2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-Segment Elevation

Prof. Marco Roffi, FESC

University Hospital
Geneva, Switzerland

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)

Authors/Task Force Members: Marco Roffi* (Chairperson) (Switzerland), Carlo Patrono * (Co-Chairperson) (Italy), Jean-Philippe Collet† (France), Christian Mueller† (Switzerland), Marco Valgimigli† (The Netherlands), Felicita Andreotti (Italy), Jeroen J. Bax (The Netherlands), Michael A. Borger (Germany), Carlos Brotons (Spain), Derek P. Chew (Australia), Baris Gencer (Switzerland), Gerd Hasenfuss (Germany), Keld Kjeldsen (Denmark), Patrizio Lancellotti (Belgium), Ulf Landmesser (Germany), Julinda Mehilli (Germany), Debabrata Mukherjee (USA), Robert F. Storey (UK), and Stephan Windecker (Switzerland)
Conflicts of Interest

Research funding

- Abbott vascular
- Biotronik
- Biosensor
- Medtronic
- Boston Scientific

Speaker fees

- Astra Zeneca
Outline

- Diagnosis
- Antiplatelet therapy
- Revascularization
- Long-term prevention
0 h/1 h Rule-in and rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) assays in patients presenting with suspected NSTEMI

*Only applicable if chest pain onset >3h

- Negative predictive value >98% for acute MI
- Positive predictive value 75-80% for acute MI
- Cut-offs for « rule-in » and « rule-out » assay specific
0 h/1 h diagnostic algorithm using high-sensitivity cardiac troponin (hs-cTn) assays

*Only applicable if chest pain onset >3h
+At the time of the publication of the guideline not yet commercially available
## Unstable angina vs NSTEMI

<table>
<thead>
<tr>
<th></th>
<th>UA</th>
<th>NSTEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute cardiomyocyte necrosis</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Risk of death/major arrhythmias</td>
<td>-/+</td>
<td>+++</td>
</tr>
<tr>
<td>Benefit from</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intensified antiplatelet therapy</td>
<td>-/+</td>
<td>+++</td>
</tr>
<tr>
<td>- early revascularization</td>
<td>-/+</td>
<td>+++</td>
</tr>
</tbody>
</table>
## Recommended unit and duration of cardiac rhythm monitoring after established NSTE-ACS diagnosis

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

<sup>a</sup> If none of the following criteria: haemodynamically unstable, major arrhythmias, LVEF <40%, failed reperfusion, additional critical coronary stenoses of major vessels or complications related to percutaneous revascularization.

<sup>b</sup> If one or more of the above criteria are present.
Antiplatelet therapy
### Recommendations for platelet inhibition in NSTE-ACS

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral antiplatelet therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aspirin</strong> is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (in aspirin-naïve patients) and a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>A <strong>P2Y₁₂ inhibitor</strong> is recommended, in addition to aspirin, for <strong>12 months</strong> unless there are contraindications such as excessive risk of bleeds.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>• <strong>Ticagrelor</strong> (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications, 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).</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>• <strong>Prasugrel</strong> (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>• <strong>Clopidogrel</strong> (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>P2Y₁₂ inhibitor</strong> administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.</td>
<td>IIb</td>
<td>A</td>
</tr>
<tr>
<td>It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>
DAPT Duration after PCI with DES: Meta-analysis of RCT

CV Mortality

Total (95% CI) 68/5977 72/6013
Test for heterogeneity: $\chi^2 = 1.40$, df = 5, $P = 0.92$, $I^2 = 0%$
Test for overall effect: $z = 0.31$, $P = 0.76$

Extended 12 month
DAPT\textsuperscript{14,19} 50/5020 52/4941
DES LATE\textsuperscript{20,21} 28/2531 19/2514
Total 78/7551 71/7455
Test for heterogeneity: $\chi^2 = 1.50$, df = 1, $P = 0.22$, $I^2 = 34%$
Test for overall effect: $z = 0.50$, $P = 0.62$

Myocardial infarction

Total (95% CI) 132/7975 120/8020
Test for heterogeneity: $\chi^2 = 3.00$, df = 6, $P = 0.81$, $I^2 = 0%$
Test for overall effect: $z = 0.84$, $P = 0.40$

Extended 12 month
ARCTIC-Interruption\textsuperscript{17,18} 9/645 9/641
DAPT\textsuperscript{14,19} 99/5020 198/4941
DES LATE\textsuperscript{20,21} 19/2531 27/2514
Total 127/8196 234/8096
Test for heterogeneity: $\chi^2 = 3.16$, df = 2, $P = 0.21$, $I^2 = 37%$
Test for overall effect: $z = 3.75$, $P = 0.001$

Short term vs 12 month

Mainly stable CAD

Navarese et al, BMJ 2015;350:h1618
### Major Bleeding

<table>
<thead>
<tr>
<th>Study</th>
<th>Short term</th>
<th>12 month</th>
<th>Weight (%)</th>
<th>Odds ratio (95% CI) M-H, fixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXCELLENT</td>
<td>2/722</td>
<td>4/721</td>
<td>8.1</td>
<td>0.50 (0.09 to 2.73)</td>
</tr>
<tr>
<td>ISAR-SAFE</td>
<td>4/1998</td>
<td>5/2007</td>
<td>10.2</td>
<td>0.80 (0.22 to 3.00)</td>
</tr>
<tr>
<td>ITALIC</td>
<td>0/926</td>
<td>3/924</td>
<td>7.1</td>
<td>0.14 (0.01 to 2.75)</td>
</tr>
<tr>
<td>OPTIMIZE</td>
<td>10/1605</td>
<td>14/1606</td>
<td>28.4</td>
<td>0.71 (0.32 to 1.61)</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>5/983</td>
<td>9/987</td>
<td>18.2</td>
<td>0.56 (0.19 to 1.66)</td>
</tr>
<tr>
<td>RESET</td>
<td>2/1059</td>
<td>6/1058</td>
<td>12.2</td>
<td>0.33 (0.07 to 1.65)</td>
</tr>
<tr>
<td>SECURITY</td>
<td>5/682</td>
<td>8/717</td>
<td>15.8</td>
<td>0.65 (0.21 to 2.01)</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>28/7975</strong></td>
<td><strong>49/8020</strong></td>
<td><strong>100.0</strong></td>
<td><strong>0.58 (0.36 to 0.92)</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2=1.90$, df=6, $P=0.93$, $I^2=0\%$

Test for overall effect: $z=2.21$, $P=0.02$

---

### Extended vs 12 month

<table>
<thead>
<tr>
<th>Study</th>
<th>Extended</th>
<th>12 month</th>
<th>Weight (%)</th>
<th>Odds ratio (95% CI) M-H, fixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARCTIC-Interruption</td>
<td>7/645</td>
<td>1/641</td>
<td>1.0</td>
<td>7.02 (0.86 to 57.24)</td>
</tr>
<tr>
<td>DAPT</td>
<td>119/5020</td>
<td>73/4941</td>
<td>74.4</td>
<td>1.62 (1.21 to 2.17)</td>
</tr>
<tr>
<td>DES LATE</td>
<td>34/2531</td>
<td>24/2514</td>
<td>24.6</td>
<td>1.41 (0.84 to 2.39)</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>160/8196</strong></td>
<td><strong>98/8096</strong></td>
<td><strong>100.0</strong></td>
<td><strong>1.62 (1.26 to 2.09)</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2=2.14$, df=2, $P=0.34$, $I^2=7\%$

Test for overall effect: $z=3.75$, $P<0.001$

---

Navarese et al, BMJ 2015;350:h1618
### Recommendations for platelet inhibition in NSTE-ACS (continued)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long-term P2Y&lt;sub&gt;12&lt;/sub&gt; inhibition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2Y&lt;sub&gt;12&lt;/sub&gt; inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischaemic and bleeding risks of the patient.</td>
<td>IIb</td>
<td>A</td>
</tr>
</tbody>
</table>

<sup>a</sup> Class: I, IIa, IIb, IIIa, IIIb

<sup>b</sup> Level: A, B, C
## META-ANALYSIS OF TRIALS EVALUATING PROLONGED DAPT FOLLOWING MI

<table>
<thead>
<tr>
<th>Trial</th>
<th>Subgroup /Population</th>
<th>N</th>
<th>Drug</th>
<th>Duration (months)</th>
<th>MACE Events</th>
<th>Bleeding EP</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHARISMA</td>
<td>Stable prior MI (mean 24 mo.)</td>
<td>3846</td>
<td>Clopi</td>
<td>28</td>
<td>287</td>
<td>GUSTO mod/severe</td>
</tr>
<tr>
<td>PRODIGY</td>
<td>PCI for ACS</td>
<td>1465</td>
<td>Clopi</td>
<td>6 vs. 24</td>
<td>132</td>
<td>TIMI major</td>
</tr>
<tr>
<td>ARCTIC-Interruption</td>
<td>PCI for ACS (excluded STEMI)</td>
<td>323</td>
<td>Clopi or Pras</td>
<td>12 vs. 24</td>
<td>7</td>
<td>STEEPLE major</td>
</tr>
<tr>
<td>DAPT</td>
<td>PCI for MI</td>
<td>3576</td>
<td>Clopi or Pras</td>
<td>12 vs. 30</td>
<td>167</td>
<td>GUSTO mod/severe</td>
</tr>
<tr>
<td>DES-Late</td>
<td>PCI for ACS</td>
<td>3063</td>
<td>Clopi</td>
<td>12 vs. 24</td>
<td>122</td>
<td>TIMI major</td>
</tr>
<tr>
<td>PEGASUS TIMI-54</td>
<td>Stable prior MI (median 20 mo.)</td>
<td>21162</td>
<td>Ticag</td>
<td>33</td>
<td>1558</td>
<td>TIMI major</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>33435</td>
<td></td>
<td>30</td>
<td>2273</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Clopi: clopidogrel; Pras: prasugrel; Ticag: ticagrelor
META-ANALYSIS: INDIVIDUAL CV AND BLEEDING ENDPOINTS

1. **MACE**
   - Extended DAPT: 6.4%
   - Aspirin Alone: 7.5%
   - HR 0.78, P = 0.001

2. **CV Death**
   - Extended DAPT: 2.3%
   - Aspirin Alone: 2.6%
   - HR 0.85, P = 0.03

3. **MI**
   - Extended DAPT: 3.5%
   - Aspirin Alone: 4.4%
   - HR 0.70, P = 0.003

4. **Stroke**
   - Extended DAPT: 1.4%
   - Aspirin Alone: 1.7%
   - HR 0.81, P = 0.02

5. **Stent Thrombosis (Def/Prob)**
   - Extended DAPT: 0.6%
   - Aspirin Alone: 1.4%
   - HR 0.50, P = 0.02

---

**Extended DAPT vs. Aspirin Alone**

- **MACE**
  - HR 0.78, P = 0.001

- **CV Death**
  - HR 0.85, P = 0.03

- **MI**
  - HR 0.70, P = 0.003

- **Non-CV Death**
  - HR 0.81, P = 0.02

- **Stent Thrombosis (Def/Prob)**
  - HR 0.50, P = 0.02

---

**Extended DAPT vs. Aspirin Alone**

- **Major Bleeding**
  - HR 1.9, P = 0.004

- **ICH**
  - HR 1.1, P = NS

- **Fatal Bleeding**
  - HR 0.4, P = NS

- **Non-CV Death**
  - HR 1.7, P = NS

- **All-Cause Death**
  - HR 1.4, P = NS

---

**Follow-up**

- **HR 1.73**, P = 0.004
- **HR 1.05**, P = 0.004
- **HR 0.92**, P = NS

---

J. Udell (Toronto, CA) FP 3913
Timing of P2Y$_{12}$ inhibitor initiation

As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated. Based on the ACCOAST results, pretreatment with prasugrel is not recommended.
Selection of NSTE-ACS treatment strategy

Risk Stratification

- Very high
  - Immediate invasive (<2hr)
  - Early invasive (<24hr)
  - Invasive (<72hr)

- High
  - Immediate transfer to PCI center
  - Same day transfer

- Intermediate
  - Transfer

- Low
  - Non-invasive testing if appropriate
  - Optional

Therapeutic strategy

First medical contact -> NSTE-ACS diagnosis

- PCI center
- EMS or Non-PCI center

Symptoms Onset

Immediate transfer to PCI center

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**Invasive Management in NSTE-ACS**


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**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
INVASIVE MANAGEMENT IN NSTE-ACS


High-risk criteria:
- Rise or fall in cardiac troponin compatible with MI
- Dynamic ST- or T-wave changes (symptomatic or silent)
- GRACE score >140
**Invasive Management in NSTE-ACS**


**Intermediate-risk criteria**

- Diabetes mellitus
- Renal insufficiency (eGFR <60 mL/min/1.73 m²)
- 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
MATRIX
Co-primary composite outcomes at 30 days

• N=8404
• NSTE-ACS + STEMI
• Radial vs. femoral

Valgimigli M et al. 
Lancet. 2015;385:2465-76

All-cause mortality, MI, stroke

Rate ratio 0.85; 95% CI 0.74–0.99, p=0.0307

All-cause mortality, MI, stroke, or BARC 3 or 5 bleeding

Rate ratio 0.83; 95% CI 0.73–0.96, p=0.0092
Radial vs femoral meta-analysis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-CABG major bleeds</td>
<td>0.58 (0.46–0.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death, MI, or stroke</td>
<td>0.86 (0.77–0.95)</td>
<td>0.0051</td>
</tr>
<tr>
<td>Death</td>
<td>0.72 (0.60–0.88)</td>
<td>0.0011</td>
</tr>
<tr>
<td>MI</td>
<td>0.91 (0.79–1.04)</td>
<td>0.16</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.05 (0.69–1.60)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Valgimigli M et al.
Lancet. 2015;385:2465-76

N>19,000

Favours radial access

Favours femoral access
## Radial approach

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class\textsuperscript{a}</th>
<th>Level\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>In centres experienced with radial access, a radial approach is recommended for coronary angiography and PCI.</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

- It is recommended that centres treating ACS patients implement a transition from transfemoral to transradial access.

- Proficiency in the femoral approach should be maintained (e.g. for IABP insertion and structural as well as peripheral procedures)
# Drug-eluting stents

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients undergoing PCI, new-generation DESs are recommended.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>In patients in whom a short DAPT duration (30 days) is planned because of an increased bleeding risk, a new-generation DES may be considered over a BMS.</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

*Valgimigli M et al. J Am Coll Cardiol 2015;65: 805–15*
a) Dual therapy with OAC and clopidogrel may be considered in selected patients (low ischaemic risk).

b) Aspirin as an alternative to clopidogrel may be considered in patients on dual therapy (i.e., oral anticoagulation plus single antiplatelet) Triple therapy may be considered up to 12 months in patients at very high risk for ischaemic events.

c) Dual therapy with oral anticoagulation and an antiplatelet agent (aspirin or clopidogrel) beyond one year may be considered in patients at very high risk of coronary events. In patients undergoing coronary stenting, dual antiplatelet therapy may be an alternative to triple or dual therapy if the CHA2DS2-VASc score is 1 (males) or 2 (females).
## Long-term prevention

<table>
<thead>
<tr>
<th>It is recommended to start high-intensity statin therapy as early as possible, unless contraindicated, and maintain it long-term.</th>
<th>Class(^a)</th>
<th>Level(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

| In patients with LDL-cholesterol \(\geq 70\, \text{mg/dL} \geq 1.8\, \text{mmol/L}\) despite a maximally tolerated statin dose, further reduction in LDL-cholesterol with a non-statin agent\(^e\) should be considered. | IIa | B |

\(^e\) At the time of finalizing these guidelines this recommendation applies only to ezetimibe
Help to implement GL in daily practice

• 40 cases each
• No reference
• Link to the dedicated sections of the GL

European Heart Journal
doi:10.1093/eurheartj/ehv409

European Heart Journal

European Heart Journal
doi:10.1093/eurheartj/ehv408

www.escardio.org

Questions and answers on diagnosis and risk assessment: a companion document of the 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-Segment Elevation†

Authors: Christian Mueller¹, Carlo Patrono², Marco Valgimigli³, Jean-Philippe Collet⁴, and Marco Roffi⁵

Questions and answers on antithrombotic therapy: a companion document of the 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-Segment Elevation†

Authors: Jean-Philippe Collet¹, Marco Roffi², Christian Mueller³, Marco Valgimigli⁴, Carlo Patrono⁵

Questions and answers on coronary revascularization: a companion document of the 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation†

Authors: Marco Valgimigli¹, Carlo Patrono², Jean-Philippe Collet³, Christian Mueller⁴, Marco Roffi⁵

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