REVIEW

Acute Coronary Syndrome Update for Hospitalists

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Acute coronary syndromes (ACSs)—unstable angina, non–ST-segment (ST, part of an electrocardiogram between the QRS complex and the T wave) or ST-segment elevation myocardial infarction (MI)—remain extremely common and clinically challenging. In addition to electrocardiography and biomarkers, formal risk stratification using risk scores has become an important part of the initial evaluation of patients with ACS. On the basis of the estimated risk of subsequent ischemic events, the optimal use and timing of cardiac catheterization and revascularization procedures can be determined. Additionally, antiplatelet and anticoagulant therapy can be instituted, with consideration given to both the ischemic and bleeding risks in an individual patient. A particular challenge in ACS management has been the rapid evolution of guidelines in response to new randomized clinical trial and registry data. Understanding and implementing the recommendations in these evidence-based guidelines are important parts of hospitalists' practice. *Journal of Hospital Medicine* 2010;5:S15–S21. © 2010 Society of Hospital Medicine.

KEYWORDS: acute coronary syndrome, non–ST-segment elevation myocardial infarction, ST-segment elevation myocardial infarction.

Acute coronary syndrome (ACS) remains a major healthcare challenge. Currently, the majority of patients with ACS have non–ST-segment (ST, part of an electrocardiogram between the QRS complex and the T wave) elevation myocardial infarction (MI) and unstable angina.[1] Nevertheless, ST-segment elevation MI is also an important cause of morbidity and mortality. In recent years, our understanding of ACS has improved as a result of several major advances based on results from multiple randomized clinical trials and registry analyses. The results of these analyses have influenced guidelines issued by professional societies and in some cases have become performance metrics. Therefore, it is particularly important for physicians involved in the care of patients with ACS to be aware of evolving treatment patterns (Table 1).

Case Study

A 64-year-old man presents to the emergency department with the chief complaint of chest pressure for the past 2 hours. His chest pressure began after he moved furniture in his home. He initially believed that a pulled muscle was the cause of the pain, but when the discomfort did not improve with rest and continued to worsen, he thought it best that his wife drive him to the emergency department, where he continues to have chest pressure. He has never had this symptom before. His past medical history is notable only for mild hypertension for which he takes hydrochlorothiazide 25 mg daily. Otherwise, he has been healthy.

Clinical Presentation and Risk Assessment

The clinical presentation of ACS is not always straightforward. Although physicians frequently inquire about chest pain, the pain often manifests as chest heaviness or chest pressure. Additionally, some patients have a more atypical presentation, where the predominant symptom of acute coronary ischemia is dyspnea or extreme fatigue. These atypical presentations are believed to be somewhat more common in women and in the elderly, but it is important to realize that they can occur in any patient. Nausea, vomiting, or diaphoresis may accompany these symptoms or occur in isolation. Chest discomfort radiating to the jaw, neck, or left arm may be present, but is not necessary to the diagnosis. Thus, we see a variety of symptoms presenting in a patient with ACS.

This varied presentation makes objective assessment of ACS particularly important. To inform assessment, biomarkers have emerged as a quick and effective tool to help with the diagnosis of ACS. In particular, troponin measurement is important and serial troponin measurement is useful to exclude myonecrosis. It should be noted that the initial troponin level may be normal during the early stages of ACS. A bedside troponin measurement can be useful for rapid identification of myocardial damage. Quantitative troponin measurement also adds value, as higher levels of troponin are associated with progressively worse outcomes, including mortality (Figure 1). Although a number of biomarkers are available, the most important commonly used at present is troponin.

TABLE 1. Hospitalist Core Competencies for Management of ACS

Hospitalists should demonstrate a knowledge of:
    ACS without enzyme leak, NSTEMI, and STEMI
    Variable presentations of unstable angina, acute MI
    Conditions that mimic ACS
    Cardiac biomarkers
    Role of noninvasive cardiac testing
    Risks; indications for cardiac catheterization
    Risk factors for CAD
    Validated risk stratification tools
    Indications for hospitalization of patients with chest pain
    Indications, contraindications for thrombolytic therapy
    Indications, contraindications, and pharmacology of drugs for ACS
    Indications for early invasive interventions
        Angiography, stenting and/or CABG
    Laboratory studies or imaging indicative of disease severity
    Safe hospital discharge
Hospitalists should demonstrate skill in:
    History and physical exam relative to cardiac disease
        Recognizing signs and severity of ACS
    Diagnosing ACS through appropriate testing
        History and physical, ECG, x-rays, biomarkers
    Risk stratification using validated tools
    Formulating an evidence-based treatment plan
    Identifying patients for thrombolytics and/or early revascularization
    Recognizing and treating patient discomfort
    Recognizing decompensation, initiating immediate therapy
    Managing complicating factors
        Bleeding, inadequate response, cardiopulmonary compromise
    Timely patient assessment, co-management with other providers
Hospitalists should demonstrate attitudes that facilitate:
    Communication with patients and families relative to cardiac disease and all
     aspects of care plan
        Obtain informed consent
    Early specialty consultation
    Initiation of secondary prevention measures before discharge
    Multidisciplinary care throughout the hospital stay
    Safe discharge and transition back into primary care

Related data were reported by the Society of Hospital Medicine.[27]

Abbreviations: ACS, Acute coronary syndrome; CABG, coronary artery bypass graft; CAD, coronary artery disease; ECG, electrocardiogram; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction.
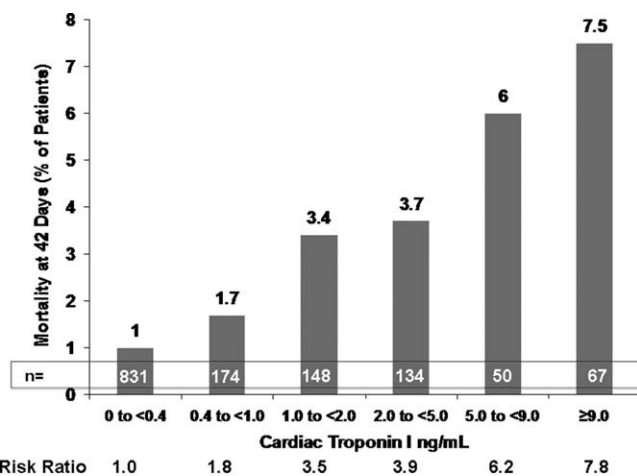

FIGURE 1. Cardiac troponin predicts the risk of mortality in UA/NSTEMI (unstable angina/non–ST-segment elevation myocardial infarction). Cardiac troponin levels measured at baseline. $P < 0.001$ for increase in mortality rate with increasing cardiac troponin I at enrollment. Source: Antman et al. *N Engl J Med.* 1996;335:1342-1349. Reprinted with permission from the *New England Journal of Medicine.* Copyright 1996 Massachusetts Medical Society. All rights reserved.
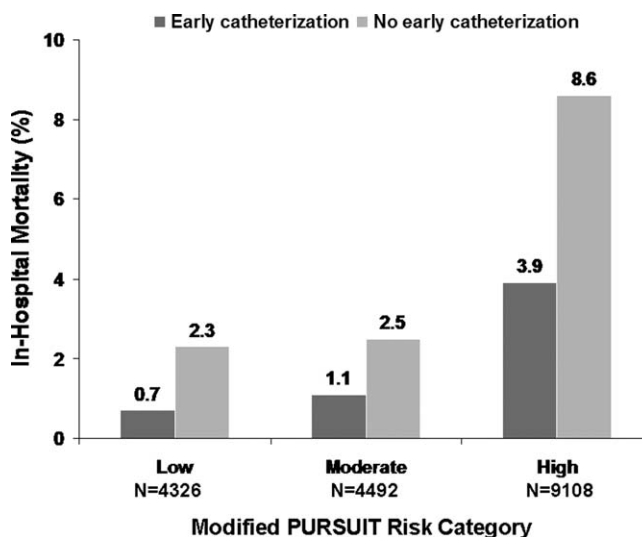

FIGURE 2. Mortality rates by early catheterization vs. no early catheterization in high-risk ACS patients. $P < 0.001$ for comparisons within each risk group. Source: Bhatt et al. *JAMA.* 2004;292:2096-2104. Reprinted with permission from the *Journal of the American Medical Association.* Copyright 2004 American Medical Association. All rights reserved.

In addition to biomarkers, the electrocardiogram (ECG) remains extremely important in diagnosis and risk stratification. In a moderate-level emergency department, the triage nurse should obtain a 12-lead ECG for a patient with a history that is suspicious for coronary ischemia, and ask the attending physician to review the ECG immediately. If there is ST-segment elevation or any new or presumed new left bundle-branch block, the patient should be triaged to the ST-segment elevation MI pathway of care. If there is ST-segment depression or marked T-wave inversion, this greatly raises the suspicion for non–ST-segment elevation MI or unstable angina. The presence of any of these features on the ECG places the patient at markedly elevated risk of short-term ischemic complications.

A protocol should be in place for rapid treatment of patients with ST-segment elevation MI.[2] If the hospital has

24/7 percutaneous coronary intervention (PCI) capability, the catheterization lab should be immediately activated and the patient should proceed to primary PCI. The goal door-to-balloon time is 90 minutes or less. A patient who presents to a hospital without primary PCI capability should receive either fibrinolysis or be transferred to a center that
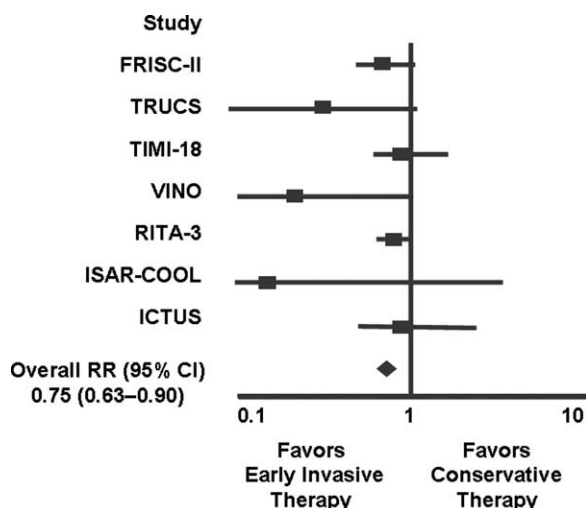
FIGURE 3. Relative risk of all-cause mortality at a mean follow-up 2 years for invasive vs. conservative strategy in high-risk ACS patients. FRISC-II, Fragmin and Fast Revascularization During Instability in Coronary Disease; ICTUS, Invasive vs. Conservative Treatment in Unstable Coronary Syndromes Investigators; ISAR-COOL, Intracoronary Stenting With Antithrombotic Regimen Cooling Off; RITA-3, Randomized Intervention Trial of Unstable Angina; TIMI-18, Thrombolysis in Myocardial Infarction-18; TRUCS, Treatment of Refractory Unstable Angina in Geographically Isolated Areas Without Cardiac Surgery; VINO, Value of First Day Coronary Angiography/Angioplasty in Evolving Non–ST-Segment Elevation Myocardial Infarction. Source: Bavry et al. *J Am Coll Cardiol.* 2006;48:1319-1325. Reprinted with permission from the *Journal of the American College of Cardiology* (Elsevier).

can perform primary PCI. If fibrinolytic therapy is planned, it is essential that the patient not have any absolute contra-indications to fibrinolytic therapy. Fibrinolysis should be administered within 30 minutes of patient contact. If transfer for primary PCI is planned, it is important that systems to support the transfer are in place so that the time from first medical contact to PCI does not exceed 90 minutes. As a practical point, it can be difficult to achieve these short transfer times in many geographic regions of the United States. However, with organized systems of care, it is certainly possible to have effective transfer systems and to achieve a short door-to-balloon time.[3]

If the patient does not have ST-segment elevation MI, the next step depends on the patient's level of risk, where risk stratification is particularly important. As mentioned above, troponin measurement and the ECG are both essential aspects of risk stratification, but they alone are not sufficient to establish risk. It is recommended that an objective risk tool also be used. This is especially important because the patient can be initially troponin-negative and have a normal ECG but still be at high risk for ischemic complications. The TIMI risk score (Table 2) is 1 of a number of resources that can help determine whether patients are at high risk for short-term ischemic complications using means more objective than the "eyeball" test (Table 3).
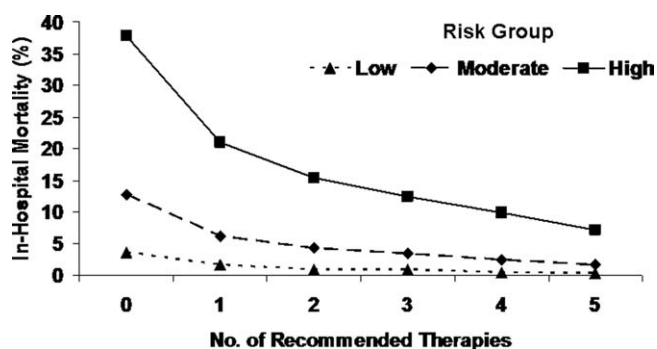

FIGURE 4. Mortality rates by the number of acute recommended therapies from the Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines (CRUSADE) National Quality Improvement Initiative. Acute therapies defined as aspirin, beta blockers, heparin, GP IIb/IIIa inhibitors, or cardiac catheterization < 48 hours. Risk group based upon CRUSADE risk score. Source: Peterson et al. *J Am Med Assoc.* 2006;295:1912-1920. Copyright 2006. Reprinted with permission of the American Medical Association. All rights reserved.

FIGURE 5. All-cause mortality for patients receiving a drug-eluting stent vs. a bare metal stent. PES, paclitaxel-eluting stent; SES, sirolimus-eluting stent; DES, drug-eluting stent; BMS, bare metal stent. Source: Bavry and Bhatt. *Lancet.* 2008;371:2134-2143. Reprinted with permission from *The Lancet* (Elsevier).

Delineation of the coronary anatomy in the catheterization lab is warranted for patients judged to be at high risk on the basis of the TIMI risk score, which would include most patients with elevated troponin or ST-segment deviation. Many patients will undergo PCI on the basis of those test results and a smaller percentage might undergo coronary artery bypass grafting (CABG). Additionally, a sizeable minority of patients will be managed medically. This latter group is challenging because it consists of patients who have either trivial coronary artery disease or extensive coronary artery disease not amenable to revascularization and who have either a very low or very high risk of ischemic complications.

Even though catheterization may not be necessary, further evaluation is warranted in patients with ACS deemed to be at low risk. Typically, some form of functional assessment is indicated. In patients who are able to exercise, this would consist of exercise stress testing, often with an imaging modality. If the stress test is abnormal, cardiac catheterization is often the next step.

Case Study (cont)

An ECG is rapidly obtained on this patient and there is ST-segment depression in leads II, III, and aVF. A bedside troponin is positive. The patient is at high risk of ischemic complications. He is diagnosed with non–ST-segment elevation MI. The next step is to initiate medical therapy. Presumably, the patient would have already (or at least should have already) received aspirin. Chewing or swallowing a dose of 325 mg nonenteric coated aspirin should provide a prompt aspirin effect. It would be reasonable to initiate anticoagulation as well, and the guidelines support a number of choices such as unfractionated heparin or low molecular weight heparin. Consideration should also be given to starting additional antiplatelet therapy, such as a loading dose of clopidogrel. Although aspirin provides some degree of antiplatelet effect, in a patient with activated platelets who presents with an ACS, additional antiplatelet therapy is necessary, although the exact timing of it is a matter of debate. Finally, consideration needs to be given to the need for catheterization. This patient, on the basis of his high ischemic risk and lack of obvious contraindications, should go to the catheterization laboratory, and the timing of catheterization requires further thought.

Guideline Update

The American College of Cardiology/American Heart Association 2009 Focused Guideline Update provides new information and recommendations pertinent to the care of patients with ACS[2] and incorporates new data relevant to the initial emergency care and subsequent inpatient care of patients with ACS. Guideline highlights are presented in Table 4.

Several studies support an invasive strategy to assess high-risk ACS patients. Randomized clinical trials and meta-analyses of these trials have confirmed a significant reduction in subsequent ischemic events, including mortality, in patients who undergo an invasive vs. a more conservative strategy.[4] Registry data have confirmed that these randomized clinical trial data reflect patients in the real-world setting of clinical practice.[5]

The timing of angiography has recently been examined in detail.[6,7] It appears that for patients with non–ST-segment elevation ACS, unlike those with ST-segment elevation MI, there is no need for emergent transfer to the catheterization laboratory, assuming patients are electrically and hemodynamically stable. Emergency transfer is warranted for unstable patients and those with ongoing chest discomfort. Otherwise, it appears sufficient to send the patient with non–ST-segment elevation ACS for catheterization within the subsequent 48 hours, or, alternatively, to adopt a more expectant approach in which catheterization is deferred until either recurrent symptoms develop or risk stratification suggests that there is substantial myocardium in jeopardy.

PCI is performed in the catheterization laboratory most often in the setting of ACS.[5] When PCI is performed, an important consideration is whether to use a bare metal stent or a drug-eluting stent.[8] Drug-eluting stents have been shown to have a significant benefit in reducing restenosis and the need for repeat revascularization. However, in aggregate, they have not been shown to either increase or decrease mortality.[9] A key issue for the referring physician is to ascertain whether patients who go to the catheterization laboratory are likely to tolerate and be compliant with prolonged dual antiplatelet therapy. If it appears that the patient can or will not be compliant, a bare metal stent is preferable to a drug-eluting stent; a bare metal stent requires dual antiplatelet therapy of shorter duration.

TABLE 4. New Recommendations From the 2009 Joint STEMI/PCI Focused Update

Intervention	Recommendation
GP IIb/IIIa receptor antagonists	
Class IIa	Start abciximab, tirofiban, or eptifibatide at primary PCI (with/without stenting) in selected patients with STEMI.
Class IIb	Uncertain value in STEMI when given before arrival at catheterization lab.
Thienopyridines	
Class I	Use loading dose for planned PCI in STEMI. Regimens for primary and nonprimary PCI are detailed within the guideline.
	Duration of therapy after stent placement of at least 12 months. Stop early if bleeding risk outweighs benefit.
	Discontinue before planned, delayed CABG ($\geq$5 d clopidogrel; $\geq$7 d prasugrel) unless the need for CABG outweighs bleeding risk.
Class IIb	After DES placement, consider continuing clopidogrel or prasugrel beyond the first 15 months of therapy.
Class III	Prasugrel is not recommended for primary PCI in patients with STEMI who have a history of stroke or TIA.
Parenteral anticoagulants	
Class I	In primary PCI, supportive anticoagulants include unfractionated heparin, enoxaparin, fondaparinux, or bivalirudin, following ASA and a thienopyridine.
Class IIa	Bivalirudin is reasonable in patients at high risk of bleeding undergoing PCI for STEMI.
Triage and transfer for PCI	
Class I	STEMI system of care is supported by dedicated teams and protocols required for all communities.
Class IIa	Transfer patients who received fibrinolytic therapy at a nonPCI-capable facility to a PCI-capable facility. Consider preparatory antithrombotic regimen before or during transfer.
Class IIb	Consider expeditious transfer of nonhigh-risk patients from a nonPCI-capable facility to a PCI-capable facility after administration of fibrinolytic. Consider preparatory antithrombotic regimen before or during transfer.
Intensive glucose control in STEMI	
Class IIa	Insulin is reasonable to maintain glucose <180 mg/dL (avoid hypoglycemia) for any patient with STEMI.
Thrombus aspiration during PCI of STEMI	
Class IIa	Aspiration thombectomy is reasonable.
Use of stents in STEMI	
Class IIa	DES is a reasonable alternative to BMS for primary PCI in STEMI.
Class IIb	Consider DES when clinical or anatomical factors suggest favorable safety and efficacy for DES.
Angiography in CKD	
Class I	Isomolar contrast or low molecular weight contrast (not ioxaglate or iohexol) is indicated for CKD patients not on dialysis.
Fractional flow reserve	
Class IIa	FFR is useful to assess a specific coronary lesion or as an alternative to noninvasive functional testing to justify PCI. Reasonable for intermediate coronary stenosis in patients with angina.
Class III	Routine use of FFR is not recommended to assess severity of CAD in patients with angina who have had a positive, unequivocal, noninvasive functional study.
PCI for unprotected left main CAD	
Class IIb	PCI of left main coronary artery with stents is an alternative to CABG for anatomy associated with low risk of PCI complications and a clinical scenario with higher risk of adverse surgical outcomes.
Timing of angiography and antiplatelet therapy in UA/NSTEMI	
Class I	Initiate dual-antiplatelet therapy for UA/NSTEMI and an invasive approach. Start ASA on presentation. Clopidogrel (before or at PCI) or prasugrel (at PCI) as a second antiplatelet agent.
Class IIa	Early invasive strategy within 12 to 24 hours of admission is reasonable for stabilized high-risk UA/NSTEMI; an early approach is also reasonable for UA/STEMI not at high-risk.

NOTE: Classification of recommendations: Class I. Benefit $\gg$ risk. Procedure or treatment *should* be performed or administered. Class IIa. Benefit $\gg$ risk. Additional studies with focused objectives are needed. It is *reasonable* to perform procedure or administer treatment. Class IIb. Benefit $\geq$ risk. Additional studies with broad objectives are needed; additional registry data would be helpful. Procedure or treatment *may be considered*. Class III. Risk $\geq$ benefit. Procedure or treatment *should not* be performed or administered *since it is not helpful and may be harmful*.
Related data were reported by Bavry et al.[4]
Abbreviations: ASA, aspirin; BMS, bare metal stent; CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; d, days; DES, drug-eluting stent; FFR, fractional flow reserve, PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIA, transient ischemic attack; UA/NSTEMI, unstable angina/non–ST-segment elevation myocardial infarction.

Additional considerations when sending patients to the catheterization laboratory are related to renal function. In patients with renal dysfunction, the most important way to prevent contrast nephropathy is adequate hydration prior to the procedure. In patients with left ventricular dysfunction, hydration must be done judiciously. Other strategies for preventing contrast nephropathy are being studied, although it is not entirely clear which strategies beyond hydration are truly effective.

Use of upstream glycoprotein IIb/IIIa inhibitors has become more common in patients with non–ST-segment elevation ACS. However, the most recent trial to examine this issue, the Early Glycoprotein IIb/IIIa Inhibition in Non–ST-Segment Elevation Acute Coronary Syndrome (EARLY ACS) trial, did not find a clear benefit for routine administration of upstream glycoprotein IIb/IIIa inhibitors when studying all patients with ACS.[10] There did appear to be a signal of benefit in troponin-positive patients, but as an

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overall strategy no significant benefit and even some detriment associated with an increase in bleeding were shown. Similarly, the results of the Acute Catheterization and Urgent Intervention Triage strategY (ACUITY) trial did not support the benefit of upstream glycoprotein IIb/IIIa inhibitors in patients with ACS.[11]

New data have also been released with respect to the thienopyridines. The Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction (TRITON–TIMI) 38 study found that the more potent thienopyridine prasugrel significantly reduced ischemic events when compared with clopidogrel in patients with ACS undergoing PCI.[12–14] A significant reduction in stent thrombosis was reported regardless of the type of stent.[15] However, the study reported a significant increase in major bleeding and a small, but statistically significant, excess of fatal bleeding. A subgroup analysis of patients with diabetes or with ST-segment elevation MI from the TRITON-TIMI 38 study showed a particularly large benefit associated with the use of prasugrel vs. clopidogrel and, interestingly, bleeding hazards were attenuated in these subgroups.[16,17] In the small subgroup of patients with prior stroke or transient ischemic attack (TIA), there was an excessive rate of intracranial hemorrhage with prasugrel vs. clopidogrel, indicating that prasugrel should not be used in these patients. Patients age 75 years or older or who weighed less than 60 kg also appeared to have a higher bleeding risk with prasugrel compared to clopidogrel. Careful thought is needed before using prasugrel in those patients identified as having a higher risk of bleeding.

Recently, a higher clopidogrel loading dose of 600 mg vs. the standard 300 mg dose was tested in patients who presented with ACS in the Clopidogrel optimal loading dose Usage to Reduce Recurrent EveNTs-Organization to Assess Strategies in Ischemic Syndromes (CURRENT-OASIS) 7 trial.[18] Patients also received 150 mg of clopidogrel daily for the ensuing 6 days vs. the standard 75 mg daily dose. All patients then received 75 mg clopidogrel for 1 month of follow-up. In the overall population, there was no benefit to using the higher clopidogrel loading dose. In contrast, there was a significant reduction in stent thrombosis in patients who received stents. The higher loading dose of clopidogrel was associated with a higher rate of bleeding.

Ticagrelor is a novel adenosine diphosphate receptor antagonist that was compared with clopidogrel in patients with ACS.[19,20] Compared to clopidogrel, ticagrelor significantly reduced ischemic events and there was also a significant reduction in cardiovascular mortality and in all-cause mortality. Surprisingly, overall major bleeding did not increase with ticagrelor, but non–CABG-related major bleeding increased.

The use of proton pump inhibitors (PPIs) in patients receiving dual antiplatelet therapy has also been a matter of vigorous recent debate.[21] Evidence to date suggests there is no significant clinical interaction between PPIs and prasugrel.

The data with clopidogrel and PPIs are mixed, although data are limited because much were derived from observational studies. Randomized clinical trial data are needed to assess whether there is an interaction between clopidogrel and PPIs that warrants clinical action, although preliminary data suggest there is no adverse cardiovascular interaction.[22]

New data regarding the intravenous anticoagulant bivalirudin have become available and have been incorporated into the Focused Guideline Update. Although bivalirudin is to be used primarily in the catheterization laboratory during PCI, it does appear to be associated with significantly less bleeding than heparin plus glycoprotein IIb/IIIa inhibitors.[11,23–26]

Case Study (cont)
The patient undergoes cardiac catheterization. An occluded dominant left circumflex artery is noted and is opened up with balloon angioplasty after aspiration thrombectomy. The patient receives 60 mg of prasugrel as a loading dose and bivalirudin as the anticoagulant during the procedure. A drug-eluting stent is implanted with excellent results. The patient is transferred to the cardiac care unit for further care. It appears that this is a patient who functionally has an ST-segment elevation MI with an occluded artery, although it manifested on the ECG as ST depression. Because of the patient's ongoing chest discomfort, it was fortunate that prompt angiography was performed.

Discussion
Patients with ACS present several challenges in management. Risk stratification is particularly important for non–ST-segment elevation ACS and requires thoughtful evaluation by the physician. Additionally, the large amount of new data and guideline updates create a rapidly evolving field, making it difficult to keep abreast of new developments. Physicians of patients with ACS need to be aware of these key developments so that they can provide optimal care to their patients with potentially life-threatening ACS.

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REFERENCES
1. Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation*. 2010;121:e46–e215.
2. Kushner FG, Hand M, Smith SC Jr, et al. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention

(updating the 2005 guideline and 2007 focused update) a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2009;54: 2205–2241.

3. Kumbhani DJ, Cannon CP, Fonarow GC, et al. Association of hospital primary angioplasty volume in ST-segment elevation myocardial infarction with quality and outcomes. *JAMA*. 2009;302:2207–2213.

4. Bavry AA, Kumbhani DJ, Rassi AN, Bhatt DL, Askari AT. Benefit of early invasive therapy in acute coronary syndromes: a meta-analysis of contemporary randomized clinical trials. *J Am Coll Cardiol*. 2006;48: 1319–1325.

5. Bhatt DL, Roe MT, Peterson ED, et al. Utilization of early invasive management strategies for high-risk patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE Quality Improvement Initiative. *JAMA*. 2004;292:2096–2104.

6. Mehta SR, Granger CB, Boden WE, et al. Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med*. 2009;360: 2165–2175.

7. Montalescot G, Cayla G, Collet JP, et al. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. *JAMA*. 2009;302:947–954.

8. Bavry AA, Bhatt DL. Drug-eluting stents: dual antiplatelet therapy for every survivor? *Circulation*. 2007;116:696–699.

9. Bavry AA, Bhatt DL. Appropriate use of drug-eluting stents: balancing the reduction in restenosis with the concern of late thrombosis. *Lancet*. 2008; 371:2134–2143.

10. Giugliano RP, White JA, Bode C, et al. Early versus delayed, provisional eptifibatide in acute coronary syndromes. *N Engl J Med*. 2009;360: 2176–2190.

11. Stone GW, Ware JH, Bertrand ME, et al. Antithrombotic strategies in patients with acute coronary syndromes undergoing early invasive management: one-year results from the ACUITY trial. *JAMA*. 2007;298: 2497–2506.

12. Bhatt DL. Intensifying platelet inhibition--navigating between Scylla and Charybdis. *N Engl J Med*. 2007;357:2078–2081.

13. Bhatt DL. Prasugrel in clinical practice. *N Engl J Med*. 2009;361:940–942.

14. Wiviott SD, Braunwald E, McCabe CH, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2007; 357:2001–2015.

15. Wiviott SD, Braunwald E, McCabe CH, et al. Intensive oral antiplatelet therapy for reduction of ischaemic events including stent thrombosis in patients with acute coronary syndromes treated with percutaneous coronary intervention and stenting in the TRITON-TIMI 38 trial: a subanalysis of a randomised trial. *Lancet*. 2008;371:1353–1363.

16. Montalescot G, Wiviott SD, Braunwald E, et al. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): double-blind, randomised controlled trial. *Lancet*. 2009;373:723–731.

17. Wiviott SD, Braunwald E, Angiolillo DJ, et al. Greater clinical benefit of more intensive oral antiplatelet therapy with prasugrel in patients with diabetes mellitus in the trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel—Thrombolysis in Myocardial Infarction 38. *Circulation*. 2008;118:1626–1636.

18. Mehta SR, CURRENT Investigators. A randomized comparison of a clopidogrel high loading and maintenance dose regimen versus standard dose and high versus low dose aspirin in 25,000 patients with acute coronary syndromes: results of the CURRENT OASIS 7 trial. Available at: http://www.escardio.org/congresses/esc-2009/congress-reports/Pages/706003-706004-mehta-vandewerf.aspx#discussant.2009. Accessed July 2010.

19. Bhatt DL. Antiplatelet therapy: ticagrelor in ACS-what does PLATO teach us? *Nat Rev Cardiol*. 2009;6:737–738.

20. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2009;361: 1045–1057.

21. Depta JP, Bhatt DL. Omeprazole and clopidogrel: Should clinicians be worried? *Cleve Clin J Med*. 2010;77:113–116.

22. Bhatt DL. COGENT: a prospective, randomized, placebo-controlled trial of omeprazole in patients receiving aspirin and clopidogrel. Transcatheter Cardiovascular Therapeutics (TCT) 2009; September 24, 2009; San Francisco, CA.

23. Mehran R, Brodie B, Cox DA, et al. The Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial: study design and rationale. *Am Heart J*. 2008;156:44–56.

24. Mehran R, Lansky AJ, Witzenbichler B, et al. Bivalirudin in patients undergoing primary angioplasty for acute myocardial infarction (HORIZONS-AMI): 1-year results of a randomised controlled trial. *Lancet*. 2009;374:1149–1159.

25. Stone GW, Bertrand M, Colombo A, et al. Acute Catheterization and Urgent Intervention Triage strategY (ACUITY) trial: study design and rationale. *Am Heart J*. 2004;148:764–775.

26. Stone GW, White HD, Ohman EM, et al. Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial. *Lancet*. 2007;369:907–919.

27. Society of Hospital Medicine. Acute coronary syndrome. *J Hosp Med*. 2006;1 (suppl 1):2–3.

28. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *JAMA*. 2000;284:835–842.