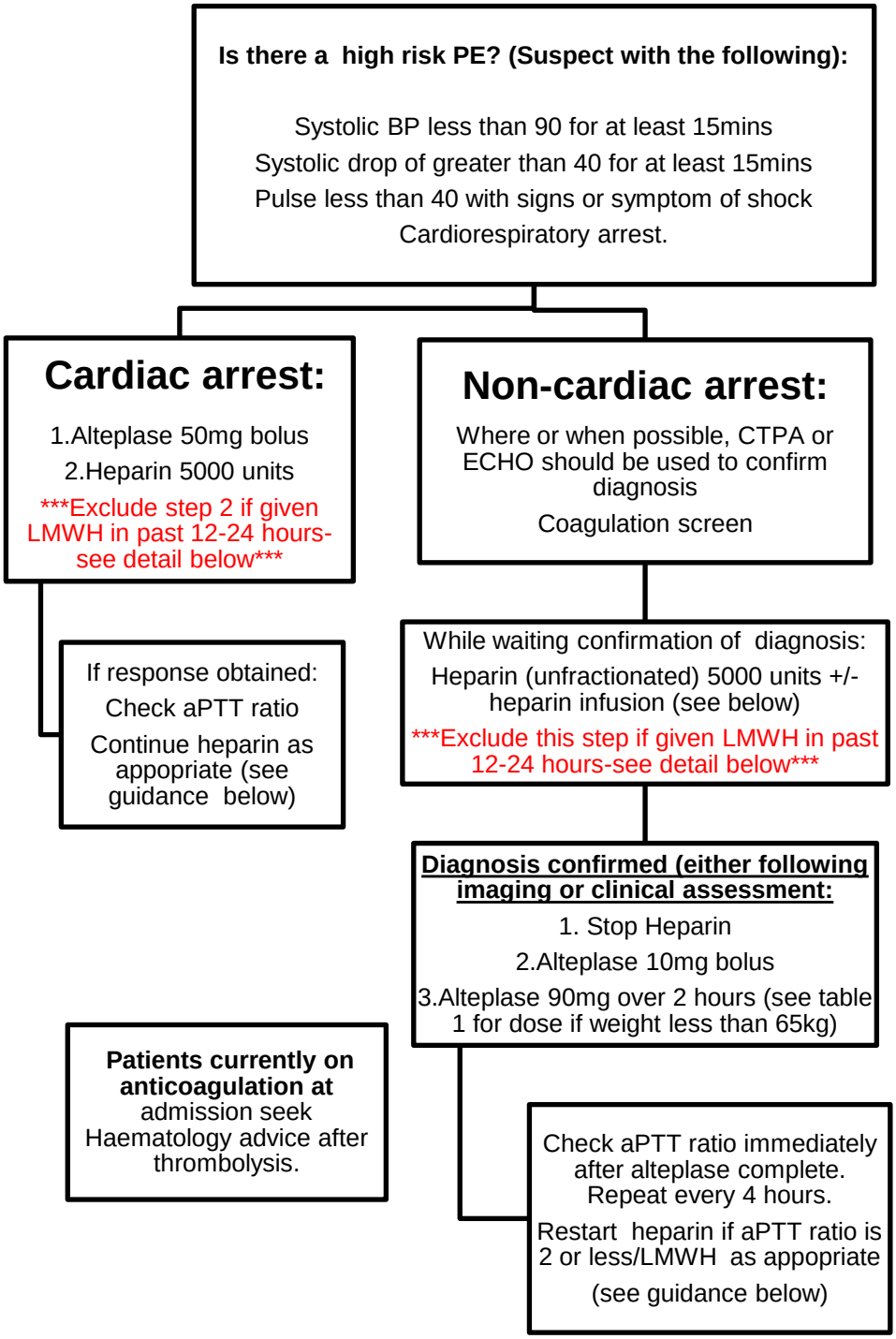
Guideline for the Diagnosis and Treatment of Suspected High Risk Pulmonary Embolus (PE) in Adults (non-pregnant*) aged 18 and over

Please note: High Risk PE can also be known as Massive PE



*For pregnant patients please refer to maternity guidelines.

Appendix 7

Dose of alteplase in patients less than 65kg (table 1)

Weight (kg)	Total dose (mg) to be administered	Dose (mg) administered as an IV Bolus over 1 to 2mins)	Dose (mg) to be administered via IV Infusion over 2 hours
40	60	10	50
42	63	10	53
44	66	10	56
46	69	10	59
48	72	10	62
50	75	10	65
52	78	10	68
54	81	10	71
56	84	10	74
58	87	10	77
60	90	10	80
62	93	10	83
64	96	10	86

Max total dose is 1.5mg/kg in patients less than 65kg. 10mg IV bolus over 2 minutes can be given to all patients.

Appendix 7

Administration of Thrombolysis for High Risk PE

1. Introduction

This is a guideline to cover the administration of thrombolysis medication for the management of high risk pulmonary embolus (PE).

Patients requiring thrombolysis ideally should be transferred to ACU/CCU or HDU if haemodynamically stable and requiring haemodynamic support. If transfer is to be delayed, thrombolysis should be given prior to transfer with appropriate monitoring in place.

2. Indications

High risk PE is defined based on the following signs:

- Systolic blood pressure less than 90 mm Hg for at least 15 minutes or requiring inotropic support, not due to a cause other than PE, such as arrhythmia, hypovolemia, sepsis or left ventricular [LV] dysfunction.
- Persistent profound bradycardia (heart rate less than 40 bpm with sign or symptoms of shock).
- Cardiorespiratory arrest (imminent or actual)

The decision to administer thrombolysis to a patient should be made by a SpR or Consultant.

Patients should be consented for thrombolysis where possible (see below) and decision documented.

3. Contraindications

Note: Although contraindications are listed, it is ultimately the doctor's decisions on whether to proceed. Seek senior/specialist advice input to consider other options (ie: catheter directed thrombolysis, surgical embolectomy, or IVC filter)

ABSOLUTE:

- Haemorrhagic shock or stroke of unknown origin at any time
- Ischaemic stroke in presiding 6 months
- CNS trauma or neoplasm
- Recent major trauma/surgery/head injury (3 weeks)
- GI bleeding within last month
- Known bleeding disorder
- Aortic dissection
- Non-compressible puncture (e.g. liver biopsy, lumbar puncture)

RELATIVE:

- TIA in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post-partum
- Uncontrolled hypertension (Sys more than 180 mmHG)
- Advanced liver disease
- Active peptic ulcer disease

4. Treatment

Alteplase (rt-PA. tissue –type plasminogen activator) (Actilyse®) is the thrombolysis agent choice in high risk PE.

Alteplase is stored on CCU/ITU/ED at Darlington Memorial Hospital and ACU/ITU/ED at University Hospital of North Durham.

If already on unfractionated heparin (UFH), discontinue prior to thrombolysis.

For cardiac arrest

1 Alteplase

- Administer 50mg (reconstituted with 50ml solvent provided or water for injection-see directions below) as an IV bolus over 1-2 minutes.

2 Heparin

- Administer UFH 5000 units (undiluted) as an IV bolus over 3-5 minutes immediately after alteplase.
- **NB:** In patients receiving therapeutic LMWH or fondaparinux at the time of (or prior to) thrombolysis, UFH **should not be given**. Instead continue LMWH 12 hours after the last LMWH injection (given twice daily), or until 24 hours after the last LMWH or fondaparinux injection (given once daily). Check antiXa level three hours after the first post thrombolysis dose.

For ongoing treatment see below.

For non-cardiac arrest

1 Heparin

- Administer UFH 5000 units (undiluted) as an IV bolus over 3-5 minutes.
- **NB**: In patients receiving therapeutic LMWH or fondaparinux at the time of (or prior to) thrombolysis, UFH should not be given. Instead administer alteplase as below once diagnosis confirmed. Continue LMWH 12 hours after the last LMWH injection (given twice daily) or until 24 hours after the last LMWH or fondaparinux injection (given once daily). Check antiXa level three hours after the first post thrombolysis dose

2. Alteplase

- Reconstitute 2 x 50mg vials with water for injection (total 100ml) to achieve a final concentration of 1mg/1ml.
  (note: 50ml of water may be used to achieve concentration of 2mg/1ml)
- Administer 10mg by slow IV injection over 1-2 minutes.
- Follow with administration of the remaining 90mg* via syringe driver over 2 hours
  - *For patients who weigh less than 65Kg give max of 1.5mg/kg total dose, therefore remaining dose should be reduced as per table 1 above.

3. **Heparin**

See below

For all patients

When above steps completed continue UFH infusion or LMWH as appropriate:

Low molecular weight heparin:

Continue on therapeutic LMWH for patients who have been initiated on treatment prior to thrombolysis. Check antiXa three hours after the first dose of post thrombolysis LMWH.

Unfractionated Heparin (for patients not previously on LMWH)

- Check aPTT ratio immediately after completion of thrombolysis and repeat every 4 hours.
- An infusion of unfractionated heparin should be initiated (or resumed) when aPTT ratio values is two or less.
- If aPTT ratio is greater than 2, wait and repeat after 4 hours.
- Infusion - **18 units per kg per hour** – using actual body weight
  (Rounded to nearest 10 units) up to a maximum 25000 units in 24 hours.
  Give over 24 hours (see protocol here for more information.)
- The infusion should be adjusted to maintain according to the aPTT ratio as per table below.
- Further oral/subcutaneous anticoagulation to be decided on by consultant or SpR. Switching from unfractionated heparin to low molecular weight heparin should be based on clinical assessment/clinical stability.

aPTT Ratio	Infusion Rate (units per kg per hour)
More than 7	Stop infusion for 30 to 60 minutes and reduce by 500units (1mL) per hour
5.1 to 7	Reduce by 500units per hour (1.0mL)
4.1 to 5	Reduce by 300units per hour (0.6mL)
3.1 to 4	Reduce by 100units per hour (0.2mL)
2.6 to 3	Reduce by 50units per hour (0.1mL)
1.5 to 2.5	No change
1.2 to 1.4	Increase by 200units per hour (0.4mL)
Less than1.2	REPEAT BOLUS DOSE, Increase by 200units per hour (0.4mL)

Reconstitution of Alteplase:

- Where possible use the solvent and transfer cannula provided.
- If not available water for injection will be adequate however any vigorous agitation should be avoided to prevent foam formation.
- If a syringe driver is unavailable, the reconstituted solution may be diluted with sterile sodium chloride 0.9 % up to a minimal concentration of 0.2 mg alteplase per ml.
- **DO NOT** mix with: Glucose 5%, Heparin, GTN or any other medicines.
- Should be administered thought a separate giving set and cannula.

5. Caution/Side Effects of Alteplase

Side Effects	Action
Sudden Hypotension	Check patient – if symptomatic, lay patient flat and monitor BP at frequent intervals. If hypotension persists, seek senior medical advice.
Severe Bleeding	Give fluid resuscitation as required. Inform senior medical staff. If heparin administered within 4 hours of onset of bleeding, protamine may be considered cautiously and the aPTT ratio rechecked.
Hypertension	If systolic BP greater than 180mmHg or diastolic greater than 105mmHg, consider buccal GTN 2-6mg or administering and IV bolus dose of metoprolol 2.5mg (provided there is no evidence of heart block, left ventricular failure, bradycardia or asthma). If ineffective, an IV infusion of glyceryl trinitrate may be commenced.
Allergic reaction	Give 0.5ml (500micrograms) Adrenaline (1mg in 1ml) 1:1000IM, Consider hydrocortisone 200mg and chlorpheniramine 10mg IV. If reaction persists or is severe, consult senior medical staff.
Arrhythmias Heart block/ Bradycardia	Check BP – if patient is symptomatic and/or hypotensive less than 90mmHg systolic) administer IV atropine 500 micrograms and repeat up to a maximum of 1mg until heart rate greater than 60bpm. If ineffective, **seek medical advice**.
Ventricular Tachycardia	Follow UK Resuscitation Council guidelines.

6. Consent for Thrombolysis

Written consent for thrombolysis is not required, however, verbal consent must be obtained where possible prior to the administration of any thrombolytic drugs and documented in the patient's notes. If the patient is unable to consent then a best interest decision should be carried out and documented.

As well as stressing the benefits of thrombolytic drugs, patients must be informed of the side effects and potential risks incurred by administering them i.e. increased risk of bleeding including:

- Cerebral bleed – incidences more than 1 in 1000, but less than 1 in 100
- Gastrointestinal bleed – incidences of more than 1 in 100, but less than 1 in 10
- Bleeding form intravascular lines, attempted venepuncture sites (common)

References:

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IV guide

With thanks to Nottingham University Hospital NHS Foundation Trust for sharing their policy format.

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https://link.springer.com/article/10.1007%2Fs00408-014-9660-z

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