Effective Health Care

Unstable Angina/NSTEMI Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Unstable angina/non-ST-elevation myocardial infarction (NSTEMI) will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase.

- When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominators: Two health care professional associations

Nomination Summary: The nominators question the effectiveness and comparative effectiveness of specific pharmacologic and revascularization strategies for patients with unstable angina (UA) and NSTEMI.

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Population(s): Adult patients with UA/NSTEMI and comorbid or multi-morbid disease
Intervention(s): Drugs (oral and intravenous antiplatelet/antithrombotic therapies, statins, beta-blockers) and surgical interventions (coronary artery bypass grafting [CABG] and percutaneous coronary intervention [PCI])
Comparator(s): Combinations of oral antiplatelet/antithrombotic therapies, or addition of oral therapies to aspirin; comparison of different PPI therapies; clopidogrel; enoxaparin; timing of CABG and PCI procedures; timing of medication initiation and/or maintenance
Outcome(s): Major adverse cardiovascular events: death, nonfatal myocardial infarction, stroke, and repeat revascularization; other clinical outcomes including heart failure, repeat hospitalization, length of hospital stay, graft failure, angina relief, quality of life, and cognitive effects; safety and adverse effects including adverse drug reactions, access site complications, renal dysfunction, anaphylaxis, arrhythmias, stent thrombosis, bleeding, and infections; cost

Key Questions from Nominator:

1. Is there an overall positive benefit to risk ratio for triple antithrombotic therapy (aspirin, clopidogrel, warfarin) in post-ACS patients with an indication for warfarin (e.g., atrial fibrillation)?
2. Added to aspirin, is there a difference in outcomes (ischemic events, bleeding risks

with intervention) between a short-acting GP IIb/IIIa inhibitor and clopidogrel as the second choice for upstream therapy (with clopidogrel being added at catheterization in PCI patients for upstream GPI patients, and selective application of GPI in upstream clopidogrel patients)?

3. Which ADP receptor antagonist agent provides the best overall benefit/risk/cost-effectiveness outcomes for initial (in-hospital) and longer-term (outpatient) antiplatelet therapy: clopidogrel, prasugrel, ticagrelor? For age >75y? For diabetics?
4. Is earlier (≤5 days) CABG preferred for UA/NSTEMI patients triaged to surgical intervention at early coronary angiography?
5. What is the optimal time-window for coronary angiography with intended PCI in UA/NSTEMI patients at higher risk (GRACE score >140) and lower risk (i.e., 4-12 h, 12-24 h, 48-96 h)?
6. What is the optimal initial dose (after loading) of aspirin (i.e., 81 vs. 325 mg/d) for patients undergoing PCI with stenting and treated with variously potent antiplatelet agents, i.e., clopidogrel? Prasugrel? Ticagrelor?
7. Is there an advantage to early (on admission), high dose statin loading over post-catheterization, evening, or next day/pre-discharge statin therapy initiation on outcomes?
8. Is long-term beta-blocker therapy effective in post-UA/NSTEMI patients with complete revascularization and normal ejection fraction (>50%)?
9. Does the incorporation of routine pre-discharge or early post-discharge platelet function testing (e.g., with VerifyNow) and titration to optimal antiplatelet effect (e.g., 100-200PFUs) using various doses of clopidogrel and/or prasugrel improve outcomes?
10. Which anticoagulant is optimal for an initial conservative approach, fondaparinux or enoxaparin?
11. If bivalirudin is selected as the anticoagulant for an invasive strategy, what is the acceptable optimal timing for co-administration of clopidogrel? prasugrel? If a GPI is not used?
12. Should a PPI be routinely used to reduce bleeding events while preserving anti-ischemic efficacy for UA/NSTEMI patients treated with clopidogrel? If so, which ones may be selected, which one(s) avoided (e.g., omeprazole)?

Considerations

- The topic meets all EHC Program selection criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- Clinicians in the rapidly evolving field of acute coronary syndromes are faced with a wide array of possible treatment algorithms and questions related to oral antiplatelet/antithrombotic therapies, intravenous/subcutaneous antiplatelet/antithrombotic therapies, timing of revascularization interventions, and other therapeutics (including statins and beta blockers).

- No current, high-quality systematic reviews, meta-analyses, or guidelines were identified that address the nominators' questions. A systematic evidence review in this topic area will reduce clinical uncertainty and aid patients and health care professionals in determining the best course from among a wide range of treatment strategies. Questions related to oral antiplatelet/antithrombotic therapies for known or suspected acute coronary syndrome and intravenous and/or subcutaneous antiplatelet/antithrombotic therapies appear to be the most critical to clinical practice at this time.