Thrombolysis for ST segment myocardial infarction (STEMI) when PPCI not available

Introduction
Current reperfusion therapy for STEMI patients is PPCI (primary percutaneous coronary intervention) delivered via a network of paramedics and cardiac catheter laboratories. Staffing and transport are essential elements. The current Covid-19 pandemic is expected to disrupt existing networks and impact delivery of 24/7 PPCI. Thrombolysis for STEMI is an established alternate reperfusion therapy and supported by current NICE pathways (http://pathways.nice.org.uk/pathways/myocardial-infarction-with-st-segment-elevation). Thrombolysis does not require patient transport out of county (Bristol) and can be delivered on Cardiac Care Units (CCU) without need for direct access to a staffed catheter laboratory.

When to consider patients for thrombolysis
- Criteria for diagnosis of STEMI are met: ST elevation on ECG or new LBBB with good history
- Patient would normally be eligible for PPCI if available under normal circumstances (ie no contraindications such as terminal prognosis, extreme old age, etc)
- Normal pathway for PPCI provision is not available:
  - Out of hours (ie 20.00-08.00 Mon-Fri and w/e) - Bristol Heart unable to take patient
  - In hours (ie 08.00-20.00 Mon-Fri) local GHT service unavailable
Discussion with the on call interventional cardiologist will be required to confirm this, if prior notification not already made.

Delivery of thrombolysis
- ECG monitoring (reperfusion arrhythmias). Ideally CCU but could be on cohort ward.
- Other care as for any other patient meeting criteria for diagnosis of STEMI.
- Response to thrombolysis (ECG appearances and symptoms) needs monitoring as may still be need for ‘rescue PCI’ if no improvement.

Drug
Recommended agent is alteplase delivered according to the following protocol:

Alteplase (rt-PA, tissue-type plasminogen activator) (Actilyse®)

Reconstitution:
Reconstitute two 50mg vials; each with 50ml Water for Injections (giving a 1mg in 1ml solution).

Administration:
90 minute (accelerated) regimen started within 6 hours after symptom onset

Step 1: Slow i.v. injection:
Give 15mg (15ml) by slow i.v. injection over 3 to 5 minutes.

Step 2: Intermittent infusion via syringe pump:
The remainder of the dose should be given as follows:

Patient body weight ≥65kg:
- 50mg (50ml) over 30 minutes, followed immediately by
- 35mg (35ml) over 60 minutes

Patient body weight <65kg: (see table overleaf)
- 0.75mg/kg over 30 minutes, followed immediately by
- 0.5mg/kg over 60 minutes

Adjunctive therapy:
Fondaparinux 2.5mg i.v. stat. followed (after 24 hours) by 2.5mg s.c. daily
(Intravenous administration should be through an existing intravenous line either directly or using a 50ml 0.9% sodium chloride minibag).

RCW/20/3/20: Covid-19/Contingency/Cardiac/PPCI
Contraindications to thrombolysis:

- significant bleeding disorder at present or within the past 6 months
- known haemorrhagic diathesis
- patients receiving effective oral anticoagulant treatment, e.g. warfarin (INR > 1.3) or DOAC (apixaban, dabigatran, edoxaban, rivaroxaban)
- manifest or recent severe or dangerous bleeding
- known history of or suspected intracranial haemorrhage
- suspected subarachnoid haemorrhage or condition after subarachnoid haemorrhage from aneurysm
- any history of central nervous system damage (i.e. neoplasm, aneurysm, intracranial or spinal surgery)
- recent (less than 10 days) traumatic external heart massage, obstetrical delivery, recent puncture of a non-compressible blood-vessel (e.g. subclavian or jugular vein puncture)
- severe uncontrolled arterial hypertension
- bacterial endocarditis, pericarditis
- acute pancreatitis
- documented ulcerative gastrointestinal disease during the last 3 months, oesophageal varices, arterial-aneurysm, arterial/venous malformations
- neoplasm with increased bleeding risk
- severe liver disease, including hepatic failure, cirrhosis, portal hypertension (oesophageal varices) and active hepatitis
- major surgery or significant trauma in past 3 months.
- any known history of haemorrhagic stroke or stroke of unknown origin
- known history of ischaemic stroke or transient ischaemic attack (TIA) in the preceding 6 months.

Alteplase dosing table (following reconstitution; 1mg/ml)

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slow i.v. injection</td>
<td>30 minute infusion</td>
<td>60 minute infusion</td>
</tr>
<tr>
<td>40kg</td>
<td>15ml</td>
<td>30ml (60ml/hr)</td>
<td>20ml (20ml/hr)</td>
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<tr>
<td>45kg</td>
<td>15ml</td>
<td>34ml (68ml/hr)</td>
<td>23ml (23ml/hr)</td>
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<tr>
<td>50kg</td>
<td>15ml</td>
<td>38ml (76ml/hr)</td>
<td>25ml (25ml/hr)</td>
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<tr>
<td>55kg</td>
<td>15ml</td>
<td>41ml (82ml/hr)</td>
<td>28ml (28ml/hr)</td>
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<tr>
<td>60kg</td>
<td>15ml</td>
<td>45ml (90ml/hr)</td>
<td>30ml (30ml/hr)</td>
</tr>
<tr>
<td>≥65kg</td>
<td>15ml</td>
<td>50ml (100ml/hr)</td>
<td>35ml (35ml/hr)</td>
</tr>
</tbody>
</table>