STEMI - ST Elevation Myocardial Infarction - Full Clinical Guideline

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1. Reperfusion

(a) Immediate (Primary) Percutaneous Coronary Intervention (Primary PCI or PPCI)

PPCI is now the management of choice for all Derby patients with acute ST elevation myocardial infarction. PPCI has the advantage of achieving higher rates of normal flow in the infarct artery, and treating the underlying lesion at the same time than thrombolysis. Trials comparing PPCI with thrombolysis have shown a small mortality reduction (7% v. 9%) and a larger reduction in reinfarction (3% v. 7%). There is also a reduction in stroke, which is uncommon after PPCI.

In Derby, we have a 24/7 PPCI service. The team is activated by telephoning 07584 407868. This dedicated mobile is held by a senior catheter suite nurse during working hours and by a senior coronary care nurse after hours. The team can be activated by the paramedics, A&E Consultants, Cardiac Outreach or Medical Registrars.

PPCI is indicated in patients with ischaemic cardiac chest pain that began <12 hours ago, with ST elevation of more than 2 mm in 2 chest leads or >1 mm in 2 limb leads, or new LBBB on their ECG. The earlier the reperfusion is given the more myocardium that will be salvaged and the better the outcome for the patient. **Therefore delays should be minimised by rapid ECG and clinical assessment**. National targets are in place and we are measured against these. Emergency PCI can also be considered for those with ongoing chest pain of over 12 hours and ST elevation, ongoing chest pain and borderline ST elevation, transient ST elevation which has resolved and ongoing chest pain with ST depression – discuss with Cardiology (via outreach in daytime or direct with Interventional Cardiologist in the cath lab or via switch out of hours).

The Paramedics will record and interpret a 12 lead ECG. They can activate the PPCI team for patients with cardiac chest pain of <12 hours duration with ST elevation of >2mm in 2 chest leads or 1mm in 2 limb leads. The paramedics will administer ***Aspirin*** 300mg. The patients will be taken directly to the cardiac catheter suite, or to a holding bay in CCU (out of hours).

Patients with LBBB, paced rhythms or other ECG changes (and those with reduced levels of consciousness or evidence of an acute hemiparesis) are taken to A&E for further assessment. The senior doctor in A&E will assess the patient and look at old ECGs and information on MUSE and Cardiobase. If they feel the patient is having an acute MI, they can discuss the case with the on call interventional Cardiologist, who will decide if the Cath Lab team should be activated.

Some patients with STEMI may present directly to A&E. They will be assessed promptly in the department. If they have cardiac chest pain <12 hours duration and ST elevation of >2mm in 2 chest leads or 1mm in 2 limb leads, the A&E registrar or consultant can activate the Cardiac Catheter Lab team by telephoning 07584 407868 directly, or via cardiac outreach. The patient is then transferred promptly to the Cath Lab or the holding bay in CCU.

When a patient arrives in the Cath Lab or CCU, they will be met by the CCU doctors or the Medical Registrar on call, who will take a focused history, briefly examine the patients, check the ECG and take bloods. They will confirm that the patient has had ***Aspirin***. Patients ≤75 yrs of age and ≥60kg without a history of CVA or TIA should also be given ***Prasugrel*** 60mg stat po. followed by Prasugrel 10mg od. for 12 months. Patients aged >75yrs, or <60kg or who have had a previous TIA or CVA should receive ***Ticagrelor 180mg stat*** followed by Ticagrelor 90mg bd. for 12 months. Patients who have a history of intracranial haemorrhage should be loaded with ***Clopidogrel*** 600mg instead continuing clopidogrel 75mg od for 12 months.

Cangrelor can be used for patients who are unable to take oral therapy prior to PPCI eg unconscious or heavy vomiting. The dose is 30mcg/kg i.v. over 1 minute followed by 4mcg/kg/min infusion for 2-4 hours. Once the patient is conscious and able to take oral therapy they should start dual antiplatelet therapy as above (including the loading dose). Prasugrel and Clopidogrel interact with Cangrelor so the loading dose must not be given until the infusion is discontinued.

Please refer to Algorithm for Anti-platelet Therapy in Primary PCI on the intranet. Other anti-thrombotic and anti-platelet drugs will be given as required by the interventional Cardiologist in the Cath Lab (see antiplatelet chart, ref CG-T/2014/143)

(b) Thrombolysis

Since the 24/7 primary PCI service started in Derby (January 2011), very few STEMI patients have been thrombolysed, as the treatment of choice for these patients is PPCI. On rare occasions, thrombolysis may be more appropriate on clinical grounds, than PPCI - but this decision will be made by the consultant cardiologist on call. Occasional patients may decline invasive management and (hopefully very rarely) there maybe logistic reasons why primary PCI is unavailable. For relevant protocols for thrombolysis refer to guidance on thrombolysis in Appendix 1 at the end of this guideline.

After initiating thrombolysis, the ECG should be repeated after 90 minutes and again at 3 hours. A significant (>50%) reduction in ST elevation on the 90 minute ECG, in association with chest pain improvement, is good evidence of successful thrombolysis.

The major complication of thrombolysis is bleeding, and this risk is increased if the patient is hypertensive. Thrombolysis should **not** be done if systolic BP >180 or diastolic BP >110. Treat with IV ***Atenolol*** 5mg, ***GTN*** infusion and give pain relief (opiate) if required and ensure the BP is <180/110 before starting thrombolysis. Patients with a systolic BP >160 have an increased bleeding risk (GUSTO) and should, therefore, receive ***Atenolol*** IV and ***GTN*** while undergoing thrombolysis (aim to get systolic BP <140).

It is important that we achieve a “door-to-needle” time for thrombolysis of <30 minutes, to meet the Department of Health target. If thrombolysis is delayed for clinical reasons, the cause for delay should be documented in the hospital notes.

2. Anti-platelet and anti-thrombotic therapy

(a) Aspirin

Aspirin (300mg chewed) should be given to all patients immediately on admission (unless already administered or contra-indicated, followed by ***Aspirin*** (75mg daily) on a long-term basis.
Patients with a history of dyspepsia (but no active peptic ulceration) should be given ***Aspirin*** 300mg + ***Lansoprazole*** 15mg stat on admission, with further regular ***Lansoprazole*** if appropriate.

(b) Clopidogrel

Clopidogrel is a thienopyridine anti-platelet agent previously shown to be beneficial in conjunction with ***Aspirin*** in NSTEMI and after coronary angioplasty. Two studies (CLARITY – TIMI 28 and COMMIT) both showed that the addition of ***Clopidogrel*** to ***Aspirin*** and thrombolysis reduced a composite end point of death, re-infarction and stroke.

In STEMI patients undergoing PPCI, antiplatelet regimens vary. Patients with a previous history of CVA or TIA will receive ***Clopidogrel*** 600mg stat on admission, followed by ***Clopidogrel*** 75 mg daily for 12 months. Patients who are >75 yrs or <60kg will be loaded with ***Prasugrel*** on admission (see below) but will then be given ***Clopidogrel*** 75mg daily for 12 months. Other patients will be loaded with ***Prasugrel*** and take this for 1 month (see below) but will then take ***Clopidogrel*** 75mg daily for 11 months. The duration of treatment must be clearly stated on the TTOs.

Clopidogrel is a prodrug, and must be converted into an active metabolite for it to exert its anti-platelet effect. This metabolism is by CYP2C19 microsomal enzymes in the liver, which may be inhibited by PPI class drugs (e.g. ***Omeprazole*** and ***Ezomeprazole***), thus reducing the anti-platelet activity of ***Clopidogrel***. Although early observational studies suggested that an interaction between ***Clopidogrel*** and PPIs could increase the risk of re-infarction, the recent prospective COGENT study showed no evidence of this. While results of other on-going studies are awaited it is suggested that patients requiring a PPI with ***Clopidogrel*** should separate the dosage times (PPI at 8.00am and ***Clopidogrel*** at 8.00pm).

(c) Prasugrel

Prasugrel is a potent thienopyridine anti-platelet drug similar to ***Clopidogrel*** which inhibits ADP platelet aggregation in a more rapid and consistent way than ***Clopidogrel***. It is particularly beneficial in STEMI patients undergoing PPCI. ***Prasugrel*** 60mg loading followed by 10mg daily maintenance + ***Aspirin*** was associated with 31% less events (death, MI and stroke) than ***Clopidogrel*** + ***Aspirin*** (TRITON-TIMI 38). ***Prasugrel*** should not be given to patients with a previous TIA or CVA. Patients >75yrs and low

weight (<60kg) have an increased bleeding risk. They can receive the loading dose but should then switch to ***Clopidogrel*** 75mg daily.

Patients in TRITON-TIMI 38 were treated with ***Prasugrel*** 10mg daily for 1 year, but most benefit seen was during the first 30 days. Prasugrel 10mg od. is continued for 12 months following PPCI.

(d) Ticagrelor

Unlike Prasugrel and Clopidogrel, ***Ticagrelor*** is not a thienopyridine but a novel nucleoside analogue which reversibly inhibits ADP-dependent activation of the platelet. It does not require hepatic activation (unlike clopidogrel and to a lesser extent Prasugrel) and thus there is little potential for 'resistance' to platelet inhibition. Aspirin doses >100mg od may inhibit the effectiveness of Ticagrelor. Due to a short half life and reversible mode of action a maintenance dose of 90mg bd. is required (after a loading dose of 180mg). There is a higher incidence of a side-effect of dyspnoea (an ADP effect) than with Clopidogrel with discontinuation due to dyspnoea in 8% in the PLATO trial. Ticagrelor 90mg bd is continued for 12 months following PPCI or high-risk NSTEMI (consultant cardiologist initiation in NSTEMI).

(e) Cangrelor

Cangrelor is an intravenous P2Y12 receptor inhibitor indicated as an adjunct to percutaneous coronary intervention (PCI) to reduce the risk of periprocedural myocardial infarction (MI), repeat coronary revascularization, and stent thrombosis (ST) in patients who have not been treated with a P2Y12 platelet inhibitor and are not being given a glycoprotein IIb/IIIa inhibitor. The loading dose is 30 mcg/kg IV bolus infused over 1 minute before PCI, then immediately follow the bolus injection with 4 mcg/kg/min IV infusion; continue for at least 2 hr or duration of PCI, whichever is longer.

(f) Anti-coagulation

Enoxaparin should be given at prophylactic dose of 40mg s/c daily (20mg if renal impairment) until discharge. ***Warfarin or NOAC*** anti-coagulation is not given routinely, but may be beneficial in special circumstances (atrial fibrillation, mural thrombus or previous thrombo-embolus).

(g) **Duration of antiplatelet therapy**

As noted above, dual antiplatelet therapy is generally given for 12 months after an ACS with aspirin lifelong, but in some circumstances a different duration may be selected. **Please follow the advice of the** Consultant.

For example, if there is a need for anticoagulation (eg AF, previous PE or metal valve), all antiplatelets may stop after 12 months, leaving the patient just on anticoagulation. Also, Clopidogrel tends to be used, rather than Prasugrel or Ticagrelor. In certain selected patients with higher bleeding risk and lower thrombosis risk, we may opt for aspirin for just 1 month (or not at all) and use clopidogrel plus warfarin or NOAC for the first 12 months. Please also note that in these circumstances a different dose of Rivaroxaban 15mg daily may be selected as this was used in the Pioneer trial.

There is always a higher risk of bleeding when combination therapy is used. In these circumstances, ensure the patient is taking a proton pump inhibitor.

Certain stents (currently biofreedom and synergy) appear to be safer with shorter courses of antiplatelet therapy and we may select these stents in patients with an indication for anticoagulation, high bleeding risk or surgery planned, for example. The minimum duration of dual antiplatelet therapy with these stents is 1 month, but we may still recommend longer is there are no bleeding issues, especially after ACS. Bare metal stents (with no drug coating) are rarely used now as they have a higher risk of restenosis (renarrowing) and require a similar course of antiplatelet therapy to these newer stents.

In certain patients at high risk of recurrent ischaemic events and a low risk of bleeding, Ticagrelor can be continued for up to 3 years (a lower dose of 60mg bd is used after the first 12 months). This reduces recurrent ischaemic events but at the cost of higher bleeding rates.

3. Anti-ischaemic therapy

(a) β Blockade

There is good evidence that early β blocker therapy (IV followed by oral) is beneficial in STEMI (ISIS 1), although patients with extensive myocardial infarction and a relative bradycardia may have an adverse haemodynamic response. Benefit is probably greater if β blockade is given early (soon after admission) and may be due partially to a reduction in acute cardiac rupture on day 1. If the patient is haemodynamically stable (heart rate >70; systolic BP >110 and no evidence of failure) consider ***Atenolol*** 5mg slowly IV over 5 minutes, repeated after 15 minutes if well tolerated, and followed by ***Atenolol*** 25-50mg bd or an equivalent β blocker (e.g. ***Timolol*** 5-10mg bd). Aim for a target heart rate of 50-60.

β blockade may be particularly beneficial in patients with a tachycardia (rate >110) and hypertension (systolic BP >160) on admission when treatment increases coronary flow and reduces cardiac oxygen demand (and therefore reduces infarct size and peri-infarction ischaemia) and also reduces the risk of cardiac rupture and cerebral haemorrhage in patients who have received thrombolysis.

There is evidence of benefit from long-term β blockade after hospital discharge. Oral ***Timolol*** (5-10mg bd) given long term has been particularly beneficial. Trials of ***Metoprolol*** and ***Propranolol*** (but not ***Atenolol***) have also been favourable.

Patients with proven acute myocardial infarction should usually be discharged on a β blocker unless there are contra-indications or unacceptable side effects.

β blockade should be avoided if sinus tachycardia is secondary to cardiac failure, shock or hypotension.

(b) Calcium Antagonists

There is some evidence (DAVIT-II) that ***Verapamil*** (40mg tds increasing in stages to 120mg tds) is a useful alternative to β blockers in secondary prevention after myocardial infarction in patients (e.g. asthmatics) in whom β blockade is contra-indicated. ***Verapamil*** should be used with caution in patients with cardiac failure and should **NOT** be used in combination with a β blocker.

Diltiazem, a non-dihydropyridine calcium antagonist, showed possible benefit

in patients with NSTEMI, but not in other post MI patients.

The ***Dihydropyridine*** group of calcium antagonists (e.g. ***Felodipine*** and ***Nifedipine***) should not be used after myocardial infarction and may cause adverse effects (TRENT) due probably to reflex tachycardia.

(c) Nitrates

IV or oral ***nitrates*** should be used in patients with angina following myocardial infarction and if pulmonary oedema is present. Both ISIS 4 and GISSI 3 have shown no benefit from the routine use of ***nitrates*** after myocardial infarction.

4. Vasodilatation using ACE inhibition after STEMI

Animal studies have shown that extensive myocardial infarction leads to progressive LV dilatation with progressive worsening of cardiac function, which is attenuated by the use of angiotensin converting enzyme inhibitor (ACEI). These findings have been confirmed in man by the SAVE trial, which showed a reduction in cardiac mortality of 21% with ***Captopril***.

Patients with a documented myocardial infarction have been shown to benefit from treatment with an ACEI, and this should be considered, unless there is a contra-indication. ***Enalapril*** (2.5-20mg bd), ***Lisinopril*** (2.5-40mg od) and

Ramipril (1.25-10mg od) have all been of proven benefit after myocardial infarction. There is no evidence of benefit by early treatment on admission (Consensus II) and treatment should be started 24-48 hours post infarction. Recent trial data would suggest that the lower the ejection fraction the worse the prognosis, and the greater the benefit from an ACEI.

There is now considerable evidence (HOPE and EUROPA) that ACE inhibition has a beneficial effect on all patients (particularly diabetics) with “high risk” vascular disease, due to a presumed primary effect on the endothelium and atheromatous plaque. This beneficial effect is in addition to blood pressure reduction (in hypertension) and after-load reduction (in heart failure).

Angiotensin receptor blockers (ARBs) such as ***Valsartan*** 40-160mg bd, or ***Candesartan*** 4-32mg od are an effective alternative in patients intolerant to ACE inhibitors (e.g. ACE inhibitor cough).

Patients should be started on a low dose of either an ACEI or ARB and up-titrated, according to their blood pressure. Renal function (U/E) should be monitored and renal artery stenosis suspected if creatinine rises by >20%.

5. Further assessment of patients after STEMI

Assessment of LV function

(i) Echocardiography

This is a simple way of assessing LV function, and is also helpful in confirming (or excluding) a pericardial effusion or diagnosing flail mitral valve (due to papillary muscle disruption) or ventricular septal defect. It may also identify left ventricular thrombus, and these patients should be considered for ***Warfarin*** anticoagulation. (Emergency echocardiography can be carried out by the

patient's bed in CCU, using a mobile machine.) Requests for emergency echocardiograms should normally be discussed with a cardiology registrar or consultant cardiologist.

Most anterior STEMIs should have a predischarge echo to exclude LV thrombus. It is preferres that all STEMIs have a pre-discharge echocardiogram, but patients who are stable, without evidence of heart failure or cardiac murmurs, can undergo echocardiography as outpatients if it avoids delayed discharge. The echo should be repeated at 6 weeks if EF <40%.

Patients with LVEF <35% at 6 weeks post ACS should be considered for an ICD or CRT-D.

(ii) Gated T^c MUGA (Multiple Gated Acquisition) Scan

This technique involves isotope blood pool imaging, and the procedure is carried out in the Nuclear Medicine department. A T^c MUGA scan is helpful if satisfactory echo data cannot be obtained (non "echogenic" patients) or if more precise data on LV function and ejection fraction are required.

(iii) **Cardiac MR**

MRI is another alternative which provides excellent reproducible information on LV function and also thickness of infraction (which can be used to predict recovery of LV function after revascularization of occluded vessels). It also can be used for identifying other conditions such as myocarditis or takotsubo cardiomyopathy, which can present in a similar way to MI. It is expensive and requests must be made after discussion with a Cardiology Consultant. Inpatient availability is low.

Assessment of residual ischaemia

(i) Coronary Angiography

The majority of STEMI patients will now have PPCI. In some patients, significant 'bystander' coronary disease in other vessels may be noted at the time of PPCI, but not treated. The Consultant Cardiologist will decide whether it is necessary to treat this later, as a staged procedure in line with emerging clinical trial evidence of benefit with complete revascularization (PRAMI and CVLPRIT trials).

In patients presenting late (and therefore not undergoing PPCI) with large enzyme rises (often with Q wave formation), coronary angiography may show the infarct vessel still to be occluded. Late opening of an infarct related artery has not been shown to be beneficial (OAT). However, angiography may still be considered in some patients to assess the other coronary vessels and guide future revascularisation.

(ii) Treadmill Exercise Testing

A pre-discharge exercise test to identify exertional ischaemia, may be helpful in selected patients who have not gone directly to angiography and PPCI, who may benefit from further investigation and possible intervention.

Documentation Controls

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Thrombolytic Therapy – Appendix 1

The standard management of STEMI in Derby is now primary PCI. Thrombolysis has been shown to be less beneficial and will therefore only be used in this situation in exceptional cases (patient declines invasive management, primary PCI contraindicated on clinical grounds or Cath Lab/ PCI Cardiologist unavailability).

Early thrombolytic therapy will produce thrombolysis and "opening" of the infarct artery in 60-80% of patients with a reduction in mortality of up to 50%. Very early thrombolysis, within one hour of symptom onset, will abort myocardial infarction in about 25% of patients. Reperfusion is usually associated with dramatic improvement in chest pain and resolution of ST elevation, but may also produce reperfusion ventricular arrhythmias and an early release of CK. Serious complications are mainly haemorrhagic, and occur in about 1%.

The tissue plasminogen activator (TPA) ***Tenecteplase*** (***TNK***) is available at the RDH and is used in combination with ***Enoxaparin.*** An alternative TPA ***Reteplase*** (***rPA***) may be used occasionally by the East Midlands Ambulance Service paramedics, usually as part of a clinical trial.

There has been concern about increased haemorrhagic stroke with TPA's especially in older patients and in those who present late after acute STEMI. In patients over 75 years, and in those treated greater than 6 hours after symptom onset, ***Streptokinase*** remains the thrombolytic of choice. However, ***Streptokinase*** is strongly allergenic, high antibody titres persist for many months, and are present in about 50% of patients at four years. TPA's are not allergenic and ***Tenecteplase*** may be given safely in a patient who has received either ***Streptokinase*** or any TPA previously. ***Streptokinase*** should **NOT** be given to any patient who has received the drug at any time before or if there is a strong history of allergy.

Aortic dissection is a less common cause of acute chest pain and in this situation thrombolysis is likely to be disastrous.
Always consider the possibility of dissection in atypical, very sudden onset, severe "tearing" chest pain, particularly in hypertensive patients (see Appendix 6).

A. **Definite Indications for Thrombolysis** - major benefit likely

1. Typical chest pains with onset within 6 hours
2. ECG showing ST elevation (1mm in limb leads or 2mm in chest leads or 1mm in posterior leads V7, V8) or LBBB
3. Younger patients

Patients who derive particular benefit appear to be those who are treated early (less than 2 hours), have an anterior infarction, have gross ST elevation, have LBBB or have LV failure.

B. **Relative Indications for Thrombolysis** - probably some benefit

1. Onset of chest pain 6-12 hours
2. Elderly patients but no major contra-indications
3. "Minor" ECG ST elevation only

A detailed meta-analysis of all the early placebo controlled trials showed that patients with a normal ECG or ST depression derive no benefit from thrombolysis (? excess hazard) and these patients should, therefore, **NOT** be thrombolysed. The risk of

haemorrhagic stroke appears to be greater in older hypertensive patients who are treated after 6 hours, who may also be at increased risk of cardiac rupture. Thrombolytic therapy should not be given to patients presenting after 12 hours.

Elderly patients (>80yrs) have the highest mortality after myocardial infarction and, although they have an increased risk of intra-cranial bleeding with thrombolytics, there is a worthwhile clinical benefit. ***Streptokinase*** is probably safer than ***Tenecteplase*** (***TNK***) in those over 75yrs.

Absolute benefit is probably greater in diabetics than non-diabetics and proliferative retinopathy is not a contra-indication to thrombolysis.

C. Contra-indications to thrombolysis

1. Possible aortic dissection.

2. Any active bleeding (peptic ulceration, colitis, etc).

3. CVA within the last 2 months, any previous cerebral haemorrhage or known cerebral tumour.

4. Recent trauma (including surgery, organ biopsy, central venous cannulation and prolonged external cardiac massage).

5. Uncontrolled hypertension (systolic >180 or diastolic >110mmHg). If BP remains high after pain relief give ***Atenolol*** 5mg IV stat, followed by a ***GTN*** infusion if required.

6. Severe renal failure, metastatic cancer, haemorrhagic diabetic retinopathy, or cavitating lung disease.

7. Pregnancy and early post partum period, heavy vaginal bleeding.

8. Previous therapy with either ***Streptokinase*** or ***Anistreplase*** is a contra-indication to repeated use. Use ***Tenecteplase***.

9. ***Warfarin*** anti-coagulation with INR >3.0 – see page 32.

10. Known intravascular thrombus, which is likely to break up and embolise (e.g. in aortic aneurysm or enlarged left atrium with mitral stenosis and AF).

If there is a history of dyspepsia, but active ulceration is considered unlikely, and there are major indications for thrombolysis, use ***Ranitidine*** 300mg nocte (for two weeks) “cover” with a thrombolytic as appropriate.

D. Treatment Regimes

(a) Thrombolysis using *Streptokinase*

1. ***Streptokinase*** 1.5 million units in 100ml saline infused IV over one hour

2. Daily ***Aspirin*** therapy (300mg stat then 75mg daily). The first ***Aspirin*** tablet should be given at the time of ***Streptokinase*** administration (if not already given) and should be chewed.

3. ***Enoxaparin*** 1mg/kg bd subcut for 5 days.

(b) **Treatment regime for *Tenecteplase* (*TNK)***

Tenecteplase should be administered as a single IV bolus over approximately 10 seconds on the basis of body weight, up to a maximum dose of 50mg. The drug is given after oral ***Aspirin*** (300mg) and ***Heparin*** is given at the same time.

Body Weight	***Tenecteplase***
<60kg	30mg
60-69kg	35mg
70-79kg	40mg
80-89kg	45mg
≥90kg	50mg

TNK is given with an IV bolus of unfractionated ***Heparin*** 5,000iu and followed without delay by subcutaneous LMWH (***Enoxaparin***) 1mg/kg every 12 hours (until hospital discharge or a maximum of 7 days).

(c) **Treatment regime for *Reteplase (rPA)***

Reteplase* 10u x 2**. An initial slow IV bolus of 10u over 1 minute (will be given by the paramedics on site), followed by a second bolus of ***Reteplase 10u administered 30 minutes later (usually on arrival in CCU).

A bolus of 5,000iu of ***Heparin*** will be given by the paramedics before the first bolus of ***Reteplase***. An intravenous ***Heparin*** infusion (see Appendix 9) should be started in hospital after the second bolus and continued for 72 hours. This should be followed by ***Enoxaparin*** (1mg/kg bd subcut) until discharge, or for a maximum of 5 days.

E. Routine Management of Patients after Thrombolytic Therapy

1. THROMBOLYTIC THERAPY MUST BE GIVEN AS EARLY AS POSSIBLE

2. Monitor in CCU for 48 hours post treatment (reperfusion arrhythmias)

3. Consider nitrate therapy (IV, patch or oral) if persistent pain or ischaemic changes on ECG. Occlusion and thrombolysis maybe associated with significant coronary spasm in some patients. Early angiography should be considered if on-going pain.

4. CK and TnT measurement on admission and 12 hours after symptom onset.

5. Pre-treatment ECG then hourly for the next 3 hours, and again at 12 hours, 24 hours and 48 hours. Further daily recordings are done on CCU, if ward transfer is delayed beyond 48 hours.

6. No central vascular cannulation or arterial puncture. Avoid unnecessary venepuncture

7. If pacing electrode needed, this should be inserted via antecubital vein cut down, internal jugular or femoral vein (**NOT subclavian vein cannulation**)

8. Routine post MI mobilisation with exercise testing at 4-6 weeks.

9. Consider cardiological referral for angiography if significant post thrombolysis angina or positive exercise test at low workload. Early angiography should also be considered in patients with a good result from thrombolysis, who may have a critical residual stenosis and viable myocardium.

Streptokinase is potentially antigenic. Acute allergic responses with urticaria and anaphylaxis have been described, as have chronic phenomena (serum sickness and vasculitis) but are rare.

F. Bleeding problems after thrombolytic therapy

The major serious complication with thrombolytic therapy is haemorrhage and, if intra-cranial, this may be fatal. By carefully excluding patients likely to bleed, the risk of major haemorrhage is small, but occurs in approximately 0.5%. Patients at risk of bleeding are hypertensive patients (systolic BP >140), females, elderly (>70yrs), underweight patients and those with renal disease. Patients who have a major bleed have a high mortality (30-50%) due to a combination of the adverse effect of the haemorrhage and also the adverse effects of withdrawing anti-thrombotic and anti-platelet therapy (LMWH, ***Aspirin*** and ***Clopidogrel***) in acute coronary syndrome.

If major bleeding complications occur, stop the thrombolytic infusion (and ***Heparin*** infusion if given IV) and arrange a full coagulation screen (FBC, platelets, INR, KCCT, Thrombin time, Fibrinogen and D Dimers). Reverse the ***Heparin*** using protamine (see Appendix 11) while awaiting coagulation data. Discontinue ***Aspirin*** and ***Clopdiogrel***. Discuss the results with the haematologist on call.

If bleeding is serious and life threatening give ***Tranexamic acid*** 1gm IV over 15 minutes while awaiting coagulation data.
When thrombin time and INR are prolonged but fibrinogen is >1gm/L give 2-4u ***FFP.*** When thrombin time is prolonged and fibrinogen is low (<1gm/L) give 10u ***Cryoprecipitate***. Repeat coagulation screen 30 minutes after treatment. Replace blood as necessary and, if indicated, arrange a CT scan or ultrasound. Surgical evacuation of clot may need to be considered but will carry significant risks if done under GA early after myocardial infarction.

G. Failed coronary thrombolysis

ST segment resolution is currently the most useful simple guide to vessel patency after thrombolysis and also correlates with outcome (30 day mortality in INJECT study). The ECG should be repeated 90 minutes after starting thrombolysis and a 50% fall in the sum of all leads with ST elevation (or the worst lead),

particularly if associate with loss of pain, is good evidence of successful thrombolysis and a favourable outcome.

The REACT study showed that patients with evidence of severe ongoing ischaemia with persistent ST segment elevation >50% (due to presumed failed thrombolysis) within 8 hours of lytic therapy, benefit from emergency 'rescue' angioplasty. Rescue PCI is very effective and of clinical benefit early (within 6 hours) after acute myocardial infarction onset, but if performed later (after 12 hours) worthwhile benefit is unlikely, as substantial myocardial necrosis will have occurred.

.Patients who have persistent ST elevation and are both clinically stable and pain free should be managed conservatively, as their prognosis is good. Some of these patients have chronic ST elevation without recent infarction and will subsequently be found to have normal cardiac enzymes.

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