Management of Non–ST Elevation Acute Coronary Syndrome: A Guideline from the AHA and ACC

Key Points for Practice

- Cardiac troponin levels should be measured on arrival and again three to six hours after the patient's symptoms began.
- ECG should be performed every 15 to 30 minutes within the first hour in patients with ACS if the original ECG did not confirm the diagnosis.
- Oral beta blockers should be started within 24 hours of presentation, if there are no contraindications.
- Treatment with ACE inhibitors is recommended in persons with a left ventricular ejection fraction less than 0.40, hypertension, diabetes mellitus, or stable chronic kidney disease.
- Chewable aspirin without an enteric coating, at a dose of 162 to 325 mg, should be administered as soon as possible.
- Dual antiplatelet therapy with ticagrelor or clopidogrel in combination with aspirin should be given for up to one year in the invasive and ischemia-guided treatment approaches.

From the AFP *Editors*

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Acute coronary syndrome (ACS), a term that encompasses a range of conditions, is caused when blood flow to the heart is suddenly reduced. The American College of Cardiology (ACC), with the American Heart Association (AHA), has provided recommendations for managing non–ST elevation ACS.

Evaluation and Management

To determine whether or not a patient should be admitted to the hospital, and to guide treatment decisions, persons with symptoms of ACS should be evaluated based on their probability of having ACS and adverse outcomes. Those with high-risk symptoms (e.g., persistent chest pain, severe dyspnea, syncope) should be transferred to the emergency department right away, and those with less severe symptoms at presentation can be referred to the emergency department, a chest pain unit, or another office that can appropriately assess the patient's symptoms.

On presentation to the emergency department, persons with symptoms consistent with ACS should be evaluated with 12-lead electrocardiography (ECG) within 10 minutes to determine if there are any ischemic changes. Additionally, cardiac troponin levels (I or T) should be measured on arrival, after which they should be measured again three to six hours after the patient's symptoms began. If it is not known when symptoms started, time of patient presentation can be used. In patients whose initial troponin levels, as well as levels obtained three to six hours after symptom onset, are normal, but who have ECG results that indicate immediate or high risk, additional measurements should be obtained. When confirming a diagnosis of ACS, creatine kinase-myocardial isoenzyme and myoglobin measurements are not useful.

If the original ECG did not confirm a diagnosis, but ACS is still suspected, ECG should be performed every 15 to 30 minutes within the first hour. Additionally, in those at intermediate or high risk whose original ECG does not confirm ACS, additional readings can be obtained in leads V7 to V9; constant monitoring with 12-lead ECG may also be an option.

B-type natriuretic peptide or N-terminal pro-B-type natriuretic peptide testing can help determine a patient's risk of ACS, and may be useful for determining prognosis. Prognosis in persons with non–ST elevation ACS should be determined using risk scores, and treatment may be helped with the use of risk-stratification models. Troponin levels, depending on the elevation, can help with determining prognosis. In persons with myocardial infarction, obtaining troponin levels again three or four days after presentation may be beneficial for estimating size of the infarct and dynamics of necrosis.

Monitoring in a chest pain or telemetry unit is an option for persons with symptoms suggestive of ACS, but who do not appear to

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have myocardial ischemia; this should be done with serial ECG and measurement of troponin levels every three to six hours. Before patients with normal findings on serial ECG and normal troponin levels are discharged from the emergency department, or in the 72 hours following, treadmill ECG, stress myocardial perfusion imaging, and stress echocardiography are options. For those with no history of coronary artery disease, coronary computed tomography angiography or resting myocardial perfusion imaging performed with a technetium-99m radiopharmaceutical are reasonable initial options to evaluate coronary artery anatomy and exclude myocardial ischemia, respectively. When these tests are performed as an initial evaluation, serial ECG and troponin measurements are not necessary. Persons at low risk of ACS who are referred for testing in an outpatient setting can receive aspirin daily, and short-acting nitroglycerin and other medication as needed; however, physicians should educate them about activity levels and schedule a follow-up appointment.

Early Management in Hospitalized Patients

OXYGEN

Persons with non–ST elevation ACS with arterial oxygen saturation less than 90%, respiratory distress, or other high-risk signs or symptoms of hypoxemia should receive supplemental oxygen.

NITRATES

Nitroglycerin, at a sublingual dosage of 0.3 to 0.4 mg every five minutes for, at most, three doses should be given to patients with persistent ischemic pain. Following administration of sublingual nitroglycerin, patients should be evaluated to determine if the intravenous formulation, which is used to manage persistent ischemia, heart failure (HF), and hypertension, might be necessary. Nitrates are contraindicated in patients who have taken a phosphodiesterase inhibitor recently, particularly within 24 hours of taking sildenafil (Viagra) or vardenafil (Levitra), or within 48 hours of taking tadalafil (Cialis).

ANALGESICS

Intravenous morphine sulfate, if not contraindicated, may be helpful in patients with non–ST elevation ACS who have persistent ischemic chest pain even though they have received treatment with anti-ischemics. Other than aspirin, nonsteroidal anti-inflammatory drugs should not be used in patients hospitalized for non–ST elevation ACS because they increase the likelihood of having an adverse cardiovascular event.

BETA BLOCKERS

In persons without evidence of HF or low-output state, a higher risk of cardiogenic shock, or other contraindications, oral beta blockers should be started within 24 hours of presentation. Other contraindications include a PR interval greater than 0.24 seconds, second- or third-degree heart block in persons without a pacemaker, asthma, and reactive airway disease. It is recommended that beta blockers can continue to be administered to patients with non–ST elevation ACS, stable HF, and reduced systolic function, using sustained-release metoprolol succinate (Toprol XL), carvedilol (Coreg), or bisoprolol (Zebeta). Additionally, beta blockers can continue to be administered in persons with non–ST elevation ACS who have normal left ventricular function. Patients in whom beta blockers are initially contraindicated should be assessed again later to find out if they are still contraindicated. Intravenous administration of beta blockers can cause harm if given to persons who have an increased risk of shock.

CALCIUM CHANNEL BLOCKERS

Patients who have ischemia that is persistent, or that recurs often and in whom beta blockers are contraindicated, can receive a nondihydropyridine calcium channel blocker if there is no significant left ventricular dysfunction, cardiogenic shock, prolonged PR interval, or second- or third-degree atrioventricular block without a pacemaker. Additionally, if a patient's symptoms of ischemia are not resolved with beta blocker treatment, or if beta blockers are contraindicated or cause adverse effects, calcium channel blockers should be used. Those who have ischemia that persists despite treatment with beta blockers and nitrates should receive oral nondihydropyridine calcium antagonist. Long-acting calcium channel blockers and nitrates should be administered to patients with coronary artery spasm. If beta blockers are not being used in persons with non–ST elevation ACS, immediate-release nifedipine is contraindicated and should also not be used.

CHOLESTEROL MANAGEMENT

Persons with non–ST elevation ACS should be treated with high-intensity statins, and a fasting lipid profile can be performed, ideally within 24 hours.

RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM INHIBITORS

Treatment with angiotensin-converting enzyme (ACE) inhibitors is recommended in persons with a left ventricular ejection fraction less than 0.40, hypertension, diabetes mellitus, or stable chronic kidney disease. Additionally, treatment with ACE inhibitors is an option in all patients with cardiac or other vascular disease. If an ACE inhibitor cannot be administered because of intolerance, persons with a left ventricular ejection fraction less than 0.40 who have HF or myocardial infarction should be

treated with an angiotensin receptor blocker. Additionally, treatment with angiotensin receptor blockers is an option in patients with cardiac or other vascular disease who cannot tolerate ACE inhibitors. After myocardial infarction, patients with a left ventricular ejection fraction of 0.40 or less, diabetes, or HF who have been administered ACE inhibitors or beta blockers at a therapeutic dosage should be treated with aldosterone blockade in the absence of renal dysfunction or hyperkalemia.

ANTIPLATELETS AND ANTICOAGULANTS

Persons with likely or definite non–ST elevation ACS should be provided with chewable aspirin without an enteric coating, at a dose of 162 to 325 mg, as soon as possible; aspirin should be continued in these patients at a dosage of 81 to 325 mg per day. Clopidogrel (Plavix) should be used instead in those in whom aspirin cannot be administered.

Those persons with non–ST elevation ACS whose treatment is based around an early invasive or ischemia-guided approach should receive dual antiplatelet therapy with ticagrelor (Brilinta), which may be the preferred $P2Y_{12}$ inhibitor, or clopidogrel in combination with aspirin for up to one year, assuming there are no contraindications to this treatment strategy. Dosing for ticagrelor is a 180-mg initial loading dose followed by 90 mg twice per day. Clopidogrel is given at a 300- or 600-mg initial loading dose followed by 75 mg per day.

A glycoprotein IIb/IIIa inhibitor, preferably eptifibatide (Integrillin) or tirofiban (Aggrastat), can be administered in persons with intermediate or high risk factors (such as elevated troponin) who are being treated using an early invasive strategy and dual antiplatelet therapy.

Regardless of how they were initially treated, it is recommended that all persons with definite non–ST elevation ACS be administered anticoagulants in combination with antiplatelets. Treatment options include: enoxaparin (Lovenox), bivalirudin (Angiomax), fondaparunix (Arixtra) and unfractionated heparin. Treatment with intravenous fibrinolytics is not recommend in persons with non–ST elevation ACS.

EARLY INVASIVE AND ISCHEMIA-GUIDED APPROACHES

Patients with non–ST elevation ACS who have refractory angina or hemodynamic or electrical instability may require immediate treatment via an invasive strategy, such as diagnostic angiography with revascularization. An invasive treatment approach can be performed early (within 24 hours of presentation) in persons who do not have serious comorbidities (e.g., pulmonary failure, cancer) or contraindications and who have a higher risk of clinical events; however, a delayed approach (24 to 72 hours from presentation) is an option for those not at intermediate or high risk. Additionally, early invasive management is not recommended in persons, particularly women, with acute chest pain who have a low risk of ACS and whose troponin levels are not elevated.

Patients with non–ST elevation ACS who do not have serious comorbidities or contraindications and who have a higher risk of clinical events may benefit from an ischemia-guided approach with medical therapy alone with further interventions as needed; however, physician and patient preference should be taken into account.

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