Acute Coronary Syndromes - Full Clinical Guideline

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Acute Coronary Syndromes - definitions and overview of initial assessment

1. Introduction

The term acute coronary syndrome is used as a diagnosis for all patients presenting with acute prolonged chest pain due to myocardial ischaemia or infarction. Patients are classified, and management planned, according to changes on ECG and cardiac enzymes (Biomarkers).

2. Definitions, Keywords

ACS, Acute Coronary Syndrome, Cardiac, Cardiology, CCU, chest pain, Coronary care, ECG, LBBB, MI, Myocardial infarction, NSTEMI, PPCI, primary PCI, TnT, Troponin, unstable angina

3. Guidelines

Myocardial infarction is defined if the following criteria are satisfied:

Rise and gradual fall of Troponin T (TnT) and/or a rise and more rapid fall of creatine kinase (CK), and at least one of the following:

I. Typical ischaemic chest pain

II. Pathological Q waves on ECG

III. ST elevation or depression or new LBBB

IV. Coronary occlusion on angiography or autopsy

V. Imaging evidence of loss of viable myocardium or a new regional wall abnormality

Myocardial infarction and ischaemia are currently classified as follows:

a. ST Elevation Myocardial Infarction (STEMI)

Initial presentation with ST segment elevation and, if untreated, subsequent pathological Q waves. These patients have usually occluded a large coronary artery and (if untreated) will sustain an extensive myocardial infarction associated with high levels of CK (>1000) and TnT (usually >1000), and extensive ventricular damage. Patients usually present with major

symptoms although occasionally, especially in the elderly, a large infarction may be “silent”. Patients with STEMI have been shown to benefit from early Primary PCI. STEMI was previously referred to as “Q wave myocardial infarction” or “full thickness myocardial infarction”. Patients with typical symptoms and presumed new left bundle branch block are treated as STEMI.

b. Non-ST Elevation Myocardial Infarction (NSTEMI)

These patients have cardiac chest pain, ST depression, T wave inversion or minor ST/T wave changes associated with elevated biomarkers. The ECG may occasionally be normal or have very minor non-diagnostic changes. These patients have usually sustained a much smaller infarction and less myocardial necrosis, as assessed by total CK release or cardiac imaging, and have been shown not to benefit from thrombolysis. High-risk patients in this group used to be referred to as “subendocardial” or “non-Q wave” myocardial infarction. High risk patients, particularly those with ST depression, can in fact have a worse overall prognosis than those with STEMI.

Patients with a history of cardiac chest pain and an elevated TnT (>100, or 14-99 increasing by >100% over 6 hours) have often sustained an intra-coronary thrombosis with partial occlusion and distal myocardial necrosis due to embolization. Smaller increases in TnT (14-99 with an increase of at least 6 over at least 2 hours) may still have sustained an NSTEMI, but consideration must be given to other causes of TnT rises. Occasionally, these other causes can result in a TnT >100. (See ACS flow chart).

c. Unstable Angina

Ischaemic cardiac chest pain at rest or mild exertion, but with normal biomarkers, and therefore no documented myocardial infarction. These patients may give a history of previous myocardial infarction or progressively worsening exertional angina.

Patients with severe transient ST segment depression associated with chest pain often have critical disease and may be at high risk, despite having a normal TnT. If appropriate, these patients should be considered for urgent investigation and intervention as per patients with NSTEMI.

NSTEMI myocardial infarction is more common than STEMI (currently about two thirds of MI patients in Derby are NSTEMI). For patients managed conservatively, the 6-month mortality rate is very similar (around 12% for both groups). However, STEMI patients are at highest

risk during the first 24 hours and often die prior to arrival in hospital, but patients who survive to leave hospital without significant LV impairment usually have a good prognosis. NSTEMI patients have a lower initial mortality but a higher risk of later re-infarction and death, which is reduced in selected patients by early intervention.

Third Universal Definition of Myocardial Infarction

In 2012 a new definition of MI was published by the European Society of Cardiology

Type 1 MI- (spontaneous infarction). This is an event related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries, leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis. The patient may have underlying severe CAD but, on occasion (5 to 20%), non-obstructive or no CAD may be found at angiography, particularly in women. These guidelines refer mainly to this group.

Type 2 MI (MI secondary to an ischaemic imbalance). e.g., coronary endothelial dysfunction, coronary artery spasm, coronary embolism, tachy-/brady-arrhythmias, anaemia, respiratory failure, hypotension, and hypertension with or without LVH.

Type 3 MI Death from likely MI without biomarkers having been taken.

Type 4 MI (related to PCI or stent thrombosis)

Type 5 MI (related to CABG).

INITIAL ASSESSMENT OF ALL PATIENTS WITH ACUTE CORONARY SYNDROME

1. Clinical History

The first, and perhaps best description of angina pectoris was made by William Heberden in an address to the Royal College of Physicians in 1772. Unstable angina, as with its stable counterpart is a clinical diagnosis defined as abrupt new onset of angina or any sudden deterioration in previously stable symptoms. The first step in assessment of the patient with ACS is therefore a careful history of the presenting complaint, modified of course if the patient is acutely unwell or requires urgent revascularization. A short variable period of unstable symptoms (over hours or days) is a common prelude to NSTEMI or STEMI and may be misinterpreted by patients without a history of angina as symptoms of indigestion. A knowledge of the major differential diagnoses is of course required. Particular mention

should be made of acute aortic dissection, an uncommon but serious condition which demands early diagnosis and avoidance of anticoagulation. Acute type A aortic dissection classically presents with immediate onset severe interscapular pain, sometimes with a tearing character along the distribution of the aorta which is most severe at onset. Typically, patients look unwell with subtle ECG changes and may exhibit hypertension, asymmetrical pulses, or signs of aortic regurgitation (often subtle) typically with an elevated D-dimer. A history of Marfan's disease, Ehlors- Danlos or pseudoxanthoma elasticum should lead to exclusion of aortic dissection with urgent CT aorta in the event of ongoing chest pain.

2. Clinical Examination

A comprehensive cardiovascular, respiratory, and abdominal examination along with brief neurological assessment is mandatory although this should be modified in the light of clinical expediency. Even patients presenting with unequivocal STEMI must be examined to exclude relevant co-existent conditions such as CVA, abdominal aortic aneurysm or the presence of an 'acute abdomen' all of which may influence the management strategy or in some cases may mimic acute MI.

Knowledge of the heart rate and rhythm, BP, SpO2 and presence or absence of peripheral pulses (e.g., radial, femoral) is essential both for initial management and prior to cardiac catheterization as is the presence of absence of cardiac murmurs which might necessitate echocardiography prior to cardiac catheterization (e.g., if an acute ventricular septal defect or severe mitral regurgitation is suspected). Acute pulmonary oedema is not an absolute contra-indication to Primary PCI in STEMI, but its presence dramatically increases procedural risk and should be detected on arrival to allow immediate treatment.

3. ECG

An ECG should be recorded immediately on admission (if not done in A&E) and initial management will be dependent on ECG changes. Paramedic ECGs must also be reviewed.

By definition, patients with diagnostic ST segment elevation have sustained an ST elevation myocardial infarction (STEMI) and should be considered for Primary PCI (see below).

Patients with cardiac chest pain who have minor ST/T wave changes, ST depression or T wave inversion may have sustained a non-ST elevation myocardial infarction (NSTEMI), but diagnosis will depend on cardiac markers. Some high-risk patients in this group will benefit from active anti-platelet/thrombotic therapy and early intervention (see below).

The ECG should be repeated after 15 minutes if the patient is still in pain, and if chest pain recurs. It then should be repeated hourly for the next three hours, and then at 12 hours and 24 hours after admission. Some patients who present early with either a normal ECG or minor changes will subsequently develop evidence of STEMI when the ECG is repeated. Patients with unstable angina (without infarction) may have transient ST depression associated with pain, which returns to normal, but no elevation in cardiac enzymes.

The ECG criteria for PPCI in the presence of cardiac chest pain of less than 12 hours duration are:

a. ST elevation of at least 1mm in 2 contiguous limb leads OR
b. ST elevation of at least 2mm in 2 contiguous chest leads OR
c. ST elevation on posterior ECG leads
d. New LBBB with prolonged cardiac chest pain (these are not accepted direct from paramedics and go to A+E for medical assessment)

If these are present, the PPCI team must be activated immediately by calling **07584407868.** Please refer to management of STEMI.

The following should be discussed urgently with the cardiologist on call or the cardiac outreach team:

a. Ongoing cardiac chest pain with borderline ST elevation, particularly in the presence of reciprocal changes.
b. Transient ST elevation which has now settles.
c. ECG changes consistent with STEMI but ongoing pain > 12 hours.

ECG interpretation is difficult in patients with left bundle branch block. Early clinical trial data suggested that patients with LBBB and strong clinical evidence of acute myocardial infarction benefited from thrombolysis or Primary PCI. In patients with LBBB the following ECG findings would support a diagnosis of acute myocardial infarction. When all three are present in the same 12 lead ECG the likelihood of acute MI is 90%.

(a) ST elevation >1mm concordant with (in the same direction as) the QRS.
(b) ST segment depression of >1mm in lead V1, V2, or V3.
(c) ST segment elevation >5mm discordant with (in the opposite direction) the QRS.

In general, patients suspected of having an MI with LBBB (new or in the absence of previous ECGs) should be discussed with the interventional cardiologist on call to decide whether

they should have PPCI. LBBB usually indicates a large anterior MI, and the patients will usually look very unwell.

Myocardial infarction can usually be diagnosed in the presence of right bundle branch block. Many older patients have chronic ECG changes (Q waves, bundle branch block and ST/T wave changes) and a review of old ECGs in the hospital notes (or on iCM) may be helpful.

“Physiological” ST segment elevation occurs in some healthy young people, in particular Afro-Caribbeans, and may be associated with sports training. It usually involves leads V1, V2 (sometimes V3) and is up sloping (early repolarisation). Occasionally there may be concave ST segment elevation in leads V3, V4. There may also be ECG voltage changes compatible with LVH. Other non IHD causes of anterior ST segment elevation include left ventricular hypertrophy, pericarditis, hyperkalaemia and the Brugada syndrome.

Occasionally additional leads are helpful. Right ventricular infarction is associated with changes in V3R, V4R, V5R, V6R and a true posterior infarction with changes in V7, V8, V9. This is usually in association with inferior myocardial infarction and right coronary artery occlusion.

In NSTEMI, ST depression confers a poor prognosis, worse than with STEMIs. These patients often have left main stem or critical 3 vessel disease. T wave inversion carried a better prognosis.

4. Cardiac Enzymes (biochemical markers)

Creatine Kinase (CK) and Troponin T (TnT-HS) should both be measured on admission and repeated 3-6 hours later. There is increasing evidence that use of early sampling of HsTnT measured down to lowest level of detection can be used to rule out NSTEMI in the many patients as early as 3 hours after pain onset. Please refer to the ACS pathway for guidance about timing of blood tests.

Most patients can give a clear-cut time when symptoms started, but in some patients, symptoms may have been intermittent for several hours (stuttering onset of ACS) when accurate timing is impossible, and the timing of the “worst pain” should be noted.

Myocardial infarction is associated with release of Troponin, and usually CK. Troponin is cardio specific, unlike CK, which may be released from skeletal muscle after trauma or surgery. There is usually no detectable TnT-HS in the blood. Release of CK and TnT-HS

begins early (3-6 hours) after myocardial infarction and they both peak around 12-18 hours. CK returns to normal after about 72 hours, whereas TnT-HS persists for 1-2 weeks.

At the Royal Derby Hospital, we use the high sensitivity Roche Troponin T assay, TnT-HS (ng/L). The 99th percentile of TnT-HS in a healthy population was determined to be 14 ng/L and hence the diagnostic cut-off for the Derby laboratories is >14 ng/L. Although TnT-HS is elevated in acute myocardial infarction chronic low level TnT-HS release (between 14 and 99 ng/L) occurs in many patients with no clinical evidence of acute myocardial infarction.

Both acute myocardial infarction and acute cardiac injury are associated with a progressive increase (“delta change”) in TnT-HS of more than 6ng/L when re-measured at least 2 hours after the first sample, or if a 6-hour TnT-HS >100. When there is doubt about the diagnosis in a patient with second TnT-HS value between 14-99, a third re-measurement of TnT-HS 6 hours later may be helpful. Most patients with clear cut clinical and ECG evidence of myocardial infarction have a TnT-HS increase of >100%. In the appropriate clinical context, a TnT-HS >100 is usually indicative of acute myocardial damage due to myocardial infarction.

A single elevated TnT-HS in the 14-99 range should not be used to diagnose myocardial infarction due to poor specificity. About 60 -70% of MAU patients with an initial diagnosis of possible ACS/MI and a TnT-HS in the 14 – 99 range are subsequently found to have no significant increase in TnT-HS, and no clinical evidence of ACS. The precise explanation for chronic low level TnT-HS release from myocytes is unknown, but it is found to occur in patients with chronic renal failure, diabetes, LVH, documented chronic IHD, LV dysfunction with elevated BNP, and in old age. There is now evidence (PEACE trial) that, in apparently stable IHD patients, troponin elevation is not benign, and any increase in TnT-HS is associated with an increased risk of heart failure and death.

Other causes of acute TnT-HS release: -

- Secondary Ischaemic Cardiac Injury (SICI)

Arrhythmias (including AF, bradycardias causing syncope), acute LVF, pulmonary embolus, coronary spasm, aortic dissection.

- Non-Ischaemic Cardiac Injury (NICI)

Myo/pericarditis, trauma, cardiotoxic drugs, CVA, subarachnoid haemorrhage, sepsis, renal failure, tako-tsubo cardiomyopathy, infiltration e.g., amyloid,

An increase in TnT-HS of >100% makes an acute myocardial infarction likely, but a smaller increase may be due to a non-cardiac illness and the clinical context should be considered. Acute coronary syndrome diagnosis (particularly NSTEMI) must therefore be a clinical diagnosis, taking into account all aspects of the case. Remember that ischaemic heart disease is very uncommon in non-smoking pre-menopausal females, and in those patients presenting with atypical chest pain, ST/T wave ECG changes and TnT-HS elevation, the diagnosis is more likely to be myocarditis (see Appendix 4) than NSTEMI.

A TnT-HS of <14ng/L measured 6 hours after the onset of chest pain confidently excludes myocardial infarction and necrosis and is therefore a good “rule out” test, with a very high predictive value for excluding myocardial infarction. Also, an increase of less than 6ng/L over at least a 2-hour period rules out acute MI in 98% of cases.

In patients with TnT-HS <14 and a convincing history of anginal symptoms, a treadmill exercise test should be done to document or exclude exertional ischaemia. This can be arranged via the cardiac outreach nurses. Some patients with suspected ACS, who are at low risk (based on normal ECG and TIMI score <4), are suitable for early exercise test and discharge, if their TnT-HS at 6 hours from last pain is <14. (Please see chart inside back cover.).

In a patient with coronary disease and NSTEMI, TnT-HS elevation is associated with an active unstable plaque with platelet aggregation and distal platelet emboli. Associated “micro infarcts” cause troponin release but often no significant CK elevation. The combination of NSTEMI with a high TnT-HS (>100) and normal (or mildly elevated) CK indicates high risk of further major adverse cardiac events, as many of these patients have a critical underlying coronary stenosis and may benefit from early revascularisation (usually PCI). The higher the level of TnT in NSTEMI the greater the risk of subsequent events, if managed conservatively. These patients should therefore be considered for active medical treatment, early investigation, and possible intervention (see below), and should normally be under the care of a cardiologist. An audit of Derby patients with NSTEMI, who underwent urgent angiography, showed that 60% of the patients required revascularisation, and the majority were suitable for angioplasty (85% PCI and 15% CABG).

Repeat CK is useful with a suspected re-infarction several days after admission, which may show a second peak. TnT-HS is not helpful in this situation, as it remains elevated for many days after the initial infarction. However, a further increase in TnT-HS may indicate a new event. In patients presenting late (3-7 days) after acute symptom onset TnT-HS should be measured.

5. Chest X-ray

In patients who are breathless or who have clinical evidence of pulmonary oedema (basal crepitations), request a portable CXR on CCU to document the presence (and severity) of pulmonary oedema. Occasionally other unexpected relevant pathology comes to light (e.g., effusions, tumour, or pneumonia).

FURTHER RISK STRATIFICATION- TIMI AND GRACE SCORES

Multiple risk scoring algorithms have been devised in ACS. These have either derived from randomized trials of ACS management (e.g., TIMI risk score) or retrospective analysis of huge retrospective global databases of 'real-world' ACS management (e.g., GRACE score). Their practical application is to provide the clinician with an accurate estimate of early and late risk of recurrent myocardial infarction or death upon which to overlay one's own holistic clinical assessment and decide upon the optimal management for the individual patient: in practice this means whether to pursue initial medical therapy or recommend an early invasive strategy of coronary angiography +/- PCI during the index admission.

The two most widely used scoring systems are currently under-utilized: it is striking that the 'true' clinical risk is often very different from that perceived by clinicians. The TIMI risk score was derived from 'first principles' by Eugene Braunwald, famously on the back of an envelope on a plane while travelling to present the findings of the TIMI IIb study from the 'Thrombolysis in Myocardial Infarction' clinical trials group and was subsequently ratified in multiple studies (among patients aged ≤80 years). It underlines the importance of clinical history (5 of 7 parameters being immediately available from the initial history) and is quick and easy to calculate.

The GRACE score is perhaps more accurate and includes data from over 140,000 patients in the Global Registry of Acute Coronary Events. A more sophisticated score, it requires information on continuous parameters (heart rate, BP etc) on admission as well as risk factors and cardiac enzymes with separate inputs to derive risk during hospital admission and at 6 months. Calculation requires access to the internet, or an 'App' downloaded to one's smartphone.

For both TIMI and GRACE there is a linear relationship between increasing risk score and observed in-hospital and late adverse events (Figure 1). A TIMI risk score on admission of ≥4 or an admission GRACE score of ≥140 indicates high risk (in-hospital death or recurrent MI) and both European and US guideline bodies recommend an early invasive management strategy for patients at high risk. Furthermore, a GRACE score ≥140 should lead to

prioritization for coronary angiography +/-PCI ideally within 24 hours. Either the TIMI or GRACE risk score should be calculated on admission and used to guide management as per the Royal Derby ACS guideline. It must also be remembered that while some of the clinical factors determining risk are relatively fixed (age, comorbidity, LV function, ischaemic burden) others are dynamic (haemodynamic, platelet activation, sympathetic tone, sepsis/dehydration etc) and therefore clinical risk is not static but must be continually re-assessed, in concert with an assessment of the risks/benefits of invasive management, throughout the admission.

ROUTINE EARLY INVASIVE VERSUS SELECTIVE INVASIVE/ INITIAL MEDICAL THERAPY IN ACS/NSTEMI.

Meta-analysis of multiple RCTs conclusively demonstrates that in ACS/NSTEMI a strategy of routine early coronary angiography and angioplasty and stenting of flow-limiting coronary stenoses is associated with an approximate 20-25% reduction (from 12% to c.9%) in the incidence of death or recurrent MI over 12 months. This reduction in ‘hard’ endpoints has not been noted following PCI in patients with stable angina, in part due to the fact that the incidence of death/MI in stable patients with optimal medical therapy (OMT) is remarkably low at 1-2% p.a.

All 19 RCTs in the Cochrane meta-analysis of PCI vs. OMT in ACS/NSTEMI recruited patients between the ages of 18 and 80 years. Data on PCI in elderly patients is largely restricted to registry studies with the few available specific RCTs small and conflicting. It is intuitive that elderly patients have higher basal risk and more severe coronary artery disease and are likely therefore to derive more benefit from an invasive approach to management of ACS than younger patients: it is also true that complication rates with PCI are higher in the elderly. Current recommendations in the absence of class A evidence are that there is no age beyond which early invasive treatment should not be offered. Most cardiologists' base decisions in patients over the age of 85yrs on an individual basis after informed discussion with the patient of the risk/benefits of coronary intervention.

Figure 1. The TIMI risk score

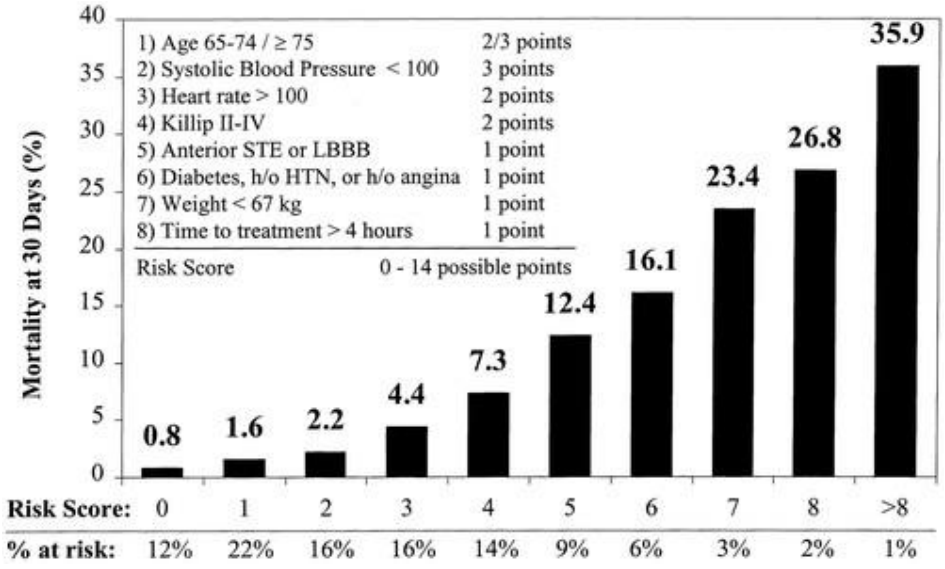

Figure 2. Predicted mortality following ACS/NSTEMI: TIMI and GRACE risk scores.

	GRACE in-hospital	TIMI 14 days	GRACE 6 months
Low risk			
Score	≤108	0–2	≤88
Mortality	<1%	1.1%	<3%
Intermediate risk			
Score	109–140	3–4	89–118
Mortality	1–3%	2%	3–8%
High risk			
Score	≥140	5–7	≥118
Mortality	>3%	5.8%	>8%

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