Chapter 9
Acute Coronary Syndromes

George Koshy and Raja Sekhar Maroju

Introduction

- Most cardiac arrests in the adult population are caused by coronary artery disease and are attributed to one of the acute coronary syndromes (ACS).
- Management of cardiac disease has evolved by the findings of large randomised clinical trials. Research and development of new cardiac biomarkers, antiplatelet agents and anticoagulants and many improvements in percutaneous revascularisation therapies have refined the care of ACS patients.
- Guidelines for care of ACS patient have been laid down by the American College of Cardiology (ACC) [1, 2], American Heart Association (AHA) and European Society of Cardiology (ESC) [3].

Time is not only cardiac muscle but also life.

Every 30-min delay from symptom onset to initiation of treatment increases 1-year mortality by 7.5 % in acute myocardial infarction (AMI).

G. Koshy, MD, DNB, DM, FACC, FESC (✉)
Pushpagiri Medical College Hospital, Tiruvalla, Kerala 689101, India
e-mail: drgkoshy@yahoo.com

R.S. Maroju, MBBS, MRCS, DipIMC, FCEM
Queen's Hospital, Rom Valley Way, Romford RM7 0AG, Essex, UK
e-mail: rsmaroju@hotmail.com

S.S. David (ed.), *Clinical Pathways in Emergency Medicine: Volume I*,
DOI 10.1007/978-81-322-2710-6_9

Table 9.1 The spectrum of ACS

ACS	Pathophysiology	Initial treatment
UA	Nonocclusive thrombus in an epicardial coronary vessel with associated ischaemia but no evidence of infarction	Aspirin
		LMWH
		Direct thrombin inhibitors (bivalirudin)
		β-blockade
NSTEMI	Nonocclusive thrombus in an epicardial coronary vessel with associated infarction	Aspirin
		Heparin
		LMWH
		β-blockade
		Consider GP IIB/IIIA inhibitor
STEMI	Occlusive thrombus in an epicardial coronary vessel with transmural ischaemia	Urgent reperfusion via thrombolysis or primary PCI

Classification

- Acute coronary syndromes (ACS) are parts of the same spectrum of disease comprising the following:
  1. Unstable angina
  2. Non-ST elevation (NSTEMI)
  3. ST elevation myocardial infarction (STEMI) (Table 9.1)
- The basic pathophysiology is in most cases initiated by rupture of an atherosclerotic plaque in a coronary artery, thus exposing subintimal collagen. This triggers platelet adhesion and activation causing subtotal occlusion of coronary artery (NSTE-ACS) or total occlusion of coronary lumen (STEMI). Fissuring can also cause hemorrhage or dissection into the plaque leading to localised swelling causing narrowing of the lumen.
- History, clinical examination, ECG analysis and cardiac biomarker results are crucial in guiding the management of ACS.

Signs and Symptoms

- The presenting symptom is classically chest/epigastric discomfort.
  - This can occur at rest or during exertion.
  - Its character is usually described as heaviness, burning, suffocation, squeezing, tightness or crushing in nature.
  - The pain can most often radiate to the jaw, neck, back, left arm or both arms.
  - This can also be usually associated with profuse sweating, nausea and vomiting.
- In elderly and diabetic patients, these symptoms may be mild or absent. They usually present with complaints of breathlessness, fatigue, episode of collapse or even confusion.

Differential Diagnoses

- Differential diagnoses to be considered are:
  - Aortic dissection
  - Acute pericarditis
  - Pulmonary embolism
  - Costochondritis
  - Acute gastritis
  - Acute cholecystitis

Enquire about recent use of phosphodiesterase inhibitors (sildenafil, tadalafil) which should preclude the use of nitrates.

Clinical Examination

- There is very little information that can be gained by clinical examination in diagnosing ACS. However, with a good history and clinical examination, other conditions causing chest pain like pneumonia, pleural effusion, aortic dissection, acute pericarditis and pericardial tamponade (Table 9.2).
- Auscultation of the heart and lungs and rapid neurologic examination (esp. when considering thrombolysis) are very important.
- Also evaluate for signs of possible cardiogenic shock (hypothermia, hypotension and low pulse pressure) [14].

Table 9.2 Physical examination findings and possible diagnosis in patients with chest pain

Examination finding	Alternative diagnosis
Markedly disparate blood pressure between the right and left arm	Aortic dissection
S3, increased jugular venous pressure, oedema	Congestive heart failure. This can also be a consequence of ACS
Irregular heart rhythm	Atrial fibrillation or other rhythms with variable blocks
Murmurs	Valvular heart disease. This could also be a consequence of ACS
Crackles, diminished breath sounds	Pneumonia
Pericardial friction rub	Pericarditis
Wheezing with decreased air movement	Bronchospasm caused by asthma, chronic obstructive pulmonary disease

Table 9.3 Criteria for STEMI

Diagnostic ECG criteria for STEMI	Additional ECG findings (supportive but not diagnostic of myocardial infarction)
New ST-segment elevation at the J point ≥0.2 mV in men {0.15 mV in women} in leads V2 and V3. ≥2 contiguous leads should be involved	Hyperacute T waves often precede ST elevation
New ST-segment elevation at the J point ≥0.1 mV in leads other than V2 or V3. ≥2 contiguous leads should be involved	Reciprocal ST-segment depressions
New left bundle branch block	Development of pathologic Q waves can be seen as the infarction progresses

Diagnosis and Management

- Two essential factors to be considered in the evaluation of a patient with ACS are:
  - Whether a patient's symptoms and signs reflect ACS
  - The likelihood of an adverse clinical outcome from ACS (risk stratification)
- The first clinical decision point is to decide if a suspected ACS patient has a STEMI (Table 9.3). This STEMI patient will need emergency reperfusion, either by primary percutaneous coronary intervention (PCI) or thrombolysis.
- If STEMI is excluded, treatment should proceed via a common pathway for initial treatment of UA and NSTEMI. Immediate contact with a cardiologist is needed to guide appropriate antiplatelet and anticoagulant treatment.
- Treatment should not be delayed to get the results of serum cardiac biomarkers from the lab. Delay in patient presentation and lack of recognition of ACS in patients without chest pain are barriers to deliver prompt treatment [4, 5].

Risk Assessment

- All treatment of ACS, be it drugs or interventional procedures, has inherent risks and benefits which should be considered. Benefits of aggressive treatment override the risks in intermediate-risk and high-risk patients, while low-risk patients may have minimal benefits and substantial risks.
- Various risk stratification/scoring tools like TIMI and GRACE are available. TIMI risk scores correlate well with 14-day, 30-day and 1-year outcomes [8]. GRACE score is also another good scoring system for NSTE-ACS, but it is more cumbersome to use [9].
- The TIMI risk score for NSTE-ACS is validated in multiple patient populations [6, 7]. It is simple and easy to use. The TIMI score for NSTE-ACS assigns one point for each risk actor: (Box 9.1)

- Patients with elevated troponin are a high-risk population and will benefit from aggressive therapies like glycoprotein 2b/3a receptor inhibitors, low-molecular-weight heparin and early invasive strategy [10–12].
- The Killip classification is another risk stratification system used in individuals with an acute myocardial infarction [13]. Patients with a low Killip class are less likely to die within the first 30 days after their myocardial infarction than individuals with a high Killip class (Box 9.2).

Box 9.1 TIMI Scoring System

1. Age 65 years or older
2. Aspirin use within last 7 days
3. Known coronary stenosis (≥50 %)
4. Three or more CAD risk factors (family h/o CAD, hypertension, hyperlipidaemia, diabetes and smoking)
5. Severe angina (at least twice within 24 h
6. Increased cardiac biomarker levels (creatine kinase-MB or troponin levels)
7. ST-segment elevation 0.05 mV or more

Box 9.2 Killip's Classification for STEMI Patients

Class	Clinical findings	Mortality rate (30 days)
Class 1	No CHF	6 %
Class 2	Mild CHF, RALES, S3 and congestion on chest x-ray	17 %
Class 3	Pulmonary oedema	38 %
Class 4	Cardiogenic shock	81 %

Investigations

ECG

- This is an indispensable tool for the evaluation and management of ACS.
- A 17-lead ECG should be the norm (standard 12-lead ECG, additional leads, viz. V7, V8, V9 and V3R, V43R) and V7–V9 leads to identify posterior wall MI and V3R and V4R to identify right ventricular MI.
- ECG should be evaluated within 10 min of patient arrival to ED. It can aid in the management of ACS in addition to identifying STEMI (see Table 9.3) by:
  - Suggesting ischaemia in patients whose symptoms are ambiguous
  - Identifying alternate diagnosis which mimic ACS (pericarditis)

  - Risk stratification in suspected ACS (TIMI score for UA/NSTEMI
  - Showing recurrent ischaemia
- ECG findings in the setting of UA/NSTEMI are as follows:
  - Transient ST-segment changes ≥0.05 mV (0.5 mm) during angina.
  - T-wave inversions ≥0.2 mv (2 mm).
  - ST-segment elevation can also be seen in LBBB, pericarditis, LVH, repolarisation abnormality and ventricular aneurysm.
- Suspected ACS patients should be continuously monitored on telemetry since they are at risk for malignant ventricular arrhythmias.

Chest X-Ray

- Useful in the diagnosis and management of ACS by:
  - Identifying noncardiac cause of chest discomfort or dyspnoea (pneumonia, pleural effusion or pneumothorax).
  - Showing pulmonary oedema as a complication of ACS.
  - Suggesting aortic dissection (widened mediastinum). Aortic dissection can involve origin of right coronary artery and so present as inferior wall MI (Figs. 9.1, 9.2 and 9.3).

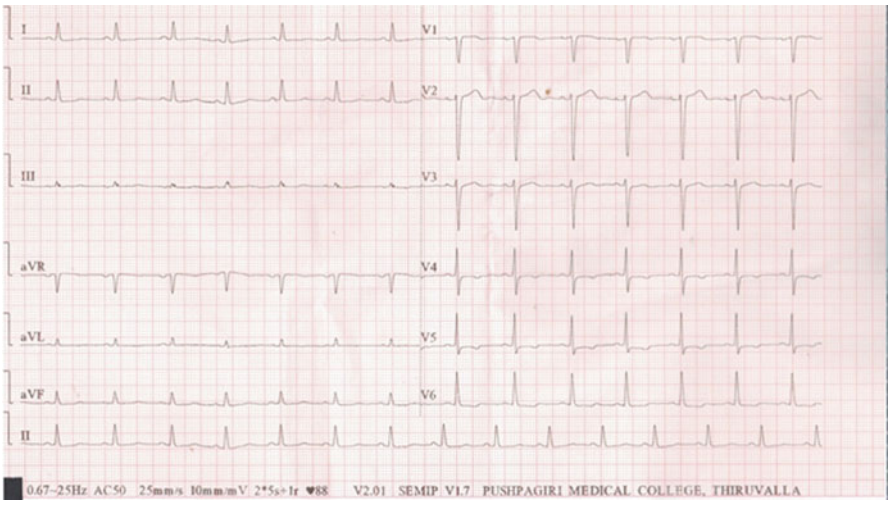


Fig. 9.1 ECG of a patient with unstable angina (Trop –ve NSTE-ACS) who could be managed with initial conservative strategy

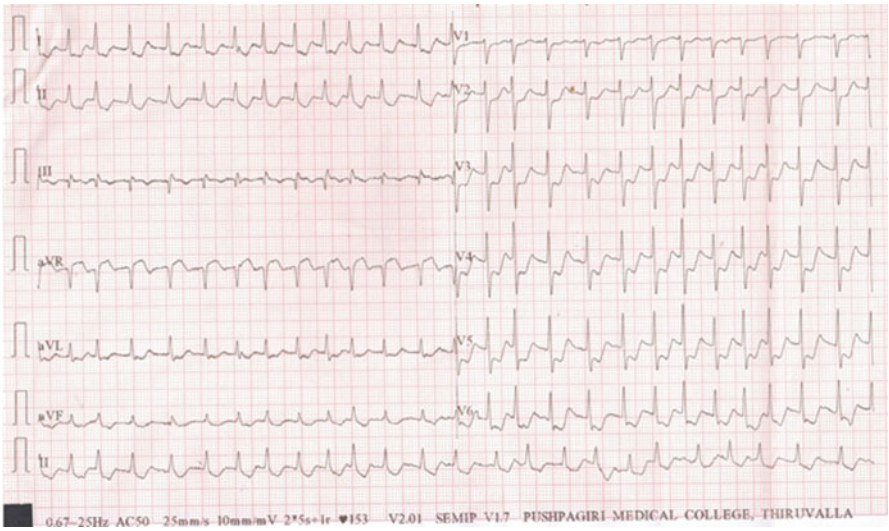


Fig. 9.2 ECG showing features of high-risk NSTE-ACS (Trop +ve) who should receive early invasive strategy

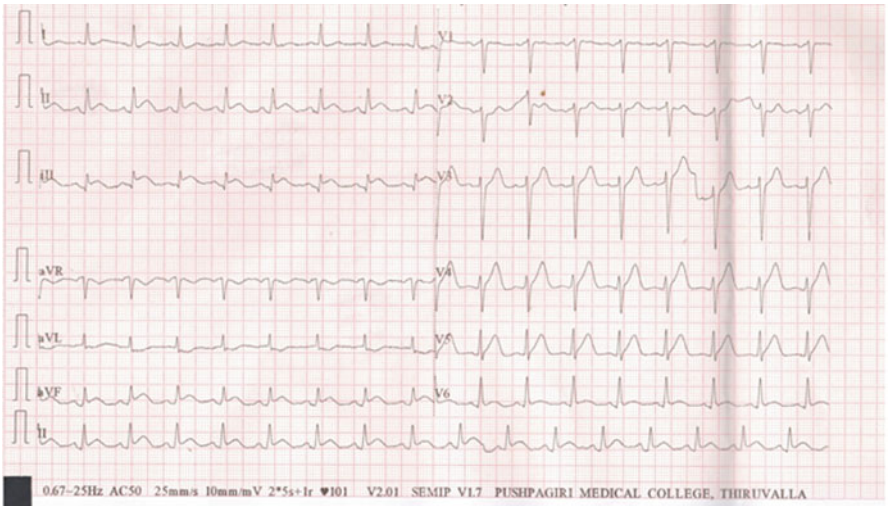


Fig. 9.3 ECG showing evidence of an acute inferior wall STEMI

Cardiac Biomarkers

- High cardiac specificity, rapid release in the setting of myocardial injury and strong correlation to the extent of myocardial damage are hallmarks of an ideal cardiac biomarker.

- Novel cardiac biomarkers like troponin I and troponin T have now largely replaced CK-MB and myoglobin as the tests of choice in ACS [15, 16].
- In the case of STEMI, reperfusion therapy (either thrombolysis or primary PCI) should not be delayed, pending results of troponin.
- Increased troponin level above 99th percentile of normal measurements is defined to represent myocardial necrosis. A single increased troponin level does not discriminate between ischaemic and nonischaemic causes. It may take 6–12 h for troponin level to rise. Hence, serial measurements may be needed to diagnose NSTEMI.
- Positive troponin signifies a high-risk cohort of ACS which benefit from aggressive treatments like low-molecular-weight heparin and early invasive strategy, viz., coronary angiogram and revascularisation.
- CK-MB has shorter half-life and so is useful to diagnose reinfarction and periprocedural MI in a setting of revascularisation.

Echocardiography

- Although not mandatory in the ED, echocardiography is useful to:
  - Confirm the presence of ischaemia (regional wall motion abnormality)
  - Assess LV and RV systolic function
  - Show mechanical complications (mitral regurgitation, VSD) of acute MI
  - See pericardial effusion or presence of cardiac tamponade

Treatment

Immediate Management

- Inhaled oxygen (if spO_2 <90 %).
- Antiplatelet agents: Dispersible aspirin 300 mg tablet stat (to inhibit platelet cyclooxygenase).
- Thienopyridines (platelet P2 Y12 receptor inhibitor): Clopidogrel 300 mg stat (if proceeding for primary PCI, 600 mg to be given) or prasugrel 60 mg stat (avoid if <65 kg weight, >75 years in age or if previous CVA) or ticagrelor 180 mg stat [17].
- IV morphine, 1–10 mg in titrated doses for analgesia and for pulmonary oedema (avoid if there is hypotension, bradycardia or shallow respiration).
- Nitrates: IV nitroglycerine from 2 mcg/min and titrate up to relieve angina and to treat hypertension. Oral isosorbide nitrate 5 mg sublingual can be given if there is no IV access.
- Beta blockers: IV metoprolol 2.5–5 mg is given as a slow IV infusion to reduce ischaemia by decreasing heart rate and BP and thus reducing myocardial O_2 demand (avoid if there is bradycardia, AV blocks, hypotension or pulmonary oedema).

- High-dose statins: Atorvastatin 80 mg or rosuvastatin 40 mg to passivate the ruptured plaque and antiplatelet effect and reversing endothelial dysfunction.

Specific Strategies for STEMI

- Primary goal should be urgent reperfusion [18]. In centers in which primary PCI is unavailable or is delayed for >90 min, prompt thrombolytic treatment is given (if no contraindications) if presenting in <12 h of onset of symptoms (Table 9.4).
- Prehospital thrombolysis: Can be given in ambulance depending on the ability of the accompanying crew in identifying STEMI based on symptoms and ECG. Tenecteplase is best suited for this. In the STREAM study, prehospital lysis vs. primary PCI remained equally effective when done in less than 3 h of symptom onset. But in view of significant increased intracranial bleed (esp. in >75 years age), emphasis should remain on transfer to primary PCI center.
- Door-to-needle time (from presentation to administering lytic drug) should be <30 min. In hospitals with the capability to perform PCI, primary PCI should be the preferred strategy.
- Patients presenting between 12 and 24 h of symptom onset should receive primary PCI if evidence of heart failure, hemodynamic instability (cardiogenic shock), malignant ventricular arrhythmia or persistent ischaemic symptom is present.

Anticoagulants in Treating UA/NSTEMI

- Heparins and direct thrombin inhibitors reduce conversion of fibrinogen to fibrin, thus limiting clot formation.
- Low-molecular-weight heparin (enoxaparin) has more predictable response and less protein binding tendency than unfractionated heparin. Enoxaparin is given in a dose of 1 mg/kg body weight, s/c, bd (od dose if renal impairment).

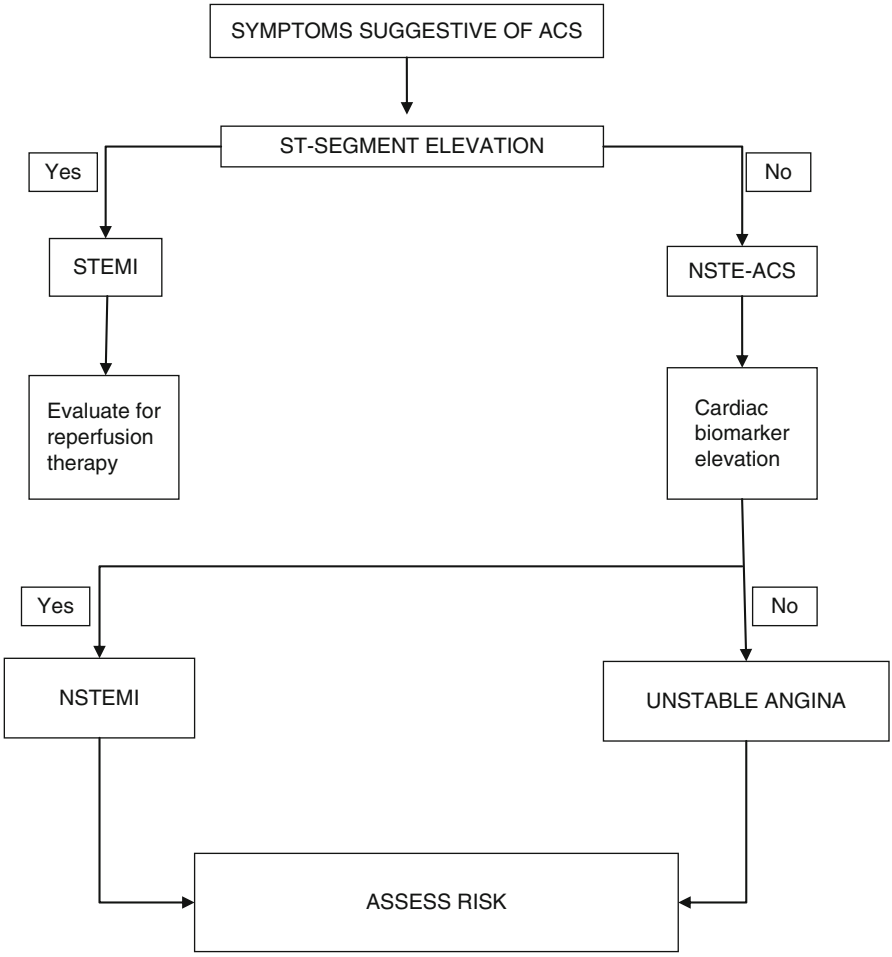
Table 9.4 Thrombolytics used for reperfusion in STEMI

Thrombolytic agent	Special attributes	Dosage
Alteplase	Recombinant tissue-type plasminogen activator. Fibrin specific	15 mg IV × 1, followed by 30 min of 0.75 mg/kg [max dose 50 mg], then 60 min of 0.5 mg/kg [max 35 mg]
Streptokinase	Low cost. Less effective than alteplase, not fibrin specific	15 lakh units over 30 min
Tenecteplase	As effective as alteplase but lower incidents of bleeding	Single IV bolus [weight based]
Reteplase	Less fibrin selective than alteplase, but with longer half-life	10 unit IV bolus followed by another 10 unit bolus IV [after 30 min]

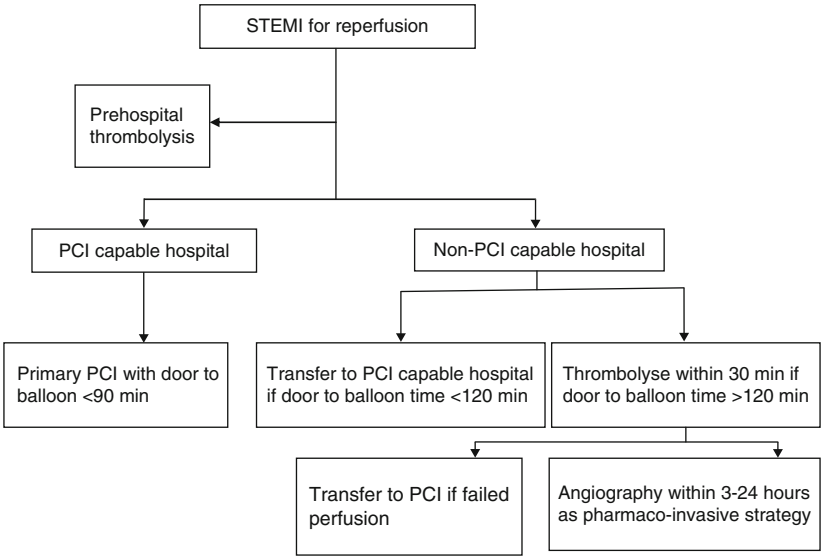
- Fondaparinux is a factor Xa inhibitor given in a dose of 2.5 mg s/c od.
- Glycoprotein 2b/3a inhibitors: Given IV as bolus and then infusion in the cath lab if heavy thrombus burden in heparinised patients.

Disposition

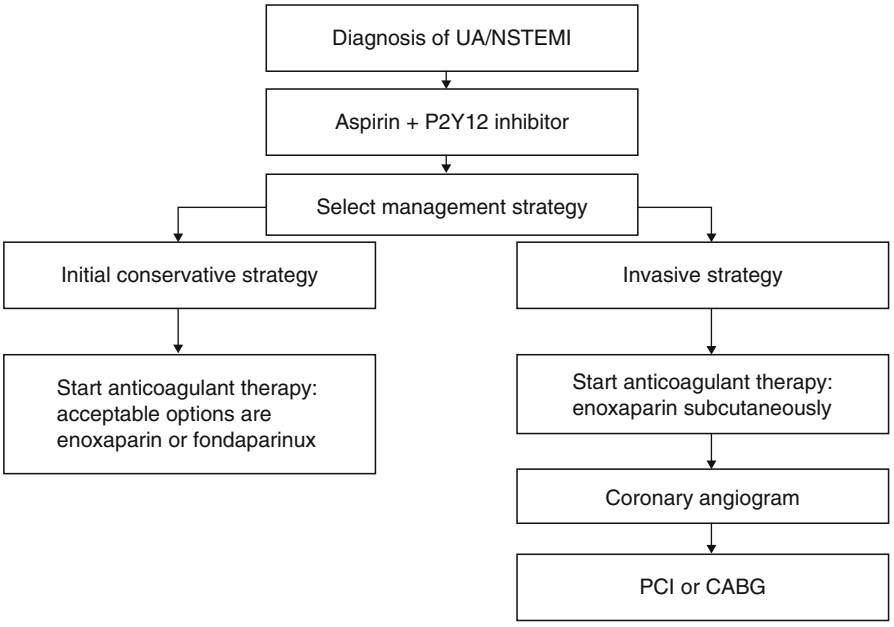
- Patients treated with thrombolytics or who are hemodynamically unstable, show ventricular dysrhythmias or show signs of new-onset heart failure in a setting of ACS should be monitored in the CCU (coronary care unit).
- After stabilisation and initiation of ACS treatment, the ED physician should also address the issue of rehabilitation and discharge (Flowcharts 9.1, 9.2 and 9.3).



Flowchart 9.1 Pathway for the management of ACS



Flowchart 9.2 Management of STEMI



Flowchart 9.3 Management of UA/NSTEMI

References

1. Anderson JL, Adams CD, Antman EM, et al. 2012 ACCF/AHA focused update incorporated into ACCF/AHA 2007 guidelines for management of patients with unstable angina/NSTEMI, a report of ACCF/AH Task Force on Practice Guidelines. Circulation. 2013;127(23):e 663–828.
2. Updated ACCF/AHA guidelines on management of STEMI. A report of ACCF/AHA Task Force on Practice Guidelines. JACC. 2013;61(4):e78–140.
3. Windecker S, et al. 2014 ESC/EACTS guidelines on myocardial revascularization. Published online: 30 Aug 2014. Eur Heart J. eurheartj.oxfordjournals.org.
4. Goff Jr DC, Feldman HA, McGovern PG, et al. Prehospital delay in patients hospitalized with heart attack symptoms in the US: REACT trial. Am Heart J. 1999;138:1046–57.
5. Canto JG, Shlipak MG, Rogers WJ. Prevalence, clinical characteristics & mortality among patients with MI presenting without chest pain. JAMA. 2000;283:3223–9.
6. Vesley MR, Keleman MD. Cardiac risk assessment matching intensity of therapy to risk. Cardiol Clin. 2006;24:67–78.
7. Sabatine MS, Antman EM. The thrombolysis in myocardial infarction risk score in UA/NSTEMI. JACC. 2003;41:89S.
8. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for UA/NSTEMI; a method for prognostication & decision making. JAMA. 2000;284:835–42.
9. Granger CB, Goldberg RC, Dabbous O, et al. Predictors of hospital mortality in Global Registry of Acute Coronary Events. Arch Int Med. 2003;163:2345.
10. Morrow DA, Antman EM, Snapinn SM, et al. An integrated clinical approach to predicting benefit of tirofiban in NSTEACS. Application of TIMI risk score for UA/NSTEMI in PRISM PLUS. Eur Heart J. 2002;23:223–9.
11. Cohen M, Demers C, Gurfinkel EP, et al. A comparison of low-molecular weight heparin with unfractionated heparin for unstable CAD. Efficacy & safety of enoxaparin in non-Q wave coronary events study group. NEJM. 1997;337:447.
12. Cannon CP, Weintraub WS, et al. Comparison of early invasive & conservative strategies in patients with unstable coronary syndromes treated with glycoprotein inhibitor tirofiban. NEJM. 2001;344:1879.
13. Mameletzi D, Kouidi E, Koutlianos N, Deligiannis A. Effects of long-term exercise training on cardiac baroreflex sensitivity in patients with coronary artery disease: a randomized controlled trial. Clin Rehabil. 2011;25:217–27.
14. Holmes DR, Berger PB, Hochman JS, et al. Cardiogenic shock in patients with acute ischemic syndromes with & without ST-segment elevation. Circulation. 1999;100:2067–73.
15. Anderson JL, Adams CD, Antman EM, et al. AAC/AHA 2007 guidelines for management of patients with UA/NSTEMI – executive summary. JACC. 2007;50:652–726.
16. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial infarction. Circulation. 2007;116:2634–53.
17. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor Vs clopidogrel in patients with acute coronary syndromes. NEJM. 2009;361:1045–57.
18. Keeley EC, Boura JA, Grines CL. Primary angioplasty Vs intravenous thrombolytic therapy for acute MI: a quantitative review of 23 randomized trials. Lancet. 2003;361(9351):13.