Acute Coronary Syndrome: Focus on Antiplatelet Therapy

Rodel V. Bobadilla, MSN, APRN, CCRN, NP-C, FNP-BC

The American Heart Association/American College of Cardiology in 2014 published a focused update of the 2007 and 2012 guidelines for non–ST-segment elevation acute coronary syndrome (NSTE-ACS). The management of ST-segment elevation myocardial infarction (STEMI) is described in a separate guideline published in 2013. The focused updates to the guidelines contain updated recommendations for dual antiplatelet therapy, including use of the P2Y<sub>12</sub> inhibitor ticagrelor, which was recently approved by the Food and Drug Administration. Nurses caring for patients with acute coronary syndrome must have a good understanding of the current treatment guidelines for such patients, to help ensure delivery of evidence-based care. This review article uses a case study–based approach to describe how the new guidelines affect clinical decision making when choosing appropriate antiplatelet therapy for patients with NSTE-ACS or STEMI, depending on the patient’s clinical history and presenting characteristics. (Critical Care Nurse. 2016;36[1]:15-27)

In 2010, there were 1,141,000 unique hospitalizations for acute coronary syndrome (ACS) in the United States. ACS describes any group of clinical signs and symptoms that are compatible with acute myocardial ischemia; thus, ACS includes both non–ST-segment elevation acute coronary syndrome (NSTE-ACS; formerly known as unstable angina and non–ST-segment elevation myocardial infarction [NSTEMI]) and ST-segment elevation myocardial infarction (STEMI). It is estimated that, each year, approximately 635,000 new ACS events and approximately 300,000 recurrent events will occur in the United States. ACS is caused by obstruction of blood flow to the myocardium as a result of blockage in the coronary artery. A common cause of such blockage is disruption of an atherosclerotic...
plaque within a coronary artery, often associated with the formation of a clot. The consequent ischemia may cause myocardial damage, and potentially necrosis, which can be detected via cardiac biomarkers (ie, troponins or creatine kinase–MB).3

ACS therapy is directed toward reestablishing coronary artery perfusion through either invasive therapy with percutaneous coronary artery intervention (PCI) or an ischemia-guided strategy. Because ACS has serious consequences, it is vital that patients be evaluated, given a diagnosis, and treated quickly to optimize outcomes.4 Major priorities for improving outcomes are better recognition of signs and symptoms and shortening the time to reperfusion.5 The American Heart Association (AHA) and American College of Cardiology Foundation (ACCF) have recently updated their guidance for the management of NSTE-ACS and STEMI, with a focus on antiplatelet therapy.5 Regardless of treatment approach, antiplatelet therapy is an important short- and long-term strategy to minimize damage and prevent recurrence of myocardial injury or infarction. This review summarizes updated information reflected in the latest AHA/ACC guidelines for the management of NSTE-ACS and STEMI, with a focus on antiplatelet therapy. NSTE-ACS and STEMI case studies are included to illustrate how the current guidelines can be applied to clinical practice.

Class of Recommendation and Level of Evidence

An evidence-based approach was taken by the guideline writing groups in analyzing the data and developing recommendations, using methods created by the ACCF/AHA Task Force on Practice Guidelines.7 Each recommendation includes a class of recommendation (COR), an estimate of the magnitude of a treatment effect, and a level of evidence (LOE), which estimates the probability or precision of the effect (Table 1).
Pathophysiology of ACS: The Role of Platelets

ACS often occurs when a vulnerable plaque in a coronary artery ruptures (Figure 1), exposing the lipid-filled core. Platelets in the blood are activated by coming into contact with the thrombogenic contents (eg, collagen) exposed by disruption of the plaque’s fibrous cap (Figure 2). Platelets adhere to sites of vascular injury, where collagen and von Willebrand factor in the extracellular matrix interact with the glycoprotein (GP) receptors on the platelet surface. This activates the platelets, causing a shape change and releasing adenosine diphosphate (ADP) and thromboxane A₂, which in turn activates surrounding platelets. Platelets express GPIIb/IIIa receptors, which bind adhesive proteins such as von Willebrand factor and fibrinogen, and stimulate the formation of thrombin on their surface to amplify aggregation and support coagulation. A number of platelet receptors are involved in this process, including the P₂Y₁₂ receptor. These receptors are activated by ADP, which mediates the release of potent prothrombotic and proinflammatory factors involved in platelet aggregation.

Figure 1 The pathophysiology of acute coronary syndromes. The rupture of an unstable atherosclerotic plaque can lead to an acute coronary event. The clinical severity of the event is influenced by the thrombotic response of the individual.

Figure 2 The process of platelet activation and thrombus formation within a blood vessel. Where the vascular surface is disrupted, collagen and von Willebrand factor (vWF) in the extracellular matrix (ECM) are exposed to the circulating blood and interact with glycoprotein (GP) receptors on the surface of platelets. Platelets then adhere to the site and become activated, changing shape, releasing adenosine diphosphate (ADP) and thromboxane A₂ (TxA₂), and stimulating the formation of thrombin. These stimuli act on surrounding platelets to accelerate and augment the process. Platelets express GPIIb/IIIa receptors, which bind adhesive proteins such as vWF and fibrinogen. The adhesion of the platelets forms the platelet-rich thrombus.
and the promotion of fibrin cross-linking to stabilize the thrombus. The P2Y$_{12}$ antagonists clopidogrel, prasugrel, and ticagrelor inhibit ADP-induced P2Y$_{12}$ receptor activation, thereby preventing GPIIb/IIIa complex activation and reducing platelet aggregation.\(^9\)

Clopidogrel and prasugrel are both orally administered, thienopyridine-based, irreversibly binding P2Y$_{12}$ inhibitors, which must be converted into an active metabolite to allow binding to the P2Y$_{12}$ receptor.\(^10\) Ticagrelor, an orally administered, reversibly binding P2Y$_{12}$ receptor antagonist, is the first in a new class of agents, cyclopentyltriazolopyrimidines, and does not need a metabolic conversion step to become active. In addition to P2Y$_{12}$ inhibition, ticagrelor also increases extracellular adenosine levels by inhibiting the equilibrative nucleoside transporter-1.\(^11\) As well as being an additional mechanism for the antiplatelet effects of ticagrelor,\(^12\) the increase in local adenosine levels enhances adenosine-mediated coronary blood flow.\(^13-15\)

**Guideline Update: NSTE-ACS**

The AHA/ACC Task Force on Practice Guidelines has published a 2014 update for the care of patients with NSTE-ACS.\(^6\) This update replaces the relevant parts of the 2007 ACC/AHA guidelines,\(^4\) which were revised during focused updates in 2011\(^16\) and 2012.\(^17\)

NSTE-ACS is characterized by ST-segment depression or prominent T-wave inversion as shown by electrocardiography and/or a positive result for a necrosis biomarker (eg, troponin) without ST-segment elevation and in the presence of other clinically relevant symptoms such as chest discomfort or anginal equivalent.\(^6\)

Patients with unstable angina or NSTEMI are often difficult to distinguish at first, and therefore are considered together in the term NSTE-ACS under AHA/ACC guidance.\(^6\) Unstable angina and NSTEMI have a similar pathogenesis and mainly differ in the degree of ischemia and whether the degree of ischemia is sufficient to cause myocardial damage that releases biomarkers of myocardial necrosis (ie, troponins or creatine kinase–MB).\(^3\) When neither of these biomarkers is detected, a patient is confirmed as having unstable angina; if a biomarker is present, a diagnosis of NSTEMI is established.\(^6\) Around 53% to 71% of patients with ACS have NSTE-ACS diagnosed at first.\(^1,18,19\)

**Antiplatelet Therapy**

In NSTE-ACS, dual antiplatelet therapy with aspirin and a P2Y$_{12}$ inhibitor remains the cornerstone of treatment, and aspirin is recommended as first-line, indefinite therapy.\(^6\) Several sections of the guidelines that include guidance on how to manage antiplatelet therapies in patients with NSTE-ACS were updated to include the newest P2Y$_{12}$ receptor antagonist, ticagrelor, in addition to clopidogrel and prasugrel.\(^6\) Recommendations for use of antiplatelet therapies in patients with NSTE-ACS managed with an invasive strategy or ischemia-guided strategy are summarized in Table 2 (available online only, at www.ccnonline.org).

Similar to guidelines for patients with STEMI, the recommendations for use of ticagrelor in patients with NSTE-ACS are primarily derived from the results of the pivotal Platelet Inhibition and Patient Outcomes (PLATO) study, which enrolled 18 624 patients with ACS\(^20\) (NSTE-ACS, n = 11 080)\(^21\) and compared cardiovascular outcomes in patients taking ticagrelor (180-mg loading dose, 90-mg twice-daily maintenance dose) with those taking clopidogrel (300- to 600-mg loading dose, 75-mg daily maintenance dose).\(^20\) An aspirin loading dose of 325 mg and a maintenance dose of 75 to 100 mg daily (325 mg daily in patients with stents was permitted up to 6 months) were recommended in the study protocol. In the overall PLATO population, ticagrelor significantly reduced the incidence of the combined (primary) end point of vascular death, myocardial infarction, or stroke (9.8% vs 11.7%; \(P < .001\)) after 12 months. These findings were driven by significantly lower rates of both vascular death and myocardial infarction in ticagrelor-treated patients.\(^20\) A statistically significant reduction in all-cause mortality was also seen with ticagrelor compared with clopidogrel (\(P < .001\)).\(^20\) These results were also reflected in the NSTE-ACS population (Table 3).\(^21\)

No significant differences in the rate of major bleeding were found, either overall or in patients undergoing a coronary artery bypass graft (CABG) in whom clopidogrel and ticagrelor were discontinued according to the study protocol before the procedure (5 days and 24-72 hours before surgery, respectively) in the overall PLATO population\(^20\) or the NSTE-ACS population.\(^21\) However, ticagrelor demonstrated significantly increased rates of major bleeding that were not related to CABG (4.5% vs 3.8%, \(P = .03\) overall; 4.8% vs 3.8%, \(P = .01\) for NSTE-ACS),\(^20,21\) dyspnea (13.8% vs 7.8%, \(P < .001\) overall;
although only 0.9% of ticagrelor recipients and 0.1% of clopidogrel recipients discontinued treatment because of dyspnea, and ventricular pauses of 3 seconds or longer during treatment week 1 that were not associated with syncope or with pacemaker implantation (5.8% vs 3.6%, \( P < .01 \) overall).

In the overall PLATO population, ticagrelor efficacy (primary composite end point) was apparently lower in patients weighing less than the median weight (for their sex) and in patients who were not receiving lipiddowering medication when randomized. Ticagrelor efficacy also appeared to be lower in patients from North America, most likely because aspirin doses commonly are higher in the United States, although a chance finding cannot be ruled out. Adjusted analyses showed that in patients taking low-dose maintenance aspirin, ticagrelor was associated with better outcomes than was clopidogrel, with statistical superiority in countries

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PLATO</th>
<th>TRITON-TIMI 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>11 080</td>
<td>7544</td>
</tr>
<tr>
<td>Median age, years</td>
<td>64</td>
<td>59</td>
</tr>
<tr>
<td>Prior myocardial infarction, No. (%) of patients</td>
<td>2810 (25)</td>
<td>1014 (13)</td>
</tr>
<tr>
<td>Prior PCI, No. (%) of patients</td>
<td>1862 (17)</td>
<td>630 (8)</td>
</tr>
<tr>
<td>PCI on study, No. (%) of patients</td>
<td>5710 (52)</td>
<td>6158 (82)</td>
</tr>
<tr>
<td>Primary end point (cardiovascular death, myocardial infarction, stroke)</td>
<td>10.0% T vs 12.3% C ( P = .001 )</td>
<td>9.4% T vs 10.8% C ( P = .07 )</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>4.3% T vs 5.8% C ( P = .002 )</td>
<td>5.0% T vs 6.1% C ( P = .05 )</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>3.7% T vs 4.9% C ( P = .007 )</td>
<td>4.5% T vs 5.5% C ( P = .07 )</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>6.6% T vs 7.7% C ( P = .04 )</td>
<td>4.7% T vs 5.8% C ( P = .03 )</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.3% T vs 1.4% C ( P = .79 )</td>
<td>1.7% T vs 1.0% C ( P = .02 )</td>
</tr>
<tr>
<td>Major bleeding( ^b )</td>
<td>13.4% T vs 12.6% C ( P = .26 )</td>
<td>9.0% T vs 9.2% C ( P = .76 )</td>
</tr>
<tr>
<td>CABG-related major bleeding( ^b )</td>
<td>NA</td>
<td>5.1% T vs 5.8% C ( P = .30 )</td>
</tr>
<tr>
<td>Non–CABG-related major bleeding( ^b )</td>
<td>4.8% T vs 3.8% ( P = .01 )</td>
<td>4.1% T vs 3.7% ( P = .61 )</td>
</tr>
<tr>
<td>Life-threatening bleeding( ^b )</td>
<td>6.6% T vs 6.5% C ( P = .56 )</td>
<td>4.7% T vs 4.9% C ( P = .86 )</td>
</tr>
<tr>
<td>Fatal bleeding( ^b )</td>
<td>0.3% T vs 0.4% C ( P = .37 )</td>
<td>0.2% T vs 0.1% C NA</td>
</tr>
</tbody>
</table>

Abbreviations: C, clopidogrel; CABG, coronary artery bypass grafting; NA, not available; P, prasugrel; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; T, ticagrelor.

\( ^a \) During index admission (PCI performed within 12 hours of randomization in 5439 [72\%] of patients with STEMI).

\( ^b \) Trial definitions of bleeding were PLATO (PLATO trial) and TIMI (TRITON-TIMI 38 trial).

\( ^c \) Includes life-threatening and fatal bleeding.

\( ^d \) Non–CABG-related fatal bleeding.
outside of the United States and similar outcomes in the US cohort. Therefore, low maintenance doses of aspirin, as approved by the Food and Drug Administration, may result in the most favorable outcomes.

Ticagrelor is recommended over clopidogrel for all patients with NSTE-ACS according to the updated AHA/ACC guidelines, irrespective of their initial treatment strategy. In line with the prescribing information for ticagrelor, which states that it should be used only with a low maintenance dose of aspirin (325-mg loading dose then a 75- to 100-mg maintenance dose), the updated guidelines recommend an aspirin loading dose of 162 to 325 mg and a maintenance dose of 81 mg daily for patients receiving ticagrelor, as it is considered to carry a lower risk for bleeding. This recommendation is also similar to the recommendations for patients with STEMI following primary PCI. The guidelines also state the importance of considering the potential for intracranial bleeding in patients who have previously experienced a stroke or a transient ischemic attack (TIA) when considering the addition of ticagrelor to aspirin, because dual antiplatelet treatment (aspirin and either clopidogrel or prasugrel) has previously been associated with an increased likelihood of intracranial bleeding, especially in patients who have previously experienced stroke.

In PLATO, ticagrelor was associated with more episodes of intracranial bleeding than clopidogrel was (26 [0.3%] vs 14 [0.2%] respectively, \( P = .06 \)). However, bleeding intracranially was not found to be related to a history of stroke or TIA (interaction \( P = .38 \)); of the 1152 patients in PLATO with a history of stroke or TIA, only 4 patients receiving ticagrelor and 4 patients receiving clopidogrel had intracranial bleeding. It is worth noting that ticagrelor is currently being evaluated as a monotherapy in a trial of “all-comers (unselected)” patients undergoing PCI (NCT01813435), with results expected in 2016. The guidelines provide recommendations on how long antiplatelet therapy should be stopped before planned cardiac surgery. It is recommended that both ticagrelor and clopidogrel be stopped 5 days before surgery. For prasugrel, the guidelines recommend stopping therapy 7 days before surgery (Table 2—available online).

Guidance on the management of patients with NSTE-ACS with platelet GPIIb/IIIa receptor antagonists (abciximab, eptifibatide and tirofiban) remains the same as that published in the 2007 guidelines, as do the recommendations for anticoagulant support of PCI.

Case Study 1: NSTE-ACS

A 65-year-old man arrives in the emergency department complaining of chest pain that has been occurring for the past 6 hours. He has coronary artery disease and had a drug-eluting stent placed 8 years previously. He is currently receiving aspirin (81 mg/d), clopidogrel (75 mg/d), metoprolol (25 mg/d), benazepril/amlodipine (10/5 mg/d), and pravastatin (40 mg/d). (Continuation of a P2Y\(_{12}\) receptor inhibitor such as clopidogrel for longer than 12 months may be possible for patients receiving a drug-eluting stent [COR: IIb; LOE: C].)

Cardiac enzymes are initially negative but reveal a slight elevation on the second test (creatine phosphokinase, 500 μg/L; creatine kinase–MB fraction, 5.2 μg/L; troponin I, 1.03 μg/L), and the 12-lead electrocardiogram shows no ischemic changes. NSTE-ACS (NSTEMI) is diagnosed, and the patient is given a loading dose of clopidogrel (300 mg) in the emergency department and admitted to cardiac telemetry. Coronary angiography is scheduled for the following day.

Coronary angiography reveals a 90% stenosis at the previously stented site in the left anterior descending artery and a 50% stenosis of the mid-left circumflex artery. A drug-eluting stent is placed in the left anterior descending artery, reducing the 90% stenosis to 0% residual.

Choice of P2Y\(_{12}\) Inhibitor for PCI

A key question in this case is the choice of P2Y\(_{12}\) inhibitor for antiplatelet therapy. The updated AHA/ACC guidelines recommend clopidogrel or ticagrelor (in addition to aspirin) for all patients with NSTE-ACS managed with either an early invasive strategy or ischemia-guided strategy (COR: I; LOE: B), and state that it is reasonable to use ticagrelor over clopidogrel (COR: IIa; LOE: B). For patients with NSTE-ACS undergoing PCI with stenting, the guidelines recommend clopidogrel, prasugrel, or ticagrelor (COR: I; LOE: B for all 3 P2Y\(_{12}\) inhibitors; Table 2—available online only), with prasugrel recommended over clopidogrel for patients who are undergoing PCI and not at high risk for bleeding complications. The removal of prasugrel from recommended initial therapy in NSTE-ACS patients managed with an ischemia-guided strategy (based in part on the TRILOGY-ACS trial results) represents a key update from the
2007 guidelines and is more similar to the approach suggested in the European Society of Cardiology (ESC) NSTE-ACS guidelines, which recommend individual P2Y12 inhibitors for particular patient subgroups. The guidance for patients with NSTE-ACS undergoing PCI is slightly different from the recommendations for antiplatelet therapy in patients with STEMI, where one P2Y12 inhibitor is not endorsed over another.

Furthermore, a number of sections in the 2012 ACCF/AHA NSTE-ACS guidelines highlight potential variability in response to clopidogrel associated with its reliance on the CYP2C19 isoenzyme, which converts clopidogrel to its active metabolite. A boxed warning in the prescribing information for clopidogrel acknowledges higher cardiovascular event rates following ACS or PCI among CYP2C19-poor metabolizers taking clopidogrel versus patients with normal CYP2C19 function. The updated 2014 AHA/ACC guidelines for NSTE-ACS do not recommend routine testing of platelet function or genetic phenotype testing, on the basis that such tests have not been associated with a decrease in ischemic complications. It is notable that the ESC guidelines recommend the consideration of these testing approaches for patients who are receiving clopidogrel.

Another consideration in the choice of treatment for this patient is concomitant therapy. Although this patient was not prescribed a proton pump inhibitor (PPI), such agents are often given to prevent gastrointestinal complications in patients receiving nonsteroidal anti-inflammatory drugs plus clopidogrel, where they may reduce the antiplatelet effects of clopidogrel via competition for CYP2C19. The effect of the interaction between PPIs and clopidogrel on cardiovascular outcomes has not been confirmed as clinically important, and the guidelines do not prohibit the use of PPIs in patients taking clopidogrel. (Remember, continuation of a P2Y12 receptor inhibitor >12 months may be possible for patients receiving a drug-eluting stent [COR: IIb; LOE: C].) The guidelines recommend that PPIs be prescribed in patients receiving triple antiplatelet therapy with a vitamin K antagonist, aspirin, and a P2Y12 receptor inhibitor who have a history of gastrointestinal bleeding, and that use of PPIs may be considered in patients without a history of gastrointestinal bleeding who are receiving P2Y12 agents.

In case study 1, the interventional cardiologist decides to change the P2Y12 inhibitor to ticagrelor, a decision based on the reduction in vascular death, myocardial infarction, or stroke found for ticagrelor relative to clopidogrel in the PLATO trial. The patient receives a loading dose of ticagrelor 180 mg by mouth and then 90 mg twice a day.

Risk Associated With Switching Antiplatelet Therapies

The patient in this case had received a 300-mg loading dose of clopidogrel before angiography and then was switched to ticagrelor. In the PLATO study, 46.0% of the patients in the ticagrelor study group had received clopidogrel in the hospital before randomization; most received 300 to 375 mg (n = 1921; 20.6%), and a number received 600 to 675 mg (n = 1282; 13.7%). Interestingly, the rate of major bleeding did not differ between patients receiving ticagrelor along with clopidogrel and patients receiving just clopidogrel, and no significant interaction was found between clopidogrel given before randomization or as a loading dose and bleeding events.

The other possible choices of P2Y12 inhibitor are continuation of clopidogrel or initiation of prasugrel.
Guideline Update: STEMI

The 2013 ACCF/AHA Guideline for the Management of STEMI contains a significantly revised version of the recommendations from the 2004 guidelines, for which focused updates were published in 2007 and 2009. The American College of Physicians, American College of Emergency Physicians, and Society for Cardiac Angiography and Interventions (SCAI) participated in a joint initiative to update the guidelines. The update focuses on recent developments in reperfusion therapy, the organization of regional care systems, transfer algorithms, antithrombotic and medical therapies (evidence-based), and approaches in secondary care that may improve patient-centered management. The following sections expand on the updates that are most relevant to critical care nurses, including the use of antiplatelet therapy in patients with STEMI.

Regional Approaches to STEMI Management and Reperfusion Treatment

PCI remains the reperfusion strategy in patients experiencing STEMI, and the 2013 ACCF/AHA guideline recommendations favor the benefits of PCI over fibrinolytic agents, despite the potential for delays associated with transport to a hospital with the capability to perform PCI. Still, several updates to the guidelines emphasize time as a key factor in STEMI outcomes. Current time-to-treatment goals are summarized in Table 4.

Antiplatelet Therapy

The 2013 ACCF/AHA STEMI guidelines encourage appropriate antithrombotic therapy, including dual antiplatelet therapy and anticoagulants, both during and after reperfusion therapy. Similar to the NSTE-ACS guidelines, the updated STEMI guidelines provide guidance on the use of the newest P2Y12 receptor antagonist, ticagrelor, with the PLATO trial (described earlier) supporting these recommendations. In a planned subgroup analysis of the PLATO cohort limited to the 7544 patients (41%) with STEMI (Table 3), the 13% risk reduction (hazard ratio = 0.87; \( P = .07 \)) in the combined primary end point (myocardial infarction, stroke, or cardiovascular death) for ticagrelor versus clopidogrel was comparable with that seen in the overall population of the study. The incidence of myocardial infarction alone was also significantly reduced with ticagrelor (4.7% vs 5.8% with clopidogrel) in STEMI patients. The treatment groups did not differ significantly with regard to major bleeding. Similar to the total study population, dyspnea was more frequent with ticagrelor (12.6%) than with clopidogrel (8.4%) in STEMI patients (\( P < .001 \)), but rarely required drug discontinuation (0.5% of ticagrelor

Table 4 2013 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) time-to-treatment goals for care of ST-segment-elevation myocardial infarction (STEMI)

<table>
<thead>
<tr>
<th>ACCF/AHA recommendations</th>
<th>Class of recommendation</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 12-lead ECG should be performed by emergency medical services personnel at the site of FMC in patients with symptoms consistent with STEMI.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Primary PCI is recommended for STEMI patients with ischemic symptoms for less than 12 hours.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>It is reasonable to perform PCI in STEMI patients with ECG or clinical evidence of ischemia up to 24 hours.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>For STEMI patients initially transported to a PCI-capable hospital, the ideal FMC-to-device goal is 90 minutes or less.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Immediate transfer to a PCI-capable hospital is recommended for patients with STEMI who initially arrive at a non-PCI-capable hospital, with an FMC-to-device time goal of 120 minutes or less.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>In the absence of contraindications, fibrinolytic therapy should be administered to patients with STEMI at non-PCI-capable hospitals when the anticipated FMC-to-device time at a PCI-capable hospital exceeds 120 minutes because of unavoidable delays.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>When fibrinolytic therapy is indicated or chosen as the primary reperfusion strategy, it should be administered within 30 minutes of hospital arrival.</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

Abbreviations: ECG, electrocardiogram; FMC, first medical contact; PCI, percutaneous coronary intervention.
and 0.1% of clopidogrel recipients discontinued treatment because of dyspnea). Results in the STEMI subgroup of the TRITON-TIMI trial are also shown in Table 3. Between 30% and 40% of patients with ACS in the United States have STEMI. The PLATO study sample reflected this national average, with approximately 38% of patients having STEMI.

The 2013 ACCF/AHA guidelines for antiplatelet therapy to support reperfusion with primary PCI in patients experiencing STEMI are summarized in Table 5. As mentioned previously, the ACCF/AHA STEMI recommendations are slightly different from those for NSTE-ACS in that clopidogrel, prasugrel, or ticagrelor are recommended without a preference for one in particular. From a comparison perspective, the STEMI recommendations are broadly in line with the ESC’s STEMI guidelines, although the ESC recommends prasugrel only in patients who are clopidogrel-naïve and less than 75 years old (in addition to having no history of stroke or TIA) and recommends clopidogrel preferably

### Table 5 2013 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines for antiplatelet therapy to support reperfusion with primary PCI in patients experiencing STEMI

<table>
<thead>
<tr>
<th>ACCF/AHA recommendations</th>
<th>Class of recommendation</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>In STEMI patients undergoing PCI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>162- to 325-mg loading dose before procedure</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>81- to 325-mg daily maintenance dose (indefinite)</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>81 mg daily is the preferred maintenance dose</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>A loading dose of a P2Y&lt;sub&gt;12&lt;/sub&gt; receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Clopidogrel 600 mg; or</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Prasugrel&lt;sup&gt;b&lt;/sup&gt; 60 mg; or</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Ticagrelor 180 mg</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>In patients receiving stents:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2Y&lt;sub&gt;12&lt;/sub&gt; inhibitor therapy should be given for 1 year to patients with STEMI who receive a drug-eluting stent or bare-metal stent during primary PCI, using the following maintenance doses:</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Clopidogrel: 75 mg daily; or</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Prasugrel&lt;sup&gt;b&lt;/sup&gt;: 10 mg daily; or</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Ticagrelor: 90 mg twice a day&lt;sup&gt;a&lt;/sup&gt;</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>In patients with a drug-eluting stent:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel, prasugrel,&lt;sup&gt;b&lt;/sup&gt; or ticagrelor&lt;sup&gt;a&lt;/sup&gt; can be continued beyond 1 year</td>
<td>IIB</td>
<td>C</td>
</tr>
<tr>
<td>In STEMI patients who are receiving antiplatelet agents and must undergo urgent CABG:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin should not be withheld</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Clopidogrel or ticagrelor should be discontinued at least 24 hours before urgent on-pump CABG, if possible</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Urgent off-pump CABG within 24 hours of clopidogrel or ticagrelor administration might be considered, especially if the benefits of prompt revascularization outweigh the risks of bleeding</td>
<td>IIB</td>
<td>B</td>
</tr>
<tr>
<td>Urgent CABG within 5 days of clopidogrel or ticagrelor administration or within 7 days of prasugrel administration might be considered, especially if the benefits of prompt revascularization outweigh the risks of bleeding</td>
<td>IIB</td>
<td>C</td>
</tr>
<tr>
<td>Short-acting intravenous glycoprotein IIb/IIIa receptor antagonists (eptifibatide, tirofiban) should be discontinued at least 2 to 4 hours before urgent CABG</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Abciximab should be discontinued at least 12 hours before urgent CABG</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

<sup>a</sup> The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.

<sup>b</sup> Prasugrel should not be administered to patients with a history of stroke or transient ischemic attack (class of recommendation: III; level of evidence: B).

<sup>c</sup> Drug-eluting stent should not be used in patients who cannot or will not comply with long-term dual antiplatelet therapy (class of recommendation: III; level of evidence: B).
in cases where prasugrel and ticagrelor are not available or cannot be used (ticagrelor can be used in all patient groups). The ACCF/AHA recommendations for supportive anticoagulant regimens are unchanged from the 2009 update and comprise the use of unfractionated heparin, including bolus doses to maintain therapeutic activated clotting times (as required), with consideration of whether the patient has received a GPIIb/IIIa receptor antagonist (LOE: C) or bivalirudin, with or without prior treatment with unfractionated heparin (LOE: B). They also note that bivalirudin monotherapy is preferred over unfractionated heparin and a GPIIb/IIIa inhibitor in patients who are at a high risk of bleeding. However, the ESC’s STEMI guidelines recommend bivalirudin (with GPIIb/IIIa inhibitors limited to bailout use) or enoxaparin (with or without a GPIIb/IIIa inhibitor) over unfractionated heparin and a GPIIb/IIIa inhibitor in all patients (although the ESC guidelines state that unfractionated heparin should be used in patients not receiving bivalirudin or enoxaparin).

The lack of consensus between the guidelines is part of a larger ongoing debate around the use of heparin versus bivalirudin in patients with STEMI who are undergoing PCI. The recently published UK HEAT-PPCI trial showed that heparin led to a lower incidence of ischemic events and a similar incidence of bleeding compared with bivalirudin, suggesting that heparin might be a more cost-effective treatment on the basis of these results and its lower cost. In addition to a significant reaction to its delayed consent strategy, the trial has generated much debate in the medical community because of the difference in results compared with previous trials of bivalirudin versus heparin. Although interestingly, a subsequent US study also yielded similar results. It is not clear whether the current debate will influence the next update to the STEMI guidelines, although it is important for all health care professionals treating cardiology patients to be aware of the potential implications with respect to clinical practice as the discussions and investigations will no doubt continue.

It should be noted that clopidogrel is the only P2Y12 receptor antagonist recommended for supporting reperfusion with fibrinolytic therapy (ie, as adjunctive antithrombotic therapy). Only clopidogrel and prasugrel are recommended in the setting of PCI after fibrinolytic therapy.

### Case Study 2: STEMI

A woman aged 67 years has an inferior wall STEMI diagnosed and undergoes emergency coronary angiography. Antithrombotic and dual oral antiplatelet therapies are not started before the coronary angiography because of the possibility of surgical revascularization. Unfortunately, the angiography reveals severe, diffuse 3-vessel coronary artery disease with decreased flow in the right coronary artery, although her left ventricular ejection fraction is normal at 60%. The surgical team determined that the patient was not suitable for bypass surgery. Medical management is recommended.

According to the 2013 STEMI recommendations, the patient should receive β-blockers (COR: I; LOE: B), angiotensin-converting enzyme inhibitors (COR: IIa; LOE: A), and high-intensity statin therapy (COR: I; LOE: B). The patient is currently receiving enteric-coated aspirin 325 mg/d, carvedilol 6.25 mg twice daily, lisinopril 5 mg/d, and atorvastatin 40 mg/d.

Table 5 describes the antiplatelet treatment options for this patient according to the 2013 ACCF/AHA STEMI guidelines. If she had been treated with a fibrinolytic agent and PCI, then there would be an indication for dual antiplatelet therapy with clopidogrel or prasugrel as the P2Y12 inhibitor. However, as neither fibrinolysis nor PCI have been used, a selection of either clopidogrel or ticagrelor would be appropriate to individualize therapy for this patient. Prasugrel should not be considered because the patient did not undergo PCI.

### The Nurse’s Role in Facilitating Guideline-Based In-Hospital Care

**Critical Care Nurses’ Central Role**

A critical care nurse may encounter patients with ACS in emergency departments, intensive care units, cardiac care units, cardiac catheter laboratories, telemetry units, progressive care units, and recovery rooms. Within these settings, nurses have a variety of responsibilities in the management of ACS patients, including explaining to patients what is happening to them, providing comfort to patients and their families, assisting with risk stratification of patients, acting as a conduit of information between different departments or members of the health care team, and assisting with decision making.

Nurses have an important role in the clinical decision process. The interpretation of vital signs, laboratory test results, and electrocardiographic tracings will speed the
Triage process and assist with determining which patients require immediate care and transfer from the emergency department to the cardiac care unit. The nurse’s understanding of the current AHA/ACC treatment guidelines for patients with ACS will not only help ensure delivery of evidence-based care, but will reduce time-to-treatment, a critical aspect of ACS response.

**Postprocedural Bleeding**

An additional key role for critical care nurses is in the early identification of postprocedural bleeding in patients with ACS. Bleeding is the most common noncardiac complication in patients undergoing PCI, due to the number of antiplatelet and anticoagulation therapies patients receive in the acute phase. Monitoring for arterial bleeding is particularly important in high-risk groups such as elderly patients, women, those with renal dysfunction, and those who had a STEMI. Monitoring should include regular assessment of wound or vascular-access sites, pain, peripheral pulses, vital signs, heart rhythm, and fluid intake and output. Bleeding should be suspected in any hypotensive patient who has recently received coronary angiography, PCI, CABG, or other surgery in a background of antiplatelet therapy.

**The Nurse’s Role in Posthospital Care Planning**

**Postdischarge Pharmacotherapy**

Nurses also have an important role in planning for discharge and posthospital management. With respect to posthospital care, the guidelines for NSTE-ACS emphasize secondary prevention, including continued use of antiplatelet therapy. Recommendations for maintenance dosing of antiplatelet agents in patients with NSTE-ACS are summarized in Table 2 (available online only). Routine pharmacotherapies recommended for posthospital care include continued use of β-blockers (when no contraindications are present) during and after hospitalization for all patients with STEMI (COR: I; LOE: B). In addition, angiotensin-converting enzyme inhibitors may be considered for all patients with STEMI (and no contraindications; COR: Ia, LOE: A), and all patients with STEMI should receive high-intensity statin therapy if there are no contraindications to its use (COR: I; LOE: B).

**New Guideline Recommendations**

Although not specifically referred to in the most recent update of the NSTE-ACS guidelines, the 2012 focused update contained a new section on quality of care and outcomes. It was recommended that key stakeholders (health care professionals and institutions) managing patients with NSTE-ACS contribute to a standardized quality-of-care data registry designed to monitor outcomes, including complications and adherence to agreed evidence-based care processes and improvement of quality for NSTE-ACS (COR: IIa; LOE: B). Among the registries listed are the National Cardiovascular Data Registry, the AHA’s Get With The Guidelines (GWTG) quality-improvement program, and the ACTION Registry-GWTG. The goal is to evaluate NSTE-ACS care, identify system problems, and implement improvements.

The 2013 ACCF/AHA STEMI guidelines have added a posthospitalization plan of care section designed to prevent hospital readmissions. It is recommended that all STEMI patients receive cardiac rehabilitation/secondary prevention programs that are exercise-based (COR: I; LOE: B); an evidence-based plan of care that encourages medication adherence (and is easy to understand), prompt follow-up with the health care team, improved diet and level of physical activity, and compliance with secondary prevention measures (COR: I; LOE: C); and smoking cessation support, including avoidance of second-hand smoke (COR: I; LOE: A).

**Postdischarge Planning**

As an in-hospital patient advocate, the critical care nurse is uniquely positioned to provide invaluable education about posthospital care to patients with ACS and their families. Such education would address medication adherence and titration, medication side effects, meeting promptly with a health care professional, smoking cessation, improved diet, physical activity levels, cardiac rehabilitation, symptom awareness, and the need for ongoing reassessment of risks for arrhythmias and heart failure. Assessment of adherence with medication is vital as evidence suggests that patients often discontinue antiplatelet therapy following hospital discharge, which may contribute to readmission and further complications, such as increased risk of stent thrombosis. Furthermore, patients should continue with a stabilized antiplatelet regimen as an outpatient unless there is a clinical need to change or discontinue treatment. Medication reconciliation is critically important during
hospitalization and at discharge to ensure no errors, omissions, and/or drug interactions occur.\textsuperscript{16,17} The nurse may also be mindful of wider socioeconomic/psychosocial challenges, including increased risk of depression and imbalance in health care provision or access that may necessitate individualization of the care plan.

A recent study by Jorstad et al\textsuperscript{52} provides evidence that nurse-coordinated education and monitoring after ACS improves cardiovascular outcomes. Patients were randomized to a program consisting of 4 outpatient nurse clinic visits within 8 months of ACS (n = 366) or to usual care alone (n = 367). Clinic visits focused on healthy lifestyles, biometric risk factors, and medication adherence and were conducted in addition to a usual-care regimen, which included outpatient cardiologist visits and referral to a 12-week cardiovascular rehabilitation program. After 12-month follow-up, the estimated 10-year cardiovascular mortality risk was reduced by 17\% in the intervention group versus usual care alone. The intervention group also experienced a significant reduction in rehospitalizations (86 vs 132 with usual care). Although the intervention used in this study was carried out after discharge, predischarge counseling may have similar benefits in patients with ACS.\textsuperscript{52}

Conclusions

Evidence-based guidelines for patient management in ACS are updated regularly, as novel treatments become available. Critical care nurses need to be familiar with the latest guidelines in order to help deliver evidence-based care, speed time to treatment, and optimize outcomes for patients with ACS. CCN

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