# NSTE-ACS

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11.2016

European Heart Journal Advance Access published September 11, 2015


European Heart Journal
doi:10.1093/eurheartj/ehv320

ESC GUIDELINES

# 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

**Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC)**

**Table I** Classes of recommendations

| Classes of recommendations | Definition | Suggested wording to use |
|---|---|---|
| Class I | Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective. | Is recommended/is indicated |
| Class II | Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure. | |
| *Class IIa* | *Weight of evidence/opinion is in favour of usefulness/efficacy.* | Should be considered |
| *Class IIb* | *Usefulness/efficacy is less well established by evidence/opinion.* | May be considered |
| Class III | Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful. | Is not recommended |

**Table 2** Levels of evidence

| | |
|---|---|
| Level of Evidence A | Data derived from multiple randomized clinical trials or meta-analyses. |
| Level of Evidence B | Data derived from a single randomized clinical trial or large non-randomized studies. |
| Level of Evidence C | Consensus of opinion of the experts and/or small studies, retrospective studies, registries. |

AHA/ACC Guideline

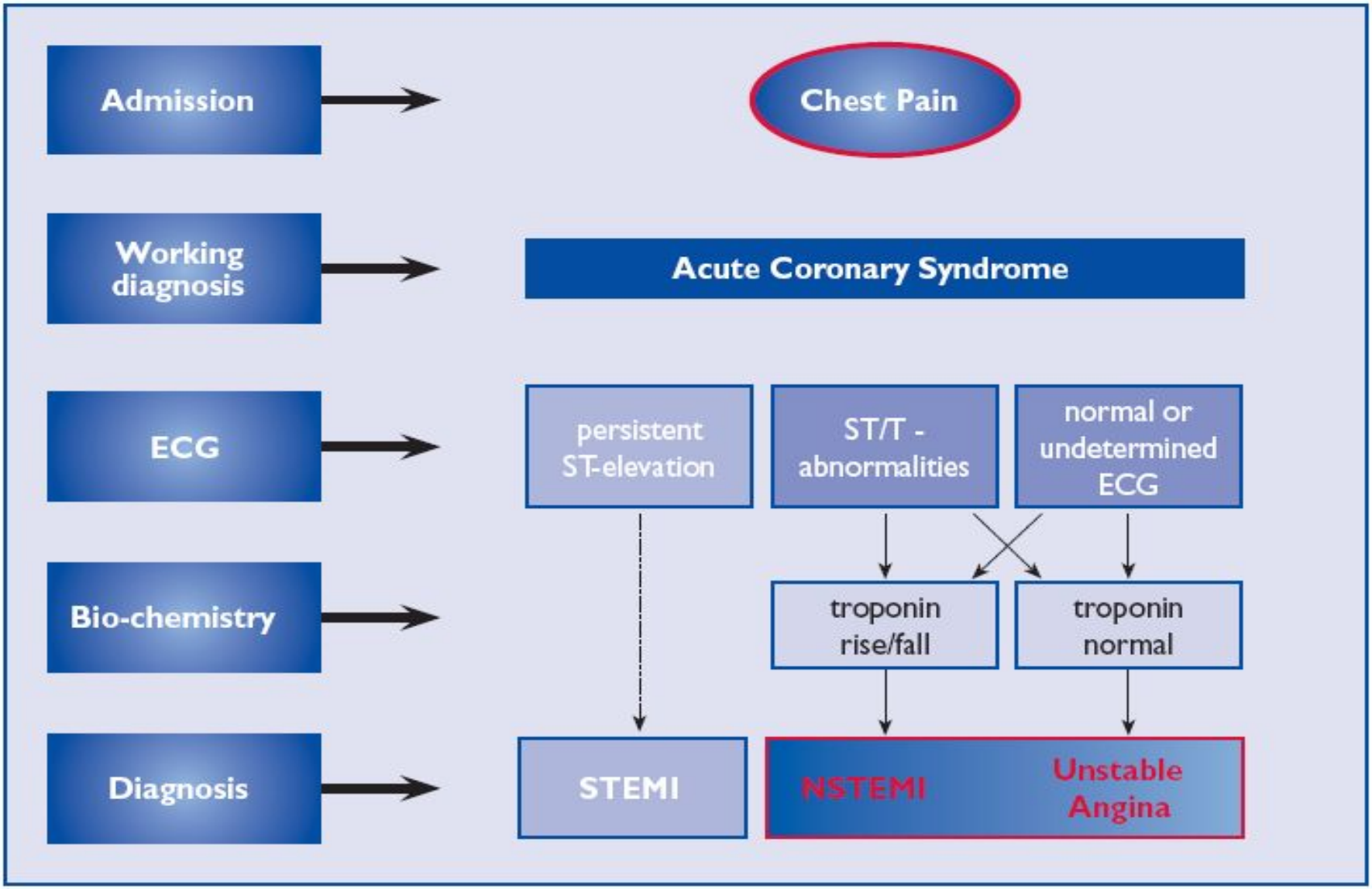
# 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

## A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

*Developed in Collaboration With the Society for Cardiovascular Angiography and Interventions and Society of Thoracic Surgeons*

*Endorsed by the American Association for Clinical Chemistry*

# The spectrum of ACS



# Clinical presentations of CAD

- Silent ischemia
- Stable angina
- Unstable angina
- Myocardial infarction
- Heart failure
- Sudden cardiac death

ACS in their different clinical presentations share a widely common pathophysiological substrate:

atherosclerotic plaque rupture or erosion, with different degrees of superimposed thrombus and distal embolization, resulting in myocardial underperfusion

(1) Patients with acute chest pain and persistent (>20 min) ST-segment elevation.

This condition is termed ST-elevation ACS and generally reflects an acute total coronary occlusion. Most patients will ultimately develop an ST-elevation myocardial infarction (STEMI). The mainstay of treatment in these patients is immediate reperfusion by primary angioplasty or fibrinolytic therapy.[1]

(2) Patients with acute chest pain but no persistent ST-segment elevation.

ECG changes may include transient ST-segment elevation, persistent or transient ST-segment depression, T-wave inversion, flat T waves or pseudo-normalization of T waves or the ECG may be normal.

# NSTE-ACS : diagnosis

- Medical Hx (timing and characteristics of CP)
- Physical examination (hypotension, heart failure signs)
- ECG
- Echocardiography (most important modality in acute setting)
- Biomarkers
- Cardiac magnetic resonance (differential Dx of non-coronary myocardial damage)
- Cardiac CT (high accuracy for exclusion of significant coronary artery stenosis)

## 3.1 Clinical presentation

Anginal pain in NSTE-ACS patients may have the following presentations:

- Prolonged (>20 min) anginal pain at rest;
- New onset (de novo) angina (class II or III of the Canadian Cardiovascular Society classification);[21]
- Recent destabilization of previously stable angina with at least Canadian Cardiovascular Society Class III angina characteristics (crescendo angina); or
- Post-MI angina.

# Chest pain

# Atypical complaints

- Epigastral pain
- Indigestion-like syndrome
- Isolated dyspnea

More often in elderly, women, patients with diabetes, renal failure, dementia

# Physical examination

- Signs of HF, hemodynamic or electrical instability  quick Dx and Rx
- Auscultation: systolic murmur of mitral regurgitation, aortic stenosis, mechanical complications
- Signs of non-coronary causes of chest pain
- Chest pain reproducible by pressure on chest wall – high negative predictive value for NSTE-ACS

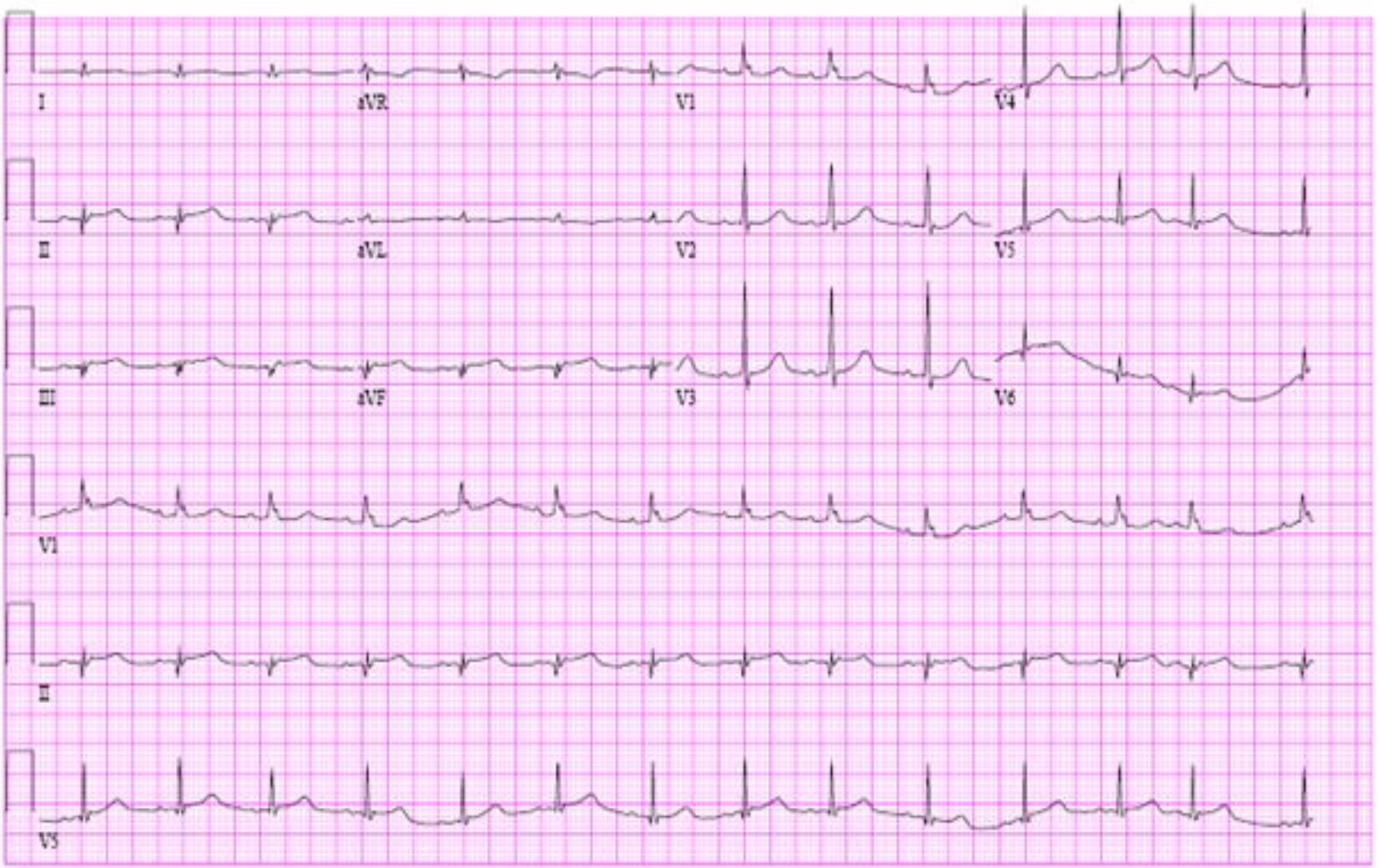
# ECG

obtain it within 10 min of the patient's arrival in the emergency room or, ideally, at first contact with emergency medical services in the pre-hospital setting and to have it immediately interpreted by a qualified physician.[28] While the ECG in the setting of NSTE-ACS may be normal in more than one-third of patients, characteristic abnormalities include ST depression, transient ST elevation and T-wave changes.[1,18]

# ECG

If the standard leads are inconclusive and the patient has signs or symptoms suggestive of ongoing myocardial ischaemia, additional leads should be recorded; left circumflex artery occlusion or right ventricular MI may be detected only in $V_7$–$V_9$ and $V_{3R}$ and $V_{4R}$, respectively.[2] In patients with suggestive signs and symptoms, the finding of persistent ST elevation indicates STEMI, which mandates immediate reperfusion.[1] Comparison with previous tracings is valuable, particularly in patients with pre-existing ECG abnormalities. It is recommended to obtain additional 12-lead ECGs in the case of persistent or recurrent symptoms or diagnostic uncertainty. In patients with bundle branch block or paced rhythm, ECG is of no help for the diagnosis of NSTE-ACS.

# AA 2022349-1



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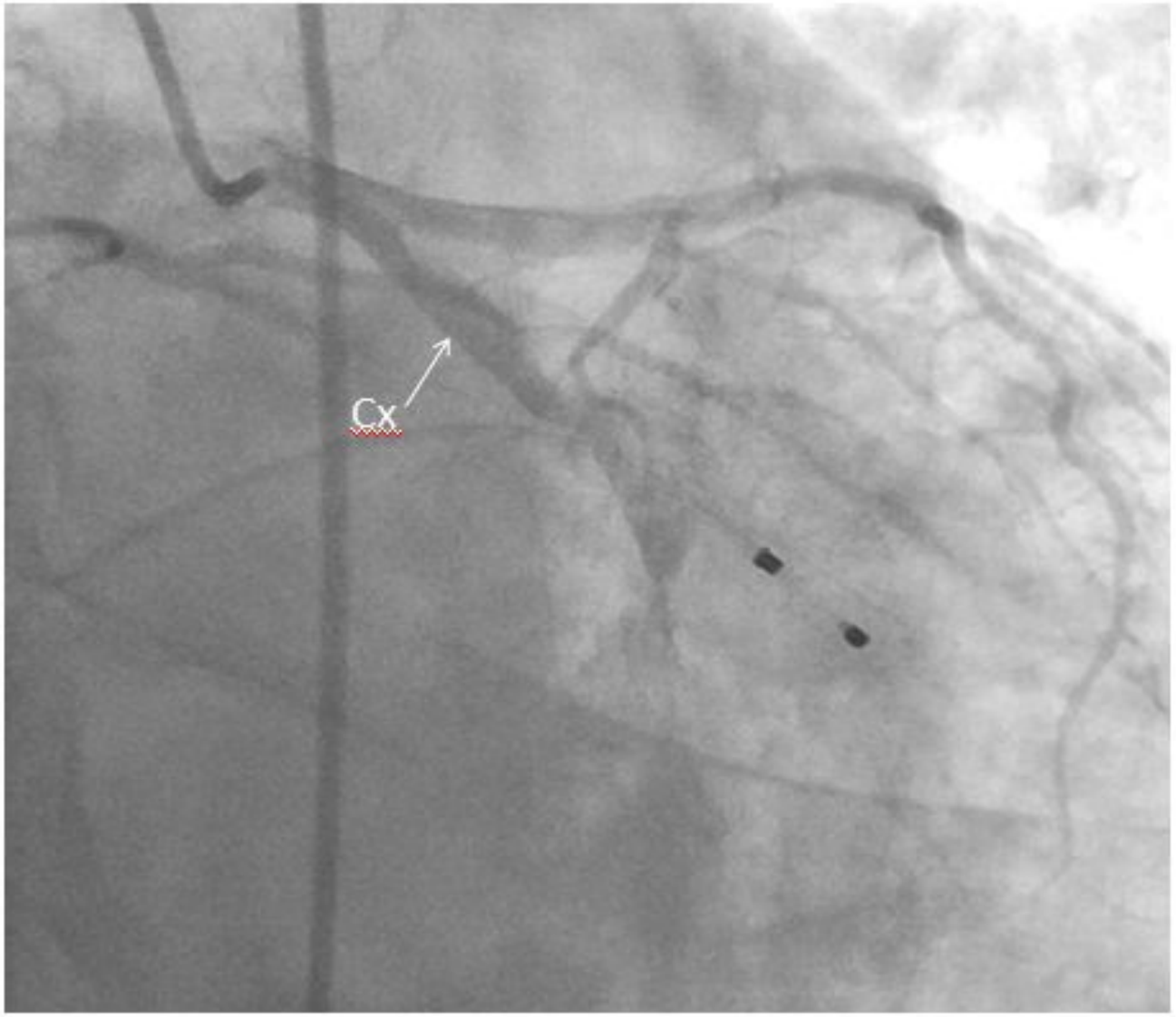

# Biomarkers

**Table 3** **Clinical implications of high-sensitivity cardiac troponin assays**

| **Compared with standard cardiac troponin assays, high-sensitivity assays:** |
|---|
| • Have higher negative predictive value for acute MI. |
| • Reduce the "troponin-blind" interval leading to earlier detection of acute MI. |
| • Result in a ~4% absolute and ~20% relative increase in the detection of type 1 MI and a corresponding decrease in the diagnosis of unstable angina. |
| • Are associated with a 2-fold increase in the detection of type 2 MI. |
| **Levels of high-sensitivity cardiac troponin should be interpreted as quantitative markers of cardiomyocyte damage (i.e. the higher the level, the greater the likelihood of MI):** |
| • Elevations beyond 5-fold the upper reference limit have high (>90%) positive predictive value for acute type 1 MI. |
| • Elevations up to 3-fold the upper reference limit have only limited (50–60%) positive predictive value for acute MI and may be associated with a broad spectrum of conditions. |
| • It is common to detect circulating levels of cardiac troponin in healthy individuals. |
| **Rising and/or falling cardiac troponin levels differentiate acute from chronic cardiomyocyte damage (the more pronounced the change, the higher the likelihood of acute MI).** |

MI = myocardial infarction.

# Biomarkers

**Table 4** **Conditions other than acute myocardial infarction type 1 associated with cardiac troponin elevation**

| |
|---|
| **Tachyarrhythmias** |
| **Heart failure** |
| **Hypertensive emergencies** |
| **Critical illness (e.g. shock/ sepsis/ burns)** |
| **Myocarditis[a]** |
| **Tako-Tsubo cardiomyopathy** |
| **Structural heart disease (e.g. aortic stenosis)** |
| **Aortic dissection** |
| **Pulmonary embolism, pulmonary hypertension** |
| **Renal dysfunction and associated cardiac disease** |
| Coronary spasm |
| Acute neurological event (e.g. stroke or subarachnoid haemorrhage) |
| Cardiac contusion or cardiac procedures (CABG, PCI, ablation, pacing, cardioversion, or endomyocardial biopsy) |
| Hypo- and hyperthyroidism |
| Infiltrative diseases (e.g. amyloidosis, haemochromatosis, sarcoidosis, scleroderma) |
| Myocardial drug toxicity or poisoning (e.g. doxorubicin, 5-fluorouracil, herceptin, snake venoms) |
| Extreme endurance efforts |
| Rhabdomyolysis |

Bold = most frequent conditions; CABG = coronary artery bypass surgery; PCI = percutaneous coronary intervention.

## Table 6 Differential diagnoses of acute coronary syndromes in the setting of acute chest pain

| Cardiac | Pulmonary | Vascular | Gastro-intestinal | Orthopaedic | Other |
|---|---|---|---|---|---|
| Myopericarditis<br>Cardiomyopathies[a] | Pulmonary embolism | Aortic dissection | Oesophagitis, reflus or spasm | Musculoskeletal disorders | Anxiety disorders |
| Tachyarrhythmias | (Tension)-Pneumothorax | Symptomatic aortic aneurysm | Peptic ulcer, gastritis | Chest trauma | Herpes zoster |
| Acute heart failure | Bronchitis, pneumonia | Stroke | Pancreatitis | Muscle injury/ inflammation | Anaemia |
| Hypertensive emergencies | Pleuritis | | Cholecystitis | Costochondritis | |
| Aortic valve stenosis | | | | Cervical spine pathologies | |
| Tako-Tsubo cardiomyopathy | | | | | |
| Coronary spasm | | | | | |
| Cardiac trauma | | | | | |

Bold = common and/or important differential diagnoses.

[a]Dilated, hypertrophic and restrictive cardiomyopathies may cause angina or chest discomfort.

# Non-invasive diagnostic modalities

- Echocardiography
- Cardiac CT
- Cardiac magnetic resonance

# Coronary angiography

- Urgently in high risk pts and in pts in whom Dx is unclear
- In hemodynamically unstable pts insertion of IABP is recommended
- For diagnosis of thrombotic occlusion of CA (e.g. Cx) in pt with ongoing symptoms but in the absence of diagnostic ECG changes
- Data from TIMI-3B and FRISC-2 trials:
  - 30-38% of pts – 1-vessel disease
  - 44-59% - multivessel disease
  - 4-8% - LMCA stenosis

# Risk criteria mandating invasive strategy

| **Very-high-risk criteria** |
| --- |
| • Haemodynamic instability or cardiogenic shock |
| • Recurrent or ongoing chest pain refractory to medical treatment |
| • Life-threatening arrhythmias or cardiac arrest |
| • Mechanical complications of MI |
| • Acute heart failure |
| • Recurrent dynamic ST-T wave changes, particularly with intermittent ST-elevation |
| **High-risk criteria** |
| • Rise or fall in cardiac troponin compatible with MI |
| • Dynamic ST- or T-wave changes (symptomatic or silent) |
| • GRACE score >140 |
| **Intermediate-risk criteria** |
| • Diabetes mellitus |
| • Renal insufficiency (eGFR <60 mL/min/1.73 $m^2$) |
| • LVEF <40% or congestive heart failure |
| • Early post-infarction angina |
| • Prior PCI |
| • Prior CABG |
| • GRACE risk score >109 and <140 |
| **Low-risk criteria** |
| • Any characteristics not mentioned above |

# A GRACE Risk Model Nomogram

1. Find Points for Each Predictive Factor:

| Killip Class | Points | SBP, mm Hg | Points | Heart Rate, Beats/min | Points | Age, y | Points | Creatinine Level, mg/dL | Points |
|---|---|---|---|---|---|---|---|---|---|
| I | 0 | ≤80 | 58 | ≤50 | 0 | ≤30 | 0 | 0-0.39 | 1 |
| II | 20 | 80-99 | 53 | 50-69 | 3 | 30-39 | 8 | 0.40-0.79 | 4 |
| III | 39 | 100-119 | 43 | 70-89 | 9 | 40-49 | 25 | 0.80-1.19 | 7 |
| IV | 59 | 120-139 | 34 | 90-109 | 15 | 50-59 | 41 | 1.20-1.59 | 10 |
| | | 140-159 | 24 | 110-149 | 24 | 60-69 | 58 | 1.60-1.99 | 13 |
| | | 160-199 | 10 | 150-199 | 38 | 70-79 | 75 | 2.00-3.99 | 21 |
| | | ≥200 | 0 | ≥200 | 46 | 80-89 | 91 | >4.0 | 28 |
| | | | | | | ≥90 | 100 | | |

| Other Risk Factors | Points |
|---|---|
| Cardiac Arrest at Admission | 39 |
| ST-Segment Deviation | 28 |
| Elevated Cardiac Enzyme Levels | 14 |

2. Sum Points for All Predictive Factors:

Killip Class + SBP + Heart Rate + Age + Creatinine Level + Cardiac Arrest at Admission + ST-Segment Deviation + Elevated Cardiac Enzyme Levels = Total Points

3. Look Up Risk Corresponding to Total Points:

| Total Points | ≤60 | 70 | 80 | 90 | 100 | 110 | 120 | 130 | 140 | 150 | 160 | 170 | 180 | 190 | 200 | 210 | 220 | 230 | 240 | ≥250 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Probability of In-Hospital Death, % | ≤0.2 | 0.3 | 0.4 | 0.6 | 0.8 | 1.1 | 1.6 | 2.1 | 2.9 | 3.9 | 5.4 | 7.3 | 9.8 | 13 | 18 | 23 | 29 | 36 | 44 | ≥52 |

GRACE
ACS RISK SCORE 2.0

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# GRACE 2.0 Risk Calculator

The GRACE 2.0 ACS Risk Calculator implements the revised GRACE algorithms for predicting death or death/myocardial infarction following an initial acute coronary syndrome (ACS).

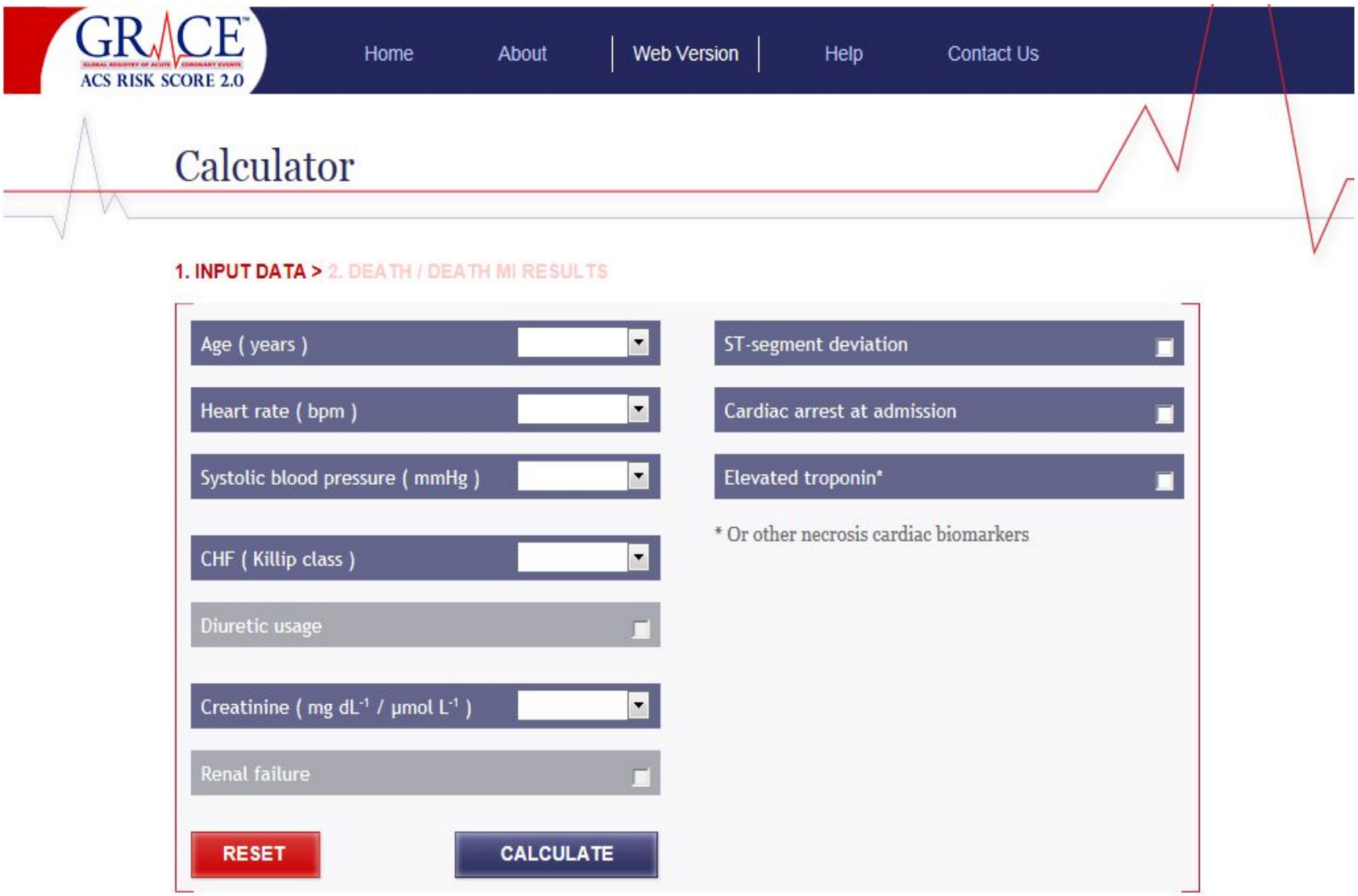
## WHAT'S NEW IN 2.0?

- "Mini-GRACE" algorithm (for use when serum creatinine and Killip class may not be available)
- New 1- and 3-year calculations
- New calculations provide probabilities directly, bypassing scores
- Population histograms with high-, medium- and low-risk markers
- The GRACE 2.0 ACS Risk Calculator app has been defined as a medical device under the Medical Device Directive (MDD) 93/42/EEC and has been CE-marked to indicate compliance with the Directive


## DOWNLOAD THE MOBILE APP

Available on the App Store

ANDROID APP ON Google play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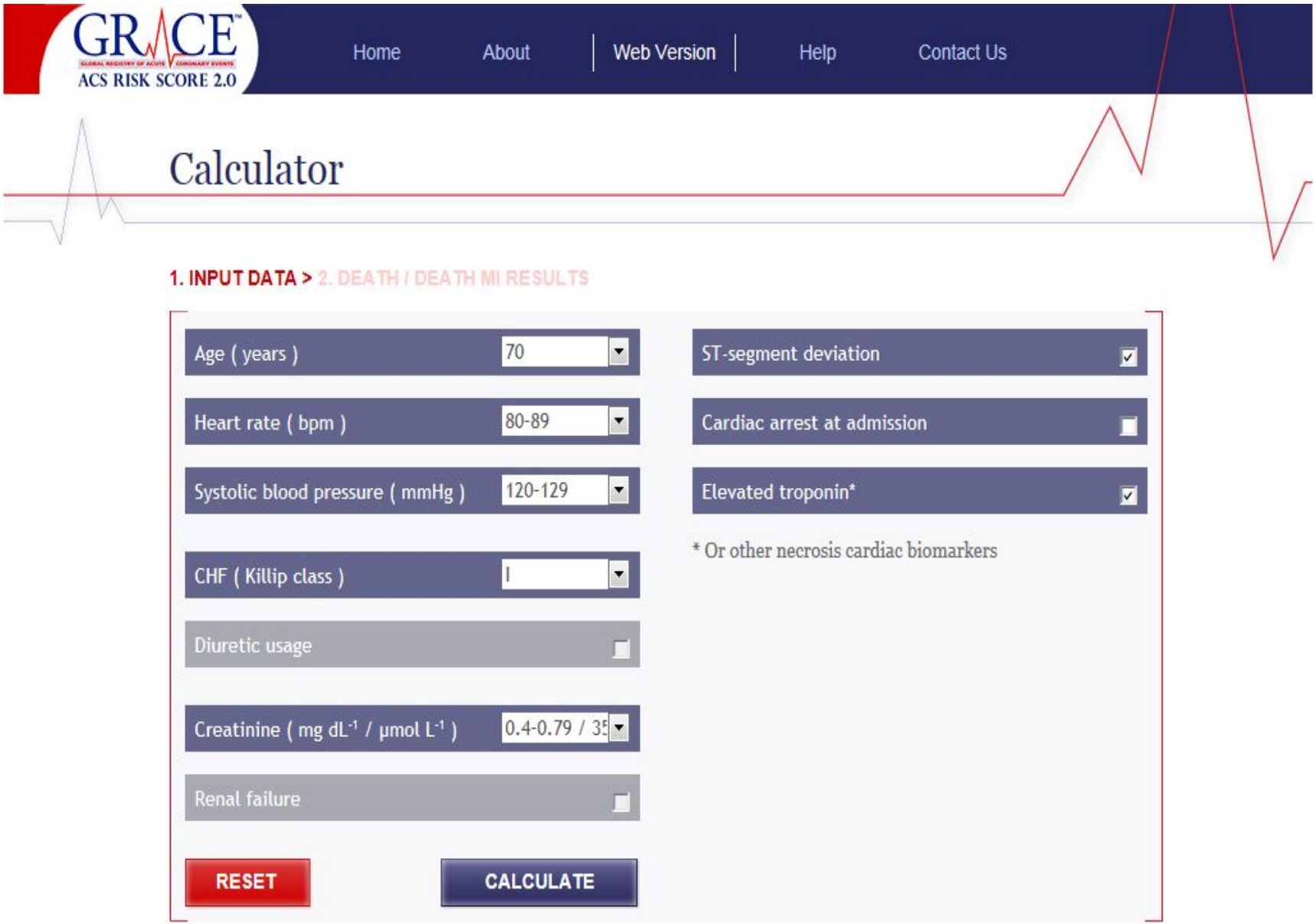
Age ( years )
Heart rate ( bpm )
Systolic blood pressure ( mmHg )
CHF ( Killip class )
Diuretic usage
Creatinine ( mg dL-1 / µmol L-1 )
Renal failure
ST-segment deviation
Cardiac arrest at admission
Elevated troponin*
* Or other necrosis cardiac biomarkers
RESET
CALCULATE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Calculator
1. INPUT DATA > 2. DEATH / DEATH MI RESULTS
Age ( years )
70
Heart rate ( bpm )
80-89
Systolic blood pressure ( mmHg )
120-129
CHF ( Killip class )
I
Diuretic usage
Creatinine ( mg dL-1 / µmol L-1 )
0.4-0.79 / 35
Renal failure
ST-segment deviation
Cardiac arrest at admission
Elevated troponin*
* Or other necrosis cardiac biomarkers
RESET
CALCULATE

# Calculator

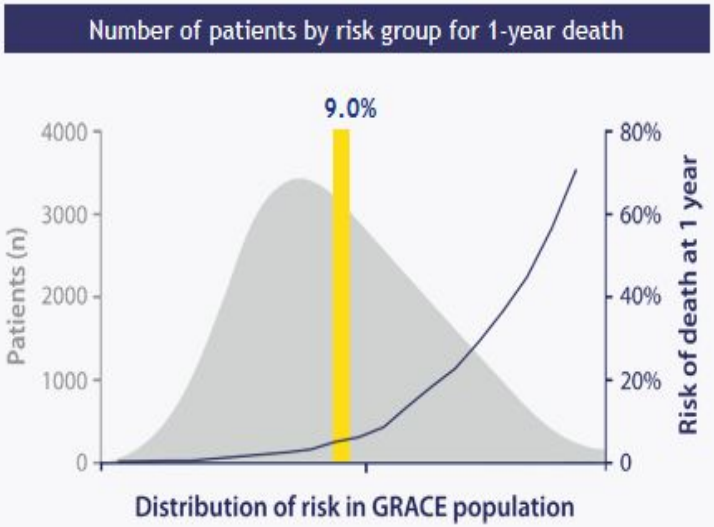
1. INPUT DATA > **2. DEATH / DEATH MI RESULTS**

| Death | | |
|---|---|---|
| Time | % Risk (Score) | Histograms |
| In hospital | 3.9 | Not available |
| 6 months | 8.3-9.7 (127) | Not available |
| 1 year | 8.3-9.7 | GRAPH |
| 3 years | 27 | GRAPH |

| Death/MI | | |
|---|---|---|
| Time | % Risk | Histograms |
| 1 year | 12 | GRAPH |

EDIT INPUT

NEW CALCULATION




Area plot: distribution (log scale) of risk based on the entire GRACE population of 102,341 patients.

Line: risk of death or death/MI

Vertical bar: individual risk of death or death/MI
green = low, yellow = intermediate, red = high

# Risk assessment: clinical markers

- Advanced age
- Younger pts – cocaine use may be considered (more extensive myocardial damage, higher rates of complications)
- Diabetes
- Renal failure
- Other co-morbidities
- Symptoms @ rest
- Tachycardia
- Hypotension
- Heart failure

# Risk assessment:  ECG markers

- ST depression > negative T waves > normal ECG
- Number of leads showing ST depression
- Magnitude of ST depression
  - ST depression > 0.1 mV – 11% death or MI @ 1 year
  - ST depression > 0.2 mV – 6-fold increased risk of death
- ST depression combined with transient ST elevation
- ST elevation in aVR – high probability of LM (left main) or 3-vessel disease

## Table 7 Recommended unit and duration of monitoring according to clinical presentation after established NSTE-ACS diagnosis

| Clinical Presentation | Unit | Rhythm monitoring |
|---|---|---|
| Unstable angina | Regular ward or discharge | None |
| NSTEMI at low risk for cardiac arrhythmias[a] | Intermediate care unit or coronary care unit | ≤24 h |
| NSTEMI at intermediate to high risk for cardiac arrhythmias[b] | Intensive/coronary care units or intermediate care unit | >24 h |

NSTEMI = Non-ST-elevation myocardial infarction.

[a]If none of the following criteria: haemodynamically unstable, major arrhythmias, left ventricular ejection fraction <40%, failed reperfusion, additional critical coronary stenoses of major vessels or complications related to percutaneous revascularization.

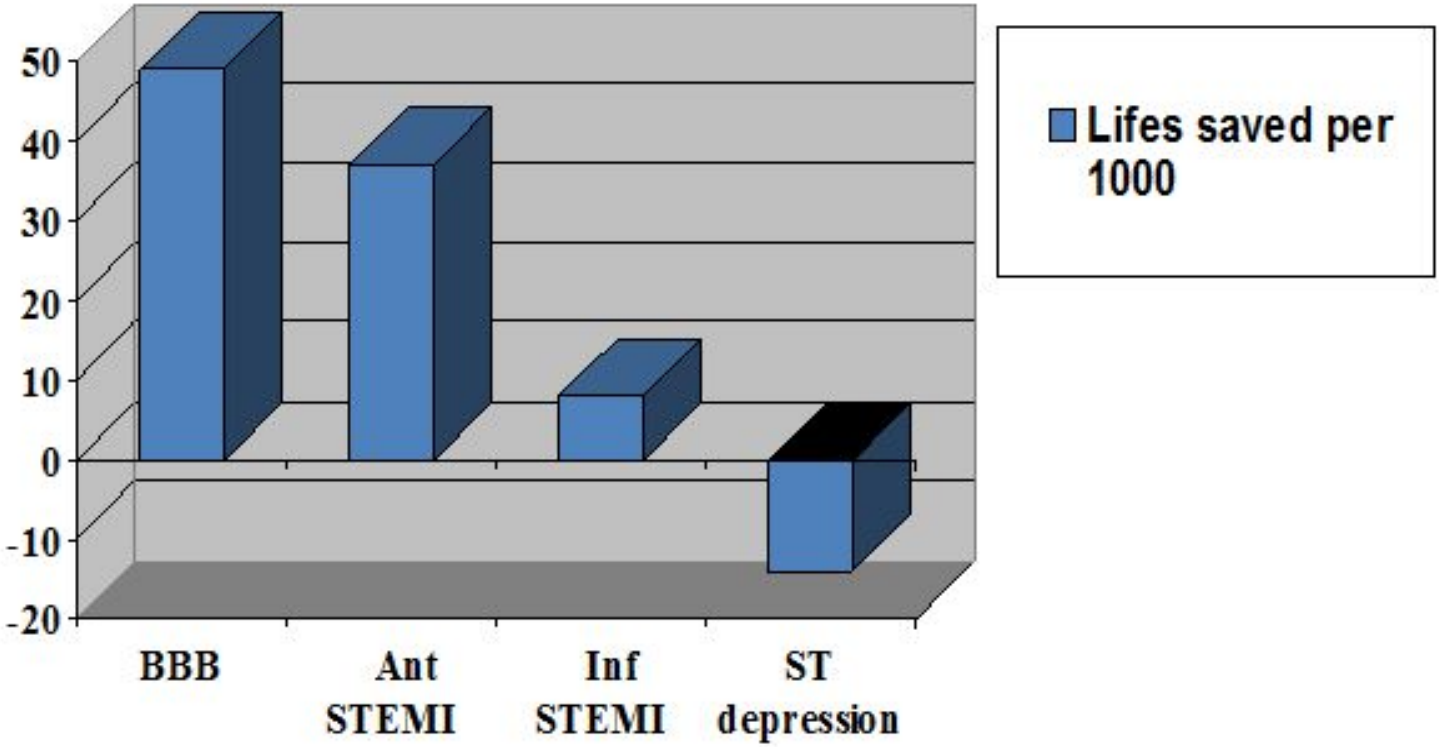
[b]If one or more of the above criteria are present.

# NSTE-ACS : medical Rx

- Anti-ischemic drugs: beta-blockers, nitrates, Ca-channel blockers
- Antiplatelet agents : aspirin, P2Y12 inhibitors (Cloidogrel, Prasugrel, Ticagrelor)
- Glicoprotein IIb/IIIa inhibitors: (Abciximab [Reo-pro], Eptifibatide [Integrilin], Tirofiban [Aggrastat]
- Anticoagulants

  - indirect thrombin inhibitors: UFH, LMWHs
  - indirect factor Xa inhibitors: LMWHs, Fondaparinux
  - direct factor Xa inhibitors: Apixaban, Rivaroxaban, Otamixaban
  - direct thrombin inhibitors: Bivalirudin, Dabigatran

# Effect of fibrinolytic therapy on mortality according to admission ECG




The Lancet 1994;343:311-322

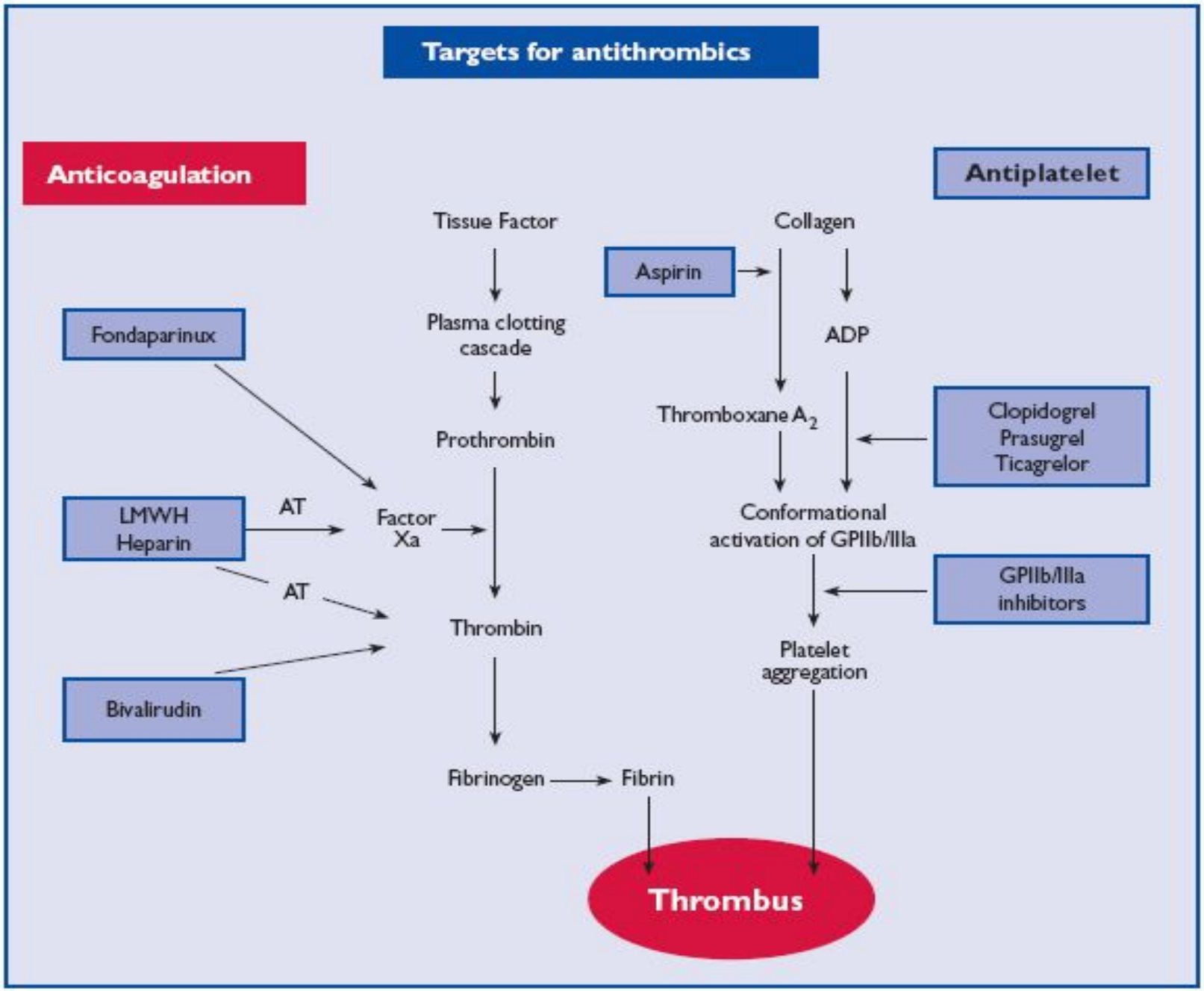
## Class III: Harm

1. **In patients with NSTE-ACS (ie, without ST-elevation, true posterior MI, or left bundle-branch block not known to be old), intravenous fibrinolytic therapy should not be used.[93,329] (*Level of Evidence: A*)**

There is no role for fibrinolytic therapy in patients with NSTE-ACS. Fibrinolysis with or without subsequent PCI in patients with NSTE-ACS was evaluated by the Fibrinolytic Trialists and TIMI investigators.[93,329] There was no benefit for mortality or MI. Intracranial hemorrhage and fatal and nonfatal MI occurred more frequently in patients treated with fibrinolytic therapy.

## Recommendations for anti-ischaemic drugs in the acute phase of non-ST-elevation acute coronary syndromes

| Recommendations | Class[a] | Level[b] | Ref.[c] |
|---|---|---|---|
| Early initiation of beta-blocker treatment is recommended in patients with ongoing ischaemic symptoms and without contraindications. | I | B | 119 |
| It is recommended to continue chronic beta-blocker therapy, unless the patient is in Killip class III or higher. | I | B | 126 |
| Sublingual or i.v. nitrates are recommended to relieve angina;[d] i.v. treatment is recommended in patients with recurrent angina, uncontrolled hypertension or signs of heart failure. | I | C | |
| In patients with suspected/confirmed vasospastic angina, calcium channel blockers and nitrates should be considered and beta-blockers avoided. | IIa | B | 127 |


Targets for antithrombics
Anticoagulation
Antiplatelet
Tissue Factor
Collagen
Aspirin
Plasma clotting cascade
ADP
Fondaparinux
Thromboxane A2
Clopidogrel
Prasugrel
Ticagrelor
Prothrombin
LMWH
Heparin
AT
Factor Xa
Conformational activation of GPIIb/IIIa
AT
GPIIb/IIIa inhibitors
Thrombin
Platelet aggregation
Bivalirudin
Fibrinogen
Fibrin
Thrombus

## Table 8 $P2Y_{12}$ inhibitors

| | Clopidogrel | Prasugrel | Ticagrelor | Cangrelor |
|---|---|---|---|---|
| **Chemical class** | Thienopyridine | Thienopyridine | Cyclopentyl-triazolopyrimidine | Stabilized ATP analogue |
| **Administration** | Oral | Oral | Oral | Intravenous |
| **Dose** | 300–600 mg orally then 75 mg a day | 60 mg orally then 10 mg a day | 180 mg orally then 90 mg twice a day | 30 μg/kg bolus and 4 μg/kg/min infusion |
| **Dosing in CKD** | | | | |
| • Stage 3 (eGFR 30–59 mL/min/1.73m$^2$) | No dose adjustment | No dose adjustment | No dose adjustment | No dose adjustment |
| • Stage 4 (eGFR 15–29 mL/min/1.73m$^2$) | No dose adjustment | No dose adjustment | No dose adjustment | No dose adjustment |
| • Stage 5 (eGFR <15 mL/min/1.73m$^2$) | Use only for selected indications (e.g. stent thrombosis prevention) | Not recommended | Not recommended | No dose adjustment |
| **Binding reversibility** | Irreversible | Irreversible | Reversible | Reversible |
| **Activation** | Prodrug, with variable liver metabolism | Prodrug, with predictable liver metabolism | Active drug, with additional active metabolite | Active drug |
| **Onset of loading dose effect**[a] | 2–6 hours[b] | 30 min[b] | 30 min[b] | 2 min |
| **Duration of effect** | 3–10 days | 7–10 days | 3–5 days | 1–2 hours |
| **Withdrawal before surgery** | 5 days[c] | 7 days[c] | 5 days[c] | 1 hour |
| **Plasma half-life of active $P2Y_{12}$ inhibitor**[d] | 30–60 min | 30–60 min[e] | 6–12 hours | 5–10 min |
| **Inhibition of adenosine reuptake** | No | No | Yes | Yes ('inactive' metabolite only) |

| | | | |
|---|---|---|---|
| Aspirin is recommended for all patients without contraindications at an initial oral loading dose[d] of 150–300 mg (in aspirin-naive patients) and a maintenance dose of 75–100 mg/day long-term regardless of treatment strategy. | I | A | 129–132 |

| | | | |
|---|---|---|---|
| A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds. | I | A | 137, 148, 153 |
| • Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications,[e] for all patients at moderate-to-high risk of ischaemic events (e.g. elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started). | I | B | 153 |
| • Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.[e] | I | B | 148, 164 |
| • Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation. | I | B | 137 |

| Intravenous antiplatelet therapy | | | |
|---|---|---|---|
| GPIIb/IIIa inhibitors during PCI should be considered for bailout situations or thrombotic complications. | IIa | C | |
| Cangrelor may be considered in $P2Y_{12}$ inhibitor–naive patients undergoing PCI. | IIb | A | 158–161 |
| It is not recommended to administer GPIIb/IIIa inhibitors in patients in whom coronary anatomy is not known. | III | A | 198, 199 |

## Table 10 Dosing of glycoprotein IIb/IIIa inhibitors in patients with normal and impaired renal function

| Drug | Recommendations | | | |
|---|---|---|---|---|
| | Normal renal function or stage 1–2 CKD (eGFR ≥60 mL/min/1.73m²) | Stage 3 CKD (eGFR 30–59 mL/min/1.73m²) | Stage 4 CKD (eGFR 15–29 mL/min/1.73m²) | Stage 5 CKD (eGFR <15 mL/min/1.73m²) |
| **Eptifibatide** | Bolus 180 µg/kg i.v., infusion 2 µg/kg/min | No adjustment of bolus, reduce infusion rate to 1 µg/kg/min if eGFR <50 mL/min/1.73m² | Not recommended | Not recommended |
| **Tirofiban** | Bolus 25 µg/kg or 10 µg/kg i.v, infusion 0.15 µg/kg/min | No dose adjustment | No adjustment of bolus, reduce infusion to 0.05 µg/kg/min | Not recommended |
| **Abciximab** | Bolus 0.25 mg/kg i.v., infusion 0.125 µg/kg/min (max.10 µg/min) | No specific recommendations for the use of abciximab, or for dose adjustment in the case of renal failure. Careful evaluation of haemorrhagic risk is needed. | | |

# Anticoagulants (1)

| Recommendations | Class [a] | Level [b] | Ref [c] |
|---|---|---|---|
| Anticoagulation is recommended for all patients in addition to antiplatelet therapy. | I | A | 171, 172 |
| The anticoagulation should be selected according to both ischaemic and bleeding risks, and according to the efficacy–safety profile of the chosen agent. | I | C | - |
| Fondaparinux (2.5 mg subcutaneously daily) is recommended as having the most favourable efficacy–safety profile with respect to anticoagulation. | I | A | 173, 175 |
| If the initial anticoagulant is fondaparinux, a single bolus of UFH (85 IU/kg adapted to ACT, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) should be added at the time of PCI. | I | B | 178 |
| Enoxaparin (1 mg/kg twice daily) is recommended when fondaparinux is not available. | I | B | 175, 193 |
| If fondaparinux or enoxaparin are not available, UFH with a target aPTT of 50–70 s or other LMWHs at the specific recommended doses are indicated. | I | C | - |

# Anticoagulants (2)

| | | | |
|---|---|---|---|
| Bivalirudin plus provisional GP IIb/IIIa receptor inhibitors are recommended as an alternative to UFH plus GP IIb/IIIa receptor inhibitors in patients with an intended urgent or early invasive strategy, particularly in patients with a high risk of bleeding. | I | B | 165, 196, 197 |
| In a purely conservative strategy, anticoagulation should be maintained up to hospital discharge. | I | A | 175, 180–182 |
| Discontinuation of anticoagulation should be considered after an invasive procedure unless otherwise indicated. | IIa | C | - |
| Crossover of heparins (UFH and LMWH) is not recommended. | III | B | 171, 183, 193 |

## Table 11 Dosing of anticoagulants in patients with normal and impaired renal function

| Drug | Recommendations | | |
|---|---|---|---|
| | Normal renal function or stage 1–3 CKD (eGFR ≥30 mL/min/1.73m²) | Stage 4 CKD (eGFR 15–29 mL/min/1.73m²) | Stage 5 CKD (eGFR <15 mL/min/1.73m²) |
| **Unfractionated heparin** | • Prior to coronary angiography: 60–70 IU/kg i.v. (max 5000 IU) and infusion (12–15 IU/kg/h) (max 1000 IU/h), target aPTT 1.5–2.5x control<br>• During PCI: 70-100 IU/kg i.v. (50–70 IU/kg if concomitant with GPIIb/IIIa inhibitors) | No dose adjustment | No dose adjustment |
| **Enoxaparin** | 1 mg/kg s.c. twice a day | 1 mg/kg s.c. once a day | Not recommended |
| **Fondaparinux** | 2.5 mg s.c. once a day | Not recommended if eGFR <20 mL/min/1.73m² | Not recommended |
| **Bivalirudin** | Bolus 0.75 mg/kg i.v., infusion 1.75 mg/kg/h | No adjustment of bolus, reduce infusion rate to 1 mg/kg/h | On dialysis, no adjustment of bolus, reduce infusion rate to 0.25 mg/kg/h |

**Table 12** **Suggested strategies to reduce bleeding risk related to PCI**

| |
|---|
| • Anticoagulant doses adjusted to bodyweight and renal function, especially in women and elderly patients. |
| • Radial approach preferred. |
| • Proton pump inhibitors in patients on DAPT at higher than average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAIDs/corticosteroid use, or two or more among age ≥65 years, dyspepsia, gastrooesophageal reflux disease, *Helicobacter pylori* infection, and chronic alcohol use). |
| • In patients on OAC<br>o PCI performed without interruption of VKAs or NOACs.<br>o In patients on VKAs, do not administer UFH if INR value >2.5.<br>o In patients on NOACs, regardless of the timing of the last administration of NOACs, add additional low-dose parenteral anticoagulation (e.g. enoxaparin 0.5 mg/kg i.v. or UFH 60 IU/kg).<br>o Aspirin indicated but avoid pretreatment with $P2Y_{12}$ inhibitors.<br>o GPIIb/IIIa inhibitors only for bailout of periprocedural complications. |

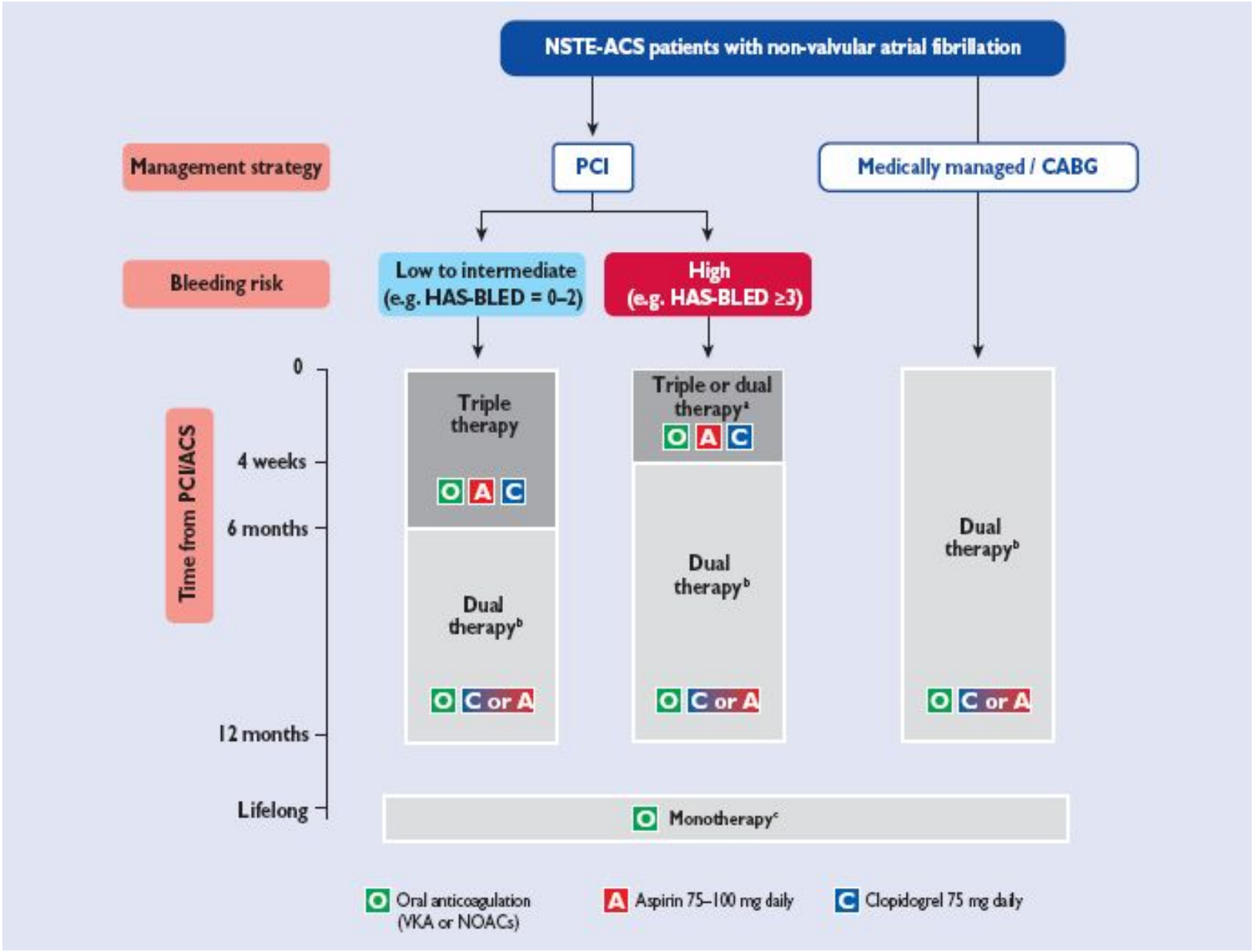

NSTE-ACS patients with non-valvular atrial fibrillation
Management strategy
PCI
Medically managed / CABG
Bleeding risk
Low to intermediate (e.g. HAS-BLED = 0–2)
High (e.g. HAS-BLED ≥3)
Time from PCI/ACS
0
4 weeks
6 months
12 months
Lifelong
Triple therapy
O A C
Dual therapy[b]
O C or A
Triple or dual therapy[a]
O A C
Dual therapy[b]
O C or A
Dual therapy[b]
O C or A
O Monotherapy[c]
O Oral anticoagulation (VKA or NOACs)
A Aspirin 75–100 mg daily
C Clopidogrel 75 mg daily

**Table 13** Checklist of treatments when an ACS diagnosis appears likely

| | |
|---|---|
| **Aspirin** | Initial dose of 150–300 mg non-enteric formulation followed by 75–100 mg/day (i.v. administration is acceptable) |
| **$P2Y_{12}$ inhibitor** | Loading dose of ticagrelor or clopidogrel[a] |
| **Anticoagulation** | Choice between different options depends on strategy:<br>• Fondaparinux 2.5 mg/daily subcutaneously<br>• Enoxaparin 1 mg/kg twice daily subcutaneously<br>• UFH i.v. bolus 60–70 IU/kg (maximum 5000 IU) followed by infusion of 12–15 IU/kg/h (maximum 1000 IU/h) titrated to aPTT 1.5–2.5 × control<br>• Bivalirudin is indicated only in patients with a planned invasive strategy |
| **Oral ß-Blocker** | If tachycardic or hypertensive without signs of heart failure |

aPTT = activated partial thromboplastin time; IU = international units; i.v. = intravenous; UFH = unfractionated heparin.

[a]Prasugrel is not mentioned as it is not approved as medical therapy before invasive strategy, but only after angiography when anatomy is known.

## Table 14 Checklist of antithrombotic treatments prior to PCI

| | |
|---|---|
| **Aspirin** | Confirm loading dose prior to PCI. |
| **$P2Y_{12}$ inhibitor** | Confirm loading dose of ticagrelor or clopidogrel prior to PCI.<br>If $P2Y_{12}$ naïve, consider prasugrel (if <75 years age, >60 kg, no prior stroke or TIA) |
| **Anticoagulation** | • Fondaparinux pre-treated: add UFH for PCI<br>• Enoxaparin pre-treated: add if indicated<br>• UFH pre-treated: titrate to ACT >250 s, or switch to bivalirudin (0.1 mg/kg bolus followed by 0.25 mg/kg/h) |
| **GP IIb/IIIa receptor inhibitor** | • Consider tirofiban or eptifibatide in patients with high-risk anatomy or troponin elevation<br>• Abciximab only prior to PCI in high-risk patients. |

ACT = activated clotting time; GP, glycoprotein; PCI = percutaneous coronary intervention; TIA = transient ischaemic attack; UFH = unfractionated heparin.

# Coronary revascularization

Revascularization for NSTE-ACS relieves symptoms, shortens hospital stay, and improves prognosis. The indications and timing for myocardial revascularization and choice of preferred approach (PCI or CABG) depend on many factors including the patient's condition, the presence of risk features, co-morbidities, and the extent and severity of the lesions as identified by coronary angiography.

A recent meta-analysis, based on individual patient data from the FRISC-2, Invasive versus Conservative Treatment in Unstable Coronary Syndromes (ICTUS), and Randomized Intervention Trial of unstable Angina-3 (RITA-3) studies comparing a routine invasive vs. a selective invasive strategy, revealed a reduction in rates of death and non-fatal MI at 5-year follow-up, with the most pronounced difference in high risk patients.[209]

Primary composite end point
( death / reinfarction / rehospitalization )
(%) in different trials

| Trial | Conserv. | Early Interv. | P value | # of pts |
|---|---|---|---|---|
| TACTICS | 19.4 | 15.9 | 0.025 | 2210 |
| INTERACT | 16.2 | 13.5 | 0.32 | 746 |
| RITA-3 | 19.5 | 13.5 | 0.001 | 1810 |
| ISAR-COOL | 11.6 | 5.9 | 0.04 | 410 |
| ICTUS | 22.7 | 21.2 | 0.33 | 1200 |
| All combined | 18.6 | 14.6 | 0.001 | |

There was a 2.0–3.8% absolute reduction in cardiovascular death or MI in the low and intermediate risk groups, and an 11.1% absolute risk reduction in the highest risk patients. These results support a routine invasive strategy, but highlight the role of risk stratification in the management decision process.

In summary, timing of angiography and revascularization should be based on patient risk profile. Patients at very high risk (as defined above) should be considered for urgent coronary angiography (<2 h). In patients at high risk with a GRACE risk score of >140 or with at least one major high risk criterion, an early invasive strategy within 24 h appears to be the reasonable time window. This implies expedited transfer for patients admitted to hospitals without on-site catheterization facilities. In lower risk subsets with a GRACE risk score of <140 but with at least one high risk criterion (*Table 9*), the invasive evaluation can be delayed without increased risk but should be performed during the same hospital stay, preferably within 72 h of admission. In such patients, immediate transfer is not mandatory, but should be organized within 72 h (e.g. diabetic patients). In other low risk patients without recurrent symptoms a non-invasive assessment of inducible ischaemia should be performed before hospital discharge. Coronary angiography should be performed if the results are positive for reversible ischaemia.

# Step 1: initial evaluation

- Quality of chest pain and a symptom-orientated physical examination
- Assessment of the likelihood of CAD (e.g. age, risk factors, previous MI, CABG, PCI)
- ECG (to detect ST-segment deviation or other abnormality).

On the basis of these findings, which should be available within 10 min of first medical contact, the patient can be assigned to one of the three major working diagnoses:

- STEMI
- NSTE-ACS;
- ACS (highly) unlikely.

# Step 2 : diagnosis validation and risk assessment

- Responsiveness to antianginal treatment.
- Routine clinical chemistry, particularly troponins (on presentation and after 6–9 h) and other markers, according to working diagnoses (e.g. D-dimers, BNP, NT-proBNP); if highly sensitive troponin assays are available, a fast track rule-out protocol (3 h) may be implemented (*Figure 5*).
- Repeat or continuous ST-segment monitoring (when available).
- Ischaemic risk score assessment (GRACE score).
- Echocardiogram;

# Step 3: invasive strategy (1)

- **invasive** (<72 h);
  - **urgent invasive** (<120 min);
  - **early invasive** (<24 h);
- primarily **conservative**.

# Step 3: invasive strategy (2)

**Urgent invasive strategy (<120 min after first medical contact)**

This should be undertaken for very high risk patients. These patients are characterized by:

- Refractory angina (indicating evolving MI without ST abnormalities).
- Recurrent angina despite intense antianginal treatment, associated with ST depression (2 mm) or deep negative T waves.
- Clinical symptoms of heart failure or haemodynamic instability ('shock').
- Life-threatening arrhythmias (ventricular fibrillation or ventricular tachycardia).

# Step 3: invasive strategy (3)

**Conservative strategy (no or elective angiography)**

Patients that fulfil all of the following criteria may be regarded as low risk and should not routinely be submitted to early invasive evaluation:

- No recurrence of chest pain.
- No signs of heart failure.
- No abnormalities in the initial ECG or a second ECG (at 6–9 h).
- No rise in troponin level (at arrival and at 6–9 h).
- No inducible ischaemia.

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### Class III: No Benefit

1. An early invasive strategy (ie, diagnostic angiography with intent to perform revascularization) is not recommended in patients with:
   a. Extensive comorbidities (eg, hepatic, renal, pulmonary failure; cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. (*Level of Evidence: C*)
   b. Acute chest pain and a low likelihood of ACS who are troponin-negative (*Level of Evidence: C*), especially women.[141] (*Level of Evidence: B*)

# Step 4: revascularization modalities

Recommendations for the choice of a revascularization modality in NSTE-ACS are similar to those for elective revascularization procedures. In patients with single-vessel disease, PCI with stenting of the culprit lesion is the first choice. In patients with multivessel disease, the decision for PCI or CABG must be made individually, according to institutional protocols designed by the 'Heart Team'. A sequential approach, consisting of treating the culprit lesion with PCI followed by elective CABG with proof of ischaemia and/or functional assessment (FFR) of the non-culprit lesions, may be advantageous in some patients.

# Step 5: hospital discharge

**Table 15 Measures checked at discharge**

| | |
|---|---|
| **Aspirin** | Continue life long |
| **$P2Y_{12}$ inhibitor** | Continue for 12 months (unless at high risk of bleeding) |
| **β-Blocker** | If LV function depressed |
| **ACE inhibitor/ ARB** | If LV function depressed<br>Consider for patients devoid of depressed LV function |
| **Aldosterone antagonist/ eplerenone** | If depressed LV function (LVEF ≤35%) and either diabetes or heart failure, without significant renal dysfunction |
| **Statin** | Titrate to achieve target LDL-C levels <1.8 mmol/L (<70 mg/dL) |
| **Lifestyle** | Risk-factor counselling, referral to cardiac rehabilitation / secondary prevention programme |

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; LDL-C = low-density lipoprotein cholesterol; LV = left ventricular; LVEF = left ventricular ejection fraction.

## Table II Performance measures in NSTEMI patients

| |
|---|
| • Use of aspirin |
| • Use of clopidogrel/prasugrel/ticagrelor |
| • Use of UFH/enoxaparin/fondaparinux/bivalirudin |
| • β-Blocker at discharge in patients with LV dysfunction |
| • Use of statins |
| • Use of ACE-inhibitor or ARB |
| • Use of early invasive procedures in intermediate- to high-risk patients. |
| • Smoking cessation advice/counselling |
| • Enrolment in a secondary prevention/ cardiac rehabilitation programme |

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; LV = left ventricular; NSTEMI, non-ST-segment elevation myocardial infarction; UFH = unfractionated heparin.

*Thank you 4 attention*

# Backup slides

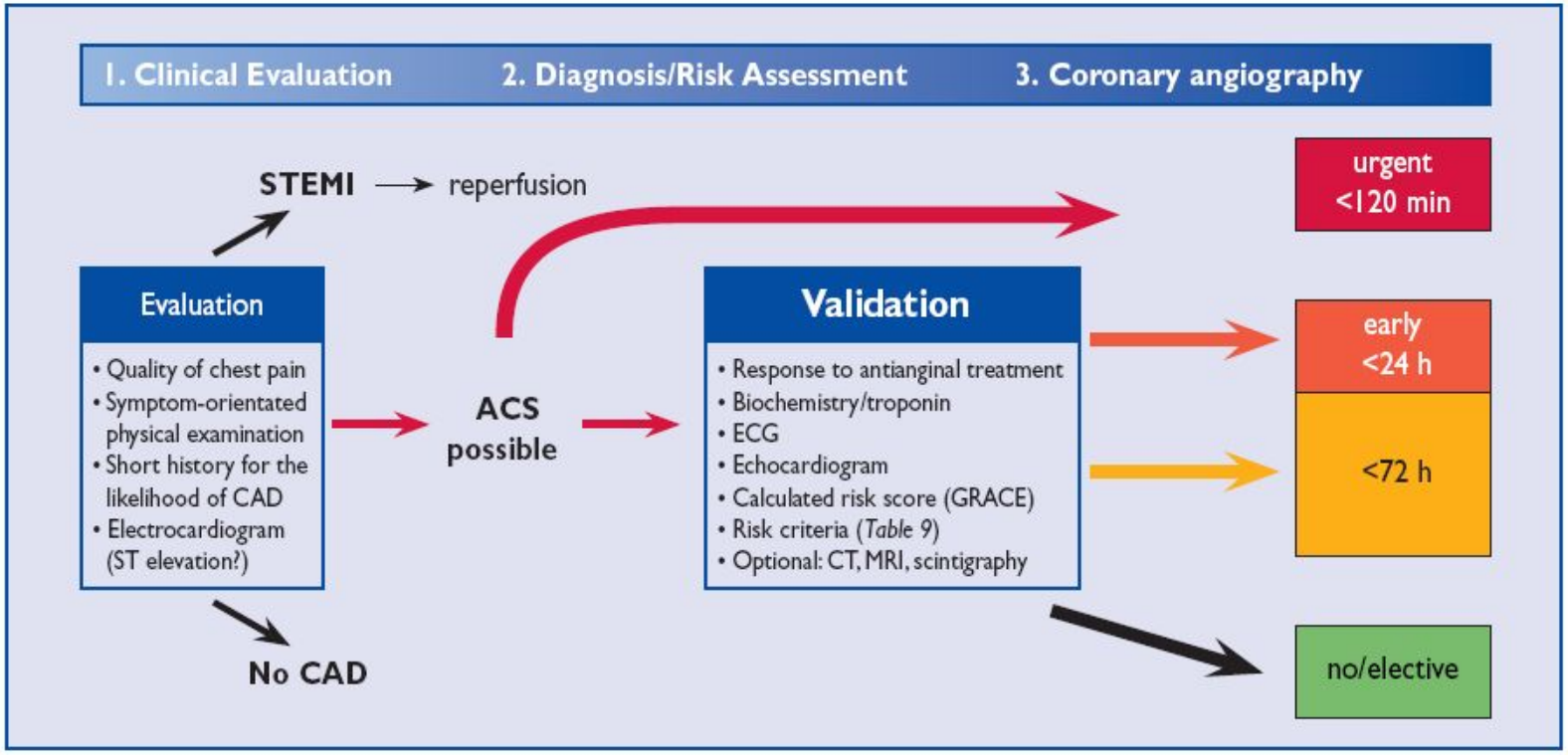



**Figure 6** Decision-making algorithm in ACS. ACS = acute coronary syndrome; CAD = coronary artery disease; CT = computed tomography; ECG, electrocardiogram; GRACE = Global Registry of Acute Coronary Events; MRI = magnetic resonance imaging; STEMI = ST-elevation myocardial infarction.

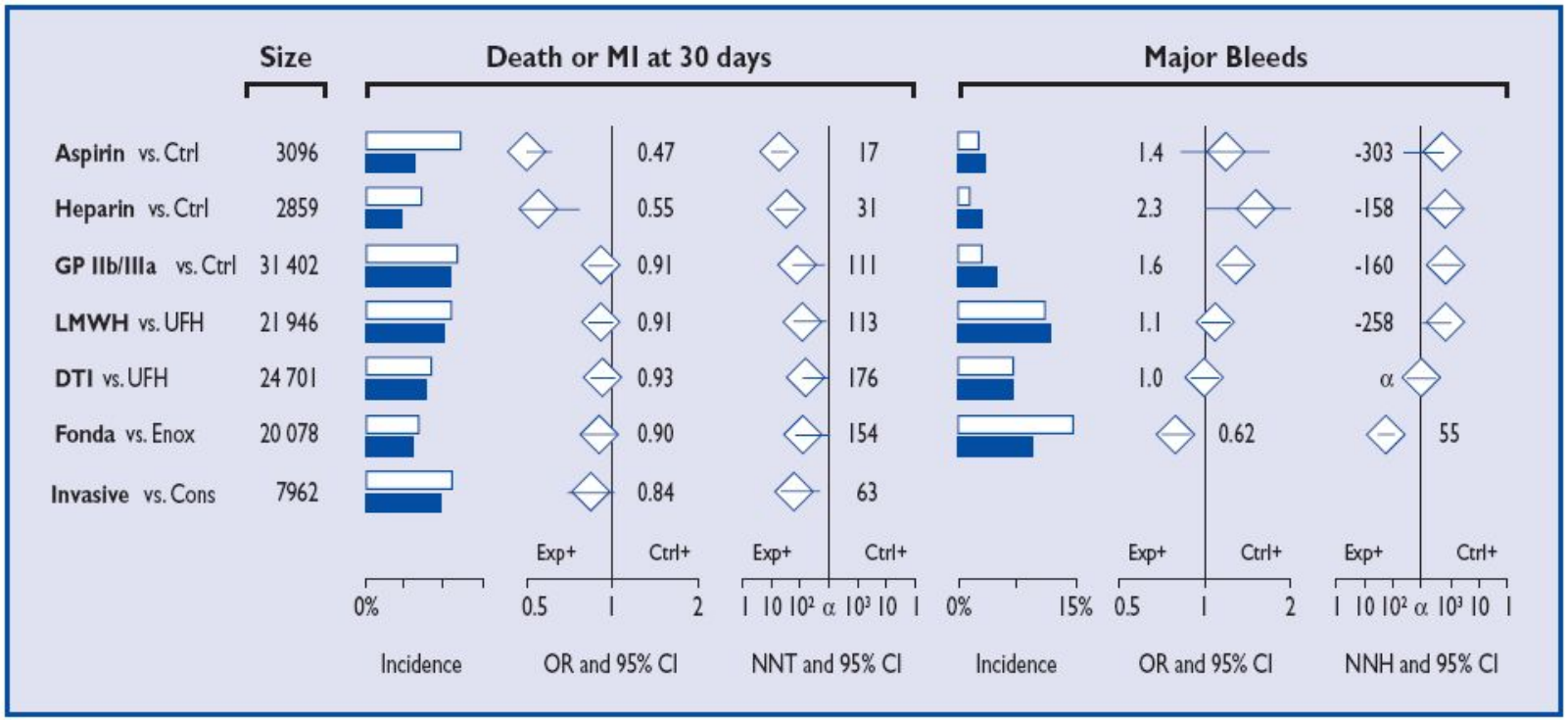



**Figure 4** Benefit and risk for different treatment modalities. CI = confidence interval; Cons = conservative; Ctrl = control; DTI = direct thrombin inhibitor; Enox = enoxaparin; Exp + = experimental therapy; Fonda = fondaparinux; GP = glycoprotein; LMWH = low molecular weight heparin; MI = myocardial infarction; NNH = numbers needed to harm; NNT = numbers needed to treat; OR = odds ratio; UFH = unfractionated heparin.

## 2014 AHA/ACC NSTE-ACS Guideline

Features not characteristic of myocardial ischemia include:

- Pleuritic pain (sharp or knifelike pain provoked by respiration or cough);
- Primary or sole location of discomfort in the middle or lower abdomen;
- Pain localized by the tip of 1 finger, particularly at the LV apex or costochondral junction;
- Pain reproduced with movement or palpation of the chest wall or arms;
- Brief episodes of pain lasting a few seconds or less;
- Pain that is of maximal intensity at onset; and
- Pain that radiates into the lower extremities.

**Table 8. Factors Associated With Appropriate Selection of Early Invasive Strategy or Ischemia-Guided Strategy in Patients With NSTE-ACS**

| | |
|---|---|
| Immediate invasive (within 2 h) | Refractory angina<br>Signs or symptoms of HF or new or worsening mitral regurgitation |
| | Hemodynamic instability |
| | Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy |
| | Sustained VT or VF |
| Ischemia-guided strategy | Low-risk score (eg, TIMI [0 or 1], GRACE [<109])<br>Low-risk Tn-negative female patients |
| | Patient or clinician preference in the absence of high-risk features |
| Early invasive (within 24 h) | None of the above, but GRACE risk score >140<br>Temporal change in Tn (Section 3.4) |
| | New or presumably new ST depression |
| Delayed invasive (within 25–72 h) | None of the above but diabetes mellitus Renal insufficiency (GFR <60 mL/min/1.73 m$^2$) |
| | Reduced LV systolic function (EF <0.40) |
| | Early postinfarction angina |
| | PCI within 6 mo |
| | Prior CABG |
| | GRACE risk score 109–140; TIMI score ≥2 |

CABG indicates coronary artery bypass graft; EF, ejection fraction; GFR, glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; LV, left ventricular; NSTE-ACS, non–ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction; Tn, troponin; VF, ventricular fibrillation; and VT, ventricular tachycardia.

# Biomarkers: possible non-ACS causes of troponin elevation

| |
|---|
| • **Chronic or acute renal dysfunction** |
| • Severe congestive **heart failure** – acute and chronic |
| • **Hypertensive crisis** |
| • **Tachy- or bradyarrhythmias** |
| • **Pulmonary embolism**, severe pulmonary hypertension |
| • Inflammatory diseases, e.g. **myocarditis** |
| • Acute neurological disease, including **stroke**, or subarachnoid haemorrhage |
| • Aortic dissection, aortic valve disease or hypertrophic cardiomyopathy |
| • Cardiac contusion, ablation, pacing, cardioversion, or endomyocardial biopsy |
| • Hypothyroidism |
| • Apical ballooning syndrome (Tako-Tsubo cardiomyopathy) |
| • Infiltrative diseases, e.g. amyloidosis, haemochromatosis, sarcoidosis, sclerodermia |
| • Drug toxicity, e.g. adriamycin, 5-fluorouracil, herceptin, snake venoms |
| • Burns, if affecting >30% of body surface area |
| • Rhabdomyolysis |
| • Critically ill patients, especially with respiratory failure, or sepsis |

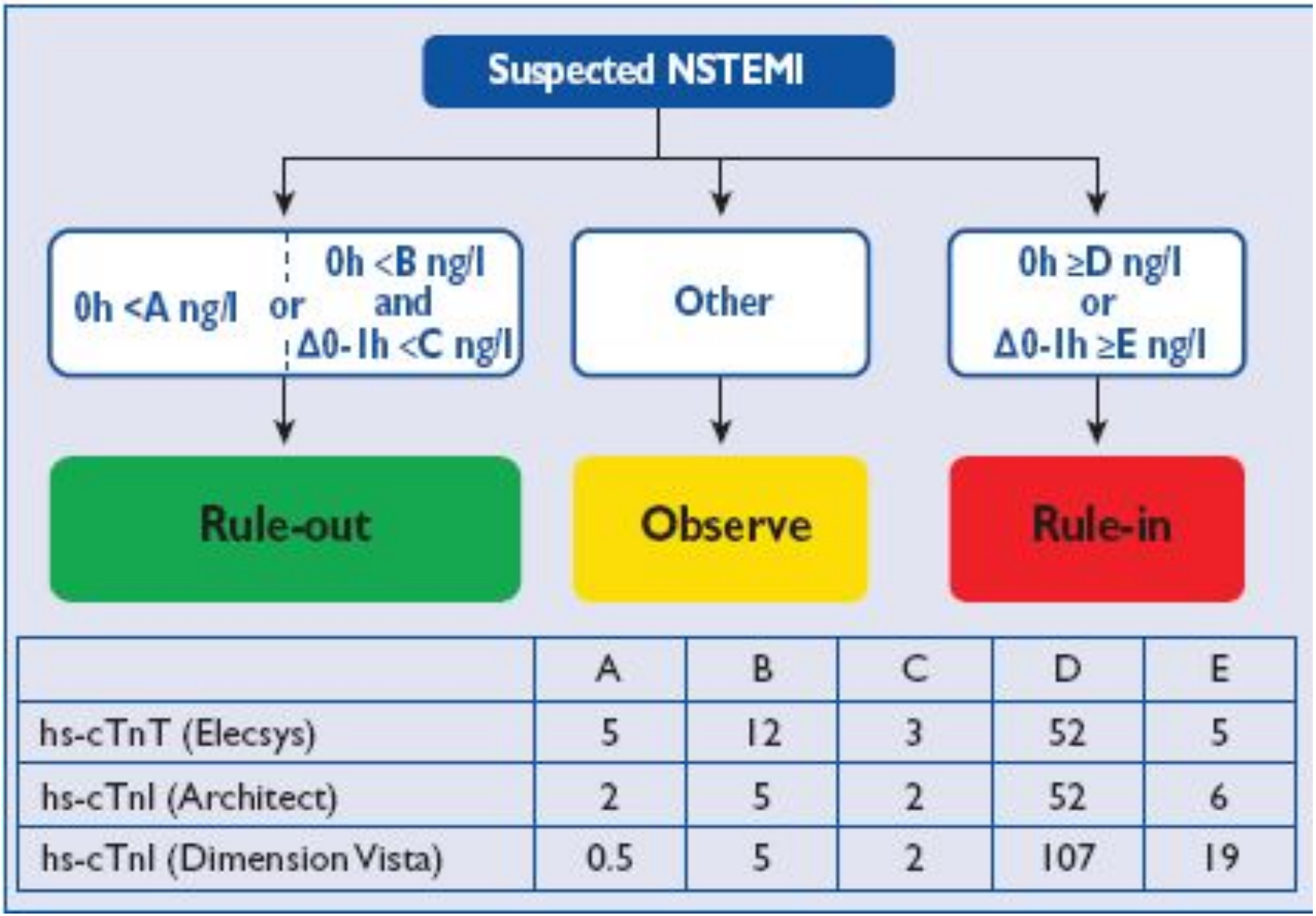
# NSTE-ACS : differential diagnosis

**Table 4** Cardiac and non-cardiac conditions that can mimic non-ST-elevation acute coronary syndomes

| Cardiac | Pulmonary | Haematological | Vascular | Gastro-intestinal | Orthopaedic/ infectious |
|---|---|---|---|---|---|
| Myocarditis | Pulmonary embolism | Sickle cell crisis | Aortic dissection | Oesophageal spasm | Cervical discopathy |
| Pericarditis | Pulmonary infarction | Anaemia | Aortic aneurysm | Oesophagitis | Rib fracture |
| Cardiomyopathy | Pneumonia<br>Pleuritis | | Cerebrovascular disease | Peptic ulcer | Muscle injury/ inflammation |
| Valvular disease | Pneumothorax | | | Pancreatitis | Costochondritis |
| Tako-Tsubo cardiomyopathy | | | | Cholecystitis | Herpes zoster |
| Cardiac trauma | | | | | |

# Two categories of patents with ACS

1. **Patients with acute chest pain and persistent (>20 min) ST-segment elevation.** This is termed ST-elevation ACS (STE-ACS) and generally reflects an acute total coronary occlusion. Most of these patients will ultimately develop an ST-elevation MI (STEMI). The therapeutic objective is to achieve rapid, complete, and sustained reperfusion by primary angioplasty or fibrinolytic therapy.
2. **Patients with acute chest pain but without persistent ST-segment elevation.** These patients have rather persistent or transient ST-segment depression or T-wave inversion, flat T waves, pseudo-normalization of T waves, or no ECG changes at presentation. The initial strategy in these patients is to alleviate ischaemia and symptoms, to monitor the patient with serial ECGs, and to repeat measurements of markers of myocardial necrosis. At presentation, the working diagnosis of non-ST-elevation ACS (NSTE-ACS), based on the measurement of troponins, will be further qualified as non-ST-elevation MI (NSTEMI) or unstable angina (*Figure 1*). In a certain number of patients, coronary heart disease will subsequently be excluded as the cause of symptoms.




| | A | B | C | D | E |
|---|---|---|---|---|---|
| hs-cTnT (Elecsys) | 5 | 12 | 3 | 52 | 5 |
| hs-cTnI (Architect) | 2 | 5 | 2 | 52 | 6 |
| hs-cTnI (Dimension Vista) | 0.5 | 5 | 2 | 107 | 19 |

# NSTE-ACS : recommendations diagnosis and risk stratification

| Recommendations | Class [a] | Level [b] | Ref [c] |
|---|---|---|---|
| In patients with a suspected NSTE-ACS, diagnosis and short-term ischaemic/bleeding risk stratification should be based on a combination of clinical history, symptoms, physical findings, ECG (repeated or continuous ST monitoring), and biomarkers. | I | A | 16, 18, 27, 30, 58 56, 57 |
| ACS patients should be admitted preferably to dedicated chest pain units or coronary care units. | I | C | 47 |
| It is recommended to use established risk scores for prognosis and bleeding (e.g. GRACE, CRUSADE). | I | B | 50, 83 |
| A 12-lead ECG should be obtained within 10 min after first medical contact and immediately read by an experienced physician. This should be repeated in the case of recurrence of symptoms, and after 6–9 and 24 h, and before hospital discharge. | I | B | 17, 18 |
| Additional ECG leads ($V_{3R}$, $V_{4R}$, $V_7$–$V_9$) are recommended when routine leads are inconclusive. | I | C | 18 |
| Blood has to be drawn promptly for troponin (cardiac troponin T or I) measurement. The result should be available within 60 min. The test should be repeated 6–9 h after initial assessment if the first measurement is not conclusive. Repeat testing after 12–24 h is advised if the clinical condition is still suggestive of ACS. | I | A | 27, 30 |
| A rapid rule-out protocol (0 and 3 h) is recommended when highly sensitive troponin tests are available (see *Figure 5*). | I | B | 20, 21, 23 |
| An echocardiogram is recommended for all patients to evaluate regional and global LV function and to rule in or rule out differential diagnoses. | I | C | - |
| Coronary angiography is indicated in patients in whom the extent of CAD or the culprit lesion has to be determined (see Section 5.4). | I | C | - |
| Coronary CT angiography should be considered as an alternative to invasive angiography to exclude ACS when there is a low to intermediate likelihood of CAD and when troponin and ECG are inconclusive. | IIa | B | 37–41 |
| In patients without recurrence of pain, normal ECG findings, negative troponins tests, and a low risk score, a non-invasive stress test for inducible ischaemia is recommended before deciding on an invasive strategy. | I | A | 35, 54, 55 |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Last Updated:
March 2008

## Enter values in drop-down boxes below:

| | | | |
|---|---|---|---|
| Baseline Hematocrit | 37 - 39.9 | Prior Vascular Disease | Yes |
| GFR: Cockcroft-Gault | 61 - 90 (Calculate GFR) | Diabetes Mellitus | Yes |
| Heart rate on admission | 81 - 90 | Signs of CHF on admission | No |
| Systolic blood pressure on admission | < 91 | Sex | Male |

Clear Selections

### CRUSADE Bleeding Score

**44**

**High Risk**

### Risk of In-Hospital Major Bleeding

**10.4%**

## Table 8 $P2Y_{12}$ inhibitors

| | Clopidogrel | Prasugrel | Ticagrelor |
|---|---|---|---|
| Class | Thienopyridine | Thienopyridine | Triazolopyrimidine |
| Reversibility | Irreversible | Irreversible | Reversible |
| Activation | Prodrug, limited by metabolization | Prodrug, not limited by metabolization | Active drug |
| Onset of effect[a] | 2–4 h | 30 min | 30 min |
| Duration of effect | 3–10 days | 5–10 days | 3–4 days |
| Withdrawal before major surgery | 5 days | 7 days | 5 days |

[a]50% inhibition of platelet aggregation.

# Recommendations for oral antiplatelet agents

| Recommendations | Class [a] | Level [b] | Ref [c] |
|---|---|---|---|
| Aspirin should be given to all patients without contraindications at an initial loading dose of 150–300 mg, and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy. | I | A | 107, 108 |
| A $P2Y_{12}$ inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding. | I | A | 110, 130, 132 |
| A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors (*H. elicobacter pylori* infection, age ≥65 years, concurrent use of anticoagulants or steroids). | I | A | 125–127 |
| Prolonged or permanent withdrawal of $P2Y_{12}$ inhibitors within 12 months after the index event is discouraged unless clinically indicated. | I | C | - |
| Ticagrelor (180-mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins) , regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced). | I | B | 132 |
| Prasugrel (60-mg loading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.[d] | I | B | 130 |
| Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel. | I | A | 110, 146, 147 |
| A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option. | I | B | 108, 114, 115 |
| A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding. | IIa | B | 108 |
| Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases. | IIb | B | 124 |
| Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used. | IIb | B | 119, 121 |
| In patients pre-treated with $P2Y_{12}$ inhibitors who need to undergo non-emergent major surgery (including CABG), postponing surgery at least for 5 days after cessation of ticagrelor or clopidogrel, and 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischaemic events should be considered. | IIa | C | - |
| Ticagrelor or clopidogrel should be considered to be (re-) started after CABG surgery as soon as considered safe. | IIa | B | 134 |
| The combination of aspirin with an NSAID (selective COX-2 inhibitors and non-selective NSAID) is not recommended. | III | C | - |

# NSTE-ACS: IIb/IIIa inhibitors

| Recommendations | Class [a] | Level [b] | Ref [c] |
|---|---|---|---|
| The choice of combination of oral antiplatelet agents, a GP IIb/IIIa receptor inhibitor, and anticoagulants should be made in relation to the risk of ischaemic and bleeding events. | I | C | - |
| Among patients who are already treated with DAPT, the addition of a GP IIb/IIIa receptor inhibitor for high-risk PCI (elevated troponin, visible thrombus) is recommended if the risk of bleeding is low. | I | B | 152, 161 |
| Eptifibatide or tirofiban added to aspirin should be considered prior to angiography in high-risk patients not preloaded with $P2Y_{12}$ inhibitors. | IIa | C | - |
| In high-risk patients eptifibatide or tirofiban may be considered prior to early angiography in addition to DAPT, if there is ongoing ischaemia and the risk of bleeding is low. | IIb | C | - |
| GP IIb/IIIa receptor inhibitors are not recommended routinely before angiography in an invasive treatment strategy. | III | A | 151, 170 |
| GP IIb/IIIa receptor inhibitors are not recommended for patients on DAPT who are treated conservatively. | III | A | 150, 151 |

Guidelines and recommendations should help the physicians to make decisions in their daily practice. However, the final decisions concerning an individual patient must be made by the responsible physician(s).

# Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

BMJ 2003; 327: 1459 - 61

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials