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Intermountain Project ECHO
Hospitalist Medicine

NSTE-ACS:
Diagnosis & Acute Management

September 15, 2021

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Intermountain Healthcare
Disclosure

The content of this presentation does not relate to any product of a commercial entity; therefore, I have no relationships to report.

Off-label indications will not be discussed.
Objectives

At the conclusion of this activity, participants should be able to successfully:

• Differentiate NSTE-ACS from other chest pain syndromes.
• Apply published risk stratification tools to guide further management of NSTE-ACS
• Manage the acute care needs of patients with NSTE-ACS
• Collaborate with the cardiovascular team in the diagnosis & management of NSTE-ACS
Diagnosis of NSTE-ACS
Pathophysiology of Acute Coronary Syndromes
Symptomatic Coronary Atherosclerosis

- Plaque formation
- Weakening of fibrosis cap
- Plaque rupture
- Platelet aggregation
- Thrombus formation
- Decreased coronary blood flow
## Risk Factors for ASCVD & CAD Equivalents

### Risk Factors for ASCVD
- Hypertension
- Cigarette Smoking
- High LDL (> 130 mg/dL)
- Low HDL
  - Males: < 40 mg/dL
  - Females: < 50 mg/dL
- Family History of Premature CAD
- Age
  - Males ≥ 45 years old
  - Females ≥ 55 years old

### CAD Risk Equivalents
- Peripheral Vascular Disease
  - Claudication
  - ABI < 0.9
- Diabetes
- Framingham Risk Score > 20 %
- Aortic Aneurysm
- Symptomatic Carotid Artery Dz
  - Stroke
  - TIA
Assessment of Chest Pain
Clinical Classification of Chest Pain

Typical Angina (definite)
- (1) Substernal chest discomfort with a characteristic quality and duration that is:
  - (2) Provoked by exertional or emotional stress
  - (3) Relieved by rest or nitroglycerin

Atypical Angina (probable)
- Meets 2 of the above characteristics

Non-Cardiac Pain
- Meets 1 or none of the typical angina chest characteristics
# Initial Assessment of Chest Pain

## TABLE 4  Summary of Recommendations for Prognosis: Early Risk Stratification

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform rapid determination of likelihood of ACS, including a 12-lead ECG within 10 min of arrival at an emergency facility, in patients whose symptoms suggest ACS</td>
<td>I</td>
<td>C</td>
<td>(21)</td>
</tr>
<tr>
<td>Perform serial ECGs at 15- to 30-min intervals during the first hour in symptomatic patients with initial nondiagnostic ECG</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Measure cardiac troponin (cTnI or cTnT) in all patients with symptoms consistent with ACS*</td>
<td>I</td>
<td>A</td>
<td>(21,64,67–71)</td>
</tr>
<tr>
<td>Measure serial cardiac troponin I or T at presentation and 3–6 h after symptom onset* in all patients with symptoms consistent with ACS</td>
<td>I</td>
<td>A</td>
<td>(21,72–74)</td>
</tr>
<tr>
<td>Use risk scores to assess prognosis in patients with NSTE-ACS</td>
<td>I</td>
<td>A</td>
<td>(42–44,75–80)</td>
</tr>
<tr>
<td>Risk-stratification models can be useful in management</td>
<td>Ila</td>
<td>B</td>
<td>(42–44,75–81)</td>
</tr>
<tr>
<td>Obtain supplemental electrocardiographic leads V₇ to V₉ in patients with initial nondiagnostic ECG at intermediate/high risk for ACS</td>
<td>Ila</td>
<td>B</td>
<td>(82–84)</td>
</tr>
<tr>
<td>Continuous monitoring with 12-lead ECG may be a reasonable alternative with initial nondiagnostic ECG in patients at intermediate/high risk for ACS</td>
<td>IIb</td>
<td>B</td>
<td>(85,86)</td>
</tr>
<tr>
<td>BNP or NT-pro-BNP may be considered to assess risk in patients with suspected ACS</td>
<td>IIb</td>
<td>B</td>
<td>(87–91)</td>
</tr>
</tbody>
</table>

*See Section 3.4, Class I, #3 recommendation if time of symptom onset is unclear.

ACS indicates acute coronary syndromes; BNP, B-type natriuretic peptide; COR, Class of Recommendation; cTnI, cardiac troponin I; cTnT, cardiac troponin T; ECG, electrocardiogram; LOE, Level of Evidence; N/A, not available; NSTE-ACS, non–ST-elevation acute coronary syndromes; and NT-pro-BNP, N-terminal pro-B-type natriuretic peptide.
# Differential Diagnosis of Chest Pain

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
</table>
| **Cardiovascular** | Acute Coronary Syndrome  
  Pericarditis  
  Hypertrophic Obstructive Cardiomyopathy  
  Acute aortic dissection  
  Aortic or Mitral stenosis |
| **Pulmonary**    | Pulmonary embolism  
  Pleuritis  
  Pneumonia  
  Tracheobronchitis  
  Pneumothorax |
| **Gastrointestinal** | Gastroesophageal reflux/Peptic ulcer disease  
  Esophageal spasm  
  Biliary colic  
  Pancreatitis |
| **Musculoskeletal** | Costochondritis  
  Spinal disease |
| **Infection**    | Shingles |
| **Psychological** | Anxiety attacks |
Definition of Myocardial Infarction

Myocardial Injury

• Evidence of elevated cardiac troponin values (cTn) with at least one value above the 99th percentile of upper reference limit (URL).
  • Acute: rise and/or fall of cTn values

Myocardial Infarction

• Clinical Definition: Acute myocardial injury + acute myocardial ischemia
  • Type 1: Acute atherothrombotic plaque disruption
  • Type 2: Oxygen supply & demand mismatch
  • Type 3: Sudden Cardiac Death
  • Type 4: MI associated with PCI
  • Type 5: MI associated with CABG
Type 1 MI

Criteria for type 1 MI
Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and with at least one of the following:

- Symptoms of acute myocardial ischaemia;
- New ischaemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology;
- Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.\(^a\)
Type 2 MI

Criteria for type 2 MI
Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to coronary thrombosis, requiring at least one of the following:

- Symptoms of acute myocardial ischaemia;
- New ischaemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology.
Type 2 MI: Consider Clinical Context & Pathophysiological Mechanisms Attributable to Acute Myocardial Ischemia

Type 2 myocardial infarction

Context
- Secondary to another illness or process
- Main reason leading to clinical presentation (e.g., chest pain)

Mechanisms
- Oxygen supply and demand imbalance
  - Fixed coronary atherosclerosis
  - Coronary spasm
  - Coronary microvascular dysfunction
  - Coronary embolism
  - Coronary artery dissection +/- Intramural haematoma
  - Sustained tachyarrhythmia
  - Severe hypertension +/- Left ventricular hypertrophy
  - Severe bradyarrhythmia
  - Respiratory failure
  - Severe anaemia
  - Hypotension/Shock

*aIschaemic thresholds vary substantially in relation to the magnitude of the stressor and the extent of underlying cardiac disease.
Attributing Troponin Elevations

TROPNIN POSITIVE

Clinical evidence of overt ischemia
- New symptoms of acute myocardial ischemia and / or
- New ischemic ECG changes and / or
- Imaging shows new infarction or wall motion abnormality
- Serial troponins show characteristic rise and fall

Acute coronary thrombus or plaque rupture on angiography (or strongly suspected when angiography unavailable or otherwise contraindicated)

Clinical context supports myocardial oxygen supply-demand mismatch

Document "Type 1 MI" (e.g., "STEMI" or "NSTEMI")

Cardiac causes:
- Tachyarrhythmias (e.g., ATRI)
- Bradycardia
- Severe aortic valve disease
- Hypertrophic cardiomyopathy
- Acute heart failure
- Coronary vasospasm
- Coronary embolism
- Coronary vasculitis
- Spontaneous coronary artery dissection (SCAD)

Systemic causes:
- Hypertensive emergency
- Non-cardiac surgery
- Critical illness
- Shock (cardiogenic or hypovolemic)
- Hypoxic respiratory failure
- Severe anemia (acute blood loss, hemolysis)

No overt ischemia
- No ischemic symptoms, ECG changes, or imaging findings
- Serial troponins show little variation, or show rise and fall

Document "Non-MI troponin elevation secondary to [underlying cause]"

Cardiac causes:
- Tachyarrhythmias (e.g., ATRI)*
- Bradycardia
- Severe aortic valve disease
- Hypertrophic cardiomyopathy
- Acute heart failure
- Stress cardiomyopathy (tako-tsubo)
- Blunt cardiac injury (contusion)
- CPR (chest compressions)
- Defibrillator shocks
- Cardiac ablation
- Cardiac (non-CABG) surgery
- Myocarditis / pericarditis
- Endocarditis
- Cardiotoxic agents, chemotherapy
- Infiltrative disease (amyloid, sarcoid)
- Cardiac tumors / malignancies
- Myopathies / muscular dystrophies

Systemic causes:
- Hypertensive emergency*
- Non-cardiac surgery*
- Critical illness*
- Pulmonary embolism
- Pulmonary hypertension
- Sepsis
- Renal failure / ESRD
- Stroke
- Subarachnoid hemorrhage
- Rhodanomysis
- Strenuous exercise
- Burn injuries to body
- Diabetic ketoacidosis
- Hemolysis
- Other emerging causes

AFRVR: atrial fibrillation with rapid ventricular response; CABG: coronary artery bypass graft surgery; ECG: electrocardiogram; ESRD: end-stage renal disease; MI: myocardial infarction; SCAD: spontaneous coronary artery dissection.

* These conditions may cause either a type 2 MI or a non-MI troponin elevation. The presence or absence of overt symptoms of acute myocardial ischemia, new ischemic ECG changes, imaging showing new MI or wall motion abnormality, and/or findings on coronary angiography may help distinguish the two.
Early Cardiac Risk Stratification
TIMI Risk Score for UA/NSTEMI

Estimates mortality for patients with unstable angina and non-ST elevation MI.

<table>
<thead>
<tr>
<th>When to Use</th>
<th>Pearls/Pitfalls</th>
<th>Why Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65</td>
<td>No</td>
<td>Yes +1</td>
</tr>
<tr>
<td>≥3 CAD risk factors</td>
<td>No</td>
<td>Yes +1</td>
</tr>
<tr>
<td>Hypertension, hypercholesterolemia, diabetes, family history of CAD, or current smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Known CAD (stenosis ≥50%)</td>
<td>No</td>
<td>Yes +1</td>
</tr>
<tr>
<td>ASA use in past 7 days</td>
<td>No</td>
<td>Yes +1</td>
</tr>
<tr>
<td>Severe angina (≥2 episodes in 24 hrs)</td>
<td>No</td>
<td>Yes +1</td>
</tr>
<tr>
<td>EKG ST changes ≥0.5mm</td>
<td>No</td>
<td>Yes +1</td>
</tr>
<tr>
<td>Positive cardiac marker</td>
<td>No</td>
<td>Yes +1</td>
</tr>
</tbody>
</table>

0 points

5% risk at 14 days of all-cause mortality, new or recurrent MI, or severe recurrent ischemia requiring urgent revascularization.
GRACE

ACS Risk Model

At Admission (in-hospital/to 6 months) | At Discharge (to 6 months)
--- | ---
Age | Years
HR | bpm
SBP | mmHg
Creat. | mg/dL
CHF | Killip Class

- Cardiac arrest at admission
- ST-segment deviation
- Elevated cardiac enzymes/markers

<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>

https://www.outcomes-umassmed.org/grace/
# HEART Score

<table>
<thead>
<tr>
<th>History (Anamnesis)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly suspicious</td>
<td>2</td>
</tr>
<tr>
<td>Moderately suspicious</td>
<td>1</td>
</tr>
<tr>
<td>Slightly suspicious</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ECG</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant ST-deviation</td>
<td>2</td>
</tr>
<tr>
<td>Non-specific repolarisation</td>
<td>1</td>
</tr>
<tr>
<td>disturbance / LBBB / PM</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 65 years</td>
<td>2</td>
</tr>
<tr>
<td>45 – 65 years</td>
<td>1</td>
</tr>
<tr>
<td>≤ 45 years</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 3 risk factors or history</td>
<td>2</td>
</tr>
<tr>
<td>of atherosclerotic disease</td>
<td></td>
</tr>
<tr>
<td>1 or 2 risk factors</td>
<td>1</td>
</tr>
<tr>
<td>No risk factors known</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Troponin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 3x normal limit</td>
<td>2</td>
</tr>
<tr>
<td>1-3x normal limit</td>
<td>1</td>
</tr>
<tr>
<td>≤ normal limit</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HEART</th>
<th>~ % pts</th>
<th>MACE/n</th>
<th>MACE</th>
<th>Death</th>
<th>Proposed Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>32%</td>
<td>38/1993</td>
<td>1.9%</td>
<td>0.05%</td>
<td>Discharge</td>
</tr>
<tr>
<td>4-6</td>
<td>51%</td>
<td>413/3136</td>
<td>13%</td>
<td>1.3%</td>
<td>Observation, risk management</td>
</tr>
<tr>
<td>7-10</td>
<td>17%</td>
<td>518/1045</td>
<td>50%</td>
<td>2.8%</td>
<td>Observation, treatment, CAG</td>
</tr>
</tbody>
</table>

Risk factors for atherosclerotic disease:
- Hypercholesterolemia
- Cigarette smoking
- Hypertension
- Positive family history
- Diabetes Mellitus
- Obesity (BMI > 30)
High-Risk Clinical Risk Factors for Short-Term Adverse Risk

TABLE A

High-Risk Features for Short-Term Risk of Death or Nonfatal MI in Patients With NSTEMI/UA

At least 1 of the following:
- History—accelerating tempo of anginal symptoms in preceding 48 hours
- Character of pain—prolonged ongoing (>20 minutes) rest pain
- Clinical findings
  - Pulmonary edema, most likely due to ischemia
  - New or worsening MR murmur
  - S₃ or new/worsening rales
  - Hypotension, bradycardia, tachycardia
  - Age >75 years
- ECG
  - Transient ST-segment deviation >0.5 mm
  - Bundle-branch block, new or presumed new
  - Sustained ventricular tachycardia
- Cardiac marker
  - Elevated cardiac TnT, Tnl, or CK-MB (e.g., TnT or Tnl >0.1 ng per ml)
Management of NSTE-ACS
Management Strategies

NSTE-ACS: Definite or Likely

- Ischemia-Guided Strategy
- Early Invasive Strategy
NSTE-ACS: Definite or Likely

Ischemia-Guided Strategy

- Initiate DAPT and Anticoagulant Therapy
  1. ASA (Class I; LOE: A)
  2. P2Y₁₂ inhibitor (in addition to ASA) (Class I; LOE: B):
     - Clopidogrel or
     - Ticagrelor
  3. Anticoagulant:
     - UFH (Class I; LOE: B) or
     - Enoxaparin (Class I; LOE: A) or
     - Fondaparinux (Class I; LOE: B)

Early Invasive Strategy

- Initiate DAPT and Anticoagulant Therapy
  1. ASA (Class I; LOE: A)
  2. P2Y₁₂ inhibitor (in addition to ASA) (Class I; LOE: B):
     - Clopidogrel or
     - Ticagrelor
  3. Anticoagulant:
     - UFH (Class I; LOE: B) or
     - Enoxaparin (Class I; LOE: A) or
     - Fondaparinux (Class I; LOE: B) or
     - Bivalirudin (Class I; LOE: B)

Can consider GPI in addition to ASA and P2Y₁₂ inhibitor in high-risk (e.g., troponin positive) pts (Class IIb; LOE: B)
- Eptifibatide
- Tirofiban
Historic Rationale for Conservative Therapy

Effects of Tissue Plasminogen Activator and a Comparison of Early Invasive and Conservative Strategies in Unstable Angina and Non–Q-Wave Myocardial Infarction
Results of the TIMI IIIB Trial

The TIMI IIIB Investigators

TIMI IIIB trial
- ~1400 patients with UA or NQWMI
- 2x2 factorial design
  - Initial Therapy: TPA vs Placebo and early invasive vs early conservative therapy
- Primary end-point: Death, MI, or positive ETT by the 6-week follow-up
  - Primary end-point occurred in 16% of Invasive 18% conservative (p=NS)

<table>
<thead>
<tr>
<th>Table 5. Outcome According to Strategy at 6-Week Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Invasive (n=743)</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>Nonfatal MI</td>
</tr>
<tr>
<td>36</td>
</tr>
<tr>
<td>Positive 6-wk ETT</td>
</tr>
<tr>
<td>64</td>
</tr>
<tr>
<td>Total (primary end point)</td>
</tr>
<tr>
<td>120</td>
</tr>
<tr>
<td>Average length of initial hospitalization, d</td>
</tr>
<tr>
<td>No. of patients rehospitalized within 6 wk*</td>
</tr>
<tr>
<td>No. of days of rehospitalization within 6 wk*</td>
</tr>
<tr>
<td>Number of antianginal medications†</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>CCSC status at 6 wk†</td>
</tr>
<tr>
<td>No angina</td>
</tr>
<tr>
<td>Class I or II</td>
</tr>
<tr>
<td>Class III or IV</td>
</tr>
</tbody>
</table>

[Note: Table 5 details outcomes comparison between Early Invasive and Early Conservative strategies at 6-week visit, including death, non-fatal MI, positive ETT, total primary endpoint, hospitalization length, and antianginal medication usage. P-values indicate statistical significance between early invasive and conservative strategies.]
Historic Rationale for Invasive therapy

Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators

FRISC II

• ~2460 randomized to invasive vs. conservative treatment strategy with (dalteparin)
• Primary endpoint: Death or MI within 6 mo
  • 9.4% in the invasive group, 12.1% in the non-invasive group (p=0.031): primarily driven by MI.
  • Symptoms of angina and re-admission were halved by the invasive strategy.
Current Practice Justification for Invasive Therapy

Decreased Risk for Subsequent Hospitalizations & further therapies
- PCI of the culprit lesion vs conservative management

Decreased early hazard of PCI
- Adjuvant therapy with GP IIb/IIIa and thienopyridines
NSTEMI – Time to Coronary Angiography & Outcomes

<table>
<thead>
<tr>
<th>Trials</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>VERDICT (2018)</td>
<td>2147</td>
</tr>
<tr>
<td>TIMACS (2009)</td>
<td>3031</td>
</tr>
<tr>
<td>SISCA (2015)</td>
<td>170</td>
</tr>
<tr>
<td>Sciahsisi et al (2010)</td>
<td>54</td>
</tr>
<tr>
<td>RIDDLE-NSTEMI (2016)</td>
<td>323</td>
</tr>
<tr>
<td>LIPSIA-NSTEMI (2012)</td>
<td>400</td>
</tr>
<tr>
<td>ISAR-COOL (2003)</td>
<td>410</td>
</tr>
<tr>
<td>ELISA-3 (2013)</td>
<td>534</td>
</tr>
<tr>
<td>ELISA (2003)</td>
<td>220</td>
</tr>
<tr>
<td>EARLY (2020)</td>
<td>709</td>
</tr>
<tr>
<td>ABOARD (2009)</td>
<td>352</td>
</tr>
</tbody>
</table>

**Primary endpoint finding**

- No difference in composite endpoint
- No difference in composite endpoint
- \( \triangle \) in MACE
- No difference in post-PCI myocardial blush grade
- \( \triangle \) in death or new MI
- No \( \triangle \) in CK-MB
- \( \triangle \) in death or large MI
- No difference in composite endpoint
- More enzymatic infarct size
- \( \triangle \) in cardiovascular death and recurrent ischaemic events
- No reduction in peak troponin level
ESC 2020 NSTEMI Guidelines – Treatment Strategy

- **Symptom onset**
  - First medical contact → NSTE-ACS diagnosis

- **Risk Identification**
  - **PCI center**
    - **YES** → **Very High**
    - Immediate invasive (< 2 h)
  - **EMS or Non-PCI center**
    - **YES** → **Very High**

- **Therapeutic Strategy**
  - **High**
    - **YES** → Immediate transfer to PCI center
    - Same day transfer
  - **Low**
    - **YES** → Selective Invasive

- **Risk Category**
  - **Very high risk**
    - Haemodynamic instability
    - Cardiogenic shock
    - Recurrent/refractory chest pain despite medical treatment
    - Life-threatening arrhythmias
    - Mechanical complications of MI
    - Acute heart failure clearly related to NSTE-ACS
    - ST-segment depression ≥1 mm/6 leads plus ST-segment elevation aVR and/or V1
  - **High risk**
    - Established NSTEMI diagnosis
    - Dynamic new or presumably new contiguous ST/T-segment changes (symptomatic or silent)
    - Resuscitated cardiac arrest without ST-segment elevation or cardiogenic shock
    - GRACE risk score >140
  - **Low risk**
    - Lack of any of the very high or high risk characteristics
| Immediate invasive  (within 2 h) | Refractory angina  
|---------------------------------|------------------
|  | 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 (e.g., TIMI [0 or 1], GRACE [<109])  
|  | 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  
|  | 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 m²)  
|  | Reduced LV systolic function (EF < 0.40)  
|  | Early postinfarction angina  
|  | PCI within 6 mo  
|  | Prior CABG  
|  | GRACE risk score 109–140; TIMI score ≥2  

Initial Medications for NSTE-ACS
## Initial Medical Management

### TABLE 6  Summary of Recommendations for Early Hospital Care

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxygen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer supplemental oxygen only with oxygen saturation &lt; 90%, respiratory</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>distress, or other high-risk features for hypoxemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nitrites</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer sublingual NTG every 5 min × 3 for continuing ischemic pain and then</td>
<td>I</td>
<td>C</td>
<td>(216-218)</td>
</tr>
<tr>
<td>assess need for IV NTG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer IV NTG for persistent ischemia, HF, or hypertension</td>
<td>I</td>
<td>B</td>
<td>(219-224)</td>
</tr>
<tr>
<td>Nitrate are contraindicated with recent use of a phosphodiesterase inhibitor</td>
<td>III: Harm</td>
<td>B</td>
<td>(225-227)</td>
</tr>
<tr>
<td><strong>Analgesic therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV morphine sulfate may be reasonable for continued ischemic chest pain</td>
<td>IIb</td>
<td>B</td>
<td>(232,233)</td>
</tr>
<tr>
<td>despite maximally tolerated anti-ischemic medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs (except aspirin) should not be initiated and should be discontinued</td>
<td>III: Harm</td>
<td>B</td>
<td>(234,35)</td>
</tr>
<tr>
<td>during hospitalization for NSTE-ACS because of the increased risk of MACE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>associated with their use</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Initial Medical Management

## Summary of Recommendations for Early Hospital Care

<table>
<thead>
<tr>
<th>Recommendations</th>
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<tbody>
<tr>
<td><strong>Beta-adrenergic blockers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate oral beta blockers within the first 24 h in the absence of HF, low-output state, risk for cardiogenic shock, or other contraindications to beta blockade</td>
<td>I</td>
<td>A</td>
<td>(240-242)</td>
</tr>
<tr>
<td>Use of sustained-release metoprolol succinate, carvedilol, or bisoprolol is recommended for beta-blocker therapy with concomitant NSTE-ACS, stabilized HF, and reduced systolic function</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Re-evaluate to determine subsequent eligibility in patients with initial contraindications to beta blockers</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>It is reasonable to continue beta-blocker therapy in patients with normal LV function with NSTE-ACS</td>
<td>IIa</td>
<td>C</td>
<td>(241,243)</td>
</tr>
<tr>
<td>IV beta blockers are potentially harmful when risk factors for shock are present</td>
<td>III: Harm</td>
<td>B</td>
<td>(244)</td>
</tr>
<tr>
<td><strong>CCBs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer initial therapy with nondihydropyridine CCBs with recurrent ischemia and contraindications to beta blockers in the absence of LV dysfunction, increased risk for cardiogenic shock, PR interval &gt;0.24 s, or second- or third-degree atrioventricular block without a cardiac pacemaker</td>
<td>I</td>
<td>B</td>
<td>(248-250)</td>
</tr>
<tr>
<td>Administer oral nondihydropyridine calcium antagonists with recurrent ischemia after use of beta blocker and nitrates in the absence of contraindications</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>CCBs are recommended for ischemic symptoms when beta blockers are not successful, are contraindicated, or cause unacceptable side effects*</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Long-acting CCBs and nitrates are recommended for patients with coronary artery spasm</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Immediate-release nifedipine is contraindicated in the absence of a beta blocker</td>
<td>III: Harm</td>
<td>B</td>
<td>(251,252)</td>
</tr>
</tbody>
</table>
# Initial Medical Management

<table>
<thead>
<tr>
<th>Recommendations</th>
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<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate or continue high-intensity statin therapy in patients with no contraindications</td>
<td>I</td>
<td>A</td>
<td>(269-273)</td>
</tr>
<tr>
<td>Obtain a fasting lipid profile, preferably within 24 h</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Short-acting dihydropyridine calcium channel antagonists should be avoided.*
Disrupting Pathophysiology
# Initial Antiplatelet Therapy

## Summary of Recommendations for Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS and PCI

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Dosing and Special Considerations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-enteric-coated aspirin to <em>all</em> patients promptly after presentation</td>
<td>162 mg-325 mg</td>
<td>I</td>
<td>A</td>
<td>(288-290)</td>
</tr>
<tr>
<td>Aspirin maintenance dose continued indefinitely</td>
<td>81 mg/d-325 mg/d*</td>
<td>I</td>
<td>A</td>
<td>(288-290, 293,391)</td>
</tr>
<tr>
<td><strong>P2Y₁₂ inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin</td>
<td>75 mg</td>
<td>I</td>
<td>B</td>
<td>(291)</td>
</tr>
</tbody>
</table>
| P2Y₁₂ inhibitor, in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy:  
  – Clopidogrel  
  – Ticagrelor* | 300-mg or 600-mg loading dose, then 75 mg/d  
  180-mg loading dose, then 90 mg BID | I | B | (289,292, 293,294) |
| P2Y₁₂ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) continued for at least 12 mo in post-PCI patients treated with coronary stents | N/A | I | B | (293,296,302, 330,331) |
| Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy | N/A | Iia | B | (293,294) |
| **GP IIb/IIIa inhibitors** |                                |     |     |            |
| GP IIb/IIIa inhibitor in patients treated with an early invasive strategy and DAPT with intermediate/high-risk features (e.g., positive troponin) | Preferred options are eptifibatide or tirofiban | IIb | B | (43,94,295) |
Importance of Antiplatelet Therapy:

**Old Dogma**

Give ASA  
Give Anticoagulation  
Give Statin  
One of 2 Class I choices:  
• P2Y12  
• IIB/IIIA

**New Guideline**

Give ASA  
**Give P2Y12**  
Give Anticoagulation  
Give Statin  
If high risk features AND positive troponins:  
• - Consider IIB/IIIA (Cardiology Consult)  
  o Eptifibatide or tirofiban
Anti Platelet Therapy Basics: Aspirin

No trial has ever been designed to look at specific dose of ASA in ACS

- Meta-analysis (~200k pts) in BMJ 1994:
  - Long term therapy for many high risk groups showed NNT was 8-12 to prevent vascular event
- A later meta-analysis including 143,000 patient data, showed 22% reduction in vascular death

- ASA 162-325mg chewed or PR at presentation, followed by 81mg daily
- If true ASA allergy, give a clopidogrel load of 300-600 mg, followed by 75mg daily
Anti Platelet Therapy Basics: P2Y12

Clopidogrel:

- Clopidogrel: load of 300-600 mg, followed by 75mg daily
- Ticagrelor: load of 180mg, followed by 90mg BID
Anti Platelet Therapy Basics: P2Y12

**Ticagrelor:**

- **Clopidogrel:** load of 300-600 mg, followed by 75mg daily
- **Ticagrelor:** load of 180mg, followed by 90mg BID
# Initial Anticoagulation Therapies

## TABLE 7  Summary of Recommendations for Initial Antiplatelet/Anticoagulant Therapy in Patients With Definite or Likely NSTE-ACS and PCI

<table>
<thead>
<tr>
<th>Recommendations</th>
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</thead>
<tbody>
<tr>
<td><strong>Parenteral anticoagulant and fibrinolytic therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• SC enoxaparin for duration of hospitalization or until PCI is performed</td>
<td>• 1 mg/kg SC every 12 h (reduce dose to 1 mg/kg/d SC in patients with CrCl &lt; 30 mL/min)</td>
<td>I</td>
<td>A</td>
<td>(133,136,309)</td>
</tr>
<tr>
<td></td>
<td>• Initial 30 mg IV loading dose in selected patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bivalirudin until diagnostic angiography or PCI is performed in patients with early invasive strategy only</td>
<td>• Loading dose 0.10 mg/kg loading dose followed by 0.25 mg/kg/h</td>
<td>I</td>
<td>B</td>
<td>(292,293,310,311)</td>
</tr>
<tr>
<td></td>
<td>• Only provisional use of GP IIb/IIIa inhibitor in patients also treated with DAPT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• SC fondaparinux for the duration of hospitalization or until PCI is performed</td>
<td>2.5 mg SC daily</td>
<td>I</td>
<td>B</td>
<td>(312-314)</td>
</tr>
<tr>
<td>• Administer additional anticoagulant with anti-Ilalpha activity if PCI is performed while patient is on fondaparinux</td>
<td>N/A</td>
<td>I</td>
<td>B</td>
<td>(313-315)</td>
</tr>
<tr>
<td>• IV UFH for 48 h or until PCI is performed</td>
<td>• Initial loading dose 60 IU/kg (max 4,000 IU) with initial infusion 12 IU/kg/h (max 1,000 IU/h)</td>
<td>I</td>
<td>B</td>
<td>(316-322)</td>
</tr>
<tr>
<td></td>
<td>• Adjusted to therapeutic aPTT range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• IV fibrinolytic treatment not recommended in patients with NSTE-ACS</td>
<td>N/A</td>
<td></td>
<td></td>
<td>(93,329)</td>
</tr>
</tbody>
</table>
LMWH vs. UFH

Multiple head to head trials

• 5 of 6 trials of enoxaparin found point estimates for death or nonfatal MI that favored enoxaparin over UFH; the pooled OR was 0.91 (95% CI 0.83 to 0.99).

• The benefit of enoxaparin appeared to be driven largely by a reduction in nonfatal MI

• Increased risk of minor bleeding and TIMI major bleeding in the SYNERGY trial

• ESSENCE trial showed an absolute RR of 3% favoring enoxaparin vs. UFH
Adjuvant Therapies

Cardiac rehab
Smoking cessation
Follow-up
Discussion
Bibliography/References


Bibliography/References


