Maximizing Patient-Case Manager Communication and Collaboration for ACS Patients: Meeting ACO Performance Targets

Faculty

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Accreditation for Cardiovascular Excellence
Washington, DC
Activity Description

Target Audience
This activity is designed for case managers, along with physicians, nurses and hospital pharmacists, who are responsible for meeting accountable care organization (ACO) performance targets when overseeing patients with acute coronary syndrome (ACS).

Statement of Need
It is estimated that 1 in 5 Medicare patients discharged from a hospital will be readmitted within 30 days, and that 67% of patients surviving a coronary event will suffer a recurrent event requiring rehospitalization. The Medicare Hospital Readmissions Reduction Program is part of the Affordable Care Act and provides a financial incentive to hospitals to lower patient readmission rates but does not provide clear guidance on how to reduce readmissions. This activity addresses provider adherence to ACS guidelines, patient education, and discharge and transition strategies between hospital and home in an effort to reduce hospital readmission. Through this webcast, our cardiologist and pharmacist faculty discuss methodologies to reduce readmission rates among ACS patients. Downloadable resources are available for case managers to employ within their practice or share with patients.

Support Statement
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Disclosures

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The following financial relationships have been provided:

Deepak L. Bhatt, MD, MPH, FACC, FAHA (Faculty)
- Advisory Board: Regado Biosciences
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- Discussion of Off-Label, Investigational, or Experimental Drug Use: Multiple antithrombotics

John Fanikos, RPh, MBA (Faculty)
- Discussion of Off-Label, Investigational, or Experimental Drug Use: None

Sheree Schroder, MSN, RN, RDCS, FASE (Planning Committee)
- No relevant financial relationships

Staff Disclosure
ACHL staff members and others involved with the planning, development, and review of the content for this activity have no relevant affiliations or financial relationships to disclose.
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Learning Objectives

For physicians, pharmacists:

- Discuss clinical guidelines for the use of antiplatelet therapies in patients with ACS who are hospitalized, undergoing percutaneous coronary intervention, or being discharged with maintenance therapy
- Compare and contrast the efficacy and safety of antiplatelet therapies and their use in diverse ACS patients
- Formulate strategies to facilitate transitions of care, improve discharge communication, ensure patient adherence, and reduce complications and hospital readmissions related to ACS

For nurses, case managers:

- Review clinical guidelines for the use of antiplatelet therapies in patients with ACS who are hospitalized, undergoing percutaneous coronary intervention, or being discharged with maintenance therapy
- Explain why specific antiplatelet therapies are selected for specific ACS patient subsets
- Formulate strategies to facilitate transitions of care, improve discharge communication, ensure patient adherence, and reduce complications and hospital readmissions related to ACS
Downloadable Resources

Downloadable resources are available with this activity to help clinicians and case managers assist with patient medication adherence, action plan development, and transitions from hospital to home or outpatient settings. Learners are encouraged to access at this time, as they will not be available following completion of the activity.

Management of ACS Patients from Presentation to Hospital Discharge

Deepak L. Bhatt, MD, MPH, FACC, FAHA
Executive Director of Interventional Cardiovascular Programs,
Brigham and Women's Hospital Heart & Vascular Center
Professor of Medicine, Harvard Medical School
Boston, MA
Medicare Hospital Readmissions Reduction Program (HRRP)

- Part of the Affordable Care Act (ACA) that provides a financial incentive to hospitals to lower readmission rates
- Hospitals do not receive any additional reimbursement to cover the costs of interventions that may prevent readmissions, such as after-discharge follow-up
- Moreover, hospitals that reduce readmissions may even lose revenues unless they can fill unused beds with other patients
- Medicare imposes a financial penalty on hospitals with excess readmissions


Rehospitalizations: Medicare Fee-for-Service

- Analysis of Medicare Claims data from 2003-2004
- Includes the 11,855,702 Medicare beneficiaries discharged from the hospital

<table>
<thead>
<tr>
<th>Summary Analysis (Cumulative Rehospitalizations by End of Period)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 19.6% (nearly 1/5) were rehospitalized within 30 days</td>
</tr>
<tr>
<td>• For 50.2% of those rehospitalized within 30 days after a medical discharge there was no bill for a visit to a physician's office</td>
</tr>
<tr>
<td>• 34% were rehospitalized within 90 days</td>
</tr>
</tbody>
</table>

Hospital Readmission Statistics and Influences\(^1\)

- Readmission rate: 1 in 5 Medicare patients discharged from a hospital are readmitted within 30 days
- Up to 67% of patients with ACS suffer a recurrent event post-discharge, and which warrants rehospitalization\(^2\)
- Factors influencing readmission rates include
  - Geographic area
  - Disease type and severity
    - Patient’s with a low-moderate stroke risk are more likely to discontinue medication therapy\(^3\)
  - Patient’s behavior
    - Adherence to discharge instructions
  - Patient’s level of health literacy
  - Patient’s cognitive health
  - Availability and quality of postdischarge care

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Coronary Artery Disease (CAD) and Acute Coronary Syndrome (ACS)

- 15.4 million Americans have CAD
- 1,141,000 ACS events in US yearly
  - 322,000 have UA (28%)
  - 577,000 have NSTEMI (51%)
  - 236,000 have STEMI (21%)

Management
- (2010) 954,000 PCI procedures
- 397,000 CABG surgeries

Leading cause of death in the Western world
- 510,000 per year in US
- 1 death every minute

Estimated cost:
- US $312 billion

UA=Unstable Angina; NSTEMI=Non-ST-Elevation Myocardial Infarction; STEMI=ST-Elevation Myocardial Infarction

2014 ACCF/AHA Select Recommendations for Antiplatelet Rx in NSTE ACS

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Invasive Strategy, Medium to High Risk Patients:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before PCI: ticagrelor, clopidogrel, or GP IIb/IIIa inhibitor (with DAPT, LOE=B, COR=IIb)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Post-PCI: clopidogrel, prasugrel, ticagrelor or GP IIb/IIIa inhibitor (LOE=B; COR=IIb)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Initial Conservative (noninvasive) Strategy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel or ticagrelor added to aspirin and continued for up to 12 months</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Class III Recommendations:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prasugrel potentially harmful as part of DAPT in patients with a prior Hx of CVA and/or TIA</td>
<td>III—Harm</td>
<td>B</td>
</tr>
</tbody>
</table>

COR=Class Of Recommendation; LOE=Level Of Evidence

2011 ACCF/AHA/SCAI PCI Recommendations: P2Y\textsubscript{12} Inhibitor Therapy with Coronary Stents

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2Y\textsubscript{12} inhibitor therapy (clopidogrel, prasugrel, or ticagrelor for at least 12 months in patients receiving a stent (BMS or DES) during PCI for ACS)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Clopidogrel for at least 12 months in patients treated with a DES for a non-ACS indication, if patients are not at high risk of bleeding</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Clopidogrel for a minimum of 1 month and ideally up to 12 months in patients receiving a BMS for a non-ACS indication (unless the patient is at increased risk of bleeding; then it should be given for a minimum of two weeks)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Counseling patients on the importance of compliance with DAPT and to not discontinue Rx before discussion with the relevant cardiologist</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Earlier discontinuation (e.g., &lt;12 months) of P2Y\textsubscript{12} inhibitor therapy after stent implantation if the risk of morbidity from bleeding outweighs the anticipated benefit afforded by a recommended duration of P2Y\textsubscript{12} inhibitor therapy</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Continuation of DAPT beyond 12 months in patients undergoing DES implantation</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

BMS=Bare Metal Stent; DES=Drug Eluting Stent


New Terminology = NSTE ACS

- 2014 guideline update to be more accurate in distinguishing NSTE MI from unstable angina
- Patient approach remains unchanged:

<table>
<thead>
<tr>
<th>Risk stratification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection of an initial management therapy</td>
</tr>
<tr>
<td>Diagnostic evaluation for MI</td>
</tr>
<tr>
<td>Medical therapy utilization and/or revascularization</td>
</tr>
<tr>
<td>Secondary preventative therapy initiation</td>
</tr>
</tbody>
</table>

2014 NSTE MI Guideline Updates

• Updates include (pertinent to this activity)
  – new Class I recommendations for patient discharge instructions and the recommendation for a plan of care for smooth transitions and systems to promote care coordination
  – Specific recommendations for patient education regarding cardiovascular risk factors (blood pressure, cholesterol levels, lifestyle modification such as exercise and smoking cessation, medications, management of recurrent angina, cardiovascular risk factors, and activity levels)


2014 NSTE MI Guideline Updates

• Diagnosis of MI via use of troponin levels
• Risk stratification
  – Ischemia-guided approaches for patients with low risk scores
  – Stratification of early invasive strategies by time
• Medical therapy
  – Class I recommendation for ACE inhibitor use in patients with CKD and either diabetes, heart failure, HTN, or LVEF <40%
  – For early initial oral antiplatelet therapy, ticagrelor received a class IIa recommendation over clopidogrel
  – Prior to PCI, ticagrelor receives a class IIa recommendation over clopidogrel
  – DAPT duration is still 12 months for both BMSs and DESs (class I recommendation). Considering DAPT for longer than 12 months with a DES received a class II recommendation.

Potential Therapeutic Targets in ACS

- Primary and secondary prevention
  - Risk factor modification, ASA, P2Y₁₂ inhibitors, statins
- Prevent platelet activation with oral DAPT
- Prevent aggregation of activated platelets
  - Intravenous GP IIb/IIIa therapy, novel agents
- Attenuate coagulation response
  - Intravenous bivalirudin, unfractionated heparin, LMWH
- Attenuate inflammatory response
  - Statins? Manage ischemia/reperfusion injury?
  - Other emerging therapies?

DAPT=Dual Antplatelet Therapy; GP=(Platelet) Glycoprotein; LMWH=Low Molecular Weight Heparin

DISCUSSION
Aspirin in ACS

Unstable Angina

- Death or MI: *P<.0001
- Reocclusion: *P=.001

Acute MI

- MI: *P=.012
- Vascular Death: *P<.001

Placebo ASA0

- Patients (%)

<table>
<thead>
<tr>
<th>Months of Follow-up</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>ASA</td>
</tr>
<tr>
<td>N= 397</td>
<td>399</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Death or MI</td>
<td></td>
</tr>
<tr>
<td>17.1</td>
<td>11.0*</td>
</tr>
<tr>
<td>6.5*</td>
<td></td>
</tr>
<tr>
<td>Reocclusion</td>
<td></td>
</tr>
<tr>
<td>25.0</td>
<td>11.0*</td>
</tr>
<tr>
<td>11.0*</td>
<td></td>
</tr>
</tbody>
</table>

Acute MI

- MI: *P=.012
- Vascular Death: *P<.001

Placebo ASA0

- Patients (%)

<table>
<thead>
<tr>
<th>Months of Follow-up</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>ASA</td>
</tr>
<tr>
<td>N= 8,587</td>
<td>8,600</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
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<tr>
<td>10</td>
<td>10</td>
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<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Death or MI</td>
<td></td>
</tr>
<tr>
<td>11.8</td>
<td>9.4*</td>
</tr>
<tr>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Reocclusion</td>
<td></td>
</tr>
<tr>
<td>3.3</td>
<td>1.9*</td>
</tr>
<tr>
<td>1.9*</td>
<td></td>
</tr>
<tr>
<td>Acute MI</td>
<td></td>
</tr>
<tr>
<td>11.8</td>
<td>9.4*</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

MI=Myocardial Infarction;
ASA=Acetylsalicylic Acid;
RISC=Research on Instability in Coronary Artery Disease


CURE Study:
Primary End Point: MI/Stroke/CV Death

- Placebo + Aspirin (n=6303)
- Clopidogrel + Aspirin (n=6259)

Placebo + Aspirin (n=6303)

- 20% Relative Risk Reduction

Placebo + Aspirin (n=6303)

- Cumulative Hazard Rate

CURRENT OASIS 7
Study Design

Patients with STEMI or UA/NSTEMI planned for early invasive strategy, i.e. intend for PCI as early as possible within 24 hrs

N = ~25,000

Clopidogrel High Dose Group
Clopidogrel 600mg loading dose Day 1 followed by 150mg from Day 2 to Day 7; 75mg from Day 8 to 30

Clopidogrel Standard Dose Group
Clopidogrel 300mg (+placebo) Day 1 followed by 75mg (+placebo) from Day 2 to Day 7; 75mg from Day 8 to 30

ASA low dose group
At least 300mg Day1; 75–100mg from D2 to D30

ASA high dose group
At least 300mg Day1; 300mg–325mg from D2 to D30

CURRENT-OASIS 7: Clopidogrel Results

Patients with UA/NSTEMI or STEMI planned for early invasive strategy (i.e., intended for PCI as early as possible within 72 hours)

Randomize

Clopidogrel Standard-dose Group
Clopidogrel 300 mg (+ placebo) day 1 followed by 75 mg (+ placebo) from days 2 to 7; 75 mg from days 8 to 30

Clopidogrel High-dose Group
Clopidogrel 600 mg LD day 1 followed by 150 mg from days 2 to 7; 75 mg from days 8 to 30

CV death/MI/Stroke

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>Double</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (N=25,086)</td>
<td>4.4</td>
<td>4.2</td>
<td>0.94 (0.83-1.06)</td>
<td>0.30</td>
</tr>
<tr>
<td>PCI (n=17,263)</td>
<td>4.5</td>
<td>3.9</td>
<td>0.86 (0.74-0.99)</td>
<td>0.039</td>
</tr>
<tr>
<td>No PCI (n=7823)</td>
<td>4.3</td>
<td>4.9</td>
<td>1.14 (0.92-1.40)</td>
<td>0.23</td>
</tr>
</tbody>
</table>

LD = loading dose.

Definite Stent Thrombosis in 4 Groups (Angiographically Proven)

**List of Graphs:**

- **Graph 1:** Cumulative Hazard over Days
  - Standard, A Low
  - Standard, A High
  - Double, A Low
  - Double, A High
  - High ASA: 1.2 0.6 0.49 0.003
  - Low ASA: 1.2 0.8 0.6 0.058 0.35

- **Graph 2:** TRITON – TIMI 38
  - CV Death, MI, Stroke
  - Clopidogrel: HR 0.80 P=0.0003
  - Prasugrel: HR 0.77 P=0.0001

**References:**

  - Slide courtesy of Dr. Shamir Mehta
  - Slide courtesy of Dr. Elliott Antman
Stent Thrombosis
(ARC Definite + Probable)

Any Stent at Index PCI
N = 12,844

Clopidogrel

Prasugrel

HR 0.48
P < 0.0001
NNT = 77


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

TIMI Major Bleeds
ARD 0.6%
HR 1.32
P=0.03
NNH=167

Life Threatening
ARD 0.3%
HR 1.52
P=0.01

Nonfatal
ARD 0.2%
P=0.23

Fatal
ARD 0.3%
P=0.002

ICH
ARD 0%
P=0.74

Clop 0 (0) %
Pras 6 (2.3) %
P=0.02

Slide courtesy of Dr. Elliott Antman
**PLATO: CV Death, MI, or Stroke**

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>9,291</td>
<td>9,333</td>
<td>8,521</td>
</tr>
<tr>
<td>8,628</td>
<td>8,460</td>
<td>8,124</td>
</tr>
<tr>
<td>8,219</td>
<td>6,743</td>
<td>6,743</td>
</tr>
<tr>
<td>5,161</td>
<td>4,147</td>
<td>4,147</td>
</tr>
</tbody>
</table>

Days after randomization

| 6,743    | 6,743      | 5,096 |
| 5,161    | 5,161      | 4,147 |
| 4,147    | 4,147      | 4,047 |

Cumulative incidence (%)

HR 0.84 (95% CI 0.77–0.92), p=0.0003

Study Chairs: Drs. Harrington and Wallentin


**PLATO: Secondary Efficacy Endpoints**

Myocardial infarction

<table>
<thead>
<tr>
<th></th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>9,333</td>
<td>8,678</td>
<td>8,560</td>
</tr>
<tr>
<td>8,628</td>
<td>8,362</td>
<td>8,117</td>
</tr>
<tr>
<td>8,279</td>
<td>6,793</td>
<td>6,793</td>
</tr>
<tr>
<td>6,916</td>
<td>5,136</td>
<td>4,109</td>
</tr>
</tbody>
</table>

Days after randomization

| 8,628    | 8,362      | 8,117       |
| 6,793    | 6,793      | 6,793       |
| 5,136    | 4,109      | 4,109       |

Cumulative incidence (%)

HR 0.84 (95% CI 0.75–0.95), p=0.005

Study Chairs: Drs. Harrington and Wallentin

PLATO: Stratification by Invasive vs Conservative Strategy

Major Bleeding: Non-CABG vs CABG

Study Chairs: Drs. Harrington and Wallentin
**DAPT Trial: Set-Up**

- The appropriate duration of DAPT following DES implantation
  - 12 mos post DES implantation, patients randomly assigned to receive either continued thienopyridine therapy + aspirin or placebo + aspirin for 18 mos
  - Primary analysis performed on data from 12-30 mos post-enrollment
  - Co-primary efficacy endpoints included impact on stent thrombosis and MACCE


**DAPT Trial: MAACE (ITT Population)**

<table>
<thead>
<tr>
<th>Event</th>
<th>Continued Thienopyridine # of patients (%)</th>
<th>Placebo # of patients (%)</th>
<th>HR (Thienopyridine vs Placebo; 95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE</td>
<td>211 (4.3)</td>
<td>285 (5.9)</td>
<td>0.71 (0.59-0.85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death</td>
<td>98 (2.0)</td>
<td>74 (1.5)</td>
<td>1.36 (1.00-1.85)</td>
<td>0.05</td>
</tr>
<tr>
<td>Cardiac</td>
<td>45 (0.9)</td>
<td>47 (1.0)</td>
<td>1.00 (0.66-1.52)</td>
<td>0.98</td>
</tr>
<tr>
<td>Vascular</td>
<td>5 (0.1)</td>
<td>5 (0.1)</td>
<td>0.98 (0.28-3.39)</td>
<td>0.98</td>
</tr>
<tr>
<td>Noncardio-vascular</td>
<td>48 (1.0)</td>
<td>22 (0.5)</td>
<td>2.23 (1.32-3.78)</td>
<td>0.002</td>
</tr>
<tr>
<td>MI</td>
<td>99 (2.1)</td>
<td>198 (4.1)</td>
<td>0.47 (0.37-0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>37 (0.8)</td>
<td>43 (0.9)</td>
<td>0.80 (0.51-1.25)</td>
<td>0.32</td>
</tr>
<tr>
<td>Ischemic</td>
<td>24 (0.5)</td>
<td>34 (0.7)</td>
<td>0.68 (0.40-1.17)</td>
<td>0.16</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>13 (0.3)</td>
<td>9 (0.2)</td>
<td>1.20 (0.50-2.91)</td>
<td>0.68</td>
</tr>
<tr>
<td>Type uncertain</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
<td>—</td>
<td>0.32</td>
</tr>
</tbody>
</table>
DAPT Trial: Stent Thrombosis (ITT Population)

<table>
<thead>
<tr>
<th>Death</th>
<th>Continued Thienopyridine # of patients (%)</th>
<th>Placebo # of patients (%)</th>
<th>HR (Thienopyridine vs Placebo; 95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent thrombosis</td>
<td>19 (0.4)</td>
<td>65 (1.4)</td>
<td>0.29 (0.17-0.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Definite</td>
<td>15 (0.3)</td>
<td>58 (1.2)</td>
<td>0.26 (0.14-0.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Probable</td>
<td>5 (0.1)</td>
<td>7 (0.1)</td>
<td>0.71 (0.22-2.23)</td>
<td>0.55</td>
</tr>
</tbody>
</table>


DAPT Trial: Safety

- The rate of moderate or severe bleeding during the primary analysis period was significantly higher in the group that continued to receive thienopyridine therapy than in the placebo group
  - (2.5% vs. 1.6%; hazard ratio 1.61 [95% CI, 1.21 to 2.16]; P=0.001)
- Treatment with thienopyridine did not meet the prespecified criterion for noninferiority to placebo (P=0.70)
- There was no significant difference between the randomized treatments with respect to severe bleeding according to the GUSTO criteria (0.81% with continued thienopyridine and 0.56% with placebo, P=0.15) or with respect to fatal bleeding (type 5 bleeding) according to the BARC criteria (0.15% and 0.09%, respectively; P=0.38).
- Possible interpretation
  - Some patients may derive protective effects with extended periods of DAPT administration. However, additional studies need to be conducted and are underway to determine a more exact timeframe.

The Latest Ongoing Platelet Function-Based Personalized Trial (TROPICAL-ACS) - HIGH RISK PATIENTS

- 15 centers in Europe, open-label, prospective, randomized trial

Primary end point: 1y composite primary endpoint of CV death, MI, stroke and bleeding.

Secondary end-point: Individual incidence of bleeding, stent thrombosis, all-cause mortality

Cost-effectiveness analysis

ACS patients undergoing successful PCI N=2600

Control group: Uniform therapy with PRS

Monitoring group: Personalized therapy with PRS or CLP

Guidelines for Platelet Function Testing and Genotyping


Hamm CW et al. Eur Heart J. 2011;32:2999-3054

Montalescot G et al. Eur Heart J. 2013;34:2949-3003

Levine GN et al, J Am Coll Cardiol. 2011;58;e44-122

Jnied H et al, J Am Coll Cardiol. 2012;60;645-681

Report from the NICE Guideline on Evidence Based Surgery

2012 Update to The Society of Thoracic Surgeons
Guideline on Use of Antiplatelet Drugs in Patients Having Cardiac and Noncardiac Operations

For patients on dual antiplatelet therapy, it is reasonable to make decisions about surgical delay based on tests of platelet inhibition rather than arbitrary use of a specified period of surgical delay.
Summary of P2Y_{12} Inhibitor Properties and Use

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>Ticagrelor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Thienopyridine</td>
<td>Thienopyridine</td>
<td>Triazolopyrimidine</td>
</tr>
<tr>
<td><strong>“Reversibility”</strong></td>
<td>Irreversible</td>
<td>Irreversible</td>
<td>Reversible</td>
</tr>
<tr>
<td><strong>Activation</strong></td>
<td>Prodrug, limited by metabolism</td>
<td>Prodrug, not limited by metabolism</td>
<td>Active drug</td>
</tr>
<tr>
<td><strong>Onset of effect</strong></td>
<td>2-4 hr</td>
<td>30 min</td>
<td>30 min</td>
</tr>
<tr>
<td><strong>Duration of effect</strong></td>
<td>3-10 days</td>
<td>5-10 days</td>
<td>3-4 days</td>
</tr>
<tr>
<td><strong>Withdrawal before major elective surgery</strong></td>
<td>5 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
</tbody>
</table>

**Contraindications/ Caveats**
- 600 mg loading dose (not FDA approved) provides faster, greater, and more reliable platelet inhibition
- CYP2C19 *2 or *3 alleles are poor metabolizers and have reduced antiplatelet effects
- Contraindicated in patients with hx CVA/TIA
- Generally not recommended in patients age ≥75 years (bleeding risk)
- Increased bleeding risk if body weight <60 kg
- Concomitant ASA dose should be ≤100 mg
- Contraindicated if severe hepatic impairment
- Avoid use with strong CYP3A inhibitors* or CYP3A inducers**

*clarithromycin, ketoconazole, indinavir,itraconazole, etc.
**rifampin, carbamazepine, dexamethasone, phenytoin, phenobarbital

Based in part from Hamm CW, et al. *Eur Heart J*. 2011, as well as drug PIs and study protocols.

Case Study

- A 77-year old man with no previous CVD presents to the hospital with chest pain. His vitals are taken along with a brief history. He also has diabetes (type II).
- He reveals he had some discomfort in his back the previous day and that today the chest pain was intense and was accompanied by shortness of breath.
- An ECG shows a tracing indicative of NSTE ACS.
- Troponin levels are elevated.
- What types of medications should be given in the short-term?
- What types of medications should be given in the long-term, especially if only minor blockages are seen?
## Primary and Secondary Prevention: Areas of Intervention

### Lifestyle Changes
- Smoking
- Physical activity
- Weight management
- Depression
- Cardiac rehabilitation

### Medical Therapy
- Blood pressure control
- Lipid management
- Diabetes mellitus management
- Antiplatelet agents
- RAAS blockers
- Beta-blockers
- Influenza vaccination

RAAS=Renin-Angiotensin-Aldosterone System


---

## Primary and Secondary Prevention: Areas of Intervention

### Medical Therapy
- Blood pressure control
- Lipid management
- Diabetes mellitus management
- Antiplatelet agents
- RAAS blockers
- Beta-blockers
- Influenza vaccination

### Medication Noncompliance

RAAS=Renin-Angiotensin-Aldosterone System

Older CV Patients are Different

- Reduced cardiovascular reserve
  - Decreased vascular compliance
  - Increased myocardial stiffness
  - β-adrenergic responsiveness + impaired sinus node
- Higher burden of comorbid illness
  - “frailness”
- Altered pharmacodynamics and pharmacokinetics
  - Decline in creatinine clearance, hepatic metabolism
  - Altered volume of distribution (adipose tissue)
- Altered clotting mechanisms
- Reduced stem cell repair
- Higher risk for adverse outcomes

Daggubati R. C3 2014. Orlando, FL.

Nonadherence >> Resistance

Conclusions

- Oral antiplatelet therapy is critical to preventing recurrent ischemic events and death
  - **Aspirin**
    - Low-dose aspirin (81 mg daily) is the preferred chronic dose based on and efficacy and safety
    - Indefinite therapy is required
  - **P2Y$_{12}$ inhibitors**
    - No clear role for platelet aggregation testing in P2Y$_{12}$ inhibitor selection
    - New agents (prasugrel and ticagrelor) provide advantages over clopidogrel
    - Optimum duration still debated, guidelines recommend at least a year with aspirin therapy
    - Tailoring selection is critical

Conclusions (cont’d)

- Differences in chemical structure, metabolic activation, and mode of P2Y12 inhibition among clopidogrel, prasugrel, and ticagrelor are likely responsible for differences in
  - Onset of action
  - Degree of platelet inhibition
  - And reversibility of action
- Platelet inhibition by oral P2Y12 inhibitors in the early hours of STEMI remains a challenge
- Knowledge of these differences is important for understanding safety (bleeding) issues while using P2Y12 inhibitors
DISCUSSION

Overseeing the Continuum of Care for ACS Patients

John Fanikos, RPh, MBA
Adjunct Clinical Professor
Massachusetts College of Pharmacy
Director of Pharmacy
Brigham & Women's Hospital
Boston, MA
U.S. Prescription Drug Use


Adherence With Initial Discharge Prescriptions Over Time in Post-MI Patients

• 74% had ALL discharge prescriptions filled (Day 120)
• 78.6% of all prescriptions filled (Day 120)

Types of Medication Noncompliance

- Failing to initially fill a prescription
- Failing to refill a prescription
- Omitting doses
- Over dosing
- Prematurely discontinuing medication
- Taking a dose at the wrong time
- Taking a medication prescribed for someone else
- Taking a dose with prohibited foods, liquids, or other medications
- Taking outdated medications
- Improperly using medication administration devices (inhalers, injection pens, etc)

Factors Associated With Adherence With Discharge Prescriptions in Post-MI Patients

- **↑ likelihood of adherence**
  - No in-hospital PCI
    - OR 3.56 (1.31-9.91, \(P=0.01\))
  - **Low income**
    - OR 1.94 (1.53-2.45, \(P<.0001\))
  - Cardiologist as most responsible MD
    - OR 1.80 (1.34-2.43, \(P<.0001\))
  - Receipt of predischarge medication counseling
    - OR 1.61 (1.26-2.04, \(P<.0001\))
  - Internist as most responsible MD
    - OR 1.34 (1.01-1.78, \(P=0.04\))

- **↓ likelihood of adherence**
  - Heart failure
    - OR 0.45 (0.31-0.66, \(P<.0001\))
  - Prior MI
    - OR 0.65 (0.52-0.82, \(P<.0001\))
  - **↑ creatinine**
    - OR 0.67 (0.53-0.84, \(P=.001\))
  - **↑ number of Rx before admit**
    - OR 0.90 (0.88-0.92, \(P<.0001\))
  - **↑ age**
    - OR 0.97 (0.96-0.99, \(P=.001\))

Medication Adherence in the Elderly

• 1/3 of the elderly never comply with their medications
• 1/3 discontinue their medication prematurely
• > 1/2 of the elderly made errors when taking their medications
• 1/5 fail to initially fill a prescription
• 95% of the elderly live outside of institutions and are responsible for their own medications

Problem Scope

• 125,000 deaths annually in U.S.
  – 340 patients daily
• 33 to 69% of all medication-related hospital and nursing home admissions are due to poor medication adherence
• Among patients receiving treatment for chronic conditions, adherence rates are estimated to be between 43% and 78%
• Resultant estimated cost of $290 billion annually


DISCUSSION

Patient–reported Reasons for Not Taking Post–MI Therapy (Evidence–Based)

<table>
<thead>
<tr>
<th>Reason</th>
<th>Aspirin (N=1,569)</th>
<th>Clopidogrel (N=1,554)</th>
<th>Beta-blocker (N=1,566)</th>
<th>ACE inhibitor (N=1,556)</th>
<th>Statin (N=1,571)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy/intolerance/side effect</td>
<td>15.4%</td>
<td>2.8%</td>
<td>7.2%</td>
<td>10.0%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Not prescribed at discharge</td>
<td>22.6%</td>
<td>42.7%</td>
<td>28.6%</td>
<td>43.5%</td>
<td>42.1%</td>
</tr>
<tr>
<td>Stopped by MD unrelated to intolerance/side effects</td>
<td>25.0%</td>
<td>19.3%</td>
<td>24.8%</td>
<td>14.9%</td>
<td>11.8%</td>
</tr>
<tr>
<td>No reason provided</td>
<td>43.3%</td>
<td>37.3%</td>
<td>41.2%</td>
<td>35.3%</td>
<td>37.5%</td>
</tr>
</tbody>
</table>

~1/3 of patients discontinued therapy without instruction from their physician

Transitions of Care in ACS: Do Patients Receive Appropriate Education?

- Lack of awareness regarding information from index admission for MI
  - Only 41% aware of MI diagnosis
  - 19% unaware of final diagnosis
  - <50% knew they had ≥1 major CAD risk factor
  - ≤67% could recall lifestyle modifications
- Top 3 areas for improvement with educational information identified by post–MI patients
  - Follow-up after discharge
  - Medication information
  - Examinations


Early Nonadherence Following Discharge: Prescriptions Abandoned at Retail Pharmacies

- 3.3% were abandoned
- 1.0% were antithrombotic medications
- New medication users had a 3X greater probability of abandonment
- Prescription Cost >$50 there was a 5X greater probability of abandonment

Consequences of Noncompliance

• Burden on emergency room care
• Increased physician visits
• Additional diagnostic tests and alternative treatments
• Adverse clinical outcomes
  – Anticoagulants → Thrombosis
  – Cardiac medications → rebound hypertension, arrhythmia
  – Antibiotics → recurrent infection, bacterial resistance
  – Birth Control → unwanted pregnancy
  – Insulin → Ketoacidosis

Clopidogrel Nonadherence and/or Delays Impact on Clinical Outcomes

- 1 in 6 patients failed to fill their prescription on the day of discharge
- Delayed therapy was associated with CV events

Best Practice Recommendations for Discharge Preparation in MI Patients

- Address educational barriers
- Thorough review of medications
- Utilize inpatient AND outpatient settings
- Assess readiness to learn
- Vary teaching methods
  - Teach back
  - Optimize written materials
- Engage caregivers & other healthcare team members
- Emphasize self-care
- Refer to disease management program(s)
- Assess patient resources
  - Cost
  - Provision of meds at discharge?
- Focus on smooth transitions of care

## Action Plan

<table>
<thead>
<tr>
<th>Step</th>
<th>Setting</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Transition</td>
<td>Provide patient &amp; family with their medication treatment plan (medications, doses, duration) at hospital discharge</td>
</tr>
<tr>
<td>2</td>
<td>Continuum</td>
<td>Eliminate delays in prescription filling, prevent premature discontinuation</td>
</tr>
<tr>
<td>3</td>
<td>Community-Initiation</td>
<td>Educate patient &amp; family about the medication, compliance, drug-food interactions, and adverse events</td>
</tr>
<tr>
<td>4</td>
<td>Community-Maintenance</td>
<td>Monitor co-morbidities, medication use, refill intervals, and over-the-counter medication purchases, and detect drug-related problems</td>
</tr>
<tr>
<td>5</td>
<td>Community-Outcomes</td>
<td>Critically evaluate with the patient the outcomes of treatment for safety, efficacy, and the need for therapy changes</td>
</tr>
</tbody>
</table>

Slide courtesy of John Fanikos, RPh.

## DISCUSSION
Ideal Transitions in Care

- “Hospitals cannot reduce their readmission rates by focusing on aspects of care within their walls. They must forge new and stronger relationships with their communities if they are to be successful.”


Continuity Improvement Projects

- National Transitions of Care Coalition
  - 30 participating associations and organizations
  - Goal: to break down silos and barriers between different health care settings and help them work more collaboratively for the good of the patient
  - Several evidence-based transitions of care models have been developed to improve patient outcomes
  - These models include many or all of the elements that are being researched as part of The Joint Commission enterprise transitions of care initiative
    - Care Transitions Intervention (CTI)
    - Transitional Care Model (TCM)
    - The Bridge Model
    - Guided Care
    - Geriatric Resources for Assessment and Care of Elders (GRACE)
## Continuity Improvement Projects

- **“Bundle”**: a set of evidenced-based interventions for a patient population that improve patient outcomes

<table>
<thead>
<tr>
<th>Project</th>
<th>Sponsors</th>
<th>“Discharge Bundle”</th>
</tr>
</thead>
<tbody>
<tr>
<td>“RED”</td>
<td>AHRQ</td>
<td>Element: Warm handoff to discharge facility</td>
</tr>
<tr>
<td>“BOOST”</td>
<td>Society of Hospital Medicine</td>
<td>Goal: Provides most important information and option for questions</td>
</tr>
<tr>
<td>“MARQUIS”</td>
<td>NHLBI</td>
<td>Follow-up appointment scheduled before leaving hospital within 7 days of discharge</td>
</tr>
<tr>
<td>“PILL-CVD”</td>
<td>ACC</td>
<td>Intervene on medical problems</td>
</tr>
<tr>
<td>“H2H”</td>
<td></td>
<td>Follow-up phone calls made within 48 hours of discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reinforces discharge instructions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MD accountability after discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enhances communication between hospital-based MD and outpatient MD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medication reconciliation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prevent medication harm</td>
</tr>
</tbody>
</table>

### Re – Engineered Discharge (Project RED)

- **Usual Care** (N=376)
- **RN Advocate for Appointments** (N=373)
- **RPh call for med review 2-4 days**

![Graph showing hospitalization, ED visits, and readmissions](image)

Pharmacist Intervention for Low Literacy in Cardiovascular Disease (PILL–CVD)

ACS or CHF patients

Intervention Counseling

Usual Care

1. Med reconciliation
2. Med counseling
3. Adherence aids
4. Telephone follow-up call after discharge

Medication errors, Adverse drug events

Med Errors (N=851)

IRR (95% CI) P-value

0.92 (0.77-1.09) 0.32

ADEs (N=851)

1.09 (0.86-1.38) 0.49

Potential ADEs (N=851)

0.79 (0.62-1.01) 0.06

IRR (95% CI)

Favors intervention 1.0
Favors usual care

IRR=incidence rate ratios; ADE=adverse drug event


Potential Process Changes

- Identify key stakeholders, committees and special groups that need to be aware
- Identify an executive sponsor, clinical champion, team leader, quality improvement facilitator
- Consider developing a business case for your organization
- Announce team rules
- Identify available resources and opportunities
- Process Map
- Gap Analysis and ‘Failure Modes’
- Prioritize
- Specify Goals
- Select metrics for evaluation
  - Process measures
  - Outcome measures
- Integrate Workflow
- Improve

Tracking

- A point-person to review unplanned readmissions that occur within 30 days of original discharge
  - How soon after readmission are cases reviewed
- Tracking patients readmitted to another hospital
- Tracking patients with an early (<7 day) readmission rate