The 2014 American College of Cardiology ACC/American Heart Association Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes

Ten Contemporary Recommendations to Aid Clinicians in Optimizing Patient Outcomes

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The new title, “Non-ST-Elevation Acute Coronary Syndromes (NSTE-ACS),” for this full revision of the 2007 American College of Cardiology Foundation/American Heart Association guideline titled “Unstable Angina/Non-ST-Elevation Myocardial Infarction,” more concisely emphasizes the continuum between unstable angina (UA) and non-ST-elevation myocardial infarction (NSTEMI). They can be indistinguishable at presentation and therefore are considered together using the terminology non-ST-elevation acute coronary syndromes. Approximately 70% of patients with an acute coronary syndrome have an NSTE-ACS, comprising more than 625 000 patients annually.¹ In the appropriate clinical context, if cardiac biomarkers are normal, the patient is deemed to have UA; if troponins are elevated, the patient is considered to have an NSTEMI.² Additional new terminology relates to the initial strategy for management of patients with NSTE-ACS. The initial treatment pathways have been recategorized into, as previously, an early invasive strategy, seeking to rapidly risk stratify patients by angiographic assessment of their coronary anatomy with intent to perform revascularization when appropriate. The new designation, an ischemia-guided strategy, has replaced the previous term, initial conservative therapy, to more clearly convey the physiologic rationale of this approach. Ischemia-guided strategy involves guideline-directed medical therapy, with coronary angiography only if the patient experiences refractory or recurrent ischemic symptoms or develops hemodynamic instability.

Finally, this guideline highlights the third universal definition of myocardial infarction,³ which differentiates myocardial infarction caused by a primary coronary artery process, such as spontaneous plaque rupture, from a myocardial infarction related to reduced myocardial oxygen supply and/or increased demand in the absence of a direct coronary artery process.

1. Patients with chest pain or other symptoms suggesting acute coronary syndromes (ACS) should have

12-lead electrocardiography (ECG) performed and evaluated within 10 minutes of arrival at an emergency facility, and serial ECGs performed to detect ischemic changes. Serial cardiac troponin I or T levels (using a contemporary assay) should be obtained at presentation and at 3 to 6 hours after symptom onset. Risk scores can help assess prognosis. In patients with symptoms consistent with ACS without objective evidence of myocardial ischemia (nonischemic ECG and normal cardiac troponin levels), noninvasive imaging is reasonable before emergency department discharge or within 72 hours after discharge.

2. Standard initial medical therapies include: supplemental oxygen for arterial oxygen saturation <90% or respiratory distress; sublingual nitroglycerin; oral β -blocker therapy within the first 24 hours in the absence of heart failure, low output state, increased risk for cardiogenic shock or other contraindications to β blockade; nondihydropyridine calcium channel blocker for continuing or recurrent ischemia and contraindication to β blockade (in the absence of clinically significant left ventricular dysfunction). Non-steroidal anti-inflammatory drugs (except aspirin) should not be initiated and should be discontinued during the hospitalization for NSTE-ACS because of the increased risk of major adverse cardiac events associated with their use.
3. Initial antiplatelet/anticoagulant therapy includes: 325-mg chewable aspirin at presentation, followed by a daily maintenance dose of aspirin at 81 to 126 mg daily. A P2Y₁₂ inhibitor (clopidogrel or ticagrelor) in addition to aspirin for up to 12 months in patients treated with either an early-invasive or ischemia-guided strategy. In addition to antiplatelet therapy, parenteral anticoagulation is indicated with enoxaparin, bivalirudin, fondaparinux, or unfractionated heparin.
4. A high-intensity statin should be initiated or continued in all patients without contraindications. Angiotensin-converting enzyme inhibitors should be started and continued indefinitely with a left ventricular ejection fraction $\leq$ 40%, or hypertension, diabetes, or stable chronic kidney disease unless contraindicated.

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Figure 1. Algorithm for management of patients with definite or likely non–ST-elevation acute coronary syndromes (NSTE-ACS). Abbreviations: ASA, American Society of Anesthesiologists; CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; GPI, glycoprotein inhibitor; LOE, level of evidence; PCI, percutaneous coronary intervention; pts, patients; UFH, unfractionated heparin. Reprinted with permission.⁴

5. An algorithm (Figure 1) details the components of an early invasive strategy or an ischemia-guided strategy. An early invasive strategy is indicated for patients with refractory angina or hemodynamic or electrical instability and those at elevated risk for clinical events. An early invasive strategy is not recommended for patients with extensive comorbidities (eg, hepatic, renal, or pulmonary failure; cancer) in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. An ischemia-guided strategy is appropriate for low-risk score patients (Thrombolysis In Myocardial Infarction or Global Registry of Acute Coronary Events), low-risk troponin-negative women, and by patient or clinician preference in the absence of high-risk features. When an ischemia-guided strategy is chosen, noninvasive stress testing is recommended prior to hospital discharge to detect severe ischemia occurring at a low-stress threshold.
6. Patients undergoing percutaneous coronary intervention (PCI) should be treated with a P2Y₁₂ inhibitor: clopidogrel, prasugrel, or ticagrelor. Discharge planning should include detailed patient education about symptoms, lifestyle interventions, standard medication with dual antiplatelet therapy, cholesterol management, referral to cardiac rehabilitation, timely follow-up with the healthcare team, and influenza and pneumococcal vaccines.
7. NSTEMI-ACS patients with prior revascularization PCI or coronary artery bypass grafting should receive antiplatelet and anticoagulant therapy and be strongly considered for an early invasive strategy because of their increased risk. Medical treatment in the acute phase of NSTEMI-ACS and decisions to perform stress testing, angiography, and revascularization should be similar in patients with and without diabetes mellitus.
8. Patients who develop NSTEMI-ACS following noncardiac surgery should receive guideline-directed medical therapy, with additional management directed at the underlying cause of the pathophysiologic process.
9. Older patients with NSTEMI-ACS, because of their high-risk status, should be treated with guideline-directed medical therapy and an early invasive strategy with revascularization as appropriate; pharmacotherapy should be individualized and dose adjusted by weight and creatinine clearance to reduce adverse events. Management decisions should be patient centered, incorporating patient preferences, comorbidities, functional and cognitive status, and life expectancy.
10. Women with NSTEMI-ACS should be managed with the same pharmacologic therapy as men for acute care and secondary prevention, with attention to weight and/or renally calculated doses of antiplatelet and anticoagulant agents to reduce bleeding risk. Women with NSTEMI-ACS and high-risk features

(eg, troponin positive) should undergo an early invasive strategy.

Despite landmark advances in the care of patients with NSTEMI-ACS, emerging diagnostic and therapeutic strategies have posed new challenges. Evidence-based decisions will require comparative effectiveness studies of available and novel potent antiplatelet agents that are indicated, in addition to anticoagulant therapy irrespective of the initial treatment strategy. The paradox of newer and more potent antithrombotic and anticoagulant drugs that reduce major adverse cardiac outcomes but increase bleeding risk occurs with the greatest frequency in patients with atrial fibrillation. Atrial fibrillation patients who develop NSTEMI-ACS and receive a coronary stent are the population at risk from triple anticoagulant/antiplatelet therapy. The optimal regimen requires ascertainment.

The use of cardiac troponin, the preferred biomarker of myocardial necrosis, is rapidly evolving. Although a truly high-sensitive cardiac troponin is not currently available in the United States, the sensitivity of contemporary assays continues to increase, accompanied by higher rates of elevated cardiac troponin unrelated to coronary plaque rupture. This diagnostic quandary necessitates investigation, potentially addressing measurement of absolute cardiac troponin change rather than traditional analysis of relative alterations.

More than half of the NSTEMI-ACS mortality occurs in older patients, with this high-risk cohort increasing as our population ages. An unmet need is to more clearly distinguish their optimal management strategies. An appreciable number of NSTEMI-ACS patients have angiographically normal or nonobstructive coronary artery disease; women predominate in this population and their prognosis is not benign. Clinical advances are predicated on clarification of the pathophysiology of this challenging syndrome.

A fundamental aspect of all clinical practice guidelines is that these evidence-based documents cannot encompass all clinical circumstances, nor can they replace the judgment of individual physicians in the management of each patient. The science of medicine is rooted in evidence and the art of medicine is based on the application of this evidence to the individual NSTEMI-ACS patient.

References

1. Go AS, Mozaffarian D, Roger VL, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6–e245.
2. Newby LK, Jesse RL, Babb JD, et al. ACCF 2012 expert consensus document on practice clinical considerations in the interpretation of troponin elevations: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol*. 2012;60:2427–2463.
3. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol*. 2012;60:1581–1598.
4. Amsterdam EA, Wenger NK, Brindis RG, et al. *J Am Coll Cardiol*. 2014. pii: S0735-1097(14)06279-2. doi: 10.1016/j.jacc.2014.09.017.