New STEMI Guidelines

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Conflict of Interest Reporting

• Research grant funding
  – GlaxoSmithKline, Bristol Myers Squibb, Merck & Company, Inc., Amylin, MURDOCK Study

• Consulting
  – Jansen Pharmaceuticals, Roche Diagnostics, LG, Navigant, Novartis, Daiichi-Sankyo, DSI-Lilly, Genentech, GlaxoSmithKline, Cubist Pharmaceuticals

• Organizations
  – Society of Chest Pain Centers, Journal of the American Heart Association
Key objectives of 2013 STEMI guidelines

- Focus on timely reperfusion therapy
- Organization of regional systems of care
- Transfer algorithms
- Evidence-based antithrombotic and medical therapy
- Secondary prevention strategies to optimize patient-centered care

Narrower scope than prior 2004 STEMI guideline

- More focused tool for practitioner

Cross-referenced to other key guidelines
Classification of Recommendations and Levels of Evidence

**SIZE OF TREATMENT EFFECT**

<table>
<thead>
<tr>
<th>CLASS I</th>
<th>Benefit &gt;&gt; Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td></td>
</tr>
</tbody>
</table>

**LEVEL A**
Multiple populations evaluated*
Data derived from multiple randomized clinical trials or meta-analyses

- Recommendation that procedure or treatment is useful/effective
- Sufficient evidence from multiple randomized trials or meta-analyses

**LEVEL B**
Limited populations evaluated*
Data derived from a single randomized trial or nonrandomized studies

- Recommendation that procedure or treatment is useful/effective
- Evidence from single randomized trial or nonrandomized studies

**LEVEL C**
Very limited populations evaluated*
Only consensus opinion of experts, case studies, or standard of care

- Recommendation that procedure or treatment is useful/effective
- Only expert opinion, case studies, or standard of care

### Comparative effectiveness phrases*

- Treatment/strategy A is recommended/indicated in preference to treatment B
- Treatment A should be chosen over treatment B
- Treatment/strategy A is probably recommended/indicated in preference to treatment B
- It is reasonable to choose treatment A over treatment B

### Corollary (COR)

<table>
<thead>
<tr>
<th>COR II:</th>
<th>No Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure/Treatment</td>
<td>Not Helpful</td>
</tr>
<tr>
<td>Treatment</td>
<td>No Proven Benefit</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COR III:</th>
<th>Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure/Treatment</td>
<td>Excess Cost/No Benefit</td>
</tr>
<tr>
<td>Treatment</td>
<td>Harmful to Patients</td>
</tr>
</tbody>
</table>

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
Background
Epidemiology of STEMI
Age and Sex Adjusted Incidence Rates of MI

Kaiser-Permanente; 46,086 MI hospitalizations

Yeh RW, et al. NEJM 2010
Epidemiology of STEMI
Guideline-Directed Medical Therapy and Outcomes

ACTION Registry-Get With The Guidelines Q1 07 to Q2 09

250 hospitals
131,980 patients

40% STEMI

250 hospitals
131,980 patients

40% STEMI

Roe MT, et al. JACC 2010
Provider-Led QI Works
Effects on Disparities in Care

Race/Ethnicity
GWTG-CAD

Cohen MG, et al Circulation 2010

Age/Sex
GWTG-CAD

Lewis WR, et al Circ Cardiovasc Qual Outcomes 2009
General Considerations
General Considerations
ECG Points of Emphasis

• Diffuse ST-segment depression with ST-segment elevation in AVR think high risk (LM or proximal LAD)
• ST-depression in ≥2 contiguous anterior leads (V₁-V₄), consider posterior STEMI
• New or presumably new LBBB at presentation
  – occurs infrequently
    • NRMI-2 Registry 6.2% of all MIs presented with LBBB
  – may interfere with ST segment analysis
  – should not be considered diagnostic of acute MI in isolation
General Considerations
Criteria for Diagnosis of STEMI if LBBB (Sgarbossa Criteria)

- Additional criteria if LBBB present were emphasized

### Odds Ratios and Scores for Independent Electrocardiographic Criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Odds Ratio (95% CI)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-elevation ≥1 mm and concordant with QRS complex</td>
<td>25.2 (11.6 - 54.7)</td>
<td>5</td>
</tr>
<tr>
<td>ST-segment depression ≥1 mm in lead V1, V2, or V3</td>
<td>6.0 (1.9 - 19.3)</td>
<td>3</td>
</tr>
<tr>
<td>ST-elevation ≥5 mm and discordant with QRS complex</td>
<td>4.3 (1.8 - 10.6)</td>
<td>2</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
Reprinted from Sgarbossa et al. (2).

- Sgarbossa score ≥3 has 98% specificity for acute STEMI
- Sgarbossa score of 0 DOES NOT rule out STEMI
General Considerations
Risk Assessment

• Early risk assessment
  – Should be global with GRACE or TIMI STEMI scores that integrate clinical features and ECG
  – Guide care decisions, inform patients and families
General Considerations
Transport of Chest Pain Patients

• Median delay to presentation approximately 1.5 hour
  – Elderly, women, blacks, Medicaid pts have longer delays
  – EMS users have shorter delays
• 98% of US population covered by 9-1-1 service
  – Use of EMS varies from 23% to 60% depending on location and type of hospital
• EMS is preferred means of transport
  – 1 in 300 people transported by private vehicle suffer cardiac arrest in route to ED
  – Strong association between EMS use and earlier reperfusion
  – Strong association between prehospital ECG and shorter reperfusion times and better outcomes
Regional Systems of STEMI Care, Reperfusion Therapy, and Time-to-Treatment Goals
What is a STEMI Regional System of Care?

• Mission Lifeline working definition
  – An integrated group of separate entities within a geographic region
    • Focused on reperfusion therapy for STEMI
      – Goal to reduce total ischemic time
    • Includes at least 1 hospital that performs percutaneous coronary intervention and at least 1 emergency medical service agency
      – PCI preferred if acceptable delays

Characteristics of Existing STEMI Systems
Benchmarks and Guideposts for Development

- Mission Lifeline survey of existing systems
  - 381 systems, 899 PCI hospitals, 47 states
  - 255 (67%) urban

Figure 1. A, Mission: Lifeline: Registered STEMI systems by state. B, Mission Lifeline: STEMI systems coverage.

Key Features of Existing US STEMI Systems

• Predominant funding source
  – PCI hospital (84%) and/or cardiology practice (23%)

• Predominant system characteristics
  – STEMI acceptance at PCI hospital regardless of bed availability (97%)
  – Single phone call activation of cath lab (92%)
  – ED physician activation of cath lab without cardiology consultation (87%)
  – Prehospital activation of cath lab through ED without cardiology notification (78%)
  – Data registry participation (84%)

• Most common barriers to system implementation
  – Hospital (37%)
  – Cardiology group competition (21%)
  – EMS transport and finances (26%)

Regional Systems of Care
Effects on STEMI Metrics and Disparities--RACE

Reperfusion Therapy for Patients with STEMI

*Patients with cardiogenic shock or severe heart failure initially seen at a non–PCI-capable hospital should be transferred for cardiac catheterization and revascularization as soon as possible, irrespective of time delay from MI onset (Class I, LOE: B). †Angiography and revascularization should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.
Regional Systems of STEMI Care, Reperfusion Therapy, and Time-to-Treatment Goals

All communities should create and maintain a regional system of STEMI care that includes assessment and continuous quality improvement of EMS and hospital-based activities. Performance can be facilitated by participating in programs such as Mission: Lifeline and the D2B Alliance.

Performance of a 12-lead ECG by EMS personnel at the site of FMC is recommended in patients with symptoms consistent with STEMI.
Regional Systems of STEMI Care, Reperfusion Therapy, and Time-to-Treatment Goals

Reperfusion therapy should be administered to all eligible patients with STEMI with symptom onset within the prior 12 hours.

Primary PCI is the recommended method of reperfusion when it can be performed in a timely fashion by experienced operators.

EMS transport directly to a PCI-capable hospital for primary PCI is the recommended triage strategy for patients with STEMI with an ideal FMC-to-device time system goal of 90 minutes or less.*

*The proposed time windows are system goals. For any individual patient, every effort should be made to provide reperfusion therapy as rapidly as possible.
Regional Systems of STEMI Care, Reperfusion Therapy, and Time-to-Treatment Goals

Immediate transfer to a PCI-capable hospital for primary PCI is the recommended triage strategy for patients with STEMI who initially arrive at or are transported to a non-PCI-capable hospital, with an FMC-to-device time system goal of 120 minutes or less.*

In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI at non-PCI-capable hospitals when the anticipated FMC-to-device time at a PCI-capable hospital exceeds 120 minutes because of unavoidable delays.

*The proposed time windows are system goals. For any individual patient, every effort should be made to provide reperfusion therapy as rapidly as possible.
Rationale for Recommended FMC-Device Times for Transfer Patients

• <10% NCDR transfer patients treated with primary PCI in <90 minutes
• DANAMI-2 showed benefit of transfer for primary PCI vs. lytics with median FMC-device time 110 minutes
• NRMI 2,3,4 propensity matched comparison of transfer for PCI vs. lytics, benefit of PCI lost if FMC-device >120 minutes
Regional Systems of STEMI Care, Reperfusion Therapy, and Time-to-Treatment Goals

When fibrinolytic therapy is indicated or chosen as the primary reperfusion strategy, it should be administered within 30 minutes of hospital arrival.*

Reperfusion therapy is reasonable for patients with STEMI and symptom onset within the prior 12 to 24 hours who have clinical and/or ECG evidence of ongoing ischemia. Primary PCI is the preferred strategy in this population.

*The proposed time windows are system goals. For any individual patient, every effort should be made to provide reperfusion therapy as rapidly as possible.
Characteristics of High Performing Systems

- Commitment to explicit goal of improving D2B times
  - Motivated by internal and external pressure
  - Senior management support
- Innovative protocols
- Flexibility in refining standards
- Collaborative teams
- Data feedback to monitor progress and identify problems and successes
- Organizational culture that fosters resilience to challenges or setbacks to QI efforts
Evaluation and Management of Patients With STEMI and Out-of-Hospital Cardiac Arrest
STEMI and Cardiac Arrest

• 70% of CHD deaths in US occur out of hospital, usually presenting as sudden death
  – EMS attempts resuscitation in 60%
• 23% of those have initially shockable rhythm
  – Median survival to discharge 22% if VF vs. 8% overall
  – Survival decrease by 7-10% for every minute delay in onset to defibrillation
• % of patients who are found in VF and the likelihood of survival better if witnessed arrest, if bystander CPR performed, and if a monitor/defibrillator can be applied quickly
Therapeutic hypothermia should be started as soon as possible in comatose patients with STEMI and out-of-hospital cardiac arrest caused by VF or pulseless VT, including patients who undergo primary PCI.

Immediate angiography and PCI when indicated should be performed in resuscitated out-of-hospital cardiac arrest patients whose initial ECG shows STEMI.
Reperfusion at a PCI-Capable Hospital

Primary PCI in STEMI
# Primary PCI in STEMI

<table>
<thead>
<tr>
<th>Condition</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic symptoms &lt; 12 h</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Ischemic symptoms &lt; 12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Cardiogenic shock or acute severe HF irrespective of time delay from MI onset</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Evidence of ongoing ischemia 12 to 24 h after symptom onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise</td>
<td>III: Harm</td>
<td>B</td>
</tr>
</tbody>
</table>
Use of Stents in Patients With STEMI

Placement of a stent (BMS or DES) is useful in primary PCI for patients with STEMI.

BMS* should be used in patients with high bleeding risk, inability to comply with 1 year of DAPT, or anticipated invasive or surgical procedures in the next year.

DES should not be used in primary PCI for patients with STEMI who are unable to tolerate or comply with a prolonged course of DAPT because of the increased risk of stent thrombosis with premature discontinuation of one or both agents.

*Balloon angioplasty without stent placement may be used in selected patients.
Adjunctive Antithrombotic Therapy for Primary PCI
Adjunctive Antithrombotic Therapy to Support Reperfusion With Primary PCI

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

**Antiplatelet therapy**

**Aspirin**
- 162- to 325-mg load before procedure
- 81- to 325-mg daily maintenance dose (indefinite)*
- 81 mg daily is the preferred maintenance dose*

**P2Y12 inhibitors**

- Loading doses:
  - Clopidogrel: 600 mg as early as possible or at time of PCI
  - Prasugrel: 60 mg as early as possible or at time of PCI
  - Ticagrelor: 180 mg as early as possible or at time of PCI

<table>
<thead>
<tr>
<th>Cor</th>
<th>LoE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Ia</td>
<td>B</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Cor</th>
<th>LoE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>
Adjunctive Antithrombotic Therapy to Support Reperfusion With Primary PCI (cont.)

**P2Y$_{12}$ inhibitors**

- **Maintenance doses and duration of therapy**
  - **DES placed:** Continue therapy for 1 y with:
    - Clopidogrel: 75 mg daily
    - Prasugrel: 10 mg daily
    - Ticagrelor: 90 mg twice a day*
  - **BMS† placed:** Continue therapy for 1 y with:
    - Clopidogrel: 75 mg daily
    - Prasugrel: 10 mg daily
    - Ticagrelor: 90 mg twice a day*
  - **DES placed:**
    - Clopidogrel, prasugrel, or ticagrelor* continued beyond 1 y
    - Patients with STEMI with prior stroke or TIA: prasugrel

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.
†Balloon angioplasty without stent placement may be used in selected patients. It might be reasonable to provide P2Y$_{12}$ inhibitor therapy to patients with STEMI undergoing balloon angioplasty alone according to the recommendations listed for BMS. (LOE: C).
### STEMI, NSTEMI, UA N~25,000

**High Dose Clopidogrel**
- 600 mg load
- 150 mg/day x 7 days
- 75 mg/daily thereafter

**Standard Dose Clopidogrel**
- 300 mg load
- 75 mg/daily thereafter

<table>
<thead>
<tr>
<th>Event</th>
<th>Standard</th>
<th>Double</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
<th>Intn P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV Death/MI/Stroke</td>
<td>4.4</td>
<td>4.2</td>
<td>0.95</td>
<td>0.84-1.07</td>
<td>0.370</td>
<td></td>
</tr>
<tr>
<td>PCI (N=17,232)</td>
<td>4.5</td>
<td>3.9</td>
<td>0.85</td>
<td>0.74-0.99</td>
<td>0.036</td>
<td>0.016</td>
</tr>
<tr>
<td>No PCI (N=7855)</td>
<td>4.2</td>
<td>4.9</td>
<td>1.17</td>
<td>0.95-1.44</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>TIMI Major Bleeding</td>
<td>0.95</td>
<td>1.04</td>
<td>1.09</td>
<td>0.85-1.40</td>
<td>0.50</td>
<td></td>
</tr>
</tbody>
</table>

**TIMI Major Bleed:** ICH, Hb drop ≥ 5 g/dL (each unit of RBC transfusion counts as 1 g/dL drop) or fatal

Mehta. ESC 2009
Study Design

ACS (STEMI or UA/NSTEMI) & Planned PCI

N= 13,600

Double-blind

ASA

CLOPIDOGREL 300 mg LD/ 75 mg MD

PRASUGREL 60 mg LD/ 10 mg MD

Median duration of therapy - 12 months

1° endpoint: CV death, MI, Stroke
2° endpoints: CV death, MI, Stroke, Rehosp-Rec Isch
CV death, MI, UTVR
Stent Thrombosis (ARC definite/prob.)

Safety endpoints: TIMI major bleeds, Life-threatening bleeds

Key Substudies: Pharmacokinetic, Genomic
TRITON TIMI-38 Results

CV Death / MI / Stroke
HR 0.81 (0.73-0.90), p=0.0004

TIMI Major Bleeding
HR 1.32 (1.03-1.68), p=0.03

Prasugrel
Clopidogrel

TRITON TIMI-38 Bleeding Events
Safety Cohort (N=13,457)

### TIMI Major Bleeds
- **Clopidogrel**: 1.8%
  - **HR**: 1.32
  - **P**: 0.03
  - **NNH**: 167
- **Prasugrel**: 2.4%

### Life Threatening
- **Clopidogrel**: 0.9%
  - **HR**: 1.52
  - **P**: 0.01
- **Prasugrel**: 1.4%

### Nonfatal
- **Clopidogrel**: 0.9%
- **Prasugrel**: 1.1%

### Fatal
- **Clopidogrel**: 0.1%
  - **HR**: 0.9
  - **P**: 0.9
- **Prasugrel**: 0.4%

### ICH in Pts w Prior Stroke/TIA (N=518)
- **Clopidogrel**: 0 (0)%
- **Prasugrel**: 6 (2.3)%
  - **P**: 0.02

---

**Net Clinical Benefit**

**Bleeding Risk Subgroups**

**Post-hoc analysis**

- **Prior Stroke / TIA**
  - Yes
  - No

- **Age**
  - >=75
  - < 75

- **Wgt**
  - < 60 kg
  - >=60 kg

<table>
<thead>
<tr>
<th>Risk (%)</th>
<th>P_int</th>
<th>HR</th>
<th>Int %</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ 37</td>
<td>0.006</td>
<td>1</td>
<td>+3</td>
</tr>
<tr>
<td>-1</td>
<td>0.18</td>
<td>1</td>
<td>-1</td>
</tr>
<tr>
<td>-16</td>
<td>0.36</td>
<td>1</td>
<td>-14</td>
</tr>
<tr>
<td>-13</td>
<td></td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
PLATO Study Design

Primary endpoint: CV death + MI + Stroke
Primary safety endpoint: Total major bleeding

PLATO Study Design

NSTE-ACS (moderate-to-high risk) STEMI (if primary PCI) Clopidogrel-treated or -naive; randomised within 24 hours of index event (N=18,624)

Clopidogrel
If pre-treated, no additional loading dose; if naive, standard 300 mg loading dose, then 75 mg qd maintenance; (additional 300 mg allowed pre PCI)

Ticagrelor
180 mg loading dose, then 90 mg bid maintenance; (additional 90 mg pre-PCI)

6–12-month exposure

PCI = percutaneous coronary intervention; ASA = acetylsalicylic acid; CV = cardiovascular; TIA = transient ischaemic attack
PLATO Primary Results: Death, MI or Stroke

<table>
<thead>
<tr>
<th>Days after randomisation</th>
<th>No. at risk Ticagrelor</th>
<th>No. at risk Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9,333</td>
<td>9,291</td>
</tr>
<tr>
<td>60</td>
<td>8,628</td>
<td>8,521</td>
</tr>
<tr>
<td>120</td>
<td>8,460</td>
<td>8,362</td>
</tr>
<tr>
<td>180</td>
<td>8,219</td>
<td>8,124</td>
</tr>
<tr>
<td>240</td>
<td>6,743</td>
<td>6,743</td>
</tr>
<tr>
<td>300</td>
<td>5,161</td>
<td>5,096</td>
</tr>
<tr>
<td>360</td>
<td>4,147</td>
<td>4,047</td>
</tr>
</tbody>
</table>

Cumulative incidence (%)

HR 0.84 (95% CI 0.77–0.92), p=0.0003

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval
PLATO Non-CABG and CABG Bleeding

- Non-CABG PLATO major bleeding: Ticagrelor 4.5, Clopidogrel 3.8, p=0.026
- Non-CABG TIMI major bleeding: Ticagrelor 2.8, Clopidogrel 2.2, p=0.025
- CABG PLATO major bleeding: Ticagrelor 7.4, Clopidogrel 7.9, NS
- CABG TIMI major bleeding: Ticagrelor 5.3, Clopidogrel 5.8, NS
PLATO Regional Variation

Hazard Ratios and Rates of Primary End Point in Predefined Subgroups of Study Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard Ratio (95% CI)</th>
<th>Total Patients</th>
<th>KM % at Month 12</th>
<th>HR (95% CI)</th>
<th>P value (Interaction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia/Australia</td>
<td></td>
<td>1714</td>
<td>11.4</td>
<td>14.8</td>
<td>0.80 (0.61, 1.04)</td>
</tr>
<tr>
<td>Central/South America</td>
<td></td>
<td>1237</td>
<td>15.2</td>
<td>17.9</td>
<td>0.86 (0.65, 1.13)</td>
</tr>
<tr>
<td>Europe/Middle East/Africa</td>
<td></td>
<td>13859</td>
<td>8.8</td>
<td>11.0</td>
<td>0.80 (0.72, 0.90)</td>
</tr>
<tr>
<td>North America</td>
<td></td>
<td>1814</td>
<td>11.9</td>
<td>9.6</td>
<td>1.25 (0.93, 1.67)</td>
</tr>
</tbody>
</table>

FDA Black box labeling for use with low dose (<100mg) aspirin
Considerations for ADP Receptor Antagonists (versus standard dose clopidogrel)

<table>
<thead>
<tr>
<th>Drug</th>
<th>CV death, MI, stroke</th>
<th>Major Bleeding</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD Clopidogrel</td>
<td>6% ↓</td>
<td>24% ↑</td>
<td>--</td>
</tr>
<tr>
<td>Prasugrel (intended PCI)</td>
<td>19% ↓</td>
<td>32% ↑</td>
<td>--</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>16% ↓</td>
<td>4% ↑</td>
<td>22% ↓</td>
</tr>
</tbody>
</table>

Other key considerations

- Each reduced stent thrombosis by 30 to 50%
- Prasugrel increased fatal bleeding, particularly in high risk group of elderly, prior stroke, low weight
- Prasugrel data limited to intended PCI pending TRILOGY; in STEMI, risk benefit for prasugrel more favorable;
- Ticagrelor increased non-CABG bleeding by 19%; Regional differences / ASA; PEGASUS for 2nd Prevention
Adjunctive Anticoagulant Therapy to Support Reperfusion With Primary PCI

<table>
<thead>
<tr>
<th>Anticoagulant therapy</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• UFH:</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>• With GP IIb/IIIa receptor antagonist planned: 50- to 70-U/kg IV bolus to achieve therapeutic ACT ‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• With no GP IIb/IIIa receptor antagonist planned: 70- to 100-U/kg bolus to achieve therapeutic ACT §</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bivalirudin: 0.75-mg/kg IV bolus, then 1.75-mg/kg/h infusion with or without prior treatment with UFH. An additional bolus of 0.3 mg/kg may be given if needed.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>• Reduce infusion to 1 mg/kg/h with estimated CrCl &lt; 30 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Preferred over UFH with GP IIb/IIIa receptor antagonist in patients at high risk of bleeding</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>• Fondaparinux: not recommended as sole anticoagulant for primary PCI</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>III: Harm</td>
<td>B</td>
</tr>
</tbody>
</table>

‡The recommended ACT with planned GP IIb/IIIa receptor antagonist treatment is 200 to 250 s.
§The recommended ACT with no planned GP IIb/IIIa receptor antagonist treatment is 250 to 300 s (HemoTec device) or 300 to 350 s (Hemochron device).
Fibrinolytic Therapy When There Is an Anticipated Delay to Performing Primary PCI Within 120 Minutes of FMC
### Indications for Fibrinolytic Therapy When There Is a >120-Minute Delay From FMC to Primary PCI

<table>
<thead>
<tr>
<th>Indication</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic symptoms &lt;12 h</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Evidence of ongoing ischemia 12 to 24 h after symptom onset and a large area of myocardium at risk or hemodynamic instability</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>ST depression, except if true posterior (inferobasal) MI is suspected or when associated with ST elevation in lead aVR</td>
<td>III: Harm</td>
<td>B</td>
</tr>
</tbody>
</table>
Adjunctive Antithrombotic Therapy to Support Reperfusion With Fibrinolytic Therapy

<table>
<thead>
<tr>
<th>Antiplatelet therapy</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● 162- to 325-mg loading dose</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>● 81- to 325-mg daily maintenance dose (indefinite)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>● 81 mg daily is the preferred maintenance dose</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>P2Y&lt;sub&gt;12&lt;/sub&gt; receptor inhibitors</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Clopidogrel:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Age ≤75 y: 300-mg loading dose</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>● Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding</td>
<td>C</td>
<td>(up to 1 y)</td>
</tr>
<tr>
<td>● Age &gt;75 y: no loading dose, give 75 mg</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>● Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding</td>
<td>C</td>
<td>(up to 1 y)</td>
</tr>
</tbody>
</table>

Helping Cardiovascular Professionals
Adjunctive Antithrombotic Therapy to Support Reperfusion With Fibrinolytic Therapy (cont.)

Anticoagulant therapy

- **UFH:**
  - Weight-based IV bolus and infusion adjusted to obtain aPTT of 1.5 to 2.0 times control for 48 h or until revascularization. IV bolus of 60 U/kg (maximum 4000 U) followed by an infusion of 12 U/kg/h (maximum 1000 U) initially, adjusted to maintain aPTT at 1.5 to 2.0 times control (approximately 50 to 70 s) for 48 h or until revascularization

- **Enoxaparin:**
  - If age <75 y: 30-mg IV bolus, followed in 15 min by 1 mg/kg subcutaneously every 12 h (maximum 100 mg for the first 2 doses)
  - If age ≥75 y: no bolus, 0.75 mg/kg subcutaneously every 12 h (maximum 75 mg for the first 2 doses)
  - Regardless of age, if CrCl <30 mL/min: 1 mg/kg subcutaneously every 24 h
  - Duration: For the index hospitalization, up to 8 d or until revascularization

- **Fondaparinux:**
  - Initial dose 2.5 mg IV, then 2.5 mg subcutaneously daily starting the following day, for the index hospitalization up to 8 d or until revascularization
  - Contraindicated if CrCl <30 mL/min
Symptoms of Acute Ischemia

Nurse Triage and ECG within 10 minutes

Enroll in Trials

ASA 325 mg initial dose; 81 mg qD until/at DC

Antithrombotic Rx

Ticagrelor or Clopidogrel 600 mg load; 150 mg qD for 7d or until DC (if PCI)

If non ST↑ ACS, mod–high risk

If pain-free, low–mod risk, neg or nonspecific ECG neg. CK-MB, TnT/I

Chest Pain Unit

< 12h Sx

Primary PCI

Ticagrelor or Prasugrel*

Bivalirudin or UFH/GP IIb/IIIa

Cath <24 hrs

UFH †

Or bivalirudin **

Cath >24 hrs

Fondaparinux or enoxaparin

No or delayed cath

Dynamic ST∆s, pos. cardiac markers

NSSTT ∆s, neg. cardiac markers

Anticoagulant Rx

Antithrombotic Rx

Fonda

UFH

cath in 12h

Prasugrel for primary PCI (if no h/o TIA or stroke)

†GP IIb/IIIa at time of PCI or if refractory ischemia

**Consider bivalirudin for cath <12 hours
Duke ACS Algorithm: STEMI

Reperfusion Rx

Activate ICC Express/AMI Hotline

1st door-to-balloon > 90 min

TT (TNK) + clopidogrel

Known Cr > 2.5 mg/dL

UFH

Cr unknown or <2.5 mg/dL

Enoxaparin
(Dose adjust to 0.75 mg/kg q 12 hours with no bolus if ≥ 75 years)

1st door-to-balloon < 90 min

Primary PCI

Primary PCI

UFH bolus

Bivalirudin or UFH/GP IIb/IIIa

Prasugrel* or clopidogrel

Prasugrel* or clopidogrel

Upstream of lab

In lab

*Presentation to Duke ED (no h/o TIA or stroke) and for clopidogrel failure; transferring RACE ERs will give clopidogrel; decision in lab if thienopyridine not administered upstream
Reperfusion at a Non-PCI-Capable Hospital

Transfer to a PCI-Capable Hospital After Fibrinolytic Therapy
**Indications for Transfer for Angiography After Fibrinolytic Therapy**

<table>
<thead>
<tr>
<th></th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate transfer for cardiogenic shock or severe acute HF irrespective of time delay from MI onset</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Urgent transfer for failed reperfusion or reocclusion</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>As part of an invasive strategy in stable* patients with PCI between 3 and 24 h after successful fibrinolysis</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.*
Early Routine vs. Ischemia-Driven or Delayed Routine Angiography after Fibrinolysis

Time (median or average) from Fibrinolysis to PCI

- SIAM-3: 50.6%
- GRACIA-1: 9%
- CAPITAL-AMI: 21%
- CARESS-in-AMI: 11.6%
- WEST: 24.9%
- TRANSFER-AMI: 4.4%
- NORTI-STEMI: 10.7%

N Risk Follow-up Composite:
- SIAM-3: 163 All 6 mo D,MI,RI,TLR D,MI,revasc
- GRACIA-1: 500 All 12 mo D,MI,RI
- CAPITAL-AMI: 170 High 6 mo D,MI,RI,stroke
- CARESS-in-AMI: 600 High 30 d D, MI, RI
- WEST: 204 High 30 d D,MI,RI,CHF,shock,arryhy
- TRANSFER-AMI: 1059 High 30 d D,MI,RI,CHF,shock
- NORTI-STEMI: 266 All 12 mo D, MI, RI, stroke
Delayed Invasive Management
**Indications for Coronary Angiography in Patients Who Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion Therapy**

<table>
<thead>
<tr>
<th>Condition</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogenic shock or acute severe HF that develops after initial presentation</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Intermediate- or high-risk findings on predischarge noninvasive ischemia testing</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Spontaneous or easily provoked myocardial ischemia</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Failed reperfusion or reocclusion after fibrinolytic therapy</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Stable* patients after successful fibrinolysis, before discharge and ideally between 3 and 24 h</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.*
Indications for PCI of an Infarct Artery in Patients Who Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion Therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogenic shock or acute severe HF</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Intermediate- or high-risk findings on predischarge noninvasive ischemia</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>testing</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Spontaneous or easily provoked myocardial ischemia</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Patients with evidence of failed reperfusion or reocclusion after fibrinolytic therapy (as soon as possible)</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Stable* patients after successful fibrinolysis, ideally between 3 and 24 h</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Stable* patients &gt;24 h after successful fibrinolysis</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Delayed PCI of a totally occluded infarct artery &gt;24 h after STEMI in stable patients</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
</tbody>
</table>

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.
PCI of a Noninfarct Artery Before Hospital Discharge

PCI is indicated in a noninfarct artery at a time separate from primary PCI in patients who have spontaneous symptoms of myocardial ischemia.

PCI is reasonable in a noninfarct artery at a time separate from primary PCI in patients with intermediate- or high-risk findings on noninvasive testing.
Guideline for STEMI

Routine Medical Therapies
Lipid Management

High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use.

It is reasonable to obtain a fasting lipid profile in patients with STEMI, preferably within 24 hours of presentation.
Posthospitalization Plan of Care

Guideline for STEMI
Assessment of Risk for SCD

Patients with an initially reduced LVEF who are possible candidates for ICD therapy should undergo reevaluation of LVEF 40 or more days after discharge.
Posthospitalization Plan of Care

Posthospital systems of care designed to prevent hospital readmissions should be used to facilitate the transition to effective, coordinated outpatient care for all patients with STEMI.

Exercise-based cardiac rehabilitation/secondary prevention programs are recommended for patients with STEMI.
A clear, detailed, and evidence-based plan of care that promotes medication adherence, timely follow-up with the healthcare team, appropriate dietary and physical activities, and compliance with interventions for secondary prevention should be provided to patients with STEMI.

Encouragement and advice to stop smoking and to avoid secondhand smoke should be provided to patients with STEMI.
Unresolved Issues and Future Directions

- Improving patient awareness and activation
- Wider implementation of systems of care
  - Prehospital EMS protocols
  - Approach to out of hospital cardiac arrest
  - Triage and transfer algorithms
  - Refinement and clarification of clinical and time-related factors that should prompt fibrinolysis with immediate transfer for PCI
- Transfer for angiography of non-high risk patients post-successful fibrinolysis and what to do with non-infarct arteries
- Optimum choice/combination of antithrombotic/anticoagulant therapy
- Addressing reperfusion injury as possible means to improve outcome post-MI
- Preventing heart failure/treating heart failure
- Preventing sudden cardiac death
Beta Blockers
Beta Blockers

Oral beta blockers should be initiated in the first 24 hours in patients with STEMI who do not have any of the following: signs of HF, evidence of a low output state, increased risk for cardiogenic shock,* or other contraindications to use of oral beta blockers (PR interval >0.24 seconds, second- or third-degree heart block, active asthma, or reactive airways disease).

Beta blockers should be continued during and after hospitalization for all patients with STEMI and with no contraindications to their use.

*Risk factors for cardiogenic shock (the greater the number of risk factors present, the higher the risk of developing cardiogenic shock) are age >70 years, systolic BP <120 mm Hg, sinus tachycardia >110 bpm or heart rate <60 bpm, and increased time since onset of symptoms of STEMI.
Beta Blockers

Patients with initial contraindications to the use of beta blockers in the first 24 hours after STEMI should be reevaluated to determine their subsequent eligibility.

It is reasonable to administer intravenous beta blockers at the time of presentation to patients with STEMI and no contraindications to their use who are hypertensive or have ongoing ischemia.
Renin-Angiotensin-Aldosterone System Inhibitors
Renin-Angiotensin-Aldosterone System Inhibitors

An ACE inhibitor should be administered within the first 24 hours to all patients with STEMI with anterior location, HF, or EF less than or equal to 0.40, unless contraindicated.

An ARB should be given to patients with STEMI who have indications for but are intolerant of ACE inhibitors.
An aldosterone antagonist should be given to patients with STEMI and no contraindications who are already receiving an ACE inhibitor and beta blocker and who have an EF less than or equal to 0.40 and either symptomatic HF or diabetes mellitus.

ACE inhibitors are reasonable for all patients with STEMI and no contraindications to their use.
Lipid Management
Complications After STEMI
Complications After STEMI

Treatment of Cardiogenic Shock
Emergency revascularization with either PCI or CABG is recommended in suitable patients with cardiogenic shock due to pump failure after STEMI irrespective of the time delay from MI onset.

In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI and cardiogenic shock who are unsuitable candidates for either PCI or CABG.
The use of intra-aortic balloon pump counterpulsation can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological.

Alternative LV assist devices for circulatory support may be considered in patients with refractory cardiogenic shock.
Electrical Complications During the Hospital Phase of STEMI
Implantable Cardioverter-Defibrillator Therapy Before Discharge

Complications After STEMI
Implantable Cardioverter-Defibrillator Therapy Before Discharge

ICD therapy is indicated before discharge in patients who develop sustained VT/VF more than 48 hours after STEMI, provided the arrhythmia is not due to transient or reversible ischemia, reinfarction, or metabolic abnormalities.
Complications After STEMI

Bradycardia, AV Block, and Intraventricular Conduction Defects
Complications After STEMI

Pacing in STEMI
Pacing in STEMI

Temporary pacing is indicated for symptomatic bradyarrhythmias unresponsive to medical treatment.
Pericarditis
Management of Pericarditis
After STEMI
Management of Pericarditis After STEMI

Aspirin is recommended for treatment of pericarditis after STEMI.

Administration of acetaminophen, colchicine, or narcotic analgesics may be reasonable if aspirin, even in higher doses, is not effective.

Glucocorticoids and nonsteroidal antiinflammatory drugs are potentially harmful for treatment of pericarditis after STEMI.
Complications After STEMI

Thromboembolic and Bleeding Complications
Complications After STEMI

Anticoagulation
The following recommendations apply to patients who receive intracoronary stents during PCI for STEMI. Among individuals with STEMI who do not receive an intracoronary stent, the duration of DAPT beyond 14 days has not been studied adequately for patients who undergo balloon angioplasty alone, are treated with fibrinolysis alone, or do not receive reperfusion therapy. In this subset of patients with STEMI who do not receive an intracoronary stent, the threshold for initiation of oral anticoagulation for secondary prevention, either alone or in combination with aspirin, may be lower, especially if a shorter duration (i.e., 14 days) of DAPT is planned.
Anticoagulation

Anticoagulant therapy with a vitamin K antagonist should be provided to patients with STEMI and atrial fibrillation with CHADS2* score greater than or equal to 2, mechanical heart valves, venous thromboembolism, or hypercoagulable disorder.

The duration of triple-antithrombotic therapy with a vitamin K antagonist, aspirin, and a P2Y$_{12}$ receptor inhibitor should be minimized to the extent possible to limit the risk of bleeding.†

*CHADS2 (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, previous Stroke/transient ischemic attack (doubled risk weight)) score.
†Individual circumstances will vary and depend on the indications for triple therapy and the type of stent placed during PCI. After this initial treatment period, consider therapy with a vitamin K antagonist plus a single antiplatelet agent. For patients treated with fibrinolysis, consider triple therapy for 14 days, followed by a vitamin K antagonist plus a single antiplatelet agent.
Anticoagulation

Anticoagulant therapy with a vitamin K antagonist is reasonable for patients with STEMI and asymptomatic LV mural thrombi.

Anticoagulant therapy may be considered for patients with STEMI and anterior-apical akinesia or dyskinesis.

Targeting vitamin K antagonist therapy to a lower international normalized ratio (e.g., 2.0 to 2.5) might be considered in patients with STEMI who are receiving DAPT.
Risk Assessment After STEMI

Use of Noninvasive Testing for Ischemia Before Discharge
Use of Noninvasive Testing for Ischemia Before Discharge

Noninvasive testing for ischemia should be performed before discharge to assess the presence and extent of inducible ischemia in patients with STEMI who have not had coronary angiography and do not have high-risk clinical features for which coronary angiography would be warranted.

Noninvasive testing for ischemia might be considered before discharge to evaluate the functional significance of a noninfarct artery stenosis previously identified at angiography.

Noninvasive testing for ischemia might be considered before discharge to guide the postdischarge exercise prescription.
Risk Assessment After STEMI

Assessment of LV Function
Assessment of LV Function

LVEF should be measured in all patients with STEMI.
Assessment of Risk for SCD
2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

Developed in Collaboration with American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions

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The full-text guidelines are also available on the following Web sites: ACC (www.cardiosource.org) and AHA (my.americanheart.org)
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3.2. Mode of Transport to the Hospital

Even though >98% of the U.S. population is covered by 9-1-1 service (63), patients with STEMI often do not call EMS or 9-1-1 and are not transported to the hospital by ambulance. In a 2011 observational study from the ACTION Registry–GWTG that used data reported from a limited number of predominantly PCI-capable U.S. hospitals, EMS transport was used for only 60% of 37,643 patients with STEMI (64). Older U.S. surveys reported EMS activation rates of 23% to 53%, with substantial geographic variability (62,65,66).

Patients with possible ischemic symptoms should be transported to the hospital by ambulance rather than by friends or relatives because 1) 1 in every 300 patients with chest pain transported to the emergency department (ED) by private vehicle suffers cardiac arrest en route (67); and 2) there is a significant association between arrival at the ED by ambulance and earlier delivery of reperfusion therapy (64–66,68).

In addition, the performance of prehospital ECGs by trained personnel is associated with shorter reperfusion times (69) and lower mortality rates from STEMI. The use of prehospital ECGs, particularly when coupled with communication of STEMI diagnosis and preferential transport to a PCI-capable hospital, has been shown to result in rapid reperfusion times and excellent clinical outcomes (70–72).
Onset of Myocardial Infarction
Community Preparedness and System Goals for Reperfusion Therapy
Guideline for STEMI

Onset of Myocardial Infarction
Community Preparedness and System Goals for Reperfusion Therapy

Onset of Myocardial Infarction
The Relationship Between Sudden Cardiac Death and STEMI
Checklist. Improving Door-to-Device Times

1. Prehospital ECG to diagnose STEMI is used to activate the PCI team while the patient is en route to the hospital.
2. Emergency physicians activate the PCI team.
3. A single call to a central page operator activates the PCI team.
4. Goal is set for the PCI team to arrive in the catheterization laboratory within 20 minutes after being paged.
5. Timely data feedback and analysis are provided to members of the STEMI care team.
Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours’ duration.

Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours’ duration who have contraindications to fibrinolytic therapy, irrespective of the time delay from FMC.

Primary PCI should be performed in patients with STEMI and cardiogenic shock or acute severe HF, irrespective of time delay from MI onset.
Primary PCI in STEMI

Primary PCI is reasonable in patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia between 12 and 24 hours after symptom onset.

PCI should not be performed in a non-infarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable.
Aspiration Thrombectomy
Manual aspiration thrombectomy is reasonable for patients undergoing primary PCI.
Antiplatelet Therapy to Support Primary PCI for STEMI

It is reasonable to start treatment with an intravenous GP IIb/IIIa receptor antagonist at the time of primary PCI (with or without stenting or clopidogrel pretreatment) in selected patients with STEMI who are receiving UFH.

• Abciximab: 0.25 mg/kg IV bolus, then 0.125 mcg/kg/min (maximum 10 mcg/min); or

• High-bolus-dose tirofiban: 25 mcg/kg IV bolus, then 0.15 mcg/kg/min; or

• Double-bolus eptifibatide: 180 mcg/kg IV bolus, then 2 mcg/kg/min; a 2nd 180-mcg/kg bolus is administered 10 min after the 1st bolus.
Antiplatelet Therapy to Support Primary PCI for STEMI

It may be reasonable to administer intravenous GP IIb/IIIa receptor antagonist in the precatheterization laboratory setting (e.g., ambulance, ED) to patients with STEMI for whom primary PCI is intended.

It may be reasonable to administer intracoronary abciximab to patients with STEMI undergoing primary PCI.

Continuation of a P2Y$_{12}$ inhibitor beyond 1 year may be considered in patients undergoing DES placement.
Antiplatelet Therapy to Support Primary PCI for STEMI

Aspirin 162 to 325 mg should be given before primary PCI.

After PCI, aspirin should be continued indefinitely.
Antiplatelet Therapy to Support Primary PCI for STEMI

It is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses after primary PCI.
Antiplatelet Therapy to Support Primary PCI for STEMI

P2Y$_{12}$ inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent (BMS or DES) during primary PCI using the following maintenance doses:

- Clopidogrel 75 mg daily; or
- Prasugrel 10 mg daily; or
- Ticagrelor 90 mg twice a day*

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.
Antiplatelet Therapy to Support Primary PCI for STEMI

A loading dose of a $\text{P2Y}_{12}$ receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI. Options include:

- Clopidogrel 600 mg; or
- Prasugrel 60 mg; or
- Ticagrelor 180 mg
Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack.
Anticoagulant Therapy to Support Primary PCI

In patients with STEMI undergoing PCI who are at high risk of bleeding, it is reasonable to use bivalirudin monotherapy in preference to the combination of UFH and a GP IIb/IIIa receptor antagonist.

Fondaparinux should not be used as the sole anticoagulant to support primary PCI because of the risk of catheter thrombosis.
Anticoagulant Therapy to Support Primary PCI

For patients with STEMI undergoing primary PCI, the following supportive anticoagulant regimens are recommended:

- UFH, with additional boluses administered as needed to maintain therapeutic activated clotting time levels, taking into account whether a GP IIb/IIa receptor antagonist has been administered; or

- Bivalirudin with or without prior treatment with UFH.
### Adjunctive Antithrombotic Therapy to Support Reperfusion With Primary PCI (cont.)

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
</tr>
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<tbody>
<tr>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

**IV GP IIb/IIIa receptor antagonists in conjunction with UFH or bivalirudin in selected patients**

- Abciximab: 0.25-mg/kg IV bolus, then 0.125 mcg/kg/min (maximum 10 mcg/min)
- Tirofiban: (high-bolus dose): 25-mcg/kg IV bolus, then 0.15 mcg/kg/min
  - In patients with CrCl <30 mL/min, reduce infusion by 50%
- Eptifibatide: (double bolus): 180-mcg/kg IV bolus, then 2 mcg/kg/min; a second 180-mcg/kg bolus is administered 10 min after the first bolus
  - In patients with CrCl <50 mL/min, reduce infusion by 50%
  - Avoid in patients on hemodialysis
- Pre-catheterization laboratory administration of IV GP IIb/IIIa receptor antagonist
- Intracoronary abciximab 0.25-mg/kg bolus
Fibrinolytic Therapy When There Is an Anticipated Delay to Performing Primary PCI Within 120 Minutes of FMC

In the absence of contraindications, fibrinolytic therapy should be given to patients with STEMI and onset of ischemic symptoms within the previous 12 hours when it is anticipated that primary PCI cannot be performed within 120 minutes of FMC.

In the absence of contraindications and when PCI is not available, fibrinolytic therapy is reasonable for patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia within 12 to 24 hours of symptom onset and a large area of myocardium at risk or hemodynamic instability.

Fibrinolytic therapy **should not be administered** to patients with ST depression except when a true posterior (inferobasal) MI is suspected or when associated with ST elevation in lead aVR.
Immediate transfer to a PCI-capable hospital for coronary angiography is recommended for suitable patients with STEMI who develop cardiogenic shock or acute severe HF, irrespective of the time delay from MI onset.

Urgent transfer to a PCI-capable hospital for coronary angiography is reasonable for patients with STEMI who demonstrate evidence of failed reperfusion or reocclusion after fibrinolytic therapy.

I IIa IIb III

[Image of classification system]
Transfer of Patients With STEMI to a PCI-Capable Hospital for Coronary Angiography After Fibrinolytic Therapy

Transfer to a PCI-capable hospital for coronary angiography is reasonable for patients with STEMI who have received fibrinolytic therapy even when hemodynamically stable* and with clinical evidence of successful reperfusion. Angiography can be performed as soon as logistically feasible at the receiving hospital, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.
Adjunctive Antiplatelet Therapy With Fibrinolysis

Aspirin (162- to 325-mg loading dose) and clopidogrel (300-mg loading dose for patients ≤75 years of age, 75-mg dose for patients >75 years of age) should be administered to patients with STEMI who receive fibrinolytic therapy.
Adjunctive Antiplatelet Therapy With Fibrinolysis

In patients with STEMI who receive fibrinolytic therapy:

- aspirin should be continued indefinitely and

  - clopidogrel (75 mg daily) for at least 14 days
  
  - and up to 1 year
Adjunctive Antiplatelet Therapy With Fibrinolysis

It is reasonable to use aspirin 81 mg per day in preference to higher maintenance doses after fibrinolytic therapy.
Adjunctive Anticoagulant Therapy With Fibrinolysis
Adjunctive Anticoagulant Therapy With Fibrinolysis

Patients with STEMI undergoing reperfusion with fibrinolytic therapy should receive anticoagulant therapy for a minimum of 48 hours, and preferably for the duration of the index hospitalization, up to 8 days or until revascularization if performed. Recommended regimens include:

a. UFH administered as a weight-adjusted intravenous bolus and infusion to obtain an activated partial thromboplastin time of 1.5 to 2.0 times control, for 48 hours or until revascularization;

b. Enoxaparin administered according to age, weight, and creatinine clearance, given as an intravenous bolus, followed in 15 minutes by subcutaneous injection for the duration of the index hospitalization, up to 8 days or until revascularization; or

c. Fondaparinux administered with initial intravenous dose, followed in 24 hours by daily subcutaneous injections if the estimated creatinine clearance is greater than 30 mL/min, for the duration of the index hospitalization, up to 8 days or until revascularization.
Guideline for STEMI

Reperfusion at a Non–PCI-Capable Hospital
Transfer of Patients With STEMI to a PCI-Capable Hospital for Coronary Angiography After Fibrinolytic Therapy
Coronary Angiography in Patients Who Initially Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion
Coronary Angiography in Patients Who Initially Were Managed With Fibrinolytic Therapy or Who Did Not Receive Reperfusion

Cardiac catheterization and coronary angiography with intent to perform revascularization should be performed after STEMI in patients with any of the following:

a. Cardiogenic shock or acute severe HF that develops after initial presentation;

b. Intermediate- or high-risk findings on predischarge noninvasive ischemia testing; or

c. Myocardial ischemia that is spontaneous or provoked by minimal exertion during hospitalization.
Coronary angiography with intent to perform revascularization is reasonable for patients with evidence of failed reperfusion or reocclusion after fibrinolytic therapy. Angiography can be performed as soon as logistically feasible.

Coronary angiography is reasonable before hospital discharge in stable* patients with STEMI after successful fibrinolytic therapy. Angiography can be performed as soon as logistically feasible, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.
PCI of an Infarct Artery in Patients Who Initially Were Managed With Fibrinolysis or Who Did Not Receive Reperfusion Therapy
PCI of an Infarct Artery in Patients Who Initially Were Managed With Fibrinolysis or Who Did Not Receive Reperfusion Therapy

PCI of an anatomically significant stenosis in the infarct artery should be performed in patients with suitable anatomy and any of the following:

a. Cardiogenic shock or acute severe HF;

b. Intermediate- or high-risk findings on predischarge noninvasive ischemia testing; or

c. Myocardial ischemia that is spontaneous or provoked by minimal exertion during hospitalization.
PCI of an Infarct Artery in Patients Who Initially Were Managed With Fibrinolysis or Who Did Not Receive Reperfusion Therapy

Delayed PCI is reasonable in patients with STEMI and evidence of failed reperfusion or reocclusion after fibrinolytic therapy. PCI can be performed as soon as logistically feasible at the receiving hospital.
PCI of an Infarct Artery in Patients Who Initially Were Managed With Fibrinolysis or Who Did Not Receive Reperfusion Therapy

Delayed PCI of a significant stenosis in a patent infarct artery is reasonable in stable* patients with STEMI after fibrinolytic therapy. PCI can be performed as soon as logistically feasible at the receiving hospital, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.

Ia IIb III

Delayed PCI of a significant stenosis in a patent infarct artery greater than 24 hours after STEMI may be considered as part of an invasive strategy in stable* patients.

*Although individual circumstances will vary, clinical stability is defined by the absence of low output, hypotension, persistent tachycardia, apparent shock, high-grade ventricular or symptomatic supraventricular tachyarrhythmias, and spontaneous recurrent ischemia.
PCI of an Infarct Artery in Patients Who Initially Were Managed With Fibrinolysis or Who Did Not Receive Reperfusion Therapy

No Benefit

Delayed PCI of a totally occluded infarct artery greater than 24 hours after STEMI should not be performed in asymptomatic patients with 1- or 2-vessel disease if they are hemodynamically and electrically stable and do not have evidence of severe ischemia.
PCI of a Noninfarct Artery Before Hospital Discharge
Adjunctive Antithrombotic Therapy to Support Delayed PCI After Fibrinolytic Therapy
Delayed Invasive Management

Antiplatelet Therapy to Support PCI After Fibrinolytic Therapy
Antiplatelet Therapy to Support PCI After Fibrinolytic Therapy

After PCI, aspirin should be continued indefinitely.

Clopidogrel should be provided as follows:

a. A 300-mg loading dose should be given before or at the time of PCI to patients who did not receive a previous loading dose and who are undergoing PCI within 24 hours of receiving fibrinolytic therapy;

b. A 600-mg loading dose should be given before or at the time of PCI to patients who did not receive a previous loading dose and who are undergoing PCI more than 24 hours after receiving fibrinolytic therapy; and

c. A dose of 75 mg daily should be given after PCI.
Antiplatelet Therapy to Support PCI After Fibrinolytic Therapy

After PCI, it is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses.

Prasugrel, in a 60-mg loading dose, is reasonable once the coronary anatomy is known in patients who did not receive a previous loading dose of clopidogrel at the time of administration of a fibrinolytic agent, but prasugrel should not be given sooner than 24 hours after administration of a fibrin-specific agent or 48 hours after administration of a non-fibrin-specific agent.

Prasugrel, in a 10-mg daily maintenance dose, is reasonable after PCI.
Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack.
Anticoagulant Therapy to Support PCI After Fibrinolytic Therapy
Anticoagulant Therapy to Support PCI After Fibrinolytic Therapy

For patients with STEMI undergoing PCI after receiving fibrinolytic therapy with intravenous UFH, additional boluses of intravenous UFH should be administered as needed to support the procedure, taking into account whether GP IIb/IIIa receptor antagonists have been administered.

For patients with STEMI undergoing PCI after receiving fibrinolytic therapy with enoxaparin, if the last subcutaneous dose was administered within the prior 8 hours, no additional enoxaparin should be given; if the last subcutaneous dose was administered between 8 and 12 hours earlier, enoxaparin 0.3 mg/kg IV should be given.
Fondaparinux should not be used as the sole anticoagulant to support PCI. An additional anticoagulant with anti-IIa activity should be administered because of the risk of catheter thrombosis.
Adjunctive Antithrombotic Therapy to Support PCI After Fibrinolytic Therapy

<table>
<thead>
<tr>
<th>Antiplatelet therapy</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>● 162- to 325-mg loading dose given with fibrinolytic agent (before PCI). (Section 5.1.4.1 and Table 7)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>● 81- to 325-mg daily maintenance dose after PCI (indefinite)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>● 81 mg daily is the preferred daily maintenance dose</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td><strong>P2Y&lt;sub&gt;12&lt;/sub&gt; receptor inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loading doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For patients who received a loading dose of clopidogrel with fibrinolytic therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● Continue clopidogrel 75 mg daily without an additional loading dose</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>For patients who have not received a loading dose of clopidogrel:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>● If PCI is performed ≤24 h after fibrinolytic therapy: clopidogrel 300-mg loading dose before or at the time of PCI</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>● If PCI is performed &gt;24 h after fibrinolytic therapy: clopidogrel 600-mg loading dose before or at the time of PCI</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>● If PCI is performed &gt;24 h after treatment with a fibrin-specific agent or &gt;48 h after a non–fibrin-specific agent: prasugrel 60 mg at the time of PCI</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>For patients with prior stroke/TIA: prasugrel</td>
<td>III: Harm</td>
<td>B</td>
</tr>
</tbody>
</table>
Balloon angioplasty without stent placement may be used in selected patients. It might be reasonable to provide P2Y$_{12}$ inhibitor therapy to patients with STEMI undergoing balloon angioplasty after fibrinolysis alone according to the recommendations listed for BMS. *(Level of Evidence: C)*

### P2Y$_{12}$ receptor inhibitors

**Maintenance doses and duration of therapy**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel</td>
<td>75 mg</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DES placed</th>
<th>Continue therapy for at least 1 y with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel</td>
<td>75 mg daily</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>10 mg daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMS* placed</th>
<th>Continue therapy for at least 30 d and up to 1 y with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel</td>
<td>75 mg daily</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>10 mg daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>
Adjunctive Antithrombotic Therapy to Support PCI After Fibrinolytic Therapy (cont.)

<table>
<thead>
<tr>
<th>Anticoagulant therapy</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue UFH through PCI, administering additional IV boluses as needed to maintain therapeutic ACT depending on use of GP IIb/IIIa receptor antagonist†</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Continue enoxaparin through PCI:</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>- No additional drug if last dose was within previous 8 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 0.3-mg/kg IV bolus if last dose was 8 to 12 h earlier</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fondaparinux:</td>
<td>III: Harm</td>
<td>C</td>
</tr>
<tr>
<td>- As sole anticoagulant for PCI</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†The recommended ACT with no planned GP IIb/IIIa receptor antagonist treatment is 250–300 s (HemoTec device) or 300–350 s (Hemochron device).
CABG in Patients With STEMI

The use of mechanical circulatory support is reasonable in patients with STEMI who are hemodynamically unstable and require urgent CABG.

Emergency CABG within 6 hours of symptom onset may be considered in patients with STEMI who do not have cardiogenic shock and are not candidates for PCI or fibrinolytic therapy.
Timing of Urgent CABG in Patients With STEMI in Relation to Use of Antiplatelet Agents
Adjunctive Antithrombotic Therapy With Fibrinolysis

Reperfusion at a Non–PCI-Capable Hospital
Use of Stents in Primary PCI
Use of Stents in Patients With STEMI
Landmark analysis

**Any Stent at Index PCI**

- **N= 12,844**

**Stent Thrombosis**

- **Wiviott, NEJM, 2007: 357: 2001**

Comparison of Prasugrel and Clopidogrel:

- **Prasugrel**
  - Loading Dose: HR 0.82, P=0.01
  - Maintenance Dose: HR 0.80, P=0.003

- **Clopidogrel**
  - Loading Dose: 5.6
  - Maintenance Dose: 6.9

**Endpoint (%)**

- **Days**
  - 0, 30, 60, 90, 180, 270, 360, 450

- **Prasugrel**
  - 1.1 (68)
  - HR 0.48, P <0.0001
  - NNT = 77

- **Clopidogrel**
  - 2.4 (142)

**End of Document**
<table>
<thead>
<tr>
<th>category</th>
<th>Ticagrelor (n=5,640)</th>
<th>Clopidogrel (n=5,649)</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td>71 (1.3)</td>
<td>106 (1.9)</td>
<td>0.67 (0.50–0.91)</td>
<td>0.009</td>
</tr>
<tr>
<td>Probable or definite</td>
<td>118 (2.1)</td>
<td>158 (2.8)</td>
<td>0.75 (0.59–0.95)</td>
<td>0.02</td>
</tr>
<tr>
<td>Possible, probable, definite</td>
<td>155 (2.8)</td>
<td>202 (3.6)</td>
<td>0.77 (0.62–0.95)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Time-at-risk is calculated from first stent insertion in the study or date of randomisation*
# PLATO Hierarchical Testing of Efficacy

<table>
<thead>
<tr>
<th>All patients*</th>
<th>Ticagrelor (n=9,333)</th>
<th>Clopidogrel (n=9,291)</th>
<th>HR for (95% CI)</th>
<th>p value†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary objective, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV death + MI + stroke</td>
<td>864 (9.8)</td>
<td>1,014 (11.7)</td>
<td>0.84 (0.77–0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Secondary objectives, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total death + MI + stroke</td>
<td>901 (10.2)</td>
<td>1,065 (12.3)</td>
<td>0.84 (0.77–0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CV death + MI + stroke + ischaemia + TIA + arterial thrombotic events</td>
<td>1,290 (14.6)</td>
<td>1,456 (16.7)</td>
<td>0.88 (0.81–0.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>504 (5.8)</td>
<td>593 (6.9)</td>
<td>0.84 (0.75–0.95)</td>
<td>0.005</td>
</tr>
<tr>
<td>CV death</td>
<td>353 (4.0)</td>
<td>442 (5.1)</td>
<td>0.79 (0.69–0.91)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>125 (1.5)</td>
<td>106 (1.3)</td>
<td>1.17 (0.91–1.52)</td>
<td>0.22</td>
</tr>
<tr>
<td>Total death</td>
<td>399 (4.5)</td>
<td>506 (5.9)</td>
<td>0.78 (0.69–0.89)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*The percentages are K-M estimates of the rate of the endpoint at 12 months.*
Antiplatelet Therapy to Support Primary PCI for STEMI
Coronary Artery Bypass Graft Surgery

CABG in Patients With STEMI
Urgent CABG is indicated in patients with STEMI and coronary anatomy not amenable to PCI who have ongoing or recurrent ischemia, cardiogenic shock, severe HF, or other high-risk features.

CABG is recommended in patients with STEMI at time of operative repair of mechanical defects.
Timing of Urgent CABG in Patients With STEMI in Relation to Use of Antiplatelet Agents

Aspirin should not be withheld before urgent CABG.

Short-acting intravenous GP IIb/IIIa receptor antagonists (eptifibatide, tirofiban) should be discontinued at least 2 to 4 hours before urgent CABG.

Clopidogrel or ticagrelor should be discontinued at least 24 hours before urgent on-pump CABG, if possible.
Abciximab should be discontinued at least 12 hours before urgent CABG.

Urgent off-pump CABG within 24 hours of clopidogrel or ticagrelor administration might be considered, especially if the benefits of prompt revascularization outweigh the risks of bleeding.

Urgent CABG within 5 days of clopidogrel or ticagrelor administration or within 7 days of prasugrel administration might be considered, especially if the benefits of prompt revascularization outweigh the risks of bleeding.
Anticoagulant Therapy to Support Primary PCI