DECLARATION OF CONFLICT OF INTEREST
Diagnosis and risk stratification
CONFLICTS OF INTEREST
DISCLOSURE

Consulting fees: Astra-Zeneca, Bayer, BMS, Daichii-Sankyo, Eli-Lilly, Novartis, sanofi-aventis

Research grants: BMS, Pfizer, Roche
ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

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4. Prognosis assessment
5. Treatment
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7. Management strategy

- Step one: initial evaluation
- Step two: diagnosis, validation and risk assessment
- Step three: invasive strategy
- Step four: revascularization modalities
- Step five: hospital discharge and postdischarge management
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7. Management strategy

1. Clinical Evaluation
   - STEMI
   - Reperfusion

2. Diagnosis/Risk Assessment
   - ACS possible
   - Evaluation:
     - Quality of chest pain
     - Symptom-orientated physical examination
     - Short history for the likelihood of CAD
     - Electrocardiogram (ST elevation?)
   - Validation:
     - Response to antianginal treatment
     - Biochemistry/troponin
     - ECG
     - Echocardiogram
     - Calculated risk score (GRACE)
     - Risk criteria (Table 9)
     - Optional: CT, MRI, scintigraphy

3. Coronary angiography
   - Urgent <120 min
   - Early <24 h
   - <72 h
   - No/elective
3. Diagnosis

3.1 Clinical presentation
3.2 Diagnostic tools
   3.2.1 Physical examination
   3.2.2 Electrocardiogram
   3.2.3 Biomarkers
      Point-of-care (bedside) biomarker testing
   3.2.4 Imaging
      Non-invasive imaging techniques
      Invasive imaging (coronary angiography)
3.3 Differential diagnoses
3. Diagnosis

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3.3 Differential diagnoses
3. Diagnosis

Admission → Working diagnosis → ECG → Bio-chemistry → Diagnosis → Chest Pain

Acute Coronary Syndrome

- persistent ST-elevation
- ST/T - abnormalities
- normal or undetermined ECG

troponin rise/fall

troponin normal

STEMI

NSTEMI

Unstable Angina
Figure 2: Rapid rule-out of ACS with high-sensitivity troponin

**Acute Chest Pain**

- **hsTn < ULN**
  - Pain > 6h
  - Re-test hsTn: 3h
    - hsTn no change
      - Painfree, GRACE < 140, differential diagnoses excluded
      - Discharge/Stress testing
    - Δ change* (1 value > ULN)
      - Highly abnormal Tn + clinical presentation
      - Invasive management
  - hsTn < ULN

- **hsTn > ULN**
  - Pain < 6h
  - Re-test hsTn: 3h
    - hsTn no change
      - Work-up differential diagnoses
    - Δ change* (1 value > ULN)
      - Highly abnormal Tn + clinical presentation
      - Invasive management

*hsTn = high-sensitivity troponin; ULN = upper limit of normal, 99th percentile of healthy controls
*Δ change, dependent on assay
Figure 2: Rapid rule-out of ACS with high-sensitivity troponin

Acute Chest Pain

hsTn < ULN

Pain > 6h

Discharge/
Stress testing

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3.1 Clinical presentation

3.2 Diagnostic tools

3.2.1 Physical examination

3.2.2 Electrocardiogram

3.2.3 Biomarkers

- Point-of-care (bedside) biomarker testing

3.2.4 Imaging

- Non-invasive imaging techniques
- Invasive imaging (coronary angiography)

3.3 Differential diagnoses

Therefore, echocardiography should be routinely available in emergency rooms or chest pain units, and used in all patients.

CT angiography, if available at a sufficient level of expertise, may be useful to exclude ACS or other causes of chest pain.

Coronary angiography provides unique information on the presence and severity of CAD and therefore remains the gold standard.

Since the radial approach has been shown to reduce the risk of bleeding when compared with the femoral approach, this access site should be preferred in patients at high risk of bleeding provided the operator has sufficient experience with this technique.
4. Prognosis assessment

4.1 Clinical risk assessment
4.2 Electrocardiogram indicators
   Stress testing for ischaemia
   Continuous ST-segment monitoring
4.3 Biomarkers
   Novel biomarkers
4.4 Risk scores
   Risk scores of outcome
   Bleeding risk scores
4.5 Long-term risk
4. Prognosis assessment

4.1 Clinical risk assessment

4.2 Electrocardiogram indicators
- Stress testing for ischaemia
- Continuous ST-segment monitoring

4.3 Biomarkers
- Novel biomarkers

4.4 Risk scores
- Risk scores of outcome
- Bleeding risk scores

4.5 Long-term risk

- hsCRP
- BNP
- Glycemia
- Haematological markers
- Renal function
- Novel biomarkers
  - Myeloperoxidases
  - GDF 15
  - LPAP
  - PLP-A2
  - FABP
  - IMA
  - Copeptin
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4.5 Long-term risk
# 4.4 Risk scores

Risk scores of outcome

<table>
<thead>
<tr>
<th>Risk category ( tertile )</th>
<th>GRACE risk score</th>
<th>In-hospital death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>≤108</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Intermediate</td>
<td>109–140</td>
<td>1–3</td>
</tr>
<tr>
<td>High</td>
<td>&gt;140</td>
<td>&gt;3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk category ( tertile )</th>
<th>GRACE risk score</th>
<th>Post-discharge to 6-month death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>≤88</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Intermediate</td>
<td>89–118</td>
<td>3-8</td>
</tr>
<tr>
<td>High</td>
<td>&gt;118</td>
<td>&gt;8</td>
</tr>
</tbody>
</table>
### 4.4 Risk scores

#### Bleeding risk scores

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Score</th>
<th>Predictor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline hematocrit, %</td>
<td></td>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>&lt;31</td>
<td>9</td>
<td>Male</td>
<td>0</td>
</tr>
<tr>
<td>31–33.9</td>
<td>7</td>
<td>Female</td>
<td>8</td>
</tr>
<tr>
<td>34–36.9</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37–39.9</td>
<td>2</td>
<td>Signs of CHF at presentation</td>
<td></td>
</tr>
<tr>
<td>≥40</td>
<td>0</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance, mL/min</td>
<td></td>
<td>Diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>≤15</td>
<td>39</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>&gt;15–30</td>
<td>35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30–60</td>
<td>28</td>
<td>Yes</td>
<td>6</td>
</tr>
<tr>
<td>&gt;60–90</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;90–120</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;120</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (b.p.m.)</td>
<td></td>
<td>Systolic blood pressure, mmHg</td>
<td></td>
</tr>
<tr>
<td>≤70</td>
<td>0</td>
<td>≤90</td>
<td>10</td>
</tr>
<tr>
<td>71–80</td>
<td>1</td>
<td>91–100</td>
<td>8</td>
</tr>
<tr>
<td>81–90</td>
<td>3</td>
<td>101–120</td>
<td>5</td>
</tr>
<tr>
<td>91–100</td>
<td>6</td>
<td>121–180</td>
<td>1</td>
</tr>
<tr>
<td>101–110</td>
<td>8</td>
<td>181–200</td>
<td>3</td>
</tr>
<tr>
<td>111–120</td>
<td>10</td>
<td>≥201</td>
<td>5</td>
</tr>
<tr>
<td>≥121</td>
<td>11</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 3:** Risk of major bleeding across the spectrum of CRUSADE bleeding score (www.crusadebleedingscore.org/)

**Table 4: CRUSADE registry bleeding risk score**

Algorithm used to determine the risk score of CRUSADE In-Hospital major bleeding.
4. Prognosis assessment

4.1 Clinical risk assessment
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   Stress testing for ischaemia
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4.5 Long-term risk
Step two: diagnosis validation and risk assessment

After the patient is assigned to the group NSTE-ACS, i.v. and oral antithrombotic treatments will be started according to Table 13. Further management of the patient will be based on additional information/data:

- 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;
- Optional: chest X-ray, CT, MRI or nuclear imaging for differential diagnoses (e.g. aortic dissection, pulmonary embolism, etc.).
- Bleeding risk assessment (CRUSADE score).
**Recommendations for diagnosis and risk stratification**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>I</td>
<td>A</td>
<td>16, 18, 27, 30, 58 56, 57</td>
</tr>
<tr>
<td><strong>ACS patients should be admitted preferably to dedicated chest pain units or coronary care units.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is recommended to use established risk scores for prognosis and bleeding (e.g. GRACE, CRUSADE).</td>
<td>I</td>
<td>B</td>
<td>50, 83</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>B</td>
<td>17, 18</td>
</tr>
<tr>
<td>Additional ECG leads (V_{3R}, V_{4R}, V_{7-8}) are recommended when routine leads are inconclusive.</td>
<td>I</td>
<td>C</td>
<td>18</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>A</td>
<td>27, 30</td>
</tr>
<tr>
<td>A rapid rule-out protocol (0 and 3 h) is recommended when highly sensitive troponin tests are available (see Figure 5).</td>
<td>I</td>
<td>B</td>
<td>20, 21, 23</td>
</tr>
<tr>
<td>An echocardiogram is recommended for all patients to evaluate regional and global LV function and to rule in or rule out differential diagnoses.</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>Coronary angiography is indicated in patients in whom the extent of CAD or the culprit lesion has to be determined (see Section 5.4).</td>
<td>I</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>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.</td>
<td>IIa</td>
<td>B</td>
<td>37-41</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>A</td>
<td>35, 54, 55</td>
</tr>
</tbody>
</table>