

REVIEW TOPIC OF THE WEEK

Management of Patients With NSTEMI-ACS

A Comparison of the Recent AHA/ACC and ESC Guidelines



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ABSTRACT

Non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) are the leading cause of morbidity and mortality from cardiovascular disease worldwide. The American Heart Association/American College of Cardiology and the European Society of Cardiology periodically release practice guidelines to guide clinicians in the management of NSTEMI-ACS, most recently in 2014 and 2015, respectively. The present review compares and contrasts the 2 guidelines, with a focus on the strength of recommendation and level of evidence in the approach to initial presentation and diagnosis of NSTEMI-ACS, risk assessment, treatments, and systems of care. Important differences include the use of a rapid rule-out protocol with high-sensitivity troponin assays, a preference for prasugrel/ticagrelor and fondaparinux for anticoagulation therapy, and a preference for radial arterial access in the European Society of Cardiology guidelines compared with the American Heart Association/American College of Cardiology guidelines. We also highlight the similarities and differences in the guidelines for special patient populations and suggest areas of further study. (J Am Coll Cardiol 2016;68:313-21) © 2016 by the American College of Cardiology Foundation.

Clinical guidelines summarize and evaluate available evidence with the aim of helping health care practitioners make informed clinical decisions for a given clinical scenario. Unstable angina (UA) and non-ST-segment elevation myocardial infarction encompass a subset of the clinical spectrum of acute coronary syndromes (ACS). Symptoms are similar in both disease states, but with non-ST-segment elevation myocardial infarction, there is evidence of myocardial necrosis, as documented by elevations in cardiac biomarkers. Given the similarity in clinical presentation and the difficulty in distinguishing the 2 syndromes, the new guidelines favor the term non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) instead of UA or non-ST-segment elevation myocardial infarction (1). ST-segment elevation myocardial

infarctions represent a complete occlusion of an artery with an urgent need for recanalization and are managed by specific clinical algorithms. The present review compares the 2015 guidelines of the European Society of Cardiology (ESC) and the 2014 guidelines of the American Heart Association (AHA)/American College of Cardiology (ACC) on the management of NSTEMI-ACS (1,2). The present paper highlights the differences and similarities in the approach to initial presentation and diagnosis, risk assessment, treatments, special populations, and systems of care.

GUIDELINES AND LEVEL OF EVIDENCE

For both the ACC/AHA and the ESC guidelines, members of the guideline writing committee (GWC)



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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndromes

COR = Class of Recommendation

DAPT = dual antiplatelet therapy

GPI = glycoprotein IIb/IIIa receptor inhibitor

GWC = guideline writing committee

hs-cTN = high-sensitivity cardiac troponin

LOE = Level of Evidence

NSTE-ACS = non-ST-segment elevation acute coronary syndromes

OAC = oral anticoagulation

UFH = unfractionated heparin

review the relevant published reports, and weigh the strength and quality of the evidence with the use of evidence-based methodologies developed by the task force. The Class of Recommendation (COR) and Level of Evidence (LOE) are then assigned by the GWC. COR considers the anticipated magnitude of benefit relative to the risk of a particular treatment or approach, and LOE rates the scientific evidence supporting each recommendation. **Tables 1** and **2** outline the COR and LOE designations.

All GWC members must disclose conflicts of interest before initiation of the writing effort. The ACC/AHA policy on relationships with industry requires that at least 50% of writing committee members, plus the Chair, have no relevant relationships (3). The ESC policy requires that GWC members report all potential conflicts, both perceived and real,

before being appointed to the task force (4).

SUMMARY INFORMATION

Substantial resources are required to prepare and revise practice guidelines. The assimilation of the data, review and interpretation, writing, and revisions after peer review are laborious and time-consuming, particularly in disease states such as ACS for which extensive research efforts exist. **Table 3** presents some overall data that compare and contrast logistical and procedural similarities and differences. Some of the differences, such as the number of references, are due, in part, to guidelines that the task forces overseeing the guideline preparation provide to the writing committees. The **Central Illustration** displays the frequency of recommendations according to COR for the AHA/ACC and ESC guidelines.

The key differences in COR I, LOE A and COR III, LOE A between the AHA/ACC and ESC guidelines are summarized in **Tables 4** and **5**, respectively.

DIAGNOSIS

The AHA/ACC 2014 update and the ESC 2015 recommendations both emphasize the importance of early evaluation by the emergency department, a clinical history, physical examination, and 12-lead electrocardiogram within 10 min of a patient's arrival (1,2). Both guidelines also stress the growing importance of biomarkers, namely high-sensitivity cardiac troponin (hs-cTN) assays, due to their high negative predictive value for ACS (5,6). In particular, the ESC guidelines recommend utilizing a shortened algorithm for diagnosis of NSTE-ACS, with the use of a 0 h/3 h or 0 h/1 h

TABLE 1 Classes of Recommendations

Clinical Significance	
Class I	Treatment or procedure should be performed, with the benefit largely outweighing the risk
Class II	It is reasonable to perform the treatment or procedure, although the evidence may, at times, be conflicting
Class IIa	Weight of evidence is in favor of treatment/procedure
Class IIb	Evidence is less well established; treatment/procedure may be considered
Class III	Procedure/test is harmful and is not recommended

algorithm measurement of hs-cTN. In large validation cohorts, the negative predictive value of such an approach exceeded 98% (2,7,8). The 2015 ESC guidelines also recommend assessment of copeptin, the C-terminal part of the vasopressin prohormone, for added sensitivity in ruling out acute myocardial infarctions, particularly when hs-cTN assays are not readily available (9–11).

The AHA/ACC 2014 guidelines recommend the use of risk scores to assess the prognosis in patients with NSTE-ACS (COR I, LOE A). Both guidelines also emphasize the value of 2 risk scores: the GRACE (Global Registry of Acute Coronary Events) (12,13), and the TIMI (Thrombolysis In Myocardial Infarction) (14) scores. The ESC favors the GRACE risk score because of its more accurate stratification and discrimination of risk during both admission and discharge (15,16). The ESC guidelines also favor the calculation of bleeding scores, particularly through the use of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA guidelines) bleeding risk score (COR IIb, LOE B). Both ESC and ACC/AHA guidelines suggest that use of these risk scores can help steer providers to early invasive strategies for the highest risk patients.

In patients with suspected NSTE-ACS without recurrence of chest pain and with normal levels of cardiac troponin, the ESC guidelines recommend a noninvasive stress test with imaging to look for inducible ischemia (COR I, LOE A) before deciding on an invasive strategy (17–19). In contrast, the AHA/ACC guidelines provide a lower strength of recommendation (COR IIa) to proceeding with a treadmill electrocardiogram, stress myocardial perfusion imaging, or coronary computed tomography angiography for patients with symptoms concerning for ACS but without objective signs (1).

The AHA/ACC 2014 update suggests several key terminology changes; this update modifies the terminology for medical and noninvasive management strategies as an “ischemia-guided strategy.” Both

guidelines note that the optimal timing of angiography for NSTEMI-ACS has not been firmly established. The early invasive strategy typically occurs within 24 h of presentation, whereas the delayed invasive strategy is deferred until 24 to 72 h. The ischemia-guided strategy avoids the use of early invasive procedures unless patients exhibit refractory ischemic symptoms or instability. Early-invasive strategies for NSTEMI-ACS in the AHA/ACC guidelines are labeled COR I for patients experiencing refractory angina or hemodynamic instability without major contraindications to procedures (LOE A), or those with an elevated risk for clinical events (LOE B). Similarly, the ESC guidelines recommend early angiography and revascularization in high-risk patients (COR I, LOE A). These guidelines recommend noninvasive assessment of inducible ischemia before hospital discharge for lower risk patients, and coronary angiography if the results are positive (COR I, LOE A).

For those who undergo coronary revascularization, the ESC guidelines specifically recommend the radial approach for vascular access (COR I, LOE A), whereas the AHA/ACC guidelines do not provide any specific recommendations on the preferred vascular access site. The ESC authors also cite additional data from a consensus paper suggesting a shift from femoral access to radial access in ACS (20), with the overall LOE favoring radial access for its lower risk of bleeding and trends toward more favorable outcomes (21,22). Both the ESC and AHA/ACC guidelines recommend the “heart team” approach to revascularization decisions regarding percutaneous coronary intervention (PCI) versus coronary artery bypass graft.

MEDICAL TREATMENT

NON-ANTITHROMBOTIC AGENTS. Both the ESC and AHA/ACC guidelines emphasize the use of anti-ischemic agents to reduce myocardial oxygen demand. Beta-blockers and nitrates are recommended (COR I) by both guidelines, although the LOE is only B and C, respectively. According to the ESC guidelines, dihydropyridines in the absence of a beta-blocker in NSTEMI-ACS should be avoided given the trend toward harm observed in HINT (Holland Interuniversity Nifedipine/Metoprolol Trial) (COR III, LOE B) (15,23), whereas the AHA/ACC guidelines only specifically contraindicate immediate-release nifedipine. The AHA/ACC and ESC guidelines recommend the initiation or continuation of a high-intensity statin (COR I, LOE A) in all patients with NSTEMI-ACS, unless otherwise contraindicated. The ESC guidelines suggest statin therapy to target low-density lipoprotein cholesterol levels <70 mg/dl after admission (COR I,

TABLE 2 Levels of Evidence	
Data Source	
Level of Evidence: A	Multiple randomized clinical trials
Level of Evidence: B	Limited populations evaluated from either a single randomized clinical trial or large nonrandomized studies
Level of Evidence: C	Expert consensus

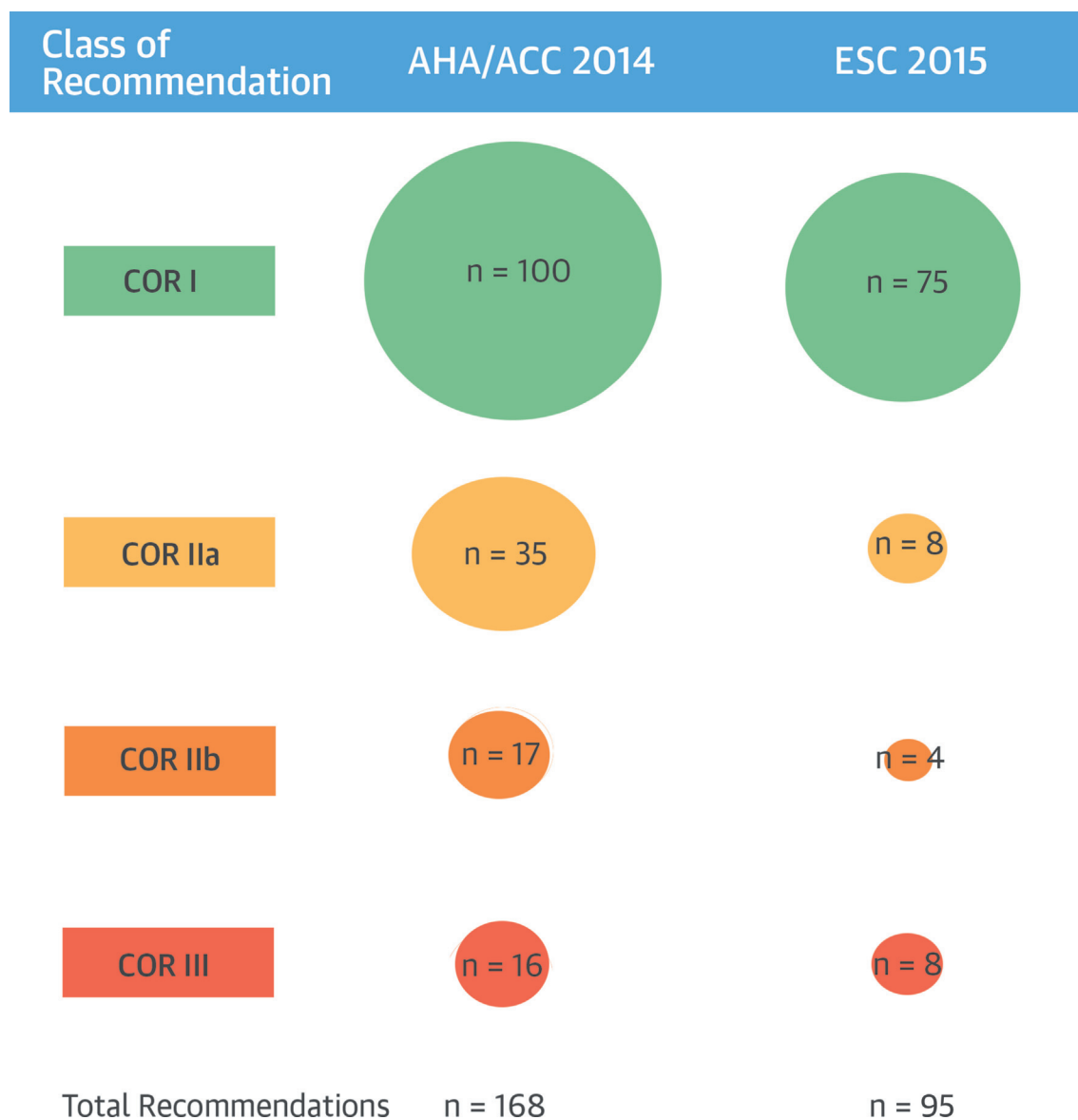
LOE B) and consideration of a non-statin agent if these levels remain higher than target levels with a maximally tolerated statin dose (COR IIa, LOE B).

ANTIPLATELET THERAPY. Dual antiplatelet therapy (DAPT) with aspirin and P2Y₁₂ inhibitors remains the cornerstone for the treatment of NSTEMI-ACS. Both the ESC and AHA/ACC NSTEMI-ACS guidelines underscore the importance of prompt administration of aspirin and a P2Y₁₂ inhibitor. Nonenteric-coated aspirin is recommended for all patients immediately after presentation, as well as indefinite aspirin for maintenance therapy (COR I, LOE A). Whereas the AHA/ACC guidelines provide recommendations for aspirin maintenance dosing to include both low and high doses (81 to 325 mg/day), the ESC guidelines suggest a low maintenance dose of 75 to 100 mg/day long-term (COR I, LOE A) (15) on the basis of CURRENT-OASIS 7 (Clopidogrel and Aspirin Optimal Dose Usage to Reduce Recurrent Events-Seventh Organization to Assess Strategies in Ischemic Syndromes) data; according to these data, there were no differences between patients with ACS undergoing an early invasive strategy using a higher dose (300 to 325 mg/day) compared with those taking a lower dose (75 to 100 mg/day) of aspirin (24).

The AHA/ACC guidelines recommend either clopidogrel or ticagrelor loading for either the invasive or ischemia-guided options, with a COR IIa, LOE B recommendation for ticagrelor over clopidogrel.

TABLE 3 ACC/AHA Versus ESC Summary Statistics for AHA/ACC Versus ESC NSTEMI-ACS Updated Guidelines		
	AHA/ACC 2014 Guidelines	ESC 2015 Guidelines
Year of previous guidelines	2007	2011
Societies involved	3	1
No. of writing committee members	17	17
No. of pages	90	56
No. of recommendations	168	99
No. of references	827	320

ACC = American College of Cardiology; AHA = American Heart Association; ESC = European Society of Cardiology; NSTEMI-ACS = non-ST-segment elevation acute coronary syndromes.

CENTRAL ILLUSTRATION Comparison of Frequency of Recommendations for NSTE-ACS Management According to AHA/ACC and ESC Guidelines by Class of Recommendation

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Demonstrates a comparison of the 2014 American Heart Association (AHA)/American College of Cardiology (ACC) and the 2015 European Society of Cardiology (ESC) non-ST-segment elevation myocardial infarction guideline recommendations according to Class of Recommendation (COR). The size of each circle is proportional to the number of recommendations in each category. NSTE-ACS = non-ST-segment elevation acute coronary syndromes.

The guidelines recommend prasugrel when a PCI is planned in those not at high risk of bleeding, on the basis of results from the TRITON-TIMI 38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel-Thrombolysis In Myocardial Infarction 38) (25)

and the TRILOGY-ACS (TaRgeted platelet Inhibition to cLarify the Optimal strateGY to medically manage Acute Coronary Syndromes) trials (26,27). Results from the PLATO (Platelet Inhibition and Patient Outcomes) trial demonstrate the benefit of ticagrelor over clopidogrel for patients at moderate to high

ischemic risk regardless of initial strategy (28), for patients both with and without revascularization (27). The ESC guidelines make several recommendations regarding the specific choice of P2Y₁₂ inhibitors. These preferences include ticagrelor for patients at moderate to high ischemic risk (COR I, LOE B), prasugrel for planned PCI after delineation of coronary anatomy (COR I, LOE B), and clopidogrel as second-line therapy if other drugs are contraindicated or are not options (COR I, LOE B). The ESC guidelines specifically advise against administration of prasugrel in patients in whom the coronary anatomy is unknown (COR III, LOE B) (2).

The ESC guidelines provide new evidence for the use of cangrelor, an adenosine triphosphate analogue that binds reversibly to the platelet P2Y₁₂ receptor with immediate, highly effective, and rapidly reversible platelet inhibition with intravenous administration of the drug (29) on the basis of findings from the 3 large clinical trials (CHAMPION-PCI, CHAMPION-PLATFORM, and CHAMPION-PHOENIX [Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition]) (30-32) that showed a reduction in periprocedural deaths among patients undergoing PCI with the use of cangrelor. The ESC guidelines state that cangrelor may be considered in P2Y₁₂ inhibitor-naïve patients undergoing PCI (COR IIB, LOE A). The most recent AHA/ACC guidelines were published in 2014, before regulatory approval of cangrelor.

PLATELET REACTIVITY TESTING. There is variability in response to clopidogrel, resulting from a genetic polymorphism leading to loss of function of the cytochrome P450 2C19 isoenzyme. Such polymorphisms result in higher platelet reactivity and have been associated with a higher incidence of cardiovascular events (33-35). However, the updated AHA/ACC guidelines do not recommend genetic testing or platelet function testing, whereas the ESC guidelines recommend that such testing may be considered in patients receiving clopidogrel (COR IIB, LOE B).

GLYCOPROTEIN IIB/IIIA RECEPTOR INHIBITORS. The ESC recommends against the routine upstream use of glycoprotein IIB/IIIA receptor inhibitors (GPIs) before angiography on the basis of results of clinical trials (COR III, LOE A) (36-38). In contrast, the AHA/ACC states that it is reasonable to use GPIs in high-risk patients with NSTEMI-ACS with a planned early invasive strategy (COR IIB, LOE B).

ANTICOAGULANT AGENTS. The AHA/ACC recommendations on the use of anticoagulant agents for NSTEMI-ACS are largely unchanged from the 2007

TABLE 4 Summary of Key Class I Recommendations From the AHA/ACC NSTEMI-ACS Guidelines

AHA/ACC 2014 Guidelines	ESC 2015 Guidelines
Diagnosis	
Measure cardiac troponin I or T at presentation and at 3-6 h after symptom onset	Measure cardiac troponin levels by using sensitive or high-sensitivity assays with results within 60 min
Obtain additional troponin levels beyond 6 h in patients with initial normal troponin levels with intermediate- or high-risk features	For rapid rule-out, 2 alternative approaches using the 0 h/1 h or 0 h/3 h algorithms of high-sensitivity troponin assays are recommended
Use of risk scores to assess prognosis in patients with NSTEMI-ACS	Use established risk scores for prognosis estimation In patients with no recurrence of chest pain and normal ECG findings and troponin levels, a noninvasive stress test (preferably with imaging) is recommended to look for ischemia
Antiplatelet therapies	
Nonenteric-coated aspirin to all patients after presentation with a dose of 162-325 mg, followed by a maintenance dose of 81-325 mg/day indefinitely	Aspirin is recommended for all patients without contraindications at an initial loading dose of 150-300 mg, followed by a maintenance dose of 75-100 mg/day long-term, regardless of treatment strategy
A P2Y ₁₂ inhibitor (either clopidogrel or ticagrelor), in addition to aspirin, should be administered for up to 12 mo to all patients with NSTEMI-ACS	A P2Y ₁₂ inhibitor (preferentially ticagrelor for moderate- or high-risk patients) is recommended in addition to aspirin for 12 months, unless there are contraindications such as excessive risk of bleeding, irrespective of revascularization strategy
In patients with high-risk features not pretreated with clopidogrel or ticagrelor, it is useful to administer a GPIIb/IIIa inhibitor at the time of PCI	
Anticoagulant agents	
SC enoxaparin for the duration of hospitalization or until PCI is performed	Fondaparinux is recommended as the first line for NSTEMI-ACS management, regardless of the management strategy
Alternatives to enoxaparin include bivalirudin, fondaparinux, and unfractionated heparin	Bivalirudin is recommended as an alternative to unfractionated heparin plus GPIIb/IIIa inhibitors during PCI
Early invasive and ischemia-guided strategies	
Urgent/immediate invasive strategy in patients with refractory angina and hemodynamic or electrical instability	An early invasive strategy is indicated for patients with high-risk features (<72 h) Radial over femoral access is recommended for coronary angiography and PCI In patients undergoing PCI, new-generation DES are recommended

DES = drug-eluting stents; ECG = electrocardiography; GPI = glycoprotein inhibitor; PCI = percutaneous coronary intervention; SC = subcutaneous; other abbreviations as in Table 3.

guidelines. For the early invasive strategy, unfractionated heparin (UFH), enoxaparin, or bivalirudin all received a COR I, with the highest LOE available for enoxaparin. In contrast, the ESC guidelines recommend the use of bivalirudin as an alternative to UFH and a GPI in patients with intended early invasive strategy at a high risk of bleeding (COR I, LOE A).

For ischemia-guided strategies, the AHA/ACC recommends UFH for 48 h or either enoxaparin or fondaparinux until hospital discharge. The ESC prefers fondaparinux as the first-line anticoagulant agent

TABLE 5 Summary of Class III, Level of Evidence A Recommendations for NSTEMI-ACS in the AHA/ACC and ESC Guidelines

AHA/ACC 2014 Guidelines	ESC 2015 Guidelines
Diagnosis	
CK-MB and myoglobin are not useful in diagnosis of ACS with contemporary troponin assays	
Antiplatelet/anticoagulation/early management	
IV fibrinolytic treatment is not recommended in patients with NSTEMI-ACS	GPIIb/IIIa inhibitors or prasugrel are not recommended in patients in whom coronary anatomy is unknown
An early invasive strategy is not recommended for patients with extensive comorbidities or low likelihood of ACS who are troponin-negative (especially women).	Crossover between unfractionated heparin and low-molecular-weight-heparin is not recommended
Secondary prevention	
Hormone therapy should not be given as new drugs for the secondary prevention of coronary events in postmenopausal women after NSTEMI-ACS and should not be continued in previous users unless benefits outweigh the risks	
Antioxidants and folic acid should not be used for secondary prevention in patients with NSTEMI-ACS	
ACS = acute coronary syndromes; CK-MB = creatine kinase-myocardial band; IV = intravenous; other abbreviations as in Tables 3 and 4.	

(39-41), given its favorable efficacy/safety profile (COR I, LOE B). The ESC guidelines advise against crossovers between UFH and enoxaparin (COR III, LOE B).

PERFORMANCE MEASURES

Regardless of which strategy is chosen (invasive or ischemia-guided), both the AHA/ACC and ESC guidelines recommend quality measures to be checked at discharge, including the use of aspirin, a P2Y₁₂ inhibitor, beta-blockers, angiotensin-converting enzyme inhibitors, statins, and life-style counseling (including referral to cardiac rehabilitation programs). To minimize variability across practice sites and improve adherence to evidence-based practice, both the AHA/ACC and ESC updated guidelines recommend monitoring through the use of quality-of-care registries (42-44). Because adherence to guidelines has been associated with improvements in patient outcomes for ACS (45,46), the ESC recommends continuous monitoring of performance indicators with feedback to individual hospitals. Similarly, the AHA/ACC guidelines emphasize that health systems should work not only with clinical providers but also with communities, payers, and public agencies to ensure guideline-driven care and prevent hospital readmissions (1). Use of performance measures are similarly recommended by the

updated AHA/ACC guidelines for NSTEMI-ACS but with a lower strength of recommendation (COR IIa, LOE B).

SPECIAL POPULATIONS

WOMEN. The ESC guidelines underscore the importance of treating both sexes presenting with NSTEMI-ACS in the same way (COR I, LOE B). Both the ESC and AHA/ACC guidelines indicate that although women may have atypical presentations for NSTEMI-ACS, outcomes and prognosis are similar to those in men (47,48). However, the AHA/ACC guidelines state that women with low-risk features should not undergo early invasive treatment because of the potential for harm (COR III, LOE B) on the basis of the evidence that women had higher bleeding complications and contrast-induced nephropathy in analyses of recent trials (49-52).

ELDERLY PATIENTS. The ESC and AHA/ACC guidelines provide specific recommendations for elderly adults (i.e., those >75 years of age) because they are at the highest risk of complications after NSTEMI-ACS (53,54) and have been largely underrepresented in many recent trials of NSTEMI-ACS (1,2). The Acute Coronary Syndrome Israeli Survey showed that patients >80 years of age referred for early coronary angiography experienced lower 30-day mortality rates (55), suggesting that older patients benefit more than younger patients with an early invasive strategy. Other studies corroborate the benefit of an early invasive strategy in older patients (56-58), with the caveat that older patients experience a 3-fold higher bleeding risk (59).

The AHA/ACC guidelines therefore recommend similar approaches for stratification of early versus delayed invasive approaches for NSTEMI-ACS in the elderly (COR I, LOE A). The ESC guidelines provide a lower class of recommendation for early invasive strategies for the elderly, after careful consideration of risks and benefits (COR IIa, LOE B). These guidelines also highlight the higher risk of bleeding in the elderly and recommend reduced dosages of anticoagulant agents, dosed according to renal function and body weight.

DIABETIC PATIENTS. Patients with diabetes presenting with NSTEMI-ACS are at higher risk of short- and long-term cardiovascular events, and they therefore require aggressive medical and early invasive management (60,61). The ESC guidelines recommend an early invasive strategy (COR I, LOE A), the use of drug-eluting stents (COR I, LOE A), and a preference for coronary artery bypass graft over PCI

in patients with diabetes with left main lesions or multivessel disease (COR I, LOE B).

Both hypoglycemia and hyperglycemia should be avoided during an NSTEMI-ACS event (COR I, LOE A). The AHA/ACC guidelines advise against stringent glycemic control after publication of the results of the NICE-SUGAR (Normoglycemia in the Intensive Care Evaluation and Survival Using Glucose Algorithm Regimen) trial; this trial found that intensive glucose control (target 81 to 108 mg/dl) resulted in increased all-cause mortality (62). Therefore, blood glucose levels should be maintained at <180 mg/dl with avoidance of hypoglycemia (1,15), according to both the ESC and AHA/ACC guidelines.

TRIPLE THERAPY. A sizeable portion of patients presenting with NSTEMI-ACS may have an indication for long-term oral anticoagulation (OAC) therapy; these indications include atrial fibrillation or venous thromboembolism. However, DAPT in combination with OAC is associated with a 3- to 4-fold higher risk of bleeding complications (63). The ESC guidelines recommend international normalized ratios of 2.0 to 2.5 when using warfarin during treatment with DAPT (15) and avoidance of prasugrel or ticagrelor as part of triple therapy. In contrast, the AHA/ACC guidelines state that there is insufficient evidence to target this lower international normalized ratio range. In patients treated with non-vitamin K oral anticoagulant agents, the ESC guidelines recommend use of the lowest tested dose of these agents for stroke prevention. In addition, on the basis of results from the WOEST (What Is the Optimal Antiplatelet and Anticoagulant Therapy in Patients With OAC and Coronary Stenting) trial (64), dual therapy with OAC and clopidogrel 75 mg/day may be considered as an alternative to triple therapy in patients at high risk of bleeding and low risk of stent thrombosis (COR IIb, LOE B). The ESC guidelines also recommend protection against spontaneous gastrointestinal bleeding through the use of a proton pump inhibitor. The recommendations are similar in the AHA/ACC guidelines (COR II, LOE C).

FUTURE RESEARCH

Clinical guidelines are systematic statements to help guide clinical practices and are updated periodically, typically every 2 to 5 years. New approaches are necessary to rapidly integrate new information more quickly and efficiently. Mini-updates, specific modifications, or clarifications of individual recommendations may need to be considered as ongoing results from clinical trials are reported. Since the

AHA/ACC guidelines were published, important information about the duration of DAPT therapy has become available that will need to be interpreted for the clinical community (65,66). Ongoing research on the optimal duration of DAPT and comparative effectiveness of new agents will continue to generate new information that may change clinical practice.

Further study is warranted to determine how busy clinicians use clinical guidelines to guide decision making and for continuing medical education. A potential area for improvement and future research includes the integration of clinical guidelines with the electronic medical record for an admission diagnosis of NSTEMI-ACS. With the growing number of guidelines and recommendations, integration with a meaningful electronic medical record would ensure that clinicians are informed of the latest evidence at the point of patient care. Finally, common conditions such as ACS are ideal for testing in the evaluation of learning health systems in which updates to care pathways occur as knowledge accrues.

As seen in the **Central Illustration** and **Tables 4 and 5**, most of the COR I findings from these contemporary clinical guidelines continue to rely on limited experimental data or expert consensus, an issue plaguing clinical practice guidelines for years (67). To circumvent many of the issues preventing the development of higher certainty of evidence, novel, more practical research approaches are warranted, including point of care randomization, leveraging existing infrastructure and electronic medical records to efficiently conduct clinical trials, and the conduct of large pragmatic clinical trials.

CONCLUSIONS

NSTEMI-ACS is a common presentation of coronary heart disease and is the leading cause of global cardiovascular morbidity and mortality. The AHA/ACC 2014 updates and the more recent ESC 2015 guidelines for management of NSTEMI-ACS offer comprehensive reviews of the available evidence as a guide for health care providers with many commonalities but also some important differences.

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