Therapies for ACS

The Articles You’ve Got to Know!!

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Objectives

• How do you treat patients after they’ve ruled IN
  - Based on initial eval (hx, PE, ECG)
  - Based on rapid rule-in protocols
• Post-cardiac arrest update
Amal Mattu, MD, FAAEM, FACEP

No financial relationships with drug or device-manufacturing companies
Non-STE ACS

Questions…

• Should you use…
  – Nitroglycerin?
  – Morphine?
Non-STE ACS

Questions...

- How do you decide if you should give...
  - Clopidogrel (Plavix)?
  - Prasugrel?
  - G2B3A inhibitors? Which one?
  - UFH vs. LMWH?
  - Fondaparinux?
  - Bivalirudin?
Non-STE ACS

Questions...

• How do you decide if you should give...
  - Clopidogrel (Plavix)?
  - Prasugrel?
  - G2B3A inhibitors?
  - UFH vs. LMWH?
  - Fondaparinux?
  - Bivalirudin?
Non-STE ACS


- Summary of literature and recommendations for management of non-STE ACS
- Just the highlights…and some evaluation first…
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Symptoms of ACS → CP, but...
- One-third of all AMI patients have no CP
  - Dyspnea
  - Fatigue
  - Diaphoresis
  - Mental status changes
  - Syncope
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- 5 most important factors on initial history, in order of importance
  - Nature of anginal symptoms (HPI)
  - Prior history of CAD
  - Male gender
  - Older age
  - Number of traditional risk factors
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• 4% of AMI patients have STE isolated to posterior leads (may be misdiagnosed as a non-STE ACS)
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Look for STD in V1-V3 → get posterior leads!
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• 12-lead ECG within 10 minutes of ED arrival!
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
- Serial ECGs (initially) every 15-30 minutes if high suspicion for ACS
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• If serial ECGs and cardiac enzymes normal, a stress test should be performed
  – In the ED
  – In a chest pain unit
  – In the hospital
  – As an outpatient
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• If risk stratified to low enough level for discharge and good follow up, follow up within 72 hours is “appropriate”

• If you start the workup, be prepared to go all the way!
  – With enzymes, provocative testing (in-patient vs. outpatient), etc.
Non-STE ACS

• Mr. Miyagi: “Either karate **do**, or karate **no do**. Karate do half-way → get squished like grape.”

• Amal’s rule: “ACS eval. same way. Either **do**, or no **do**. Do half-way → get squished like grape.”
Non-STE ACS

“If the glove don’t fit, you must acquit!”
Non-STE ACS

“If the story don’t fit, you must admit!”
Non-STE ACS

You’re gonna miss some MIs, so you better show that what you did was reasonable!

Discharge after one set of enzymes is NOT.

Discharge purely based on a negative ECG, prior stress test, or prior angiogram is NOT.

Discharge without early follow up is NOT.
Key Point!

We don’t “rule out” ACS in the ED!!
We risk stratify ACS in the ED.

Risk stratify to:
1. Not cardiac…I’m not even starting a workup!
2. Low risk…need provocative test!
   - Outpatient workup
   - Chest pain center workup
   - In-patient workup
3. Moderate or high risk
   - In-patient workup, cath lab (how soon?), etc.
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Beta-blockers
  - Should be initiated orally within 24 hours
  - Only indication for IV use in the ED mentioned is if patient has severe hypertension [though NTG probably more sensible] and no risk factors for cardiogenic shock
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Beta-blockers
  - Risk factors for cardiogenic shock
    - Age > 70
    - SBP < 120
    - **Sinus tachycardia > 110** or HR < 60
    - 1\textsuperscript{st} degree AVB with PR > 240 msec, 2\textsuperscript{nd} degree AVB, 3\textsuperscript{rd} degree AVB
    - Active asthma/reactive airway disease
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Beta-blockers
  - **Class III, level of evidence A:** “It may be harmful to administer IV beta blockers to UA/NSTEMI patients who have contraindications to beta blockade, signs of HF, or low-output state, or other risk factors for cardiogenic shock.”

[note previous set of risk factors]
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Beta-blockers
  - Oral administration at the end of the first day derives all the benefits (Vfib prevention, remodeling) without the drawbacks (increased risk of shock)
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Beta-blockers and JCAHO’s Core Measures:
  “AMI - 6 Beta Blocker at Arrival- Acute myocardial infarction (AMI) patients without beta blocker contraindications who received a beta blocker within 24 hours after hospital arrival.”
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Beta-blockers given early
  - No longer a Core Measure
  - No longer an ACC “performance measure”
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Antiplatelet therapy...
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• Clopidogrel instead if severe allergy
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• When to give ASA plus clopidogrel???
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• ASA plus clopidogrel???
  - Benefits (some debate about this)
    • Early administration + subsequent use:
      1% absolute reduction in death/MI/stroke at 9 months
    • Early reduction in recurrent ischemic events within hours of administration (300-600 mg)
    • → give it early? (even before PCI)
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• ASA plus clopidogrel??
  – Drawbacks
    • Benefits found mainly in very high-risk patients…
    • …who are also most likely to need early CABG
    • Uncertain who needs CABG until PCI done
      – i.e. emergency physician can’t be sure
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
- ASA plus clopidogrel??
  - Drawbacks
    - CABG within 5 days of clopidogrel use associated with increased…
      - PRBC and platelet transfusion
      - Re-operation for hemostasis
      - Perioperative mortality (?)
      - CT surgeons hate it
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• Guidelines state...
  - If early invasive therapy (PCI within 24 hours) is planned, give
    • ASA + clopidogrel (300 mg, 600 mg), OR
    • ASA + IV G2B3A inhibitor

  before angiography
  - Increasing support for ED administration
    • ...though not standard

  - Discuss this with your admitting cardiologist!
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• Guidelines state…
  – If non-invasive therapy (medical management) is planned, give
    • ASA + clopidogrel (300 mg, 600 mg)
    • A
    • b
  – Increasing support for ED administration
    • …though not standard
  – Discuss this with your admitting cardiologist!
Non-STE ACS

Efficacy of High-Dose Clopidogrel Treatment (600 mg) Less Than Two Hours Before Percutaneous Coronary Intervention in Patients With Non-STEMI
(Feldman, et al. Am J Cardiol 2010)

Effectiveness of In-Laboratory High-Dose Clopidogrel Loading Versus Routine Pre-Load in Patients Undergoing PCI
Non-STE ACS

Clopidogrel before PCI

- Both studies → no improvement in short-term or long-term outcome with pre-dosing of clopidogrel 600mg
- Can be safely deferred to post-cath (e.g. at the time of PCI)
Non-STE ACS

ACC/AHA 2011 Focused Update of the Non-STE ACS Guidelines
Non-STE ACS

ACC/AHA 2011 Focused Update
• Primarily addressed prasugrel
  – Alternative thienopyridine to clopidogrel
  – Some patients are genetically resistant to clopidogrel
    • Difficult to predict without genetic testing
  – Much less chance of resistance to prasugrel
Non-STE ACS

ACC/AHA 2011 Focused Update

- Primarily addressed prasugrel vs. clopidogrel
  - Slight benefit (death/MI/stroke) but slight increased risk of bleeding
  - Guidelines do not favor one over other
Non-STE ACS

ACC/AHA 2011 Focused Update

• Primarily addressed prasugrel
  – 60 mg po
  – Give at time of PCI or immediately after
    • Generally not to be given before PCI
    • Contraindicated in patients with history of stroke or TIA
    • Avoid within 7 days of CABG
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Additional points regarding antiplatelet agents
  – Other than ASA, all NSAIDS (including COX-2 agents) should be discontinued during acute Tx and hospitalization
• Increased risk of hypertension, reinfarction, heart failure, myocardial rupture, death
  – If history of GIB, add a PPI when giving ASA and/or clopidogrel…
Non-STE ACS

ACC/AHA 2011 Focused Update

- PPIs should be avoided if clopidogrel is given
  - Appear to attenuate the effect of clopidogrel (and to a lesser extent prasugrel)
  - One study showed increased risk of death or rehospitalization for ACS when clopidogrel was combined in PPI
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• Anticoagulant therapy
  - If early invasive therapy (PCI within 24 hours) is planned, add
    • either enoxaparin, UFH, bivalirudin, or fondaparinux
    • (all are Class I)
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Anticoagulant therapy
  - If non-invasive therapy (medical management) is planned, add
  - either enoxaparin, UFH, or fondaparinux
  - (all are Class I)
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Anticoagulant therapy
  – Fondaparinux is preferred if patient has increased risk of bleeding
• [also may be preferable in patients with history of HIT or renal failure]
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- Anticoagulant therapy — note…
  - Remember that these guidelines are written for non-STE ACS patients! (not low risk chest pain patients)
  - Anticoagulation not needed for low risk chest pain!
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• When is “early invasive therapy” recommended in non-STE ACS?
  - Refractory pain
  - Elevated TN
  - New STD
  - SSx of HF
  - New or worsening MR
  - Hemodynamic or electrical instability (e.g. VT)
  - Prior PCI (6 months) or CABG
  - High TIMI or GRACE score
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

- These patients have higher risk of in-hospital adverse cardiac events
- If no cath lab at your facility, strongly consider immediate transfer for PCI
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines

• Special groups
  - Women, elderly, and patients with CRI must have renally-excreted medications dosed based on estimated creatinine clearance, NOT serum creatinine!
  - These patients are frequently overdosed on anticoagulant and antiplatelet medications

• Higher morbidity and mortality
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Special groups
  – Creatinine clearance calculation
Non-STE ACS

ACC/AHA 2007 Non-STE ACS Guidelines
• Special groups
  – Google: creatinine clearance calculation
    • Enter age, weight, sex, and serum creatinine
  – If estimated creat. clearance < 30 mL/min, dose must be adjusted!
  – Example: 85 yo. woman, 110 lbs, serum creatinine 1.2 mg/dL
ACC/AHA 2007 Non-STE ACS Guidelines

- Special groups
  - Google: creatinine clearance calculation
    - Enter age, weight, sex, and serum creatinine
    - If estimated creat. clearance < 30 mL/min, dose must be adjusted!
    - Example: 85 yo. woman, 110 lbs, serum creatinine 1.2 mg/dL
      Est. creatinine clearance = 27 mL/ min
January 2008 publications
Update of the ACC/AHA 2004 STEMI Guidelines
Update of the ACC/AHA 2005 PCI Guidelines
STEMI and PCI

Updated STEMI and PCI Guidelines

• Some review
  - You MUST know how to diagnose PMI!
Isolated PMI — Posterior Leads

[ECG waveform image]
STEMI and PCI

Updated STEMI and PCI Guidelines

- Some review
  - Up to 6% of patients with chest pain and completely normal ECG prove to have AMI
  - Additional 4% will be found to have UA (neg. TN), may later develop AMI
STEMI and PCI

Updated STEMI and PCI Guidelines
• Patient with chest pain and nausea
STEMI and PCI

Updated STEMI and PCI Guidelines
• 4 days later with identical symptoms
STEMI and PCI

Updated STEMI and PCI Guidelines

• Some review
  - Time from first medical contact to balloon < 90 minutes
  - Otherwise give lytics
    • Door to lytic < 30 minutes
Updated STEMI and PCI Guidelines

- Some review
  - **Chronic kidney disease** is an independent risk factor for accelerated atherogenesis
  - Cardiovascular death is 10-30 times higher in HD patients than in general population
  - Also higher risk of bleeding complications
STEMI and PCI

Cornary artery disease risk factors

- Smoking
- Hyperlipidemia
- Early family history
- Diabetes
- Hypertension
- Male gender
- Age > 55

- Chronic kidney disease
- Cocaine use
- HIV
- Lupus, inflammatory diseases
Updated STEMI and PCI Guidelines

• Beta blockers in STEMI…
  – 2007 STEMI Guidelines → no rush!
  – Routine early use increases the risk of cardiogenic shock without improving overall survival
Updated STEMI and PCI Guidelines

- Beta blockers in STEMI…
  - Should be initiated orally within 24 hours
  - Only indication for IV use in the ED mentioned is if patient has severe hypertension [though NTG probably more sensible] and no risk factors for cardiogenic shock
Updated STEMI and PCI Guidelines

• Beta blockers in ACS
  - Oral administration at the end of the first day derives all the benefits (Vfib prevention, remodeling) without the drawbacks (increased risk of shock)
STEMI and PCI

Question…
• Should I give a dose of lytics (to “buy some time”) before the PCI?
STEMI and PCI

Updated STEMI and PCI Guidelines

- Facilitated PCI
  - Planned strategy of full-dose lytics followed by immediate PCI → NO
Updated STEMI and PCI Guidelines

- Facilitated PCI
  - Planned strategy of half-dose lytics or abciximab followed by immediate PCI → maybe...?? (class IIb, level of evidence C)
STEMI and PCI

Updated STEMI and PCI Guidelines

- Rescue PCI
  - Urgent PCI after failed lytics ➔ yes
Updated STEMI and PCI Guidelines

- “Failed” lytics
  - Pts. developing cardiogenic shock
  - Pts. developing CHF
  - Persistent ischemia after 90 min
  - Failure of 50% STE resolution after 90 min
    (in lead with greatest amt. of STE)
Updated STEMI and PCI Guidelines

• Anticoagulant therapy
  – Balance is tipping back in favor of enoxaparin
  – Increased risk of HIT if UFH used > 48 hrs
• Though UFH still has Class I rating
Updated STEMI and PCI Guidelines

- Anticoagulant therapy
  - Class I choices
    - Enoxaparin
    - UFH
    - Fondaparinux
Updated STEMI and PCI Guidelines

- Anticoagulant therapy
  - Enoxaparin: IV bolus, then SQ
- Reduce dose in elderly and patients with creat clearance < 30 mL/min
STEMI and PCI

Updated STEMI and PCI Guidelines
• Addition of clopidogrel to aspirin
STEMI and PCI

Updated STEMI and PCI Guidelines
- Addition of clopidogrel to aspirin
  - If patient gets lytics and is < 75 yo, give 300 mg oral load (Class IIa)
  - If patient going for PCI, give 600 mg oral load (Class I)
  - NOT mandatory in the ED...can be done in the cath lab...for now...
- Discuss with your cardiology consultant!
STEMI and PCI

Updated STEMI and PCI Guidelines

- IV GPIIb/IIIa receptor antagonists
  - Class I for UA/NSTEMI pts going for PCI
  - Not mandatory in the ED
- Alternatively can give bivalirudin instead of GPIIb/IIIa RA + heparin
STEMI and PCI

STEMI and PCI

Unfractionated heparin dosing

• Evaluated patients enrolled in the CRUSADE registry
  – Heparin dosing correlated with complications and mortality
• 35% of patients received excessive dosing of UFH (bolus and/or infusion)
• 5000/1000 dosing → 19% were overdosed
Unfractionated heparin dosing

• Results
  - 27% increased risk of major bleeding
  - 35% higher mortality
  - Bolus and infusion were individually predictive of complications
STEMI and PCI

Unfractionated heparin dosing

- Results
  - Initial (ED) dosing alone was predictive
  - Most common OD in women and elderly
STEMI and PCI

Unfractionated heparin dosing

- Current recommendation for UFH in ACS
  - 60 U/kg (max 4000 U) bolus
  - 12 U/kg/hr (max 1000 U/hr) infusion
Cardiac Arrest

• Question…
  - What if your patient has a cardiac arrest
  - Then gets ROSC but still unconscious
  - (Pre- or) Post-arrest ECG…
Cardiac Arrest

• (Pre- or) Post-arrest ECG...
Cardiac Arrest

- Do you activate the cath lab??
Cardiac Arrest

Survival and Neurologic Recovery in Patients With STEMI Resuscitated From Cardiac Arrest

Emergency PCI in Patients With STEMI Complicated by OOHCA
Cardiac Arrest

Survival and Neurologic Recovery in Patients With STEMI Resuscitated From Cardiac Arrest

- 98 pts underwent PCI after resuscitation
  - 64% survived
  - 92% of these had full neurological recovery
Cardiac Arrest

Survival and Neurologic Recovery in Patients With STEMI Resuscitated From Cardiac Arrest

• What about unconscious post-resus?
  - 59 pts
  - 44% survival
  - 88% of these had full neurologic recovery
Emergency PCI in Patients With STEMI Complicated by OOHCA

• OOHCA patients with STEMI going for PCI (and surviving) had similar 6-month outcome to non-CA patients
• 87% favorable neuro status at 1 year
Regional Systems of Care for OOHCA: A Policy Statement from the AHA (Circulation Feb 9, 2010)

- If OOHCA associated with STEMI, field providers should bypass nearest hospitals and go directly to a cardiac resus receiving hospital so patients can receive angiography within 90 minutes
What if…

• ECGs show non-STEMI…activate cath?
Cardiac Arrest

Coronary Angiography Predicts Improved Outcome Following CA (Reynolds, et al. J Int Care Med 2009)

• Improved survival and outcome associated with cath, regardless of…
  – Presenting rhythm
  – Presence of STEMI or new LBBB
  – Neurologic status

• Cath independently associated with good outcome
Cardiac Arrest

Immediate PCI Is Associated With Better Survival After OOHCA


• Cath independently associated with good outcome
Cardiac Arrest

Regional Systems of Care for OOHCA: A Policy Statement from the AHA (Circulation Feb 9, 2010)

- “Absence of STE on 12-lead ECG…is not strongly predictive of the absence of coronary occlusion on acute angiography.”
- Increasing support for rapid PCI regardless of ECG after ROSC
Cardiac Arrest

Recent Advances in CPR: CCR
(Ewy, et al. *J Am Coll Cardiol* 2009)

- Urgent cardiac catheterization
  - The most influential factor in survival
  - Regardless of whether or not STEMI!
Cardiac Arrest

Historical advances in Tx of cardiac arrest
• 1980s-1990s → rapid defibrillation
• 2000s → therapeutic hypothermia
• 2010s → CCR, rapid PCI
ACS Prevention...?

Dark Chocolate Improves Endothelial and Platelet Function
(Hermann F, Heart 2006)

Cocoa and Cardiovascular Health
(Corti R, Circulation 2009)
Dark Chocolate and CV Health

• Summary…
  - Dark chocolate is rich in polyphenols
    • Beneficial antioxidant effects
    • Improve endothelial and platelet function
  - Between 2-8 hours after ingestion of dark (not white!) chocolate, endothelial and platelet reactivity parameters improved
ACS Prevention...?

Dark Chocolate and CV Health

• Summary...
  - “...a small daily treat of dark chocolate may substantially...benefit vascular health.”
Summary

• Non-STE ACS
  - Aspirin → always in!
  - Early cath for high-risk patients in
  - Beta blockers → no rush
Summary

- **STEMI**
  - Beta blockers → no rush
  - Greater emphasis in new Guidelines on
    - Enoxaparin
    - Clopidogrel
- Discuss with your consultants what they prefer
- Review the data behind hospital protocols
Summary

• What should you routinely give in the ED for ACS?
  – Aspirin
  – Lytics if STEMI and no immediate PCI

• What about…
  – Beta-blocker?  ➔ no rush
  – Heparin?  ➔ not if your cardiologist prefers bivalirudin
    • Which heparin?
    – Clopidogrel or GIIb/IIIa RA?  ➔ no rush
Summary

• Dose renally-excreted meds with creatinine clearance
• Be wary of the dose for UFH
Thanks!