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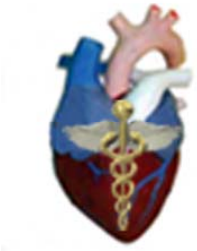

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EDITORIAL

New (2014) Guidelines for Managing Patients with Non–ST-Elevation Acute Coronary Syndromes

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The American Heart Association (AHA) and the American College of Cardiology (ACC) have just issued (September 23, 2014) new guidelines for the management of patients with non-ST elevation (NSTE) acute coronary syndromes (ACS).[1] They start with definitions. Absence of persistent ST elevation defines NSTE-ACS (except in patients with true posterior myocardial infarction –MI). Further classification of NSTE-ACS is based on whether cardiac troponin is elevated (NSTEMI) or not (unstable angina - UA). ST depression, transient ST elevation, and/or T-wave inversion may be present but are not required for a diagnosis of NSTEMI. Abnormalities on the electrocardiogram (ECG) and elevated cardiac troponins in isolation are insufficient to make the diagnosis of ACS but must be interpreted in the appropriate clinical context.[1,2] Thus, UA and NSTEMI differ primarily by whether ischemia causes myocardial damage with a detectable cardiac biomarker. With the increasing sensitivity of cardiac troponin assays, biomarker-negative ACS (UA) is becoming rarer.

The recommendation for clinical assessment and initial evaluation is as follows: "Patients with suspected ACS should be risk stratified based on the likelihood of ACS and adverse outcome(s) to decide on the need for hospitalization and assist in the selection of treatment options" (*Class I / Level of Evidence-LOE: B).*

For risk stratification, guidelines advocate the use of tools such as the ***TIMI*** risk score and the Global Registry of Acute Coronary Events ***(GRACE)*** risk score. An attempt should be made to identify low-risk patients with chest pain who are not having an ACS and who may safely be discharged home early. With regards to discharging or triaging patients from the emergency room (ER), the guidelines recommend to observe patients with symptoms consistent with ACS but without evidence of myocardial ischemia on ECG and with normal cardiac troponin, in a

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chest or telemetry unit with serial ECGs and cardiac troponin at 3- to 6-hour intervals *(Class IIa / LOE: B).* For patients with possible ACS who have normal serial ECGs and cardiac troponins, it is recommended to have a treadmill ECG (*LOE: A)*, or stress myocardial perfusion imaging, or stress echocardiography before discharge or within 72 hours after discharge *(LOE: B).* Indeed, low-risk patients can be discharged home and may be referred for outpatient testing.

Differential diagnosis of the causes of chest pain is provided and emphasis is placed on history and physical examination to aid in diagnosis of ACS. In patients with symptoms suggestive of ACS, a 12-lead ***ECG*** should be performed and evaluated for ischemic changes within 10 minutes of the patient's arrival in the ER. If the initial ECG is normal (1-6%), it should be repeated, e.g., at 15- to 30-minute intervals during the first hour, especially if symptoms recur. Indeed, when the ischemia is due to left circumflex or right coronary artery occlusions, the 12-lead ECG may be normal, in which case a 15-lead ECG by obtaining additional posterior ECG leads (V_7 - V_9) may be helpful.[1,3] Right-sided leads (V_3R - V_4R) are helpful in the case of inferior ST-elevation MI (STEMI) to detect right ventricular infarction. Left ventricular (LV) hypertrophy, bundle-branch blocks with repolarization abnormalities, and ventricular pacing may mask signs of ischemia.

Emphasis is placed on the use of *troponin* improving the diagnostic accuracy. A rising and/or falling pattern in cardiac-specific troponin (troponin I or T) levels should be sought by obtaining measurements on arrival in the ER and 3-6 hours after symptom onset in all patients who present with symptoms consistent with ACS. A negative cardiac troponin obtained with high-sensitivity assays confers a negative predictive value ≥99%.[1,4] In patients with normal troponin, additional troponin levels should be obtained beyond 6 hours after symptom onset when there is a high index of suspicion for ACS based on ECG changes and/or clinical symptoms. The following is an important statement of the new guidelines: "With contemporary troponin assays, creatine kinase myocardial isoenzyme (CK-MB) and myoglobin are not useful for diagnosis of ACS". With regards to estimating infarct size without measuring CK, the guidelines point to remeasuring troponin once on day 3 - 4 in patients with MI as an index of infarct size.

Among the *imaging* studies that are recommended to guide differential diagnosis, emphasis is placed on chest X-ray (for pulmonary causes of chest pain and aortic dissection), chest computed tomography (CT) (for pulmonary embolism and aortic dissection), transthoracic echocardiography (for pericardial effusion and also for regional wall motion abnormalities), and transesophageal echocardiography (for aortic dissection). Importantly, these guidelines indicate that in low-risk patients with chest pain, coronary CT angiography can result in a more expedient and cost-effective diagnosis than stress myocardial scintigraphy.

Admission for inpatient management is the standard of care for patients who present with NSTE-ACS. The goals of treatment are the immediate relief of ischemia and the prevention of MI and death. Medical treatment includes antianginal, antiplatelet, and anticoagulant agents.

An early invasive or ischemia-guided approach (instead of an "initial conservative management") is recommended for management of patients NSTE-ACS. Patients with continuing angina, hemodynamic instability, uncontrolled arrhythmias, or a large MI should be admitted to a coronary care unit (CCU). An assessment of LV function is recommended because depressed LV function will likely influence pharmacological therapies or choice of revascularization.

An urgent/immediate invasive strategy, starting with diagnostic angiography and intending to proceed with percutaneous coronary intervention (PCI), if appropriate, is indicated in patients with NSTE-ACS who have refractory angina or hemodynamic or electrical instability and absent serious comorbidities or contraindications to these procedures. An early invasive strategy is also indicated in initially stabilized patients with NSTE-ACS who have an increased risk for clinical adverse events. An early invasive strategy is not recommended in patients with extensive comorbidities (e.g., hepatic, renal, pulmonary failure, cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. Also, an invasive strategy is not recommended in those with acute chest pain and a low likelihood of ACS who are troponin-negative, particularly women. In both strategies, patients should receive optimal anti-ischemic and antithrombotic medical therapy. In the invasive strategy, the optimal timing of coronary angiography has not been clearly defined. In general, there are 2 options: early invasive (i.e., within 24 hours) or delayed invasive (i.e., within 24 to 72 hours). The ischemia-guided strategy seeks to avoid the routine early use of invasive procedures unless patients experience refractory or recurrent ischemic symptoms or develop hemodynamic instability. When the ischemia-guided strategy is followed, noninvasive evaluation is performed and if severe ischemia occurs at a low threshold of stress, the patient is promptly referred for coronary angiography and revascularization. By following the ischemia-guided strategy, some patients get stabilized and will not require an invasive procedure and thus avoid its attendant cost and risk. However, several studies and meta-analyses have

indicated that a strategy of routine invasive therapy is generally superior to an ischemia-guided strategy or selectively invasive approach. The invasive strategy demonstrated its greatest advantage in the highest-risk stratum of patients, with no significant benefit on mortality over the noninvasive approach in moderate- and low-risk patients. An ischemia-guided strategy has been used with favorable results in initially stabilized patients with NSTE-ACS at high risk for clinical events, including those with positive troponin levels.

Oral beta-blocker therapy should be started within the first 24 hours in patients with no contraindications, such as signs of heart failure, evidence of low-output state, increased risk for cardiogenic shock, or other contraindications to beta blockade, e.g., first degree (PR interval >0.24 s), second- or third-degree AV block, active asthma, or reactive airway disease. In patients with a contraindication to beta blockers or those who have recurrent ischemia despite use of beta-blockers and nitrates, a non-dihydropyridine calcium channel blocker (e.g., verapamil or diltiazem) should be given as initial therapy in the absence of clinically significant LV dysfunction, increased risk for cardiogenic shock, PR interval >0.24 s, or second- or third degree AV block. *(Class I / LOE: B).* Angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) for those who are ACE inhibitor intolerant, should be started and continued indefinitely in all patients with LV ejection fraction <40% and in those with hypertension, diabetes mellitus, or stable chronic kidney disease (CKD) (Class I / *LOE: A*). In these latter patients, additional therapy with aldosterone blockade is recommended when post–MI and without significant renal dysfunction (creatinine >2.5 mg/dL in men or >2.0 mg/dL in women) or hyperkalemia (K >5.0 mEq/L) *(Class I / LOE: A).* High-intensity statin therapy should be initiated or continued in all patients with NSTE-ACS and no contraindications to its use.

In patients with NSTE-ACS, anticoagulation, in addition to antiplatelet therapy, is recommended for all patients (*Class I*) in the form of either subcutaneous (sc) enoxaparin *(LOE: A),* or intravenous (IV) bivalirudin *(LOE: B)*, or fondaparinux *(LOE: B)* (if PCI is performed additional unfractionated heparin-UFH or bivalirudin is needed) *(LOE: B)*, or UFH *(LOE: B).* An anticoagulant should be administered to patients with NSTE-ACS undergoing PCI to reduce the risk of intracoronary and catheter thrombus formation *(Class I / Level of Evidence: C).*

The guidelines also discuss the newer more potent antithrombotics and anticoagulants that reduce the risk of major adverse cardiac outcomes vs the increased risk of bleeding. Dual antiplatelet therapy with a $P2Y_{12}$ inhibitor, either clopidogrel or one of the newer agents, ticagrelor or prasugrel, in addition to aspirin should be administered for up to 1 year to all patients with NSTE-ACS without contraindications who are treated with either an early invasive or ischemia-guided strategy. $P2Y_{12}$ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) should be continued for at least 1 year in post–PCI patients treated with coronary stents. It is reasonable to use ticagrelor in preference to clopidogrel for $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo an early invasive or ischemia-guided strategy. It is also reasonable to choose prasugrel (initiated during PCI) over clopidogrel for $P2Y_{12}$ treatment in patients with NSTE-ACS who undergo PCI who are not at high risk of bleeding complications.

In patients with NSTE-ACS, anticoagulation, in addition to antiplatelet therapy, is recommended for all patients irrespective of initial treatment strategy. In patients with NSTE-ACS, anticoagulant therapy should be discontinued after PCI unless there is other reason to continue such therapy. With regards to use of glycoprotein (GP) IIb/IIIa inhibitors (abciximab, eptifibatide, or tirofiban), the guidelines recommend their use in patients with NSTE-ACS and high-risk features (e.g., elevated troponin) and not adequately pretreated with clopidogrel or ticagrelor *(Class I / LOE: A).*

Patients with atrial fibrillation who develop NSTE ACS and receive a coronary stent are a special and important group at increased risk of bleeding as they are in need of triple antithrombotic (anticoagulant/antiplatelet) therapy. Withdrawing aspirin from triple therapy may decrease the risk,[5] but confirmation studies are lacking. Also the issue of using the new oral anticoagulants in these patients remains moot.[6]

The guidelines also refer to specific groups of patients, including women, older patients (>75 years), heart failure patients, patients with arrhythmias, patients in cardiogenic shock, diabetics and their adjunctive therapies, post-CABG patients, patients with perioperative NSTE-ACS related to noncardiac surgery, patients with CKD and issues with antiplatelet therapy in this group, patients with anemia/bleeding/transfusion or thrombocytopenia, cocaine and methamphetamine users, and patients with vasospastic (Prinzmetal) angina. A specific group are patients with NSTE-ACS who have angiographically normal or nonobstructive CAD, a group in which women predominate. Also patients with stress (Takotsubo) cardiomyopathy, obese patients and patients taking antineoplastic/immunosuppressive therapy are discussed separately. Instructions are also given for the pneumococcal vaccine recommended for patients ≥65 years of age and in high-risk patients with cardiovascular disease, for use of non-steroidal anti-inflammatory agents

(NSAIDs), use of hormone therapy, use of vitamins, and influenza vaccination.

Post-hospital discharge advice and instructions should be provided to all patients with ACS, including advice for medication adherence, aggressive risk factor modification, proper follow-up with the healthcare team, appropriate dietary and physical activities, compliance with interventions for secondary prevention, and plan for a rehabilitation program. In addition to detailed instructions for daily exercise, patients should be given specific instruction on activities (e.g., lifting, climbing stairs, yard work, and household activities) that are permissible and those to avoid. Specific mention should be made of resumption of driving, return to work, and sexual activity (http://www.cardiosource.org/en/Science-And-Quality/Journal-Scan/2014/09/2014-AHA-ACC-Guideline-for-the-Management-of-NSTE-ACS.aspx).

The guidelines provide summary tables with up-to-date and easily accessible information. They include tables with risk scores (TIMI, GRACE), early risk stratification, cardiac biomarkers, recommendations for early hospital care, recommendations for initial antiplatelet/ anticoagulant therapy, factors associated with appropriate selection of early invasive strategy or ischemia-guided strategy, dosing of parenteral anticoagulants during PCI, plan of care for patients with NSTE-ACS, and a summary of recommendations for special patient groups. A pedantic management algorithm and an algorithm with a stepped-care approach to pharmacological therapy for musculoskeletal symptoms in patients with known cardiovascular disease or risk factors for ischemic heart disease are also provided. In the appendix we find additional tables on universal classification of MI, pharmacological therapy in older patients with NSTE-ACS, age-related physiological changes and their clinical impact in older patients with NSTE-ACS, and the key outcomes at 2 and 5 years after randomization of the FREEDOM Trial.

Finally, the guidelines discuss quality of care and outcomes for ACS—use of performance measures and registries, and acknowledge the need for an individualized patient care.

REFERENCES

1. Amsterdam EA, Wenger NK, Brindis RG, et al, 2014 AHA/ACC Guideline for the management of patients with non–ST-elevation acute coronary syndromes, *J Am Coll Cardiol* 2014; doi: 10.1016/j.jacc.2014.09.017. / *Circulation* 2014 Sep 23. pii: CIR.0000000000000134. [Epub ahead of print]

2. IJkema BB, Bonnier JJ, Schoors D, Schalij MJ, Swenne CA. Role of the ECG in initial acute coronary syndrome triage: primary PCI regardless presence of ST elevation or of non-ST elevation. *Neth Heart J* 2014 Sep 9. [Epub ahead of print]

3. Metaxa S, Koulouris S, Stalikas D, Velissariou G, Manolis AS. Concealed myocardial infarction revealed by high lateral and posterior electrocardiographic leads. *Hosp Chronicles* 2011;6:91-95.

4. Manolis AS. High sensitivity cardiac troponins: a curse or a blessing? *Hosp Chronicles* 2011;6:56-59.

5. Dewilde WJ, Oirbans T, Verheugt FW, et al. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. *Lancet* 2013;381:1107-1115.

6. Ahrens I, Bode C. Direct oral anticoagulants in acute coronary syndrome. *Semin Hematol* 2014;51:147-151.