Management of Non-ST Segment Elevation Acute Coronary Syndrome: The Managed Care Perspective

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A CME version of this article is available at www.namcp.org/cmeonline.htm.

Summary

Issues in managing Non-ST Segment Elevation Acute Coronary Syndrome (NSTE-ACS) were discussed at the NAMCP Fall Managed Care Forum in 2005. Central to this discussion were the American Heart Association/American College of Cardiology (AHA/ACC) treatment guidelines.

Key Points

- ACS is common and costly to the healthcare system.
- The ACC/AHA guidelines can help steer appropriate treatment and cost-effective management.
- Managed care has significant opportunities to have an impact on the care of ACS patients by ensuring physician compliance with treatment guidelines, and by ensuring appropriate patient management and education to prevent or reduce morbidity and mortality.

ATHEROTHROMBOSIS, defined as ischemic heart disease and cerebrovascular disease, is the leading cause of death worldwide, exceeding deaths from AIDS, cancer, or infectious disease (see Exhibit 1). More than 500,000 deaths related to cardiovascular disease occur annually in the United States,[1] accounting for one of every 2.6 deaths. About 1.1 million Americans will have a new or recurrent coronary event each year, and about 45 percent will die. Approximately 2.2 million hospitalizations for ACS occur every year in the U.S. (see Exhibit 2).[1] Acute coronary syndrome includes stable angina, unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST elevation MI (STEMI).[2]

The prevalence of individuals living with a history of MI, angina, or both, is skyrocketing, partly due to successful treatment. As the healthcare profession effectively treats cardiovascular disease, extending lives and getting people through the acute phase of a heart attack, the prevalence rises correspondingly.

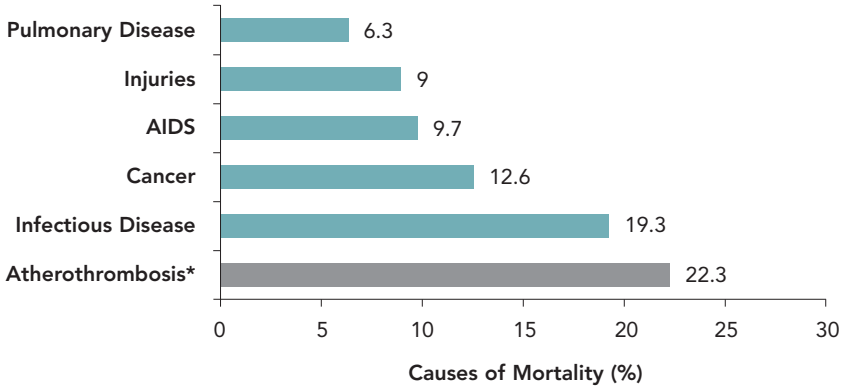
In addition to causing significant morbidity and mortality, the economic impact of coronary heart disease is equally staggering. In 2005, the estimated total cost was $393.5 billion (see Exhibit 3).[1] Approximately $249 billion of direct costs are attributable to hospitalization, health professionals, medication, nursing homes, etc. Indirect costs of CHD are estimated at $144.5 billion.

Educational Issues

Healthcare providers stand to benefit from additional education on ACS and its appropriate treatment. Many are not aware of the seriousness and risks of ACS. In addition to a high rate of in-hospital ischemic episodes and in-hospital MI or recurrent MI, patients with ACS have a high long-term mortality rate. Events such as MI and death occur most often during the first year after an episode of ACS.[2] Managed care has an opportunity to increase awareness of the significance of ACS.

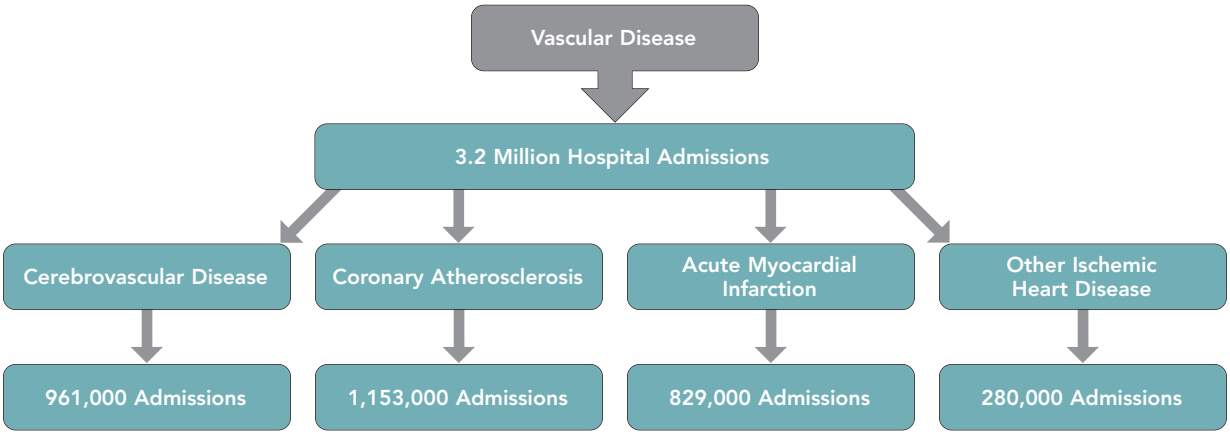
Atherosclerosis and its consequences is also a significant preventive health issue. Lifestyle changes and various medications can reduce the long-term consequences of atherosclerosis. Physicians and providers can encourage patients to seek additional education and offer assistance with complying with prevention recommendations such as smoking cessation, antiplatelet therapy, dietary changes, and exercise.

Exhibit 1: Atherothrombosis* Is the Leading Cause of Death Wordwide[1]



*Atherothrombosis defined as ischemic heart disease and cerebrovascular disease.
[1]The World Health Report 2001. Geneva: WHO:2001.
Reproduced with permission from Cannon CP. Atherothrombosis slide compendium. Available at: www.theheart.org.

Exhibit 2: Hospitalizations in the U.S. Due to Atherosclerotic Disease

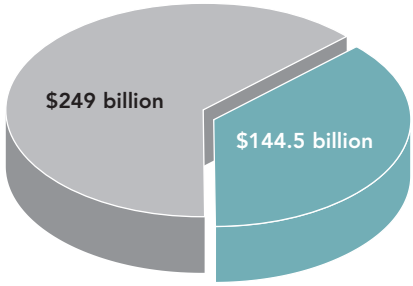


From Popovic JR, Mall MJ. Advance Data. 2001;319:1-20. Slide produced with permission from Cannon CP. Atherothrombosis slide compendium.

Exhibit 3: Coronary Heart Disease Economic Impact in the U.S.

2005 Estimated Total Cost = $393.5 billion

Direct Cost
- Hospital/nursing home
- Medication
- Home health/other medical durables
- Physicians/other professionals



Indirect Cost
- Loss of productivity

American Heart Association. 2005 Heart and Stroke Statistical Update.

Treatment Guidelines for NTSE-ACS

The ACC and AHA have developed guidelines for treatment and appropriate disease management of various cardiovascular diseases. The guidelines are regularly updated and are evidence-based. Recommendations are divided into the customary ACC/AHA classifications of I, II, and III evidence. Class I recommendations have the most consistent evidence supporting their use. The most recent version of each guideline is available at www.acc.org.

The prevalence of ACS ensures that many healthcare providers who are not cardiovascular specialists will encounter patients with NSTE-MI in the course of the treatment of other diseases. [2] This is especially true in outpatient and emergency department settings.

The optimal management of NSTE-ACS has twin goals of immediate relief of ischemia and the prevention of serious adverse outcomes (i.e., death or MI).2 This is best accomplished with a combination of anti-ischemic therapy, antiplatelet and antithrombotic therapy, ongoing risk stratification, and the use of invasive procedures such as percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG).2 The medical management recommendations for NTSE-ACS are summarized in Exhibit 4.

Antithrombotic therapy is essential to modify the ACS disease process and its progression to death, MI, or recurrent MI. A combination of aspirin, unfractionated heparin (UFH) or low molecular weight heparin (LMWH), and a platelet GP IIb/IIIa receptor antagonist represents the most effective therapy.[2] The intensity of treatment is tailored to individual risk. For example, triple antithrombotic treatment is used in patients with continuing ischemia or with other high-risk features and in patients who will be undergoing an early invasive procedure.[2] At least two studies, TIMI 11b and ESSENCE, have shown enoxaparin, a LMWH, to reduce adverse cardiovascular events more than UFH.[2] A major advantage of LMWHs is that they do not usually require the same laboratory monitoring of activity required when UFH is used.

Combination antiplatelet therapy with aspirin and clopidogrel (Plavix®) is recommended for nine months after NTSE ACS. Aspirin, if tolerated, should be continued indefinitely after the end of nine months. Clopidogrel is an alternative for long-term treatment in cases of aspirin intolerance or resistance.

It is estimated that 40 percent of patients are aspirin nonresponders. Identifying these nonresponders who possibly should be on more expensive antiplatelet therapy, primarily clopidogrel, is not currently standardized. Tests to assess platelet function and effectiveness of antiplatelet agents are not widely used. In clinical practice, many times patients having a repeat angioplasty or repeat acute coronary syndrome who are already on aspirin and other appropriate therapies such as beta blockers and angiotensin converting enzyme inhibitors are considered aspirin failures and are placed on clopidogrel therapy.

Evidence for clopidogrel effectiveness in NSTE ACS comes from the CURE trial (see Exhibit 5). This study compared aspirin plus placebo versus aspirin plus clopidogrel up to 12 months after an ACS event. Cardiovascular death, MI, or stroke occurred in 11.5 percent of patients assigned to aspirin plus placebo, and 9.3 percent assigned to aspirin plus clopidogrel.[3] In addition, clopidogrel use was associated with significant reduction in the rate of in-hospital severe ischemia and revascularization, as well as the need for thrombolytic therapy or intravenous GP IIb/IIIa receptor antagonists.

Exhibit 4: ACC/AHA Recommendations for In-Hospital Treatment of Patients With NSTE-ACS[2]

General Management	Anti-ischemic Therapy	Antiplatelet Therapy	Antithrombin Therapy
• Bed rest • Continuous ECG monitoring • Supplemental oxygen • IV morphine as needed for pain, anxiety, and/or HF • ACEI for persistent hypertension with LV systolic dysfunction or HF	• Nitroglycerin • Beta-blockers	• Aspirin • Clopidogrel (Plavix®) • GP IIb/IIIa inhibitor [abciximab (ReoPro), eptifibatide (Integrilin®), tirofiban (Aggrastat®)]	• Subcutaneous LMWH or IV UFH

ECG (electrocardiogram); HF (heart failure); ACEI (angiotensin converting enzyme inhibitor); LV (left ventricular); LMWH (low molecular weight heparin); UFH (unfractioned heparin)

Exhibit 5: The Primary Composite End Point in the CURE Trial

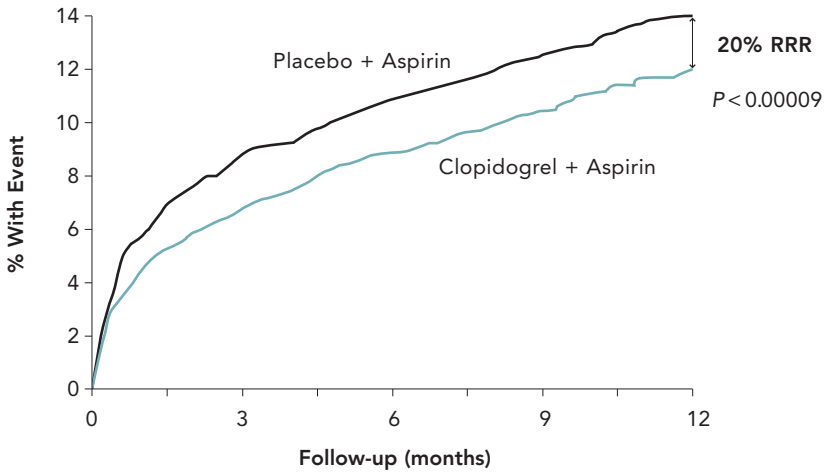


Exhibit 6: ACC/AHA Recommendations for Long-Term Medical Therapy in Patients With NSTE-ACS[2]

- Instructions on smoking cessation, weight, diet, and exercise
- Antiplatelet therapy*
- Beta blockers, unless contraindicated
- Lipid-lowering agents and diet if LDL-C >100 mg/dL
- Niacin or fibrate if HDL-C <40 mg/dl
- Blood pressure <130/85 mm Hg
- ACEI for patients with HF, LV dysfunction (EF <40%), hypertension, or diabetes
- Tight glycemic control in diabetics

*Combined aspirin + clopidogrel for nine months after NSTE-ACS then, aspirin or clopidogrel when aspirin is not tolerated.

NSTE-ACS (non-ST segment elevation acute coronary syndrome)
LDL-C (low-density lipoprotein cholesterol)
HDL-C (high density lipoprotein cholesterol)
ACEI (angiotensin converting enzyme inhibitor)
HF (heart failure)
LV (left ventricular)
EF (ejection fraction)
TG (triglycerides)

Managed Care Opportunities

Because of the significant morbidity, mortality, and costs of ACS, the treatment guidelines provide a framework for many managed care interventions. Those may include drug utilization reviews or provider profiling.

An example intervention might entail identifying patients who are frequently hospitalized for ACS and placing them within a disease management program that includes education, interventions to maximize appropriate therapy to prevent subsequent hospitalizations, and patient and provider support.

Another example may be examining cost-effective use of antiplatelet therapy. Ensuring patients receive appropriate length of combination antiplatelet therapy after an episode of NTSE ACS could be another intervention.

To prevent re-hospitalization, death, and MI, the ACC/AHA guidelines provide some recommendations for hospital discharge therapeutic strategies (see Exhibit 6).[2] The selection of a medical regimen is individualized to the specific needs of the patients based on in-hospital issues and procedures. The mnemonic ABCDE (aspirin and antianginals, beta-blockers and blood pressure, cholesterol and cigarettes, diet and diabetes, and education and exercise) helps clinicians remember all of the issues that should be addressed.[2]

Overall, ACS results in significant costs to the healthcare system and takes patients' lives. Managed care has significant opportunities to impact the care of ACS patients. The possible managed care strategies to prevent or reduce morbidity and mortality are numerous. **JMCM**

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References

1. American Heart Association. 2005 Heart and Stroke Statistical Update. Dallas, Texas: American Heart Association. 2005. Available at www.americanheart.org. Accessed Dec. 5, 2005.
2. Braunwald et al. ACC/AHA 2002 Guideline Update for the Management of Patients With Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction. Available at www.acc.org/clinical/guidelines/unstable/update_index.htm. Accessed Dec. 5, 2005.
3. Yusuf S, Zhao F, Mehta SR et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001;345:494-502.