Treatment Guideline

Gloucestershire Hospitals
NHS Foundation Trust

Acute Coronary Syndrome (ACS) Trust Protocol

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Contents

**Gloucestershire Royal Hospital is a percutaneous coronary intervention (PCI) capable hospital.*

1. Introduction

1.1 Classification

Acute coronary syndrome (ACS) includes a spectrum of conditions:

- ST-elevation myocardial infarction (STEMI)
- Non-ST-elevation acute coronary syndrome (NSTE-ACS)
    - Non-ST-elevation myocardial infarction (NSTEMI)
    - Unstable angina (UA)

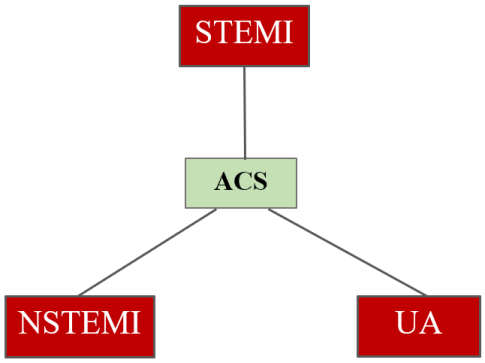

***Figure 1**. ACS spectrum.*
ACS, acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

1.2 Risk factors

Established risk factors:

- Family history of early myocardial infarction (≤55 years of age)
- Smoking
- Diabetes mellitus
- Hyperlipidaemia
- Hypertension

Other possible risk factors:

- Physical inactivity
- Obesity
- Recreational drug (e.g. cocaine)

2. Diagnosis

The following algorithm is for clinical suspicion of a high likelihood of ACS.

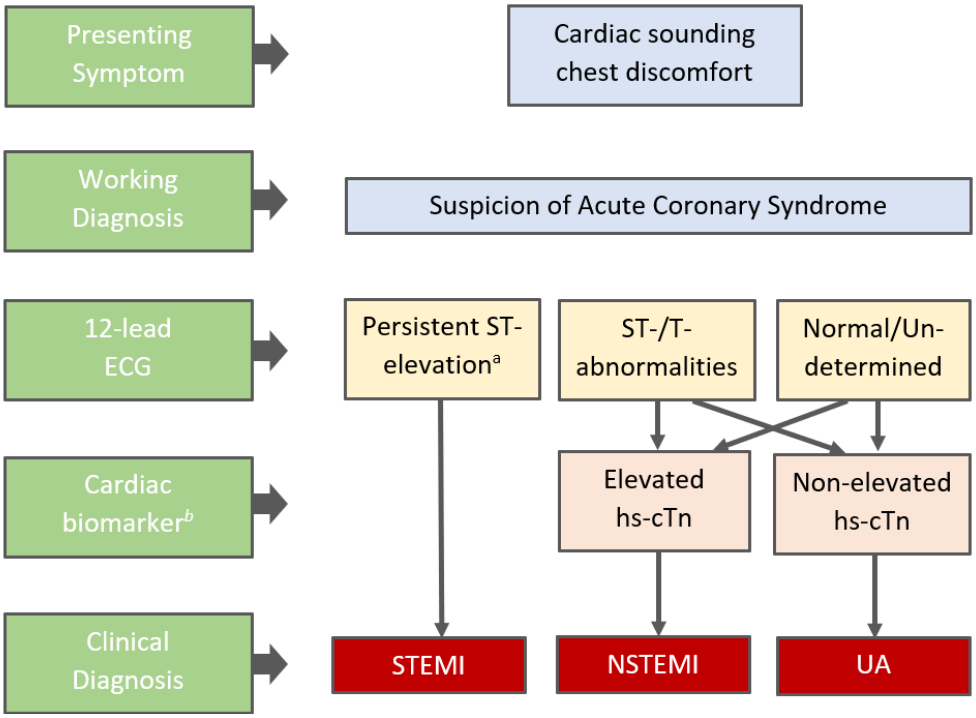

***Figure 2**. Algorithm of diagnosing ACS.*
ACS, acute coronary syndrome; ECG, electrocardiogram; hs-cTn, high-sensitivity cardiac troponin; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.
[a]refer to Heading 2.1
[b]refer to Figure 3

2.1 Diagnosis of ACS

Acute myocardial infarction (AMI) is defined as an **acute myocardial injury** with clinical evidence of **acute myocardial ischaemia**, a rise and/or fall of **cardiac troponin (cTn) values (**at least one value above the 99th percentile URL) and at least one of the following:

- Symptoms of myocardial ischaemia
- New ischaemic ECG changes
- Development of pathological Q waves

STEMI

- Symptoms of myocardial ischaemia and new ST elevation at the J-point in at least 2 contiguous leads
  - In leads V2-V3:
    - ≥2.5 mm in men <40 years old
    - ≥2 mm for men ≥40 years old
    - ≥1.5 mm for women of all ages
- ST depression in leads V1-3 (especially with dominant R wave and positive terminal T wave) is highly suggestive of posterior coronary artery occlusion.

- ST depression ≥1 mm in ≥6 surface leads (inferolateral depression), coupled with ST elevation in aVR and/or V1 suggests multivessel ischaemia or left main coronary artery obstruction (particularly in the presence of haemodynamic compromise).

NSTEMI

- AMI with either a normal ECG or with ECG changes of ST depression and/or T wave inversion; alongside hs-cTn T level of ≥14 ng/L; or a dynamic hs-cTn trend of ≥ 20% rise or fall of hs-cTn levels (refer to *Figure 3*).

UA

- Defined as myocardial ischaemia at rest or upon minimal exertion in the absence of acute cardiomyocyte injury/necrosis (normal 12-lead ECG and negative hs-cTn).
- It is characterised by:
  - Prolonged angina at rest/on minimal exertion (>20 minutes)
  - New onset of severe angina
  - Angina that is increasing in frequency/longer in duration/lower in threshold
  - Angina that occurs after a recent episode of myocardial infarction (MI)

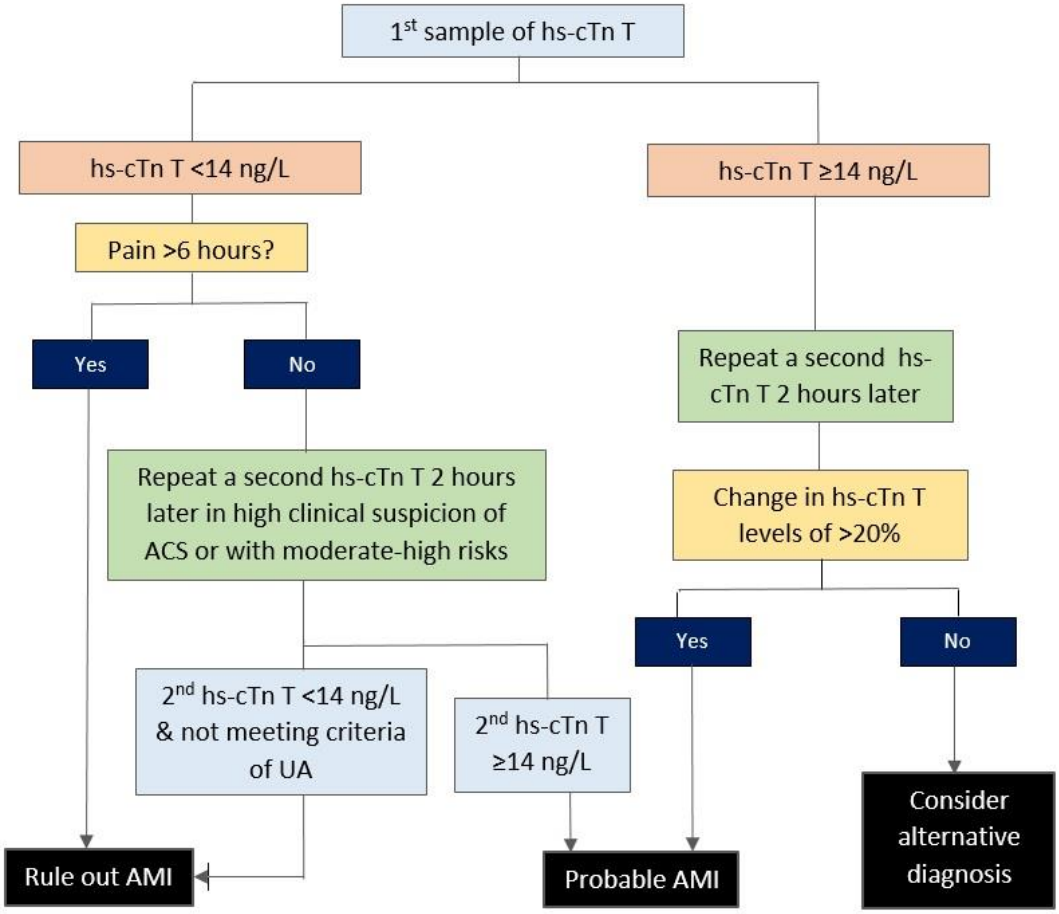

Figure 3. *'Rule-in' and 'rule-out' pathway for ACS based on hs-cTn T level and risk stratification.*
ACS, acute coronary syndrome; AMI, acute myocardial infarction; hs-cTn T, high-sensitivity cardiac troponin T; UA, unstable angina.

3. Management

3.1 Acute/early management of STEMI

Coronary angiography with follow-on primary PCI is the choice of reperfusion therapy in a PCI-capable hospital. However, in cases when PCI is not possible, fibrinolysis should be considered instead (refer to *Appendix 1 for 'Fibrinolysis pathway'*).

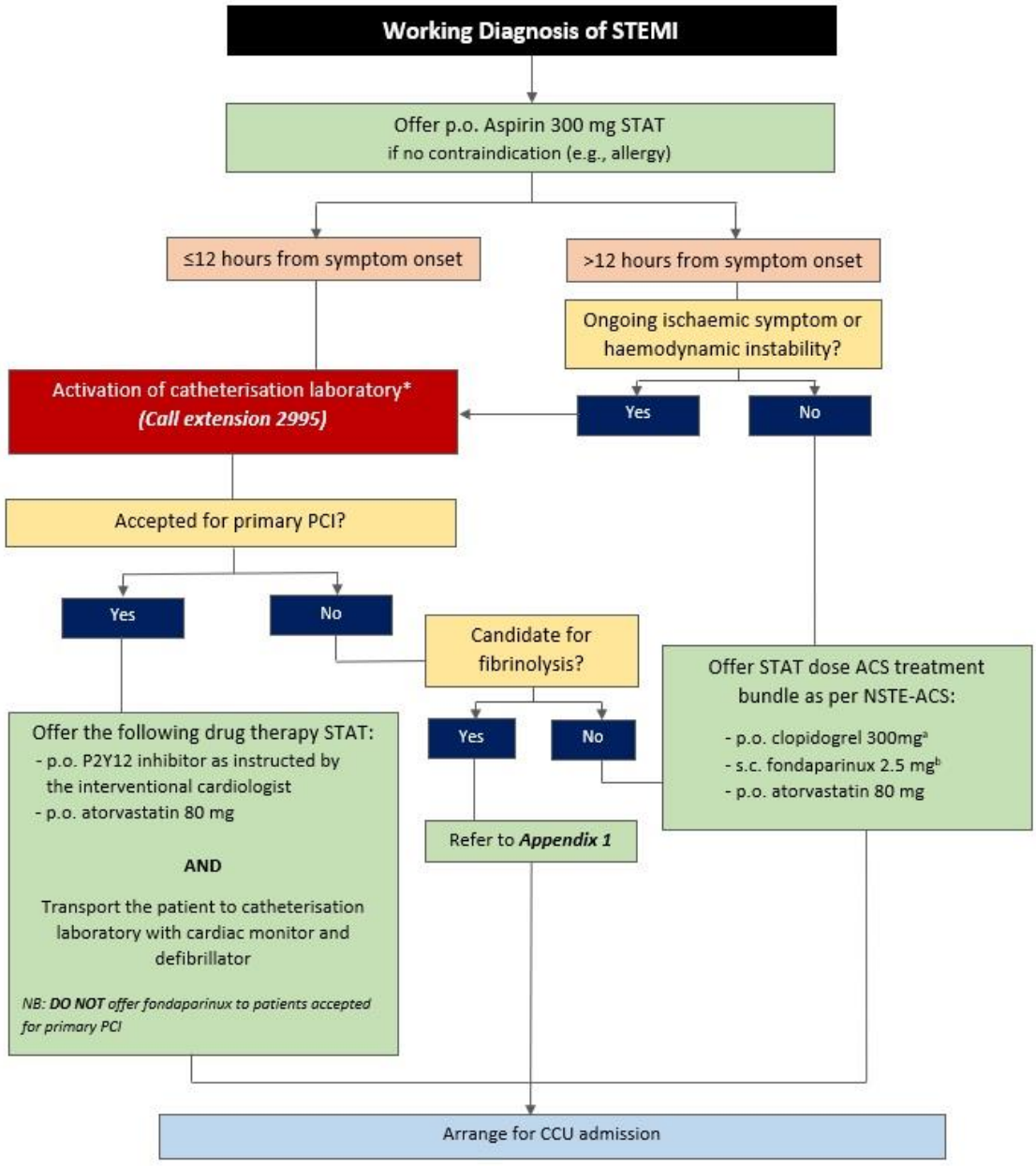

Figure 4. *STEMI pathway.*
ACS, acute coronary syndrome; NSTE-ACS, non-ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; p.o., per oral; s.c., subcutaneous; STEMI, ST-elevation myocardial infarction.
[a]p.o. ticagrelor 180mg can be used in patients allergic to clopidogrel but avoided in patients with high bleeding risk.
*[b]s.c. enoxaparin 1mg/kg in patients with renal impairment (i.e., creatinine > 265 µmol/L or creatinine clearance <20 mL/min), on warfarin/OAC or newly diagnosed atrial fibrillation, **avoid** in patients considered for coronary angiography with follow-on primary PCI in the presence of high-risk clinical features.*
** Activation of the catheterisation laboratory should only be a consultant/registrar-to-PCI consultant discussion.*

3.2 Acute/early management of NSTEMI/unstable angina

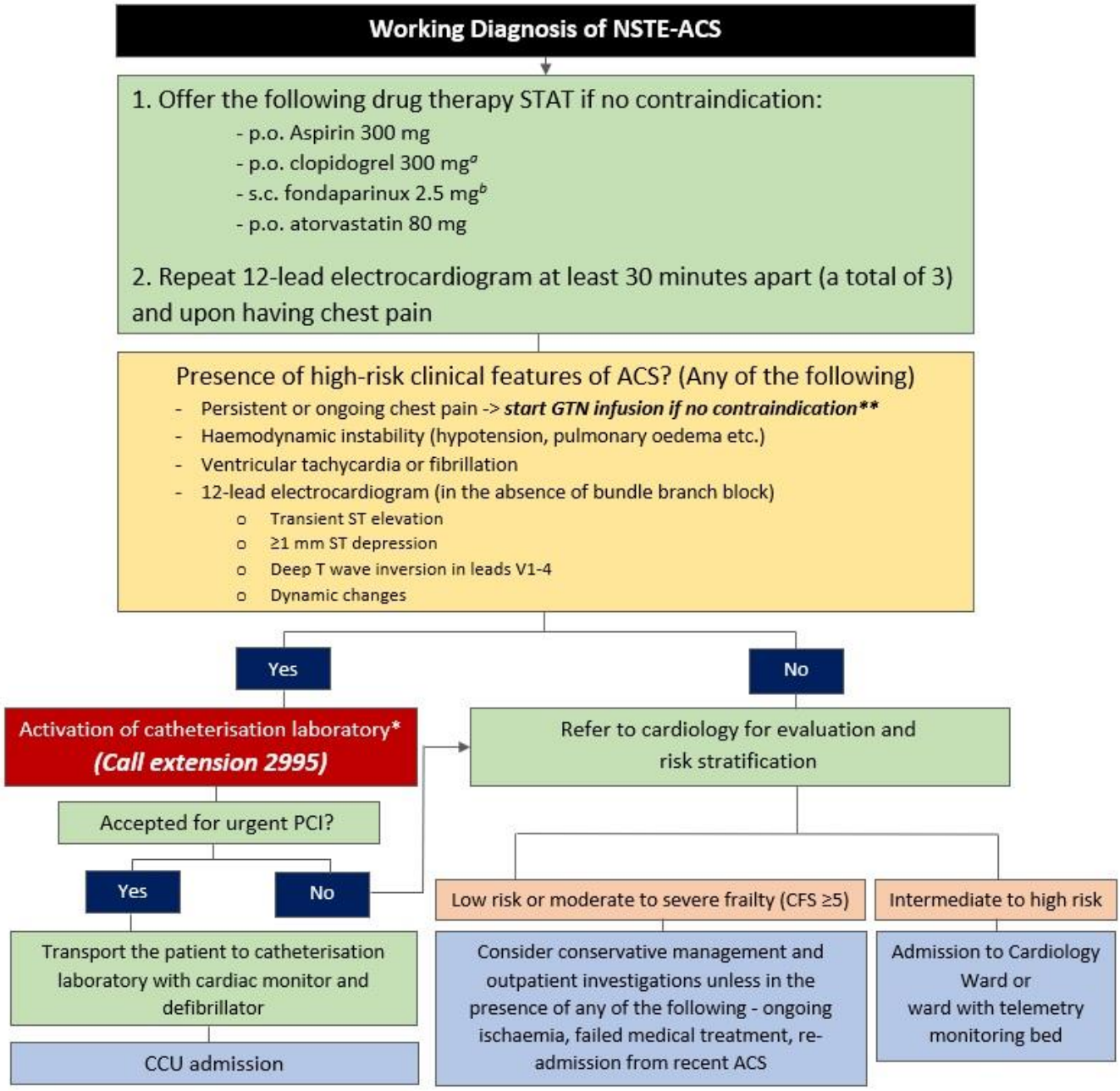

Figure 5. *NSTE-ACS pathway.*
ACS, acute coronary syndrome; CFS, Clinical Frailty Scale; GTN, glyceryl trinitrate; NSTE-ACS, non-ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; p.o., per oral; s.c., subcutaneous; TIMI, Thrombolysis in Myocardial Infarction.
[a]p.o. ticagrelor 180mg can be used in patients allergic to clopidogrel but to avoid in patients with high bleeding risk.
[b]s.c. enoxaparin 1mg/kg in patients with renal impairment (i.e., creatinine > 265 µmol/L or creatinine clearance <20 mL/min), on warfarin/OAC or newly diagnosed atrial fibrillation, ***avoid*** *in patients considered for coronary angiography with follow-on primary PCI in the presence of high-risk clinical features.*
**Activation of catheterisation laboratory should only be a consultant/registrar-to-PCI consultant discussion.*
***If GTN infusion is being started for a patient, this needs to be escalated to the cardiology consultant or registrar for urgent intervention. The patient should be moved to a cardiology bed in the first instance.*

3.3 Summary of approach to ACS diagnosis and management

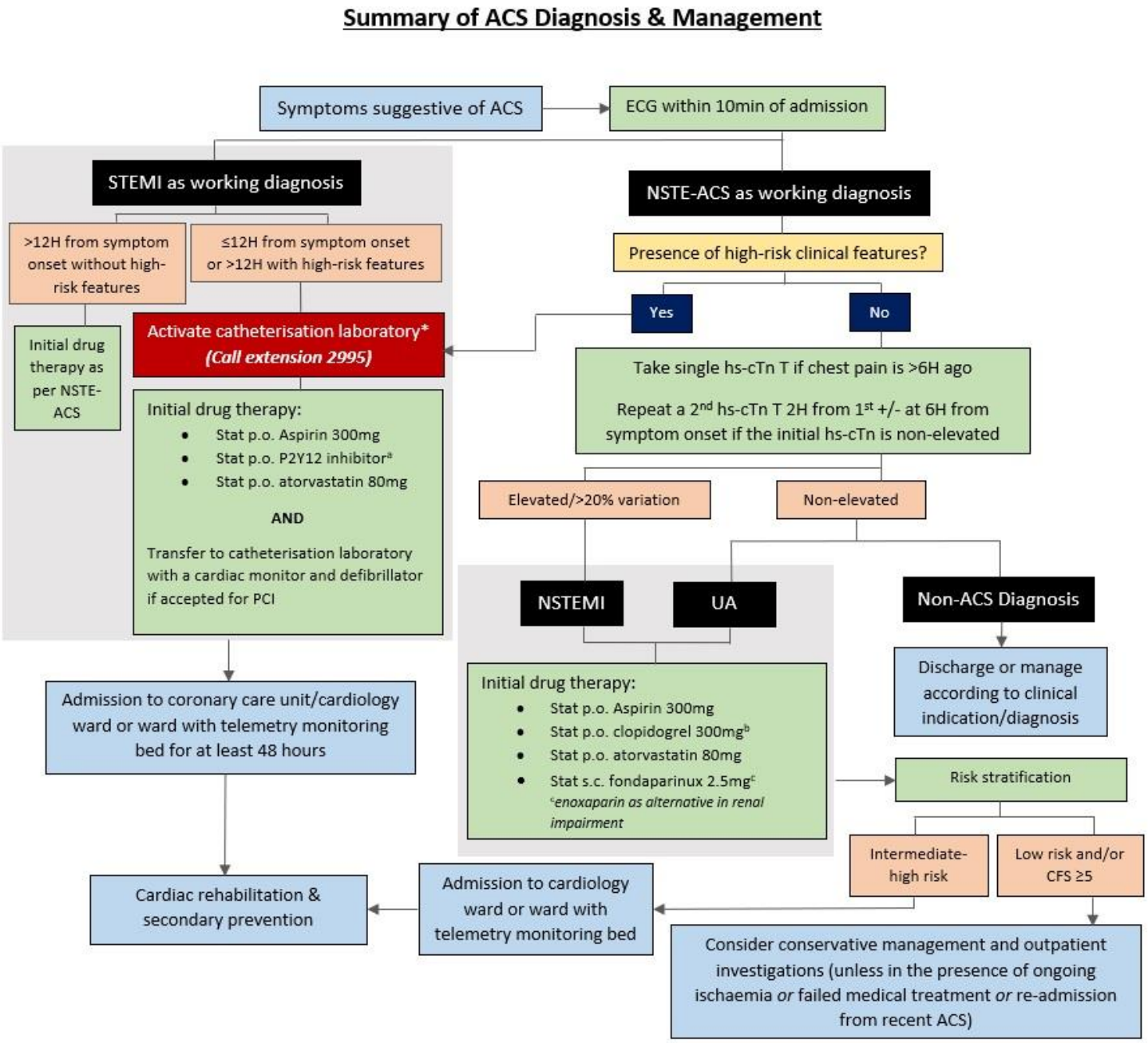

***Figure 6**. Summary of diagnosis and management of ACS.*
ACS, acute coronary syndrome; CFS, Clinical Frailty Scale; ECG, electrocardiogram; hs-cTn, highly-sensitive cardiac troponin; NSTE-ACS, non-ST-elevation acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PPI, proton pump inhibitor; STEMI, ST-elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction; UA, unstable angina.
[a]for STEMI, as instructed by the interventional cardiologist; for NSTE-ACS with high-risk clinical features, p.o. clopidogrel 300mg STAT
[b]p.o. ticagrelor 180mg can be used in patients allergic to clopidogrel but avoided in patients with high bleeding risk.
*[c]s.c. enoxaparin 1mg/kg in patients with renal impairment (i.e., creatinine > 265 µmol/L or creatinine clearance <20 mL/min), on warfarin/OAC or newly diagnosed atrial fibrillation, **avoid** in patients considered for coronary angiography with follow-on primary PCI in the presence of high-risk clinical features.*
**Activation of the catheterisation laboratory should only be a consultant/registrar-to-PCI consultant discussion.*

Appendix 1: Fibrinolysis

- Offer if presenting within 12 hours from symptom onset and PCI is not possible (refer to ***Figure 7*** for *'Fibrinolysis pathway'*).
- It should be delivered within 10 minutes of STEMI diagnosis and should not be delayed by waiting for cardiac biomarkers results.

Contraindications to fibrinolysis therapy:

Absolute:

- Previous intracranial haemorrhage or stroke of unknown origin at any time
- Ischaemic stroke in the preceding 6 months
- Central nervous system damage or neoplasms, or arteriovenous malformation
- Recent major trauma/surgery/head injury (within the preceding month)
- Gastrointestinal bleeding within the past month
- Known bleeding disorder (excluding menstrual)
- Aortic dissection
- Non-compressible punctures in the past 24 hours (e.g. liver biopsy, lumbar puncture)

Relative:

- Transient ischaemic attack in the preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post-partum
- Refractory hypertension (systolic blood pressure >180 mmHg and/or diastolic blood pressure >110 mmHg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer
- Prolonged or traumatic resuscitation

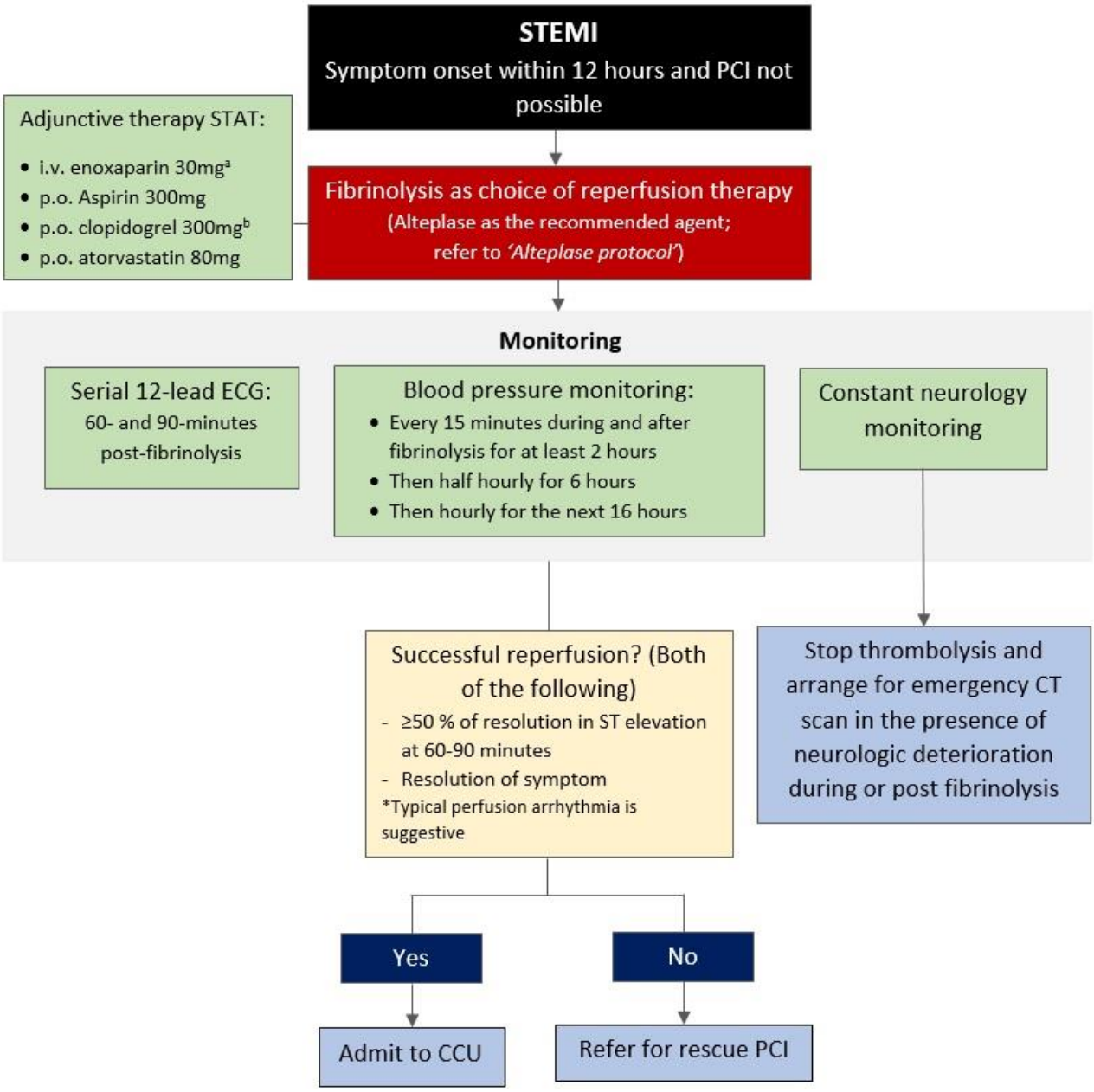

Figure 7. *Fibrinolysis pathway.*
CCU, coronary care unit; CT, computed tomography; ECG, electrocardiogram; PCI, percutaneous coronary intervention.
[a]no loading dose in patients >75 years of age
[b]loading dose of 75mg in patients >75 years of age

Alteplase (recombinant plasminogen activator, rt-PA) Protocol:

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

Administration:
90-minute (accelerated) regimen:

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 (refer to 'Alteplase dosing table' below):
0.75mL/kg over 30 minutes, followed immediately by
0.5mL/kg over 60 minutes

Alteplase dosing table (1 mg/mL following reconstitution):

Patient weight	Step 1 Slow i.v. injection	Step 2 30 minutes infusion	Step 3 60 minutes infusion
40kg	15mL	30mL (60mL/hr)	20mL (20mL/hr)
45kg	15mL	34mL (64mL/hr)	23mL (23mL/hr)
50kg	15mL	38mL (76mL/hr)	25mL (25mL/hr)
55kg	15mL	41mL (82mL/hr)	28mL (28mL/hr)
60kg	15mL	45mL (90mL/hr)	30mL (30mL/hr)
≥65kg	15mL	50mL (100mL/hr)	35mL (35mL/hr)

Appendix 2: Maintenance Therapy Regimen

All ACS patients should be started on maintenance therapy following admission to the ward after the commencement of the loading dose of acute ACS treatment.

All ACS patients after revascularisation with PCI:

- p.o. Aspirin 75mg once daily
- p.o. P2Y12 inhibitor of choice by the consultant interventional cardiologist:
    - p.o. prasugrel 10mg once daily (5mg once daily for 75 years and older; or less than 60 kg) ***or***
    - p.o. ticagrelor 90mg twice daily ***or***
    - p.o. clopidogrel 75mg once daily
- p.o. atorvastatin 80mg once daily

All ACS patients before revascularisation with PCI or for conservative management:

- p.o. Aspirin 75mg once daily
- p.o. clopidogrel 75mg once daily (unless specified otherwise by consultant cardiologist)
- p.o. atorvastatin 80mg once daily
- s.c. fondaparinux 2.5mg once daily[a] for a maximum of 8 days

All ACS patients after fibrinolysis but before revascularisation with PCI:

- p.o. Aspirin 75mg once daily
- p.o. clopidogrel 75mg once daily
- p.o. atorvastatin 80mg once daily
- s.c. enoxaparin 1mg/kg every 12 hours[b] for a maximum of 8 days

ACS patients allergic to Aspirin*:

- p.o. ticagrelor 90mg twice daily (unless specified otherwise by consultant cardiologist)
- p.o. atorvastatin 80mg once daily
- s.c. fondaparinux 2.5mg once daily

Figure 8*: Maintenance therapy.*
ACS, acute coronary syndrome; PCI, percutaneous coronary intervention
[a]for patients on warfarin/OAC or newly diagnosed atrial fibrillation: s.c. enoxaparin 1mg/kg (maximum per dose 100mg) every 12 hours if creatinine clearance >30mL/min or every 24 hours if creatinine clearance <30mL/min.
[b] every 24 hours if creatinine clearance <30mL/min.
**consider Aspirin desensitisation therapy.*

Appendix 3: Consideration of Anti-platelets

Consideration regarding Ticagrelor:

- Contraindicated with strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, nefazodone, ritonavir, atazanavir).
- Should be avoided due to reduction in efficacy with strong CYP3A4 enzyme inducers (e.g. rifampicin, dexamethasone, phenytoin, carbamazepine, phenobarbital).
- May not be tolerated due to side effects/adverse reactions (e.g., unexpected bradycardia, dyspnea).
- A possible concern with patients' compliance with its twice-daily dosing (if so consider once-daily alternatives such as Prasugrel or Clopidogrel).

Consideration regarding Prasugrel:

- Contraindicated in previous stroke/transient ischaemic attack
- Avoid in patients already taking oral anticoagulant
- Use with caution in patients aged ≥75 years and with high bleeding risk
- Particularly considered in diabetics
- For treatment of acute stent thrombosis on Clopidogrel

Clopidogrel:

- To be used as part of dual antiplatelet therapy with aspirin if they are already taking an oral anticoagulant.
- To consider for patients: aged ≥75 years, with a high clinical risk of upper gastrointestinal bleeding, weight <60kg

Appendix 4: Cardiac Rehabilitation & Secondary Prevention

Offer all ACS patients the following before discharge:

- **Transthoracic echocardiogram** to assess left ventricular function and to identify other structural complications post ACS and mural thrombus.
- **Nicotine replacement therapy** with smoking cessation advice for patients who are active smokers.
- Other lifestyle advice:
    - **Diet**: Mediterranean diet
    - **Alcohol**: Low-risk drinking (<14 units per week)
    - **Regular physical exercise**: 20-30 minutes a day (gradual increment of duration and intensity)

Cardiac Rehabilitation (refer to primary care service):

- Physical activity: adapted to clinical condition and ability
- Lifestyle advice: advice on driving, flying and sex
- Stress management
- Health education

Drug therapy:

- **Dual anti-platelet therapy**: aspirin (unless contraindicated) + a second anti-platelet for up to 12 months and to continue aspirin for life.
- **Statin**: to intensify statin therapy during admission
- **Angiotensin-converting enzyme inhibitor (ACE-i)/Angiotensin II receptor blocker (ARB)**: titrate every 12-24 hours over 4 to 6 weeks with monitoring of renal function, electrolytes and blood pressure; and continue indefinitely
- **Beta-blockers**: titrate to a maximum tolerated dose and continue for at least 12 months or indefinitely for patients with reduced left ventricular ejection fraction. (To consider **ivabradine** if beta-blocker is contraindicated)
- **Aldosterone antagonist** for heart failure with reduced ejection fraction: start 3 to 4 days post-MI, preferably after ACE-i/ARB, with renal function and serum potassium level monitoring.