Chest Pain in 2014

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Overview

• Overview of NSTEMI in 2014
• Overview of STEMI in 2014
• Changes in assessment
• Changes in treatment options
• Future directions/controversies
Overview of NSTEMI in 2014

• Adapted from The ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal (2011) 32: 2999–3054)


Epidemiology

• **NSTE-ACS compared to STEMI:**
  – More frequent.
  – Patients are older and with more comorbidities.
  – Initial mortality lower; 6 months mortality equal and long term mortality higher.
Investigations: ECG

- *Should be obtained within 10min of first medical contact.*
- *Consider additional leads, if normal.*
- *Check for: ST-segment depression and/or T wave inversion.*
- *Comparison with previous ECG - if obtainable - useful.*
- *Always serial ECGs or continuous monitoring.*
- *A normal ECG does not exclude the diagnosis (hidden ischaemia in CX and right ventricular involvement).*
Investigations: Biomarkers

• *Troponin I or T are gold standard.*
• *High sensitivity troponins rise within 2 to 4 hours.*
• *Minor elevations usually resolve within 2-3 days, but with larger necrosis elevations may remain for up to 2 weeks.*
• *Cut off for MI diagnosis > 99 percentile of normal population*
• *High sensitivity assays yield a negative predictive value of 95% as a single test on admission and nearly 100% by a repeat sample after 3 hours, but sacrifice specificity (see controversies).*
• *Use bedside tests if results from a central laboratory are not possible within 1 hour.*
Investigations: Non-invasive

• *Echocardiography should be routinely available in emergency departments or chest pain units, and used early in all patients.*
  – Evaluation of global LV function.
  – Diagnose regional hypokinesia by wall motion analysis.
  – Rule out some differential diagnosis.

• *Stress testing to rule out obstructive CAD in pain free patients with normal ECG and negative biomarkers.*

• *Multislice Cardiac CT (MSCT) is useful and recommended to rule out CAD as cause of pain in patients with low to intermediate likelihood of CAD and when troponin and ECG are inconclusive.*

• *MRI can integrate imaging of function, perfusion and necrosis.*
Investigations: Invasive

• *Coronary angiography should be performed urgently for diagnostic purpose in patients at high risk.*
Indicators of Increased Risk

• **Clinical**
  – Continuous or frequent episodes of pain.
  – Tachycardia.
  – Hypotension.
  – Heart failure.

• **ECG**
  – ST-segment depression or T-wave inversion on admission.
  – Deep T-wave inversion in anterior leads.
  – ST-segment depression $\geq 0.1 mV$ in a single lead or $\geq 0.05 mV$ in two or more contiguous leads.
  – ST-segment elevation ($\geq 0.1 mV$) in lead aVR.
Treatment: Anti ischaemia

- **Nitrates** (oral or intravenous) to relieve angina.
- **β adrenergic blocker (BB)** in patients with tachycardia and/or hypertension.
- **BB indicated in all patients with LV dysfunction (EF <40%).**
- **Non-dihydropyridine calcium channel blocker** considered in patients without heart failure with continued symptoms already on BB or with contraindication to BB.
- **No role of oxygen unless saturations <93%**
Treatment: Antiplatelet Therapy

- Aspirin lifelong for all.
- Clopidogrel or equivalent should be added and kept for 12 months unless there are contraindications such as excessive bleeding risk.
- Ticagrelor indicated in all-comers, prasugrel only prior PCI in clopidogrel naïve patients without prior stroke/TIA whose anatomy is known, clopidogrel if ticagrelor and prasugrel are not an option.
- Glycoprotein IIb/IIIa in high risk PCI patients, but not routinely upstream.
- A proton pump inhibitor in combination with DAPT is recommended in patients at risk with a previous history of gastrointestinal haemorrhage or peptic ulcer.
Treatment: Anticoagulation

- LMH heparin is preferred to UFH.
- Fondaparinux best benefit/risk profile.
- Consider triple antithrombotic therapy (TOAT) for those with ischaemia and AF.
- For patients on dual antiplatelet therapy who need initiation of oral anticoagulant therapy to prevent embolization in atrial fibrillation, use either dabigatran (thrombin inhibitor) at the 110 mg dose or apixaban (Xa inhibitor) 5 mg (both twice daily) in preference to warfarin.
Treatment: PCI

Ideally the timing of revascularization should be customized according to risk.

- Within 72 hours all patients at risk, but
  - Within 2 hours for very high risk patients (life-threatening symptoms)
  - Within 24 hours for patients with high risk criteria (GRACE score > 140(1), TIMI > 3 (2), troponin release, ST-T changes)

Overview of STEMI in 2014

• Adapted from The ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation (European Heart Journal 2012;33(15))

• And Third universal definition of myocardial infarction. European Heart Journal (2012) 33, 2551–2567
Investigations: Biomarkers Plus

• Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
  – Symptoms of ischaemia.
  – New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).
  – Development of pathological Q waves in the ECG.
  – Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
  – Identification of an intracoronary thrombus by angiography or autopsy.
Investigations: ECG

• Should be obtained within 10min of first medical contact.
• Consider additional leads, if normal.
• New universal definition of MI
• New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).
• Development of pathological Q waves in the ECG.
• New ST elevation at the J point in two contiguous leads with the cut-points: ≥0.1 mV in all leads other than leads V2–V3 where the following cut points apply: ≥0.2 mV in men ≥40 years; ≥0.25 mV in men <40 years, or ≥0.15 mV in women.
New or presumed new significant ST-segment–T wave (ST–T) changes are defined as:

- **New ST elevation at the J point in two contiguous leads with:**
- \( \geq 0.1 \text{ mV} \) in all leads other than leads V2–V3 where the following cut points apply:
  - \( \geq 0.2 \text{ mV} \) in men \( \geq 40 \text{ years} \);
  - \( \geq 0.25 \text{ mV} \) in men \( < 40 \text{ years} \);
  - \( \geq 0.15 \text{ mV} \) in women.
Investigations: Non-invasive

- *Echocardiography should be routinely available in emergency rooms or chest pain units, and used early in all patients.*
- *In the acute phase, when diagnosis is uncertain, emergency echocardiography may be useful. However, if inconclusive or unavailable and persistent doubt, emergency angiography should be considered.*
- *After the acute phase, all patients should have an echocardiography for assessment of infarct size and resting LV function. If echocardiography is not feasible, MRI may be used as an alternative.*
Treatment: Emergency Systems

• The pre-hospital management of STEMI patients must be based on regional networks designed to deliver reperfusion therapy expeditiously and effectively, with efforts made to make primary PCI available to as many patients as possible.

• Primary PCI-capable centres must deliver 24/7 service, be able to start primary PCI as soon as possible and within 60 min from the initial call.
Treatment: Targets

• All hospitals and EMSs participating in the care of patients with STEMI must record and monitor delay times and work to achieve and maintain the following quality targets:
  – First medical contact to first ECG ≤10 min;
  – First medical contact to reperfusion therapy;
    • For fibrinolysis ≤30 min;
    • For primary PCI ≤90 min (≤60 min if the patient presents within 120 minutes of symptom onset or directly to a PCI-capable hospital).
Treatment: Reperfusion Indications

- **Reperfusion therapy is indicated in all patients with symptoms of <12 hours duration and persistent ST-segment elevation or (presumed) new LBBB.**

- **Reperfusion therapy (preferably primary PCI) is indicated if there is evidence of ongoing ischaemia, even if symptoms may have started >12 hours beforehand or if pain and ECG changes have been stuttering.**
Treatment: Thrombolysis Timing

- **Fibrinolytic therapy is recommended within 12 hours of symptom onset in patients without contraindications if primary PCI cannot be performed by an experienced team within 120 min of first medical contact.**

- **In patients presenting early (<2 hours after symptom onset) with a large infarct and low bleeding risk, fibrinolysis should be considered if time from first medical contact to balloon inflation is >90 min.**

- **If possible, fibrinolysis should start in the pre-hospital setting.**
Treatment: Thrombolysis Process

- A fibrin-specific agent (tenecteplase, alteplase, reteplase) is recommended (over non-fibrin specific agents).
- Aspirin must be administered. Clopidogrel is indicated in addition to aspirin.
- Anticoagulation is recommended in STEMI patients treated with lytics until revascularization (if performed) or for the duration of hospital stay up to 8 days. The anticoagulant can be:
  - Enoxaparin i.v followed by s.c. (preferred over unfractionated heparin),
  - Unfractionated heparin given as a weight adjusted IV bolus and infusion,
  - In patients treated with streptokinase, Fondaparinux i.v. bolus followed by s.c. dose 24 hours later.
Treatment: Thrombolysis Process (cont)

• Transfer to a PCI-capable centre following fibrinolysis is indicated in all patients after fibrinolysis.

• Rescue PCI is indicated immediately when fibrinolysis has failed (<50% ST-segment resolution at 60 min).

• Emergency PCI is indicated in the case of recurrent ischaemia or evidence of re-occlusion after initial successful fibrinolysis.

• Emergency angiography with a view to revascularization is indicated in heart failure/shock patients after initial fibrinolysis.
Treatment: Primary PCI Process

• **Primary PCI is the recommended reperfusion therapy over fibrinolysis if performed by an experienced team within 120 minutes of FMC.**
• **Primary PCI is indicated for patients with severe acute heart failure or cardiogenic shock, unless the expected PCI related delay is excessive and the patient presents early after symptom onset.**
• **Stenting is recommended (over balloon angioplasty alone) for primary PCI.**
Treatment: Primary PCI Adjunctive Therapy

- Dual antiplatelet therapy with aspirin and an ADP-receptor blocker is recommended with
  - Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA and age <75
  - Ticagrelor
  - Clopidogrel, if prasugrel or ticagrelor are not available or contraindicated

- An injectable anticoagulant must be used
  - Bivalirudin is preferred over heparin. Enoxaparin may be preferred over unfractionated heparin
  - Unfractionated heparin must be used in patients not receiving either bivalirudin or enoxaparin
Changes in Assessments

- High sensitivity troponins
- Multislice coronary CT angiography
- Post PCI chest pain risk calculator
High Sensitivity Troponins

The new high sensitivity assays achieve increased sensitivity in early diagnosis at the cost of reduced specificity.

The cumulative results for a sensitive TnI for the diagnosis of acute MI, using a cut-off value of 99th centile (0.07 g/L), has been reported as:

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>30min</td>
<td>93%</td>
<td>57%</td>
</tr>
<tr>
<td>2 hours</td>
<td>98%</td>
<td>54%</td>
</tr>
<tr>
<td>3 hours</td>
<td>100%</td>
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</table>

Recommendations for Interpretation of High Sensitivity Troponins

• A test should be interpreted as positive if level is $\geq$99th centile for reference population OR there is a change of $>50\%$ above an initial baseline level.

• At 3 hours after presentation, a test should be interpreted as negative if level is $<99$th percentile AND change from baseline is $<50\%$ (with at least one of these assays having been performed $>6$ hours from symptom onset).
Recommendations for Interpretation of High Sensitivity Troponins

• Simply put:
  – Negative rules our ACS
  – Positive is an indication to investigate further and consider other causes of so called troponinitis.
Causes of Troponinitis

- Cardiac contusion, or other trauma including surgery, ablation, pacing, etc.
- Congestive heart failure—acute and chronic
- Aortic dissection
- Aortic valve disease
- Hypertrophic cardiomyopathy
- Tachy-or bradyarrhythmias, or heart block
- Apical ballooning syndrome
- Rhabdomyolysis with cardiac injury
- Pulmonary embolism, severe pulmonary hypertension
- Renal failure
- Acute neurological disease, e.g. subarachnoid hemorrhage
- Critical illness, e.g. acute neurological disease, including stroke or subarachnoid hemorrhages, and infiltrative diseases, e.g. amyloidosis, hemochromatosis, sarcoidosis, and scleroderma
- Inflammatory diseases, e.g. myocarditis or myocardial extension of endo-/pericarditis
- Drug toxicity or toxins
- Critically ill patients, especially with respiratory failure or sepsis
- Burns, especially if affecting >30% of body surface area
- Extreme exertion
Multislice Coronary CT Angiography

- Increasingly used for low/intermediate risk pretest patients with indeterminate Tni or ECG
- Has limitations:
  - Heart rate greater than 60 or 70 beats/min
  - Irregular heart rhythm (atrial fibrillation or frequent atrial or ventricular extrasystoles)
  - Inability to sustain a breath hold for at least five seconds
  - Severe coronary calcification or the presence of coronary artery stents, since image reconstruction artifacts related to radiodense material such as calcium or metal can obscure the coronary artery lumen
  - Segments with a diameter <1.5 mm can usually not be assessed for stenosis. Such small vessel calibre is typical of distal coronary artery segments and some side branches.
Multislice Coronary CT Angiography

• Limited experience means limited evidence, but:
  – ACCURACY trial (1), 230 patients. Patient-based sensitivity and specificity of CCTA were 95 percent and 83 percent, respectively.
  – CORE 64 study(2), 291 patients. Patient-based sensitivity and specificity of CCTA were 85 percent and 90 percent, respectively.
  – Dutch study, no acronym!(3), 360 patients. Patient-based sensitivity and specificity of CCTA were 99 percent and 64 percent, respectively.

Troponin The New D-Dimer?

• Could we be going the way of pretest low probability
  – check troponin
    • if negative ACS ruled out, OPD EST
    • if positive CTCA?

• High probability
  – check troponin
    • if negative CTCA
    • if positive PCI?

• What is the role of GRACE or TIMI RS scores?
Post PCI Chest Pain Risk Calculator

- Of 36,060 PCI patients surviving to discharge, 10.4% (n = 3,760) were readmitted within 30 days.
- A risk score developed from the pre-PCI model.
- The risk score was able to discriminate among patients at low (< 9%), intermediate (10%-21%) and high risk (> 24%) of 30-day readmission after PCI.

• Yet to be externally validated

• A score of less than 6 denotes low risk, 6 to 10 equals intermediate risk, and ≥ 11 signifies high risk.

### 30-day Readmission after PCI - Risk Calculator

This tool calculates the predicted risk of 30-day readmission for patients undergoing percutaneous coronary intervention (PCI). Using variables known at the time of the procedure, this model can discriminate among patients at low risk (<9%), intermediate risk (10% to 21%), and high risk (>24%) of 30-day readmission after PCI.

This calculator is based on the American Heart Association Circulation: Cardiovascular Quality & Outcomes, July 2013 article, A Prediction Model to Identify Patients at High Risk for 30-Day Readmission After Percutaneous Coronary Intervention, Table 2, by Wasfy, et.al.

Disclaimer: This risk calculator should be used for informational purposes only. If you have questions or concerns about the risk factor results, please consult with your health care provider.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Point Value</th>
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<tbody>
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<td>Cardiogenic shock</td>
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<tr>
<td>Age of patient in years</td>
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<td>Under 50</td>
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<td>50 or older</td>
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<td>Glomerular filtration rate (GFR) in mL/min</td>
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<td>30-60</td>
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<td>Over 60</td>
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<td>Admission Status</td>
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<td>Transfer from acute care facility</td>
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<tr>
<td>Transfer from nursing home</td>
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</tr>
<tr>
<td>Emergency department</td>
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<tr>
<td>None of the above</td>
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<td>Insurance Status</td>
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<td>Medicare/state</td>
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<td>Unknown</td>
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<tr>
<td>Other</td>
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</tr>
</tbody>
</table>

**Predicted 30-Day Readmission:** Low Risk (<9%)
Changes in Treatment Options

- Prehospital thrombolysis
- New antiplatelet drugs particularly ticagrelor
- New oral anti coagulant agents
- New oxygen guidelines
Prehospital Thrombolysis

• Will be a system wide challenge to define the appropriate structure

• Controversies:
  – Medico-legal, whose clinical decision to proceed?
  – Networks? (1)
  – Equipment, limitations in remote areas and moving vehicles
  – Costings

Ticagrelor 180mg load then 90mg BD

• Now preferred to clopidogel
• Binds reversibly rather than irreversibly to P2Y12 platelet receptor and has a more rapid onset of action than clopidogrel
• PLATO trial at 12 months, the composite primary end point (first event of death from vascular causes, MI, or stroke) occurred significantly less often in patients receiving ticagrelor (9.8 versus 11.7 percent, hazard ratio [HR] 0.84, 95% CI 0.77-0.92). There was no significant difference in the rates of major bleeding between the ticagrelor and clopidogrel groups (11.6 versus 11.2 percent respectively)

New Oral Anti Coagulant Agents

• In the RE-LY and ARISTOTLE trials, dabigatran at the 110 mg dose and apixaban at the 5 mg dose (respectively) were found to have a significantly lower incidence of major bleeding than warfarin (as well as equal or better efficacy, respectively).

• This benefit was confirmed (at an abstract presentation during the 2011 European Society of Cardiology Congress) in the subgroup of patients taking dual antiplatelet therapy in RE-LY.

• In the ROCKET-AF trial, there was not a statistically significant difference in the rates of major bleeding or ischaemic outcomes between rivaroxaban and warfarin.
New Oxygen Guidelines

• A 2013 Cochrane review evaluated four trials of 430 patients with presumed myocardial infarction (MI) who were randomly assigned to supplemental oxygen or room air. Enrolled patients were either hypoxic and normoxic. The study found no significant difference in mortality.

• Theoretically hyperoxia, which might occur with the administration of oxygen to normoxic individuals, has been shown to have a direct vasoconstrictor effect on the coronary arteries.
Thank You