

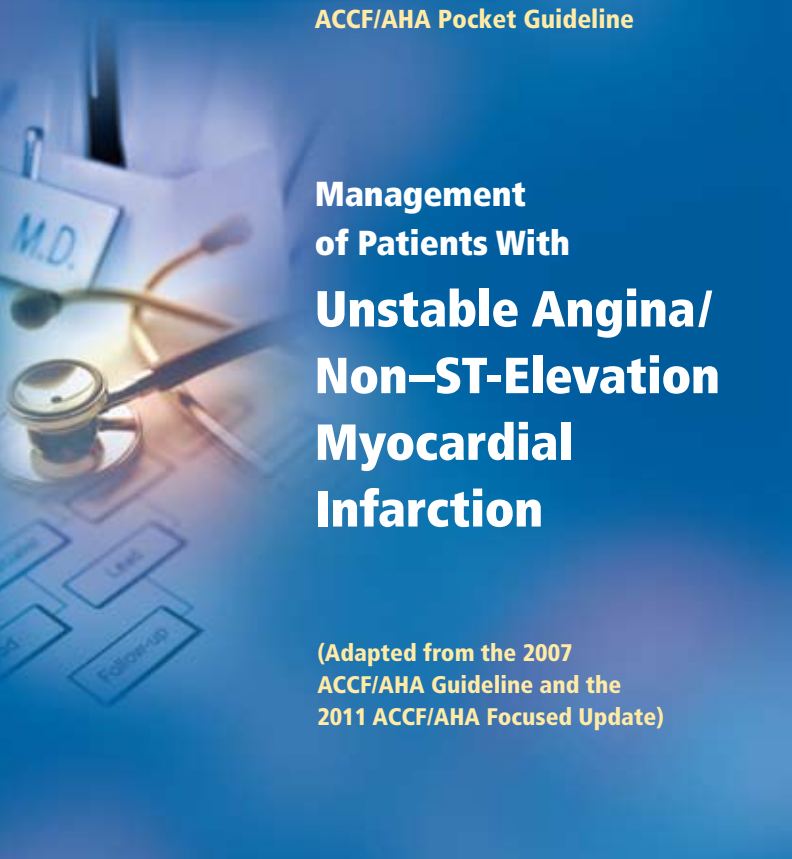


AMERICAN
COLLEGE *of*
CARDIOLOGY
FOUNDATION



American
Heart
Association®

ACCF/AHA Pocket Guideline



**Management
of Patients With
Unstable Angina/
Non–ST-Elevation
Myocardial
Infarction**

**(Adapted from the 2007
ACCF/AHA Guideline and the
2011 ACCF/AHA Focused Update)**

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The following material was adapted from the 2011 ACCF/AHA Focused Update Incorporated Into the ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction. (J Am Coll Cardiol 2011;57:e215-367). This pocket guideline is available on the Web sites of the American College of Cardiology (www.cardiosource.org) and the American Heart Association (my.americanheart.org).

For a copy of the full report or published executive summary, visit ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction (J Am Coll Cardiol 2007;50:e1-e157) and the 2011 ACCF/AHA Focused Update (J Am Coll Cardiol 2011;57:1920-1959).

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1. Introduction

Coronary artery disease is the leading cause of death in the United States. Unstable angina (UA) and the closely related condition non-ST-segment elevation myocardial infarction (MI) (NSTEMI) are very common manifestations of this disease and are responsible for approximately 1.5 million hospitalizations in the United States each year. UA and NSTEMI are examples of acute coronary syndrome (ACS), which is characterized by an imbalance between myocardial oxygen supply and demand. The most common cause is the reduced myocardial perfusion that results from coronary artery narrowing caused by a nonocclusive thrombus that has developed on a disrupted atherosclerotic plaque. UA and NSTEMI are considered to be closely related conditions whose pathogenesis and clinical presentations are similar but of differing severity; they differ primarily in whether the ischemia is severe enough to cause sufficient myocardial damage to release detectable quantities of a marker of myocardial injury.

The customary American College of Cardiology Foundation/American Heart Association (ACCF/AHA) classification of recommendations and levels of evidence is used and displayed in *Table 1*.



Table 1. Applying Classification of Recommendations and Level of Evidence[†]

		SIZE OF TREATMENT EFFECT	
		CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/administered	CLASS IIa <i>Benefit >> Risk</i> <i>Additional studies with focused objectives needed</i> IT IS REASONABLE to perform procedure/administer treatment
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> ■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> ■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses
	LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> ■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> ■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies
	LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> ■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> ■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard-of-care
	Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated
Comparative effectiveness phrases[†]		treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B



Class IIb <i>Benefit ≥ Risk</i> <i>Additional studies with broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment MAY BE CONSIDERED	Class III No Benefit or Class III Harm									
<ul style="list-style-type: none"> ■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses 	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th></th> <th style="text-align: center;">Procedure/ Test</th> <th style="text-align: center;">Treatment</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">COR III: No Benefit</td> <td style="text-align: center;">Not Helpful</td> <td style="text-align: center;">No Proven Benefit</td> </tr> <tr> <td style="text-align: center;">COR III: Harm</td> <td style="text-align: center;">Excess Cost w/o Benefit or Harmful</td> <td style="text-align: center;">Harmful to Patients</td> </tr> </tbody> </table> <ul style="list-style-type: none"> ■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses 		Procedure/ Test	Treatment	COR III: No Benefit	Not Helpful	No Proven Benefit	COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients
	Procedure/ Test	Treatment								
COR III: No Benefit	Not Helpful	No Proven Benefit								
COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients								
<ul style="list-style-type: none"> ■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> ■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies 									
<ul style="list-style-type: none"> ■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard-of-care 	<ul style="list-style-type: none"> ■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard-of-care 									

* Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

† For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

may/might be considered
may/might be reasonable
usefulness/effectiveness is
unknown /unclear/uncertain or
not well established

COR III:
No Benefit
is not
recommended
is not indicated
should not
be done
is not useful/
beneficial/
effective

COR III:
Harm
potentially
harmful
causes harm
associated with
excess morbidity/mortality
should not
be done

2. Initial Evaluation and Management

A. Clinical Assessment

Recommendations for Initial Triage

Class I

1. Patients with symptoms of ACS (chest discomfort with or without radiation to the arm[s], back, neck, jaw or epigastrium; shortness of breath; weakness; diaphoresis; nausea; lightheadedness) should be instructed to call 9-1-1 and should be transported to the hospital by ambulance rather than by friends or relatives. *(Level of Evidence: B)*
2. Prehospital emergency medical services (EMS) providers should administer 162 to 325 mg of aspirin (ASA; chewed) to chest pain patients suspected of having ACS unless contraindicated or already taken by the patient. *(Level of Evidence: C)*
3. Health care providers should instruct patients with suspected ACS for whom nitroglycerin (NTG) has been prescribed previously to take not more than 1 dose of NTG sublingually in response to chest discomfort/pain. If chest discomfort/pain is unimproved or is worsening 5 minutes after 1 NTG dose has been taken, it is recommended that the patient or family member/friend/caregiver call 9-1-1 immediately to access EMS before taking additional NTG. In patients with chronic stable angina, if symptoms are significantly improved by 1 NTG, it is appropriate to instruct the patient or family

member/friend/caregiver to repeat NTG every 5 minutes for a maximum of 3 doses and call 9-1-1 if symptoms have not resolved completely. *(Level of Evidence: C)*

4. Patients with a suspected ACS with chest discomfort or other ischemic symptoms at rest for greater than 20 minutes, hemodynamic instability, or recent syncope or presyncope should be referred immediately to an emergency department (ED). *(Level of Evidence: C)*

B. Early Risk Stratification

Recommendations

Class I

1. Patients who present with chest discomfort or other ischemic symptoms should undergo early risk stratification for the risk of cardiovascular events (e.g., death or re-MI) that focuses on history, including anginal symptoms, physical findings, electrocardiogram (ECG) findings, and biomarkers of cardiac injury *(Table 2)*. *(Level of Evidence: C)*
2. A 12-lead ECG should be performed and shown to an experienced emergency physician as soon as possible after ED arrival, with a goal of within 10 minutes for all patients with symptoms suggestive of ACS. *(Level of Evidence: B)*
3. If the initial ECG is not diagnostic but the patient remains symptomatic and there is high clinical suspicion for ACS, serial ECGs, initially at 15- to

30-minute intervals, should be performed to detect the potential for development of ST-segment elevation or depression. *(Level of Evidence: B)*

4. Cardiac biomarkers should be measured in all patients who present with chest discomfort consistent with ACS. A cardiac-specific troponin is the preferred biomarker. Patients with negative cardiac biomarkers within 6 hours of the onset of symptoms consistent with ACS should have biomarkers remeasured in the time frame of 8 to 12 hours after symptom onset. *(Level of Evidence: B)*

5. The initial evaluation of the patient with suspected ACS should include the consideration of noncoronary causes for the development of unexplained symptoms. *(Level of Evidence: C)*

-
- Class IIa** 1. Use of risk stratification models, such as the TIMI or GRACE risk score or PURSUIT risk model, can be useful to assist in decision making regarding treatment options in patients with suspected ACS *(Table 2 and Figure 1)*. *(Level of Evidence: B)*

Table 2. TIMI Risk Score for Unstable Angina/Non–ST Elevation MI

TIMI Risk Score	All-Cause Mortality, New or Recurrent MI, or Severe Recurrent Ischemia Requiring Urgent Revascularization Through 14 d After Randomization, %
0–1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6–7	40.9

The TIMI risk score is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables:

- age 65 y or older;
- at least 3 risk factors for CAD;
- prior coronary stenosis of 50% or more;
- ST-segment deviation on ECG presentation;
- at least 2 anginal events in prior 24 h;
- use of aspirin in prior 7 d;
- elevated serum cardiac biomarkers.

Prior coronary stenosis of 50% or more remained relatively insensitive to missing information and remained a significant predictor of events.

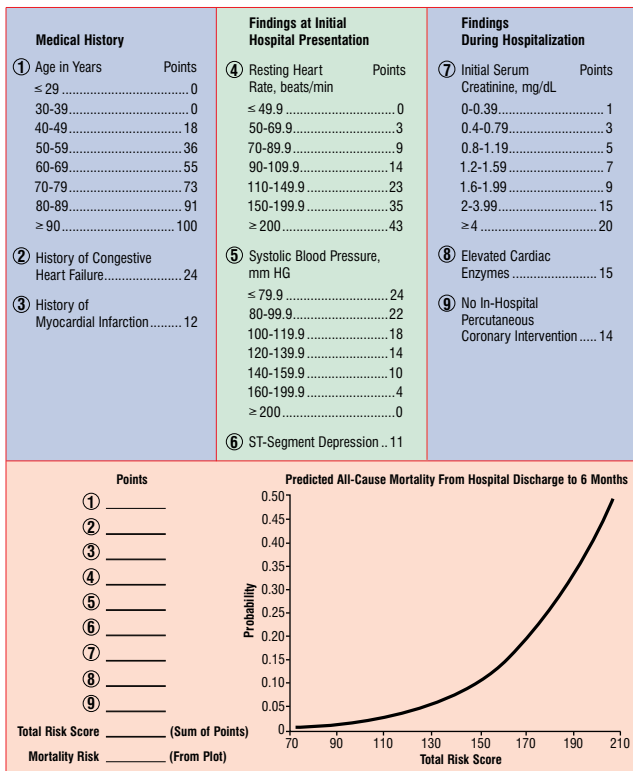
Reprinted with permission from Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *JAMA* 2000; 284:835-42. Copyright © 2000 American Medical Association.

CAD indicates coronary artery disease; ECG, electrocardiogram; MI, myocardial infarction.

Figure 1. GRACE Prediction Score Card and Nomogram for All-Cause Mortality From Discharge to 6 Months

Risk Calculator for 6-Month Post-Discharge Mortality After Hospitalization for Acute Coronary Syndrome

Record the points for each variable at the bottom left and sum the points to calculate the total risk score. Find the total score on the x-axis of the nomogram plot. The corresponding probability on the y-axis is the estimated probability of all-cause mortality from hospital discharge to 6 months.



Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month post-discharge death in an international registry. JAMA 2004; 291:2727-33. © Copyright 2004 American Medical Association.

C. Immediate Management

Recommendations

- Class I**
1. The history, physical examination, 12-lead ECG, and initial cardiac biomarker tests should be integrated to assign patients with chest pain to 1 of 4 categories: a noncardiac diagnosis, chronic stable angina, possible ACS, and definite ACS. (*Level of Evidence: C*)
 2. Patients with probable or possible ACS but whose initial 12-lead ECG and cardiac biomarker levels are normal should be observed in a facility with cardiac monitoring and repeat ECG (or continuous 12-lead ECG monitoring) and repeat cardiac biomarker measurement(s) should be obtained at predetermined, specified time intervals. (*Level of Evidence: B*)
 3. In patients with suspected ACS in whom ischemic heart disease is present or suspected, if the follow-up 12-lead ECG and biomarker measurements are normal, a stress test (exercise or pharmacological) to provoke ischemia should be performed in the ED, in a chest pain unit, or on an outpatient basis in a timely fashion (within 72 h) as an alternative to inpatient admission. Low-risk patients with a negative stress diagnostic test can be managed as outpatients. (*Level of Evidence: C*)

4. In low-risk patients who are referred for outpatient stress testing (see above), precautionary pharmacotherapy (e.g., ASA, sublingual NTG, and/or beta blockers) should be considered while awaiting results of the stress test. *(Level of Evidence: C)*

5. Patients with definite ACS and ongoing ischemic symptoms, positive cardiac biomarkers, new ST-segment deviations, new deep T-wave inversions, hemodynamic abnormalities, or a positive stress test should be admitted to the hospital for further management. Admission to the critical care unit is recommended for those with active, ongoing ischemia/injury and hemodynamic or electrical instability. Otherwise, a telemetry step-down unit is reasonable. *(Level of Evidence: C)*

5. Patients with possible ACS and negative cardiac biomarkers who are unable to exercise or who have an abnormal resting ECG should undergo a pharmacological stress test. *(Level of Evidence: B)*

6. Patients discharged from the ED or chest pain unit should be given specific instructions for activity, medications, additional testing, and follow-up with a personal physician. *(Level of Evidence: C)*

3. Early Hospital Care

A. Anti-Ischemic Therapy

Recommendations

Class I

1. Bed/chair rest with continuous ECG monitoring is recommended for all UA/NSTEMI patients during the early hospital phase. *(Level of Evidence: C)*
2. Supplemental oxygen should be administered to UA/NSTEMI patients with an arterial saturation less than 90%, respiratory distress, or other high-risk features for hypoxemia. *(Level of Evidence: B)*
3. Patients with UA/NSTEMI with ongoing ischemic discomfort should receive sublingual NTG (0.4 mg) every 5 minutes for a total of 3 doses, after which assessment should be made about the need for intravenous NTG, if not contraindicated. *(Level of Evidence: C)*
4. Intravenous NTG is indicated in the first 48 hours in patients with UA/NSTEMI for treatment of persistent ischemia, heart failure, or hypertension. The decision to administer intravenous NTG and the dose used should not preclude therapy with other proven mortality-reducing interventions such as beta blockers or angiotensin-converting enzyme (ACE) inhibitors. *(Level of Evidence: B)*

5. Oral beta-blocker therapy within 24 hours should be administered to patients without a contraindication (*Level of Evidence: B*)
 6. In UA/NSTEMI patients with continuing or frequently recurring ischemia and in whom beta blockers are contraindicated, a nondihydropyridine calcium channel blocker antagonist (e.g., verapamil or diltiazem) should be given as initial therapy in the absence of clinically significant left ventricular (LV) dysfunction or other contraindications. (*Level of Evidence: B*)
 7. An ACE inhibitor should be administered orally within the first 24 hours to patients with pulmonary congestion or left ventricular ejection fraction (LVEF) less than or equal to 0.40 in the absence of hypotension (systolic blood pressure <100 mm Hg or <30 mm Hg below baseline) or known contraindications. An angiotensin receptor blocker may be used for ACE intolerant patients. (*Level of Evidence: A*)
-



B. Initial Conservative Versus Initial Invasive Strategies (UPDATED)

Recommendations

- Class I**
1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in UA/NSTEMI patients who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures). (*Level of Evidence: B*)
 2. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in initially stabilized UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (*Table 3*). (*Level of Evidence: A*)
 3. In women with low-risk features, a conservative strategy is recommended. (*Level of Evidence: B*)
-

- Class IIa**
1. It is reasonable to choose an early invasive strategy (within 12 to 24 h of admission) over a delayed invasive strategy for initially stabilized *high-risk* patients with UA/NSTEMI. For patients *not at high risk*, a delayed invasive approach is also reasonable. (*Level of Evidence: B*)

Class IIb

1. In initially stabilized patients, an initially conservative (i.e., a selectively invasive) strategy may be considered as a treatment strategy for UA/NSTEMI patients (without serious comorbidity or contraindications) who have an elevated risk of clinical events (*Table 4*) including those who are troponin positive. (*Level of Evidence B*) The decision to implement an initial conservative strategy in these patients may be made considering physician and patient preference. (*Level of Evidence: C*)



**Table 3. Selection of Initial Treatment Strategy:
Invasive Versus Conservative Strategy (Updated)**

Strategy	Status	Patient Characteristics
Invasive	Generally preferred	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy Elevated cardiac biomarkers (TnT or TnI) New or presumably new ST-segment depression Signs or symptoms of HF or new or worsening mitral regurgitation High-risk findings from noninvasive testing Hemodynamic instability Sustained ventricular tachycardia PCI within 6 mo Prior CABG High-risk score (e.g., TIMI, GRACE) Mild to moderate renal dysfunction Diabetes mellitus Reduced left ventricular function (LVEF <40%)
Conservative	Generally preferred	Low risk score (e.g., TIMI, GRACE) Patient or physician preference in the absence of high-risk features

CABG indicates coronary artery bypass graft surgery; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction; TnI, troponin I; and TnT, troponin T.

Table 4. Short-Term Risk of Death or Nonfatal MI in Patients With UA/NSTEMI*

Feature	High Risk <i>At least 1 of the following features must be present:</i>
History	Accelerating tempo of ischemic symptoms in preceding 48 h
Character of pain	Prolonged ongoing (>20 min) rest pain
Clinical findings	Pulmonary edema, most likely due to ischemia New or worsening MR murmur S ₃ or new/worsening rales Hypotension, bradycardia, tachycardia Age >75 y
ECG	Angina at rest with transient ST-segment changes >0.5 mm Bundle-branch block, new or presumed new Sustained ventricular tachycardia
Cardiac markers	Elevated cardiac TnT, TnI, or CK-MB (e.g., TnT or TnI >0.1 ng per mL)

*Estimation of the short-term risks of death and nonfatal cardiac ischemic events in UA (or NSTEMI) is a complex multivariable problem that cannot be fully specified in a table such as this; therefore, this table is meant to offer general guidance and illustration rather than rigid algorithms.

Adapted from AHCPR Clinical Practice Guidelines No.10, Unstable Angina: Diagnosis and Management, May 1994.

Intermediate Risk

No high-risk feature, but must have 1 of the following:

Prior MI, peripheral or cerebrovascular disease, or CABG; prior aspirin use

Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD

Rest angina (>20 min) or relieved with rest or sublingual NTG

Nocturnal angina

New-onset or progressive CCS class III or IV angina in the past 2 wk without prolonged (>20 min) rest pain but with intermediate or high likelihood of CAD

Age >70 years

Low Risk

No high- or intermediate-risk feature but may have any of the following features:

Increased angina frequency, severity, or duration

Angina provoked at a lower threshold

New onset angina with onset 2 wk to 2 mo prior to presentation

T-wave changes

Pathological Q waves or resting

ST-depression < 1 mm in multiple lead groups (anterior, inferior, lateral)

Normal or unchanged ECG

Slightly elevated cardiac TnT, Tnl, or

CK-MB (e.g., TnT >0.01 but <0.1 ng per mL)

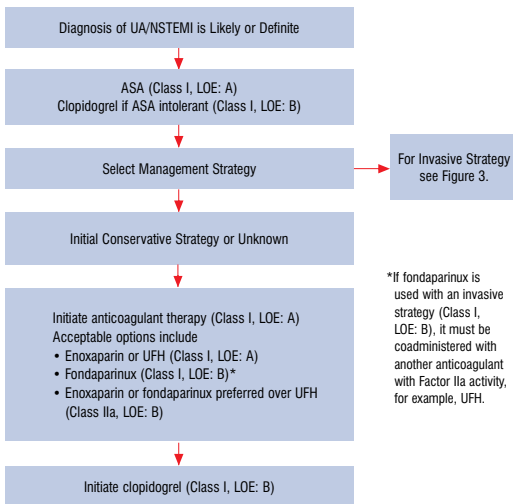
Normal

CABG indicates coronary artery bypass graft surgery; CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; CK-MB, creatine kinase, MB fraction; ECG, electrocardiogram; MI, myocardial infarction; MR, mitral regurgitation; NTG, nitroglycerin; Tnl, troponin I; TnT, troponin T; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction.

C. Antiplatelet and Anticoagulation Therapy (UPDATED)

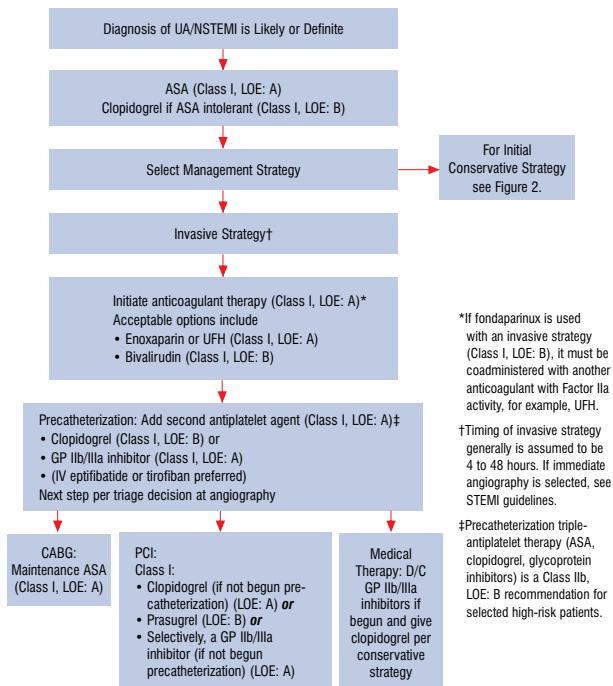
A growing number of antiplatelet and antithrombotic agents are now available for use in ACS. The decision of which agents to use, when to administer them and at what doses is complex. See *Figures 2, 3, 4, and 5*; and *Table 5* for guidance.

Figure 2. Flowchart for Class I and Class IIa Recommendations for Initial Management of UA/NSTEMI (Initial Conservative Strategy) (Updated)



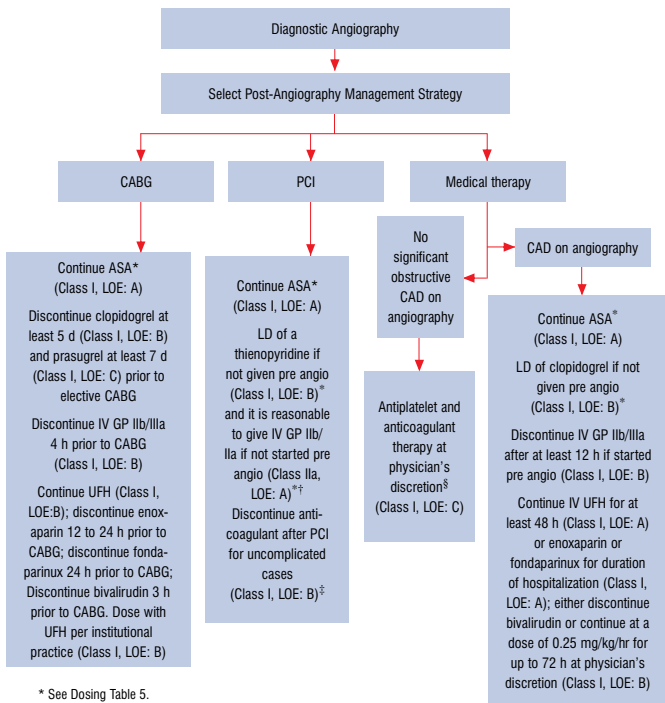
ASA indicates aspirin; CABG, coronary artery bypass graft; D/C, discontinue; GP, glycoprotein; IV, intravenous; LOE, level of evidence; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction; and UFH, unfractionated heparin.

Figure 3. Flowchart for Class I and Class IIa Recommendations for Initial Management of UA/NSTEMI (Invasive Strategy) (Updated)



ASA indicates aspirin; CABG, coronary artery bypass graft; D/C, discontinue; GP, glycoprotein; IV, intravenous; LOE, level of evidence; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction; and UFH, unfractionated heparin.

Figure 4. Management After Diagnostic Angiography in Patients With UA/NSTEMI (Updated)



* See Dosing Table 5.

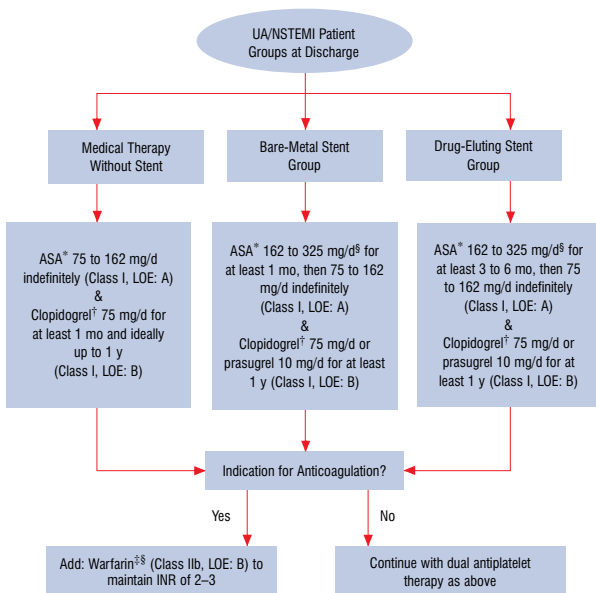
† Evidence exists that GP IIb/IIIa inhibitors may not be necessary if the patient received a preloading dose of at least 300 mg of clopidogrel at least 6 h earlier (Class I, LOE: B for clopidogrel administration) and bivalirudin is selected as anticoagulant (Class IIa, LOE: B).

‡ Additional bolus of UFH is recommended if fondaparinux is selected as anticoagulant (see Dosing Table 5).

§ For patients in whom the clinician believes coronary atherosclerosis is present, albeit without any significant, flow-limiting stenosis, long-term treatment with antiplatelet agents and other secondary prevention measures should be considered.

ASA indicates aspirin; CABG, coronary artery bypass graft; CAD, coronary artery disease; GP, glycoprotein; IV, intravenous; LD, loading dose; PCI, percutaneous coronary intervention; pre angio, before angiography; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction; UFH, unfractionated heparin.

Figure 5. Long-Term Antithrombotic Therapy at Hospital Discharge After UA/NSTEMI (Updated)



* For ASA allergic patients, use clopidogrel alone (indefinitely), or try ASA desensitization.

† For clopidogrel allergic patients, use ticlopidine, 250 mg by mouth twice daily, or prasugrel.

‡ Continue ASA indefinitely and warfarin longer term as indicated for specific conditions such as atrial fibrillation; LV thrombus, cerebral, venous or pulmonary emboli.

§ When risk of bleeding is a concern, a lower initial ASA (75 to 162 mg/d) after PCI is reasonable (Class IIa, LOE: C)

ASA indicates aspirin; INR, international normalized ratio; LOE, Level of Evidence; LV, left ventricular; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction.

Table 5. Dosing Table for Selected Antiplatelet and Anticoagulant Therapies (Updated)

Drug*	During PCI	
	Patient Received Initial Medical Treatment (With a Thienopyridine)	Patient Did Not Receive Initial Medical Treatment (With a Thienopyridine)
Glycoprotein IIb/IIIa Receptor Antagonists		
Abciximab	Of uncertain benefit	LD of 0.25 mg/kg IV bolus MD of 0.125 mcg/kg per min (maximum 10 mcg/min) (Class I, LOE: A)
Eptifibatide	Of uncertain benefit	LD of 180 mcg/kg IV bolus followed 10 min later by second IV bolus of 180 mcg/kg MD of 2.0 mcg/kg per min, started after first bolus; reduce infusion by 50% in patients with estimated creatinine clearance <50 mL/min (Class I, LOE: A)
Tirofiban	Of uncertain benefit	LD of 25 mcg/kg IV bolus MD of IV infusion of 0.15 mcg/kg per min; reduce rate of infusion by 50% in patients with estimated creatinine clearance <30 mL/min (Class I, LOE: B)
Thienopyridines		
Clopidogrel†	If 600 mg given orally, then no additional treatment A second LD of 300 mg may be given orally to supplement a prior LD of 300 mg (Class I, LOE: C)	LD of 300-600 mg orally (Class I, LOE: A) MD of 75 mg orally per d (Class I, LOE: A) An MD of 150 mg orally per d for initial 6 d may be considered (Class IIb, LOE: B)
Prasugrel†	No data are available to guide decision making	LD of 60 mg orally MD of 10 mg orally per d (Class I, LOE: B)

Comments

► All Patients to Receive ASA (162–325 mg)

- Continue for up to 12 h at the discretion of the physician.
-
- A LD of eptifibatid is FDA approved when the medication is initiated in UA/NSTEMI patients who are started on medical therapy and when there is an appreciable delay in angiography/PCI: LD of 180 mcg/kg IV bolus followed by MD of 2.0 mcg/kg per min started after bolus reduce infusion by 50% in patients with estimated creatinine clearance <50 mL/min (Class I, LOE: B)
 - Infusion should be continued for 12 to 18 h at the discretion of the physician.
-
- Increased dosing over previous recommendation.
 - Continue for up to 18 h at the discretion of the physician.
 - A lower-dose regimen for tirofiban is FDA approved and has been shown to be effective when used to treat UA/NSTEMI patients who are started on medical therapy and when there is a substantial delay to angiography/PCI (e.g., 48 h):
LD of 50 mcg/mL administered at an initial rate of 0.4 mcg/kg per min for 30 min
MD of a continuous infusion of 0.1 mcg/kg per min. Continue the infusion through angiography and for 12 to 24 h after angioplasty or atherectomy.
-
- Optimum LD requires clinical consideration.
 - Dose for patients >75 y of age has not been established.
 - There is a recommended duration of therapy for all post-PCI patients receiving a BMS or DES.
 - Caution should be exercised for use with a PPI.
 - Period of withdrawal before surgery should be at least 5 d.
- (For full explanations, see footnote.)*
-
- There are no data for treatment with prasugrel before PCI.
 - MD of 5 mg orally per d in special circumstances.
 - Special dosing for patients <60 kg or >75 y of age.
 - There is a recommended duration of therapy for all post-PCI patients receiving a BMS or DES.
 - Contraindicated for use in patients with prior history of TIA or stroke.

(For full explanations, see footnote.)

Table 5. Dosing Table for Selected Antiplatelet and Anticoagulant Therapies *continued from previous page*

Drug*	During PCI	
	Patient Received Initial Medical Treatment (With a Thienopyridine)	Patient Did Not Receive Initial Medical Treatment (With a Thienopyridine)
Parenteral Anticoagulants		
Bivalirudin	For patients who have received UFH, wait 30 min, then give 0.75 mg/kg bolus, then 1.75 mg/kg per h infusion (Class I, LOE: B)	0.75 mg/kg bolus, 1.75 mg/kg per h infusion
UFH	IV GP IIb/IIIa planned: target ACT 200–250 s No IV GP IIb/IIIa planned: target ACT 250–300 s for HemoTec, 300–350 s for HemoChron (Class I, LOE: B)	IV GP IIb/IIIa planned: 50–70 U/kg bolus to achieve an ACT of 200–250 s No IV GP IIb/IIIa planned: 70–100 U/kg bolus to achieve target ACT of 250–300 s for HemoTec, 300–350 s for HemoChron (Class I, LOE: B)

* This list is in alphabetical order and is not meant to indicate a particular therapy preference. This drug table does not make recommendations for combinations of listed drugs. It is only meant to indicate an approved or recommended dosage if a drug is chosen for a given situation.

† For post-PCI patients receiving a DES or BMS, a daily MD should be given for at least 12 mo unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine. The necessity for giving an LD of clopidogrel before PCI is driven by the pharmacokinetics of clopidogrel, for which a period of several hours is required to achieve desired levels of platelet inhibition. Patients who have a reduced-function CYP2C19 allele have significantly lower levels of the active metabolite of clopidogrel, diminished platelet inhibition, and a higher rate of MACE, including stent thrombosis. In NSTEMI patients taking clopidogrel for whom CABG is planned and can be delayed, it is reasonable to discontinue the clopidogrel to allow for dissipation of the antiplatelet effect unless the urgency for revascularization and/or the net benefit of clopidogrel outweigh the potential risks of excess bleeding. The period of withdrawal should be at least 5 d in patients receiving clopidogrel.

Comments

► All Patients to Receive ASA (162–325 mg)

- Bivalirudin may be used to support PCI and UA/NSTEMI with or without previously administered UFH with the addition of 600 mg of clopidogrel.
- In UA/NSTEMI patients undergoing PCI who are at high risk of bleeding, bivalirudin anticoagulation is reasonable.

† Patients weighing <60 kg have an increased exposure to the active metabolite of prasugrel and an increased risk of bleeding on a 10-mg once-daily MD. Consider lowering the MD to 5 mg in patients who weigh <60 kg. The effectiveness and safety of the 5-mg dose have not been studied prospectively. For post-PCI patients receiving a DES or BMS, a daily MD should be given for at least 12 and up to 15 mo unless the risk of bleeding outweighs the anticipated net benefit afforded by a thienopyridine. Do not use prasugrel in patients with active pathological bleeding or a history of TIA or stroke. In patients ≥75 years of age, prasugrel is generally not recommended because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior MI), for which its effect appears to be greater and its use may be considered. Do not start prasugrel in patients likely to undergo urgent CABG. When possible, discontinue prasugrel at least 7 d before any surgery. Additional risk factors for bleeding include body weight <60 kg, propensity to bleed, concomitant use of medications that increase the risk of bleeding (e.g., warfarin, heparin, fibrinolytic therapy, or long-term use of nonsteroidal anti-inflammatory drugs).

ACT indicates activated clotting time; BMS, bare-metal stent; GP, glycoprotein; IU, international unit; IV, intravenous; LD, loading dose; MD, maintenance dose; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stent; SC, subcutaneous; SES, sirolimus-eluting stent; U, units; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction; UFH, unfractionated heparin.

D. Risk Stratification

Recommendations

Class I

1. Noninvasive stress testing is recommended in low- and intermediate-risk patients who have been free of ischemia at rest or with low-level activity and of heart failure for a minimum of 12 to 24 hours

(Level of Evidence: C)

2. Choice of stress test is based on the resting ECG, ability to perform exercise, local expertise, and technologies available. Treadmill exercise is useful in patients able to exercise in whom the ECG is free of baseline ST-segment abnormalities, bundle-branch block, LV hypertrophy, intraventricular conduction defect, paced rhythm, preexcitation, and digoxin effect. *(Level of Evidence: C)*

3. An imaging modality should be added in patients with resting ST-segment depression (≥ 0.10 mV), LV hypertrophy, bundle-branch block, intraventricular conduction defect, preexcitation, or digoxin who are able to exercise. In patients undergoing a low-level exercise test, an imaging modality can add sensitivity. *(Level of Evidence: B)*

4. Pharmacological stress testing with imaging is recommended when physical limitations (e.g., arthritis, amputation, severe peripheral vascular disease, severe chronic obstructive pulmonary disease, general debility) preclude adequate exercise stress. *(Level of Evidence: B)*

5. Prompt angiography without noninvasive risk stratification should be performed for failure of stabilization with intensive medical treatment. *(Level of Evidence: B)*

6. A noninvasive test (echocardiogram or radionuclide angiogram) is recommended to evaluate LV function in patients with definite ACS who are not scheduled for coronary angiography and left ventriculography. *(Level of Evidence: B)*



4. Hospital Discharge and Post-Hospital Discharge Care

The acute phase of UA/NSTEMI is usually over within 2 months. The risk of progression to MI or the development of recurrent MI or death is highest during this period. Most patients then resume a clinical course similar to that of patients with chronic, stable coronary artery disease.

A. Medical Regimen

An effort of the entire staff (physicians, nurses, dietitians, pharmacists, rehabilitation specialists, and physical and occupational therapists) is often necessary to prepare the patient for discharge. Direct patient instruction is important and should be reinforced and documented with written instruction sheets. Enrollment in a cardiac rehabilitation program after discharge may enhance patient education and compliance with the medical regimen.

Recommendations

- Class I** 1. Medications required in the hospital to control ischemia should be continued after hospital discharge in patients with UA/NSTEMI who do not undergo coronary revascularization, patients with unsuccessful revascularization, and patients with recurrent symptoms after revascularization. Upward or downward titration of the doses may be required. *(Level of Evidence: C)*

2. All post-UA/NSTEMI patients should be given sublingual or spray NTG and instructed in its use.

(Level of Evidence: C)

3. Before hospital discharge, patients with UA/NSTEMI should be informed about symptoms of worsening myocardial ischemia and MI and should be instructed in how and when to seek emergency care and assistance if such symptoms occur. *(Level of Evidence: C)*

(Level of Evidence: C)

4. Before hospital discharge, post-UA/NSTEMI patients and/or designated responsible caregivers should be provided with supportable, easily understood, and culturally sensitive instructions with respect to medication type, purpose, dose, frequency, and pertinent side effects. *(Level of Evidence: C)*

5. In post-UA/NSTEMI patients, anginal discomfort lasting more than 2 or 3 minutes should prompt the patient to discontinue physical activity or remove himself or herself from any stressful event. If pain does not subside immediately, the patient should be instructed to take 1 dose of NTG sublingually. If the chest discomfort/pain is unimproved or worsening 5 minutes after 1 NTG dose has been taken, it is recommended that the patient or a family member/friend call 9-1-1 immediately to access EMS. While activating EMS access, additional NTG (at 5-minute intervals 2 times) may be taken while lying down or sitting. *(Level of Evidence: C)*

6. If the pattern or severity of anginal symptoms changes, which suggests worsening myocardial

ischemia (e.g., pain is more frequent or severe or is precipitated by less effort or now occurs at rest), the patient should contact his or her physician without delay to assess the need for additional treatment or testing. (*Level of Evidence: C*)

B. Convalescent and Long-Term Medical Therapy and Secondary Prevention (UPDATED)

1. Antiplatelet Therapy (Updated)

- Class I** 1. Aspirin 75 to 162 mg daily should be given and continued indefinitely for medically-treated patients recovering from UA/NSTEMI. (*Level of Evidence: A*) For patients who have undergone PCI, ASA 162 to 325 mg daily should be given for at least 1 month after bare-metal stent implantation, 3 months after sirolimus-eluting stent implantation, and 6 months after paclitaxel-eluting stent implantation, after which daily chronic ASA use should be continued indefinitely at a dose of 75 to 162 mg. (*Level of Evidence: B*)



2. Clopidogrel 75 mg daily (preferred) or ticlopidine (in the absence of contraindications) should be given to patients recovering from UA/NSTEMI when ASA is contraindicated or not tolerated because of hypersensitivity or gastrointestinal intolerance (despite use of gastroprotective agents such as proton pump inhibitors). *(Level of Evidence: B)*

3. The duration and maintenance dose of thienopyridine therapy should be as follows:

a. In UA/NSTEMI patients undergoing percutaneous coronary intervention (PCI) with a drug-eluting stent or bare-metal stent, clopidogrel 75 mg daily or prasugrel 10 mg daily should be given for at least 12 months. *(Level of Evidence: B)*

b. If the risk of morbidity because of bleeding outweighs the anticipated benefits afforded by thienopyridine therapy, earlier discontinuation should be considered. *(Level of Evidence: C)*

c. For UA/NSTEMI patients treated medically without stenting, clopidogrel 75 mg daily should be prescribed for at least 1 month and ideally up to 1 year. *(Level of Evidence: B)*



Class IIa 1. For UA/NSTEMI patients in whom the physician is concerned about the risk of bleeding, a lower initial ASA dose (75 to 162 mg/day) after PCI is reasonable. *(Level of Evidence: C)*

Class IIb 1. Platelet function testing to determine platelet inhibitory response in patients with UA/NSTEMI (or, after ACS and PCI) on thienopyridine therapy may be considered if results of testing may alter management. *(Level of Evidence: B)*

2. Continuation of clopidogrel or prasugrel beyond 15 months may be considered in patients following drug-eluting stent placement. *(Level of Evidence: C)*

Class III: In UA/NSTEMI patients with a prior history of stroke and/or transient ischemic attack for whom PCI is planned, prasugrel is potentially harmful as part of a dual-antiplatelet therapy regimen. *(Level of Evidence: B)*

Harm

2. Beta Blockers

Class I 1. Beta blockers are indicated for all patients recovering from UA/NSTEMI unless contraindicated and should be continued indefinitely. *(Level of Evidence: B)*

2. Patients recovering from UA/NSTEMI with moderate or severe LV failure should receive beta-blocker therapy with a gradual titration scheme.

(Level of Evidence: B)

3. Inhibition of the Renin-Angiotensin-Aldosterone System

Class I

1. ACE inhibitors should be given and continued indefinitely for patients recovering from UA/NSTEMI with HF, LV dysfunction ($EF < 0.40$), hypertension, or diabetes mellitus unless contraindicated. *(Level of Evidence: A)*

2. An angiotensin receptor blocker should be prescribed at discharge to those patients who are intolerant of an ACE inhibitor and who have either clinical or radiological signs of HF and LVEF less than 0.40. *(Level of Evidence: A)*

3. Long-term aldosterone receptor blockade should be prescribed for post-UA/NSTEMI patients without significant renal dysfunction (estimated creatinine clearance should be >30 mL per min) or hyperkalemia (potassium should be ≤ 5 mEq per L) who are already receiving therapeutic doses of an ACE inhibitor, have an LVEF less than or equal to 0.40, and have either symptomatic HF or diabetes mellitus. *(Level of Evidence: A)*

-
- Class IIa** 1. ACE inhibitors are reasonable for patients recovering from UA/NSTEMI in the absence of LV dysfunction, hypertension, or diabetes mellitus unless contraindicated. *(Level of Evidence: A)*

4. Nitroglycerin

- Class I** 1. NTG to treat ischemic symptoms is recommended. *(Level of Evidence: C)*

5. Calcium Channel Blockers

- Class I** 1. Calcium channel blockers* are recommended for ischemic symptoms when beta blockers are not successful. *(Level of Evidence: B)*
2. Calcium channel blockers* are recommended for ischemic symptoms when beta blockers are contraindicated or cause unacceptable side effects. *(Level of Evidence: C)*

** Short-acting dihydropyridine calcium channel blockers should be avoided.*

6. Warfarin Therapy (Updated)

- Class I** 1. Use of warfarin in conjunction with ASA and/or a thienopyridine agent is associated with an increased risk of bleeding and patients and clinicians should watch for bleeding, especially gastrointestinal, and seek medical evaluation for evidence of bleeding. *(Level of Evidence: A)*

-
- Class IIb** 1. Warfarin either without (international normalized ratio 2.5 to 3.5) or with low-dose ASA (75 to 81 mg per day; international normalized ratio 2.0 to 2.5) may be reasonable for patients at high coronary artery disease risk and low bleeding risk who do not require or are intolerant of a thienopyridine. *(Level of Evidence: B)*

7. Lipid Management

- Class I** 1. The following lipid recommendations are beneficial:
- Lipid management should include assessment of a fasting lipid profile for all patients, within 24 hours of hospitalization. *(Level of Evidence: C)*
 - Statins, in the absence of contraindications, regardless of baseline low-density lipoprotein (LDL)-cholesterol and diet modification, should be given to post-UA/NSTEMI patients, including postrevascularization patients. *(Level of Evidence: A)*
 - For patients with elevated LDL-cholesterol (≥ 100 mg per dL), cholesterol-lowering therapy should be initiated or intensified to achieve an LDL-cholesterol of less than 100 mg per dL. *(Level of Evidence: A)*

2. Treatment of triglycerides and non-HDL-cholesterol is useful, including the following:
 - a. If triglycerides are 200 to 499 mg per dL, non-high-density lipoprotein (HDL)-cholesterol* should be less than 130 mg per dL. (*Level of Evidence: B*)
 - b. If triglycerides are greater than or equal to 500 mg per dL[†], therapeutic options to prevent pancreatitis are fibrate[‡] or niacin[‡] before LDL-lowering therapy is recommended. It is also recommended that LDL-cholesterol be treated to goal after triglyceride-lowering therapy. Achievement of a non-HDL-cholesterol* less than 130 mg per dL (i.e., 30 mg per dL >LDL-cholesterol target) if possible is recommended. (*Level of Evidence: C*)

Class IIa 1. The following lipid management strategies can be beneficial:

- a. Further reduction of LDL-cholesterol to less than 70 mg per dL is reasonable. (*Level of Evidence: A*)
- b. If baseline LDL cholesterol is 70 to 100 mg per dL, it is reasonable to treat LDL-cholesterol to less than 70 mg per dL. (*Level of Evidence: B*)

* Non-HDL-cholesterol = total cholesterol minus HDL-cholesterol.

† Patients with very high triglycerides should not consume alcohol. The use of bile acid sequestrants is relatively contraindicated when triglycerides are >200 mg per dL.

‡ The combination of high-dose statin plus fibrate can increase risk for severe myopathy. Statin doses should be kept relatively low with this combination. Dietary supplement niacin must not be used as a substitute for prescription niacin.

8. Blood Pressure Control

- Class I** 1. Blood pressure control to less than 140/90 mm Hg (or <130/80 mm Hg if the patient has diabetes mellitus or chronic kidney disease). (*Level of Evidence: A*) Additional measures recommended to treat and control blood pressure include the following:
- a. Patients should initiate and/or maintain lifestyle modifications, including weight control; increased physical activity; alcohol moderation; sodium reduction; and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products. (*Level of Evidence: B*)
 - b. For patients with blood pressure greater than or equal to 140/90 mm Hg (or $\geq 130/80$ mm Hg for individuals with chronic kidney disease or diabetes mellitus), it is useful to add blood pressure medication as tolerated, treating initially with beta blockers and/or ACE inhibitors, with addition of other drugs such as thiazides as needed to achieve target blood pressure. (*Level of Evidence: A*)

9. Diabetes Mellitus (Updated)

- Class I** 1. Diabetes management should include lifestyle and pharmacotherapy measures to achieve a near-normal hemoglobin A1c level of less than 7% (*Level of Evidence: B*). Diabetes management should also include the following:

a. Vigorous modification of other risk factors (e.g., physical activity, weight management, blood pressure control, and cholesterol management) as recommended should be initiated and maintained.

(Level of Evidence: B)

b. It is useful to coordinate the patient's diabetic care with the patient's primary care physician or endocrinologist. *(Level of Evidence: C)*

Class IIa

1. It is reasonable to use an insulin-based regimen to achieve and maintain glucose levels less than 180 mg/dL while avoiding hypoglycemia* for hospitalized patients with UA/NSTEMI with either a complicated or uncomplicated course. *(Level of Evidence: B)*

10. Chronic Kidney Disease (Updated)

Class I

1. Creatinine clearance should be estimated in UA/NSTEMI patients and the doses of renally-cleared medications should be adjusted according to the pharmacokinetic data for specific medications. *(Level of Evidence: B)*

2. Patients undergoing cardiac catheterization with receipt of contrast media should receive adequate preparatory hydration. *(Level of Evidence: B)*

* There is uncertainty about the ideal target range for glucose necessary to achieve an optimal risk-benefit ratio.

3. Calculation of the contrast volume to creatinine clearance ratio is useful to predict the maximum volume of contrast media that can be given without significantly increasing the risk of contrast-associated nephropathy. *(Level of Evidence: B)*

Class IIa 1. An invasive strategy is reasonable in patients with mild (stage II) and moderate (stage III) chronic kidney disease. *(Level of Evidence: B) (There are insufficient data on benefit/risk of invasive strategy in UA/NSTEMI patients with advanced chronic kidney disease [stages IV, V].)*

11. Smoking Cessation

Class I 1. Smoking cessation and avoidance of exposure to environmental tobacco smoke at work and home are recommended. Follow-up, referral to special programs, or pharmacotherapy (including nicotine replacement) is useful, as is adopting a stepwise strategy aimed at smoking cessation (the 5 As: Ask, Advise, Assess, Assist, and Arrange). *(Level of Evidence: B)*

12. Weight Management

Class I 1. Weight management, as measured by body mass index and/or waist circumference, should be assessed on each visit. A body mass index of 18.5 to 24.9 kg per m² and a waist circumference (measured horizontally at the iliac crest) of less than 40 inches for men and less than 35 inches for women is recommended. *(Level of Evidence: B)*

13. Physical Activity

Class I

1. The patient's risk after UA/NSTEMI should be assessed on the basis of an in-hospital determination of risk. A physical activity history or an exercise test to guide initial prescription is beneficial. *(Level of Evidence: B)*
2. Guided/modified by an individualized exercise prescription, patients recovering from UA/NSTEMI generally should be encouraged to achieve physical activity duration of 30 to 60 minutes per day, preferably in the form of 7 (but at least 5) days per week of moderate aerobic activity, such as brisk walking, supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, and household work). *(Level of Evidence: B)*
3. Cardiac rehabilitation/secondary prevention programs are recommended for patients with UA/NSTEMI, particularly those with multiple modifiable risk factors and/or those moderate- to high-risk patients in whom supervised exercise training is particularly warranted. *(Level of Evidence: B)*

14. Patient Education

Class I

1. Beyond the detailed instructions for daily exercise, patients should be given specific instruction on activities (e.g., heavy lifting, climbing stairs, yard work, and household activities) that are permissible

and those that should be avoided. Specific mention should be made regarding resumption of driving, return to work, and sexual activity. *(Level of Evidence: C)*

15. Influenza

- Class I** 1. An annual influenza vaccination is recommended for patients with cardiovascular disease. *(Level of Evidence: B)*

16. Depression

- Class IIa** 1. It is reasonable to consider screening UA/NSTEMI patients for depression and refer for treatment when indicated. *(Level of Evidence: B)*

17. Hormone Therapy

- Class III** 1. Hormone therapy with estrogen plus progestin, or estrogen alone, should not be given de novo to postmenopausal women after UA/NSTEMI for secondary prevention of coronary events. *(Level of Evidence: A)*
2. Postmenopausal women who are already taking estrogen plus progestin, or estrogen alone, at the time of UA/NSTEMI in general should not continue hormone therapy. However, women who are more than 1 to 2 years past the initiation of hormone therapy who wish to continue such therapy for another compelling indication should weigh the

risks and benefits, recognizing the greater risk of cardiovascular events and breast cancer (combination therapy) or stroke (estrogen). Hormone therapy should not be continued while patients are on bedrest in the hospital. *(Level of Evidence: B)*

18. Quality Care and Outcomes (Updated)

- Class IIa** 1. It is reasonable for clinicians and hospitals that provide care to patients with UA/NSTEMI to participate in a standardized quality-of-care data registry designed to track and measure outcomes, complications, and adherence to evidence-based processes of care and quality improvement for UA/NSTEMI. *(Level of Evidence: B)*

5. Coronary Revascularization

See 2011 Percutaneous Coronary Intervention and Coronary Artery Bypass Graft Surgery Guidelines for the most current recommendations on revascularization.

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