertensive – in which case medical advice should be sought

- Ensure patient has sufficient analgesia prescribed

IF THROMBOLYSIS GIVEN

- Avoid central venous access, arterial puncture and injections in the first 24 hours

- Avoid nasogastric tube insertion in the first 24 hours

- Avoid placement of indwelling urinary catheter during infusion and 30 minutes after the end of the infusion and preferably not for 24 hours

- No heparin, anti-platelet agents, warfarin or NSAIDs for 24 hours

ACUTE STROKE MANAGEMENT

Management as per the Acute Stroke Guidelines except where they differ in those areas specified above also apply to all thrombolysis patients / thrombectomy patients, with regards to management of physiology and interventions such as intermittent compression stockings.