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ACC/AHA Pocket Guideline

Based on the ACC/AHA 2007 Guideline Revision

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

October 2007

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

October 2007

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The following material was adapted from the *ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction*. For a copy of the executive summary (J Am Coll Cardiol 2007;50:652–726; Circulation 2007;116:803–877) and full report, visit our Web sites at *http://www.acc.org* or *http://www.americanheart.org* or call the ACC Resource Center at 1-800-253-4636, ext. 5603.

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Introduction

Coronary artery disease (CAD) is the leading cause of death in the United States. Unstable angina (UA) and the closely related condition non–ST-segment elevation myocardial infarction (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/American Heart Association (ACC/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†

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT — CLASS I *Benefit >>> Risk* Procedure/Treatment SHOULD be performed/ administered	SIZE OF TREATMENT EFFECT — CLASS IIA *Benefit >> Risk* *Additional studies with focused objectives needed* IT IS REASONABLE to perform procedure/administer treatment
LEVEL A Multiple (3-5) population risk strata evaluated* General consistency of direction and magnitude of effect	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses
LEVEL B Limited (2-3) population risk strata evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Limited evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited (1-2) population risk strata evaluated*	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard-of-care	■ 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

Class IIb	Class III
Benefit ≥ Risk ***Additional studies with broad objectives needed; additional registry data would be helpful*** **Procedure/Treatment MAY BE CONSIDERED**	***Risk ≥ Benefit*** ***No additional studies needed*** **Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Limited evidence from single randomized trial or nonrandomized studies
■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard-of-care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard-of-care
may/might be considered may/might be reasonable usefulness/effectiveness is unknown /unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

* Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, 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. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

I. 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 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 min 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 emergency medical service (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 min 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 min, 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-myocardial infarction [MI]) that focuses on history, including anginal symptoms, physical findings, electrocardiogram (ECG) findings, and biomarkers of cardiac injury *(see 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 min 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-min

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 h of the onset of symptoms consistent with ACS should have biomarkers remeasured in the time frame of 8 to 12 h 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. *(Level of Evidence: B) (See Table 2 and Figure 1.)*

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.

CAD = coronary artery disease; **d** = day; **ECG** = electrocardiogram; **h** = hour; **MI** = myocardial infarction; **y** = year.

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.

Medical History

① Age in Years	Points
≤29	0
30-39	0
40-49	18
50-59	36
60-69	55
70-79	73
80-89	91
≥90	100

② History of Congestive Heart Failure 24

③ History of Myocardial Infarction 12

Findings at Initial Hospital Presentation

④ Resting Heart Rate, beats/min	Points
≤49.9	0
50-69.9	3
70-89.9	9
90-109.9	14
110-149.9	23
150-199.9	35
≥200	43

⑤ Systolic Blood Pressure, mm HG	
≤79.9	24
80-99.9	22
100-119.9	18
120-139.9	14
140-159.9	10
160-199.9	4
≥200	0

⑥ ST-Segment Depression .. 11

Findings During Hospitalization

⑦ Initial Serum Creatinine, mg/dL	Points
0-0.39	1
0.4-0.79	3
0.8-1.19	5
1.2-1.59	7
1.6-1.99	9
2-3.99	15
≥4	20

⑧ Elevated Cardiac Enzymes 15

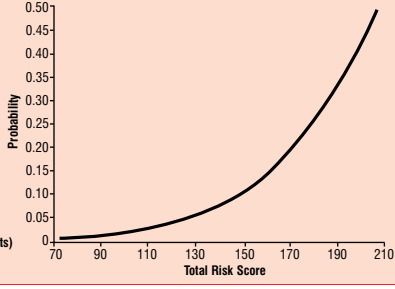
⑨ No In-Hospital Percutaneous Coronary Intervention 14

Points

① _____
② _____
③ _____
④ _____
⑤ _____
⑥ _____
⑦ _____
⑧ _____
⑨ _____

Total Risk Score _____ **(Sum of Points)**

Mortality Risk _____ **(From Plot)**



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.

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)*

II. 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 min 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 h in patients with UA/NSTEMI for treatment of persistent ischemia, heart failure (HF), 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 h 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 dysfunction or other contraindications. *(Level of Evidence: B)*

7. An ACE inhibitor should be administered orally within the first 24 h 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 less than 100 mm Hg or less than 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

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. *(Level of Evidence: A)* *(See Table 3.)*

3. In women with low-risk features, a conservative strategy is recommended. *(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 *(see 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

Preferred Strategy	Patient Characteristics
Invasive	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 months
	Prior CABG
	High risk score (e.g., TIMI, GRACE)
	Reduced left ventricular function (LVEF less than 40%)
Conservative	Low risk score (e.g., TIMI, GRACE)
	Patient or physician preference in the absence of high-risk features

CABG = 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; **TnT** = troponin T.

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

Feature	High Risk *At least 1 of the following features must be present:*
History	Accelerating tempo of ischemic symptoms in preceding 48 h
Character of pain	Prolonged ongoing (greater than 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 greater than 75 years
ECG	Angina at rest with transient ST-segment changes greater than 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 greater than 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.

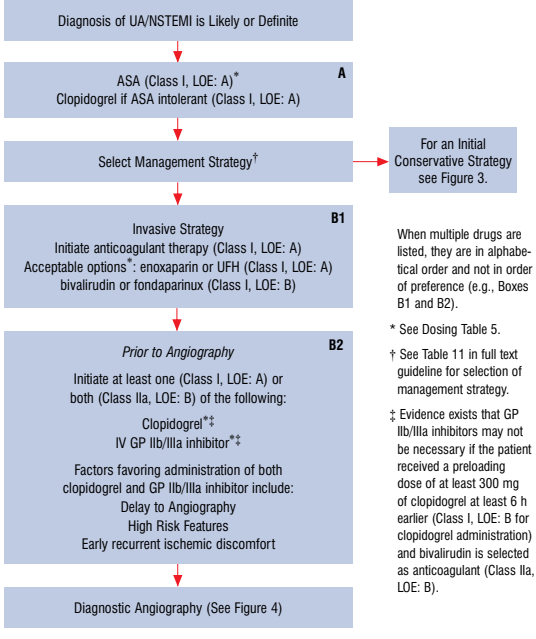
Intermediate Risk *No high-risk feature, but must have 1 of the following:*	**Low Risk** *No high- or intermediate-risk feature but may have any of the following features:*
Prior MI, peripheral or cerebrovascular disease, or CABG; prior aspirin use	
Prolonged (greater than 20 min) rest angina, now resolved, with moderate or high likelihood of CAD Rest angina (greater than 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 weeks without prolonged (greater than 20 min) rest pain but with intermediate or high likelihood of CAD	Increased angina frequency, severity, or duration Angina provoked at a lower threshold New onset angina with onset 2 weeks to 2 months prior to presentation
Age greater than 70 years	
T-wave changes Pathological Q waves or resting ST-depression less than 1 mm in multiple lead groups (anterior, inferior, lateral)	Normal or unchanged ECG
Slightly elevated cardiac TnT, TnI, or CK-MB (e.g., TnT greater than 0.01 but less than 0.1 ng per mL)	Normal

CABG = 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; **TnI** = troponin I; **TnT** = troponin T; **UA/NSTEMI** = unstable angina/non–ST-elevation myocardial infarction.

C. Antiplatelet and Anticoagulation Therapy

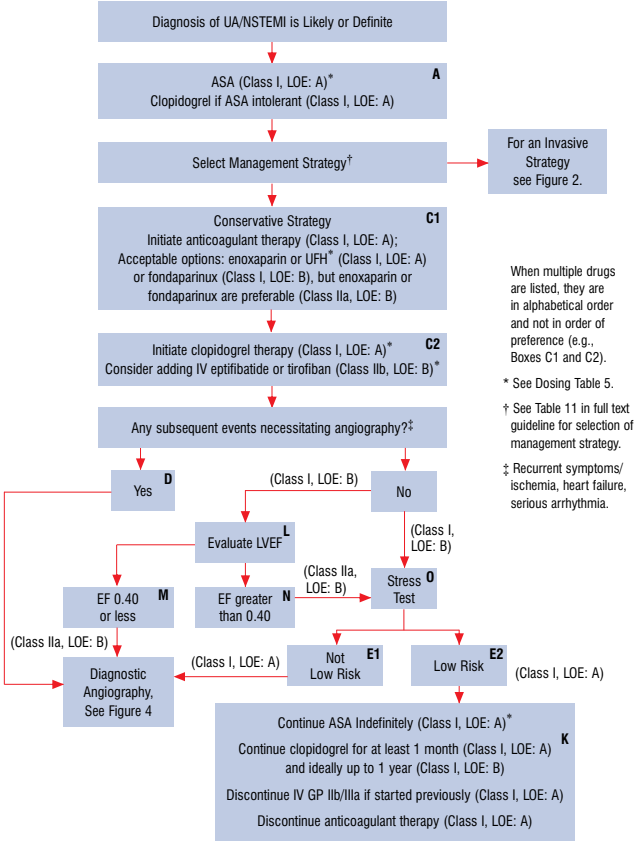
A number of antiplatelet and antithrombotic agents are now available for use in ACS. The decision of which agents to use, when to administer them and at what doses is complex. Please *see Figures 2, 3, 4 and 5* and *Table 5* for guidance.

Figure 2. Algorithm for Patients With UA/NSTEMI Managed by an Initial Invasive Strategy



ASA = aspirin; **GP** = glycoprotein; **IV** = intravenous; **LOE** = level of evidence; **UA/NSTEMI** = unstable angina/non–ST-elevation myocardial infarction; **UFH** = unfractionated heparin.

Figure 3. Algorithm for Patients With UA/NSTEMI Managed by an Initial Conservative Strategy



When multiple drugs are listed, they are in alphabetical order and not in order of preference (e.g., Boxes C1 and C2).

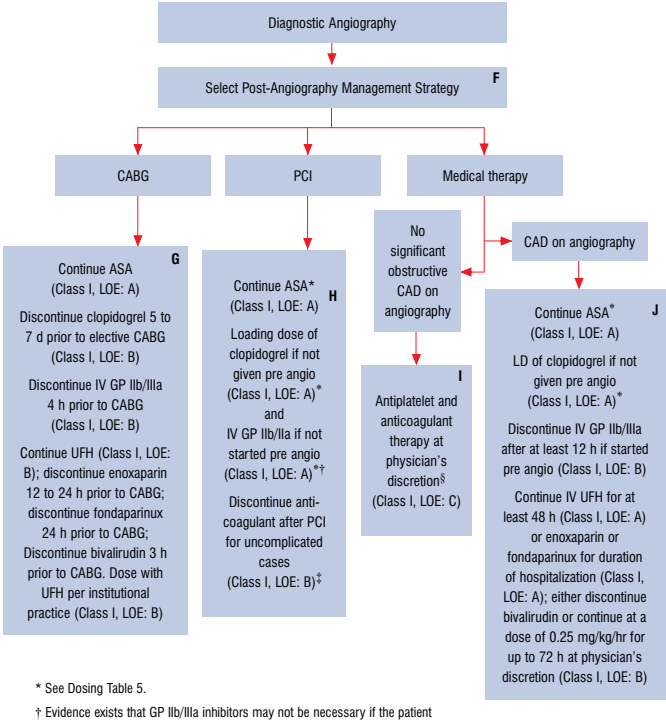
* See Dosing Table 5.

† See Table 11 in full text guideline for selection of management strategy.

‡ Recurrent symptoms/ischemia, heart failure, serious arrhythmia.

ASA = aspirin; **EF** = ejection fraction; **GP** = glycoprotein; **IV** = intravenous; **LOE** = level of evidence; **LVEF** = left ventricular ejection fraction; **UA/NSTEMI** = unstable angina/non–ST-elevation myocardial infarction; **UFH** = unfractionated heparin.

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



* See Dosing Table 5.

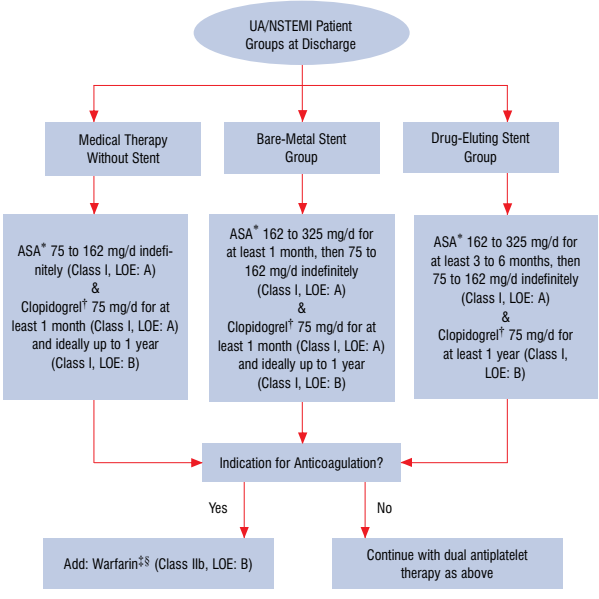
† Evidence exists that GP IIb/IIIa inhibitors may not be necessary if the patient received a preloading dose of at least 300 mg of clopidogrel at least 6 h earlier (Class I, LOE: B for clopidogrel administration) and bivalidrudin is selected as antithrombin (Class IIa, LOE: B).

‡ Additional bolus of UFH is recommended if fondaparinux is selected as antithrombin (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 = 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



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

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

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

§ When warfarin is added to aspirin plus clopidogrel, an INR of 2.0 to 2.5 is recommended.

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 Antiplatelet and Anticoagulant Therapy in Patients With UA/NSTEMI

Drug*	Initial Medical Treatment	During Patient Received Initial Medical Treatment
Oral antiplatelet therapy		
Aspirin	162 to 325 mg nonenteric formulation, orally or chewed	No additional treatment
Clopidogrel	LD of 300 to 600 mg orally MD of 75 mg orally per day	A second LD of 300 mg orally may be given to supplement a prior LD of 300 mg
Ticlopidine	LD of 500 mg orally MD of 250 mg orally twice daily	No additional treatment
Anticoagulants		
Bivalirudin	0.1 mg per kg bolus, 0.25 mg per kg per h infusion	0.5 mg per kg bolus, increase infusion to 1.75 mg per kg per h
Dalteparin	120 IU per kg SC every 12 h (maximum 10,000 IU twice daily)‡	IV GP IIb/IIIa planned: target ACT 200 s using UFH No IV GP IIb/IIIa planned: target ACT 250 to 300 s for HemoTec; 300 to 350 s for Hemochron using UFH
Enoxaparin	LD of 30 mg IV bolus may be given‖ MD=1 mg per kg SC every 12 h‖; extend dosing interval to 1 mg per kg every 24 h if estimated creatinine clearance less than 30 ml per min‖	Last SC dose less than 8 h: no additional treatment Last SC dose greater than 8 h: 0.3 mg per kg IV bolus
Fondaparinux	2.5 mg SC once daily. Avoid for creatinine clearance less than 30 mL per min‖	50 to 60 U per kg IV bolus of UFH is recommended by the OASIS 5 Investigators¶

PCI		
Patient Did Not Receive Initial Medical Treatment	**After PCI**	**At Hospital Discharge**
162 to 325 mg nonenteric formulation orally or chewed	162 to 325 mg daily should be given† for at least 1 month after BMS implantation, 3 months after SES implantation, and 6 months after PES implantation, after which daily chronic aspirin should be continued indefinitely at a dose of 75 to 162 mg	162 to 325 mg daily should be given† for at least 1 month after BMS implantation, 3 months after SES implantation, and 6 months after PES implantation, after which daily chronic aspirin should be continued indefinitely at a dose of 75 to 162 mg
LD of 300 to 600 mg orally	For BMS: 75 mg daily for at least 1 month and ideally up to 1 year. For DES, 75 mg daily for at least 1 year (in patients who are not at high risk of bleeding) (See Figure 5)	For BMS: 75 mg daily for at least 1 month and ideally up to 1 year. For DES, 75 mg daily for at least 1 year (in patients who are not at high risk of bleeding) (See Figure 5)
LD of 500 mg orally	MD of 250 mg orally twice daily (duration same as clopidogrel)	MD of 250 mg orally twice daily (duration same as clopidogrel)
0.75 mg per kg bolus, 1.75 mg per kg per h infusion	No additional treatment or continue infusion for up to 4 hours	
IV GP IIb/IIIa planned: 60 to 70 U per kg§ of UFH No IV GP IIb/IIIa planned: 100 to 140 U per kg of UFH	No additional treatment	
0.5 to 0.75 mg per kg IV bolus	No additional treatment	
50 to 60 U per kg IV bolus of UFH is recommended by the OASIS 5 Investigators¶	No additional treatment	

continued next page

Table 5. Dosing Table for Antiplatelet and Anticoagulant Therapy in Patients With UA/NSTEMI *continued from previous page*

Drug*	Initial Medical Treatment	During: Patient Received Initial Medical Treatment
Anticoagulants cont'd		
Unfractionated heparin	LD of 60 U per kg (max 4,000 U) as IV bolus ‖ MD of IV infusion of 12 U per kg per h (max 1000 U per h) to maintain aPTT at 1.5 to 2.0 times control (approximately 50 to 70 s) ‖	IV GP IIb/IIIa planned: target ACT 200 s No IV GP IIb/IIIa planned: target ACT 250 to 300 s for HemoTec; 300 to 350 s for Hemochron
Intravenous antiplatelet therapy		
Abciximab	Not applicable	Not applicable
Eptifibatide	LD of IV bolus of 180 mcg per kg MD of IV infusion of 2.0 mcg per kg per min; reduce infusion by 50% in patients with estimated creatinine clearance less than 50 mL per min	Continue infusion
Tirofiban	LD of IV infusion of 0.4 mcg per kg per min for 30 min MD of IV infusion of 0.1 mcg per kg per min; reduce rate of infusion by 50% in patients with estimated creatinine clearance less than 30 mL per min	Continue infusion

Additional considerations include the possibility that a conservatively managed patient may develop a need for PCI, in which case an intravenous bolus of 50 to 60 U per kg of UFH is recommended if fondaparinux was given for initial medical treatment; the safety of this drug combination is not well established. For conservatively managed patients in whom enoxaparin was the initial medical treatment, as noted in the table, additional intravenous enoxaparin is an acceptable option.

*This list is in alphabetical order and is not meant to indicate a particular therapy preference † In patients in whom the physician is concerned about the risk of bleeding, a lower initial ASA dose after PCI of 75 to 162 mg/d is reasonable (Class IIa, LOE: C) ‡ Dalteparin was evaluated for management of patients with UA/NSTEMI in an era before the widespread use of important therapies such as stents, clopidogrel, and GP IIb/IIIa inhibitors. Its relative efficacy and safety in the contemporary management era is not well established. § Some operators use less than 60 U per kg of UFH with GP IIb/IIIa blockade, although no clinical trial data exist to demonstrate the efficacy of doses below 60 U per kg in this setting. ‖ For patients

PCI		
Patient Did Not Receive Initial Medical Treatment	**After PCI**	**At Hospital Discharge**
IV GP IIb/IIIa planned: 60 to 70 U per kg§ No IV GP IIb/IIIa planned: 100 to 140 U per kg	No additional treatment	
LD of 0.25 mg per kg IV bolus MD of 0.125 mcg per kg per min (max 10 mcg per min)	Continue MD infusion for 12 h	
LD of IV bolus of 180 mcg per kg followed 10 min later by second IV bolus of 180 mcg per kg MD of 2.0 mcg per kg per min; reduce infusion by 50% in patients with estimated creatinine clearance less than 50 mL per min	Continue MD infusion for 18 to 24 h	
LD of IV infusion of 0.4 mcg per kg per min for 30 min MD of IV infusion of 0.1 mcg per kg per min; reduce rate of infusion by 50% in patients with estimated creatinine clearance less than 30 mL per min	Continue MD infusion for 18 to 24 h	

managed by an initial conservative strategy, agents such as enoxaparin and fondaparinux offer the convenience advantage of SC administration compared with an intravenous infusion of UFH. They are also less likely to provoke heparin-induced thrombocytopenia than UFH. Available data suggest fondaparinux is associated with less bleeding than enoxaparin in conservatively managed patients using the regimens listed. ¶ Personal communication, OASIS 5 Investigators, July 7, 2006. Note that this regimen has not been rigorously tested in prospective randomized trials.

ACT = 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 h. *(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, left ventricular (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 (greater than or equal to 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)*

III. Coronary Revascularization

Recommendations for Revascularization With PCI and CABG in Patients With UA/NSTEMI

Class I

1. An early invasive percutaneous coronary intervention (PCI) strategy is indicated for patients with UA/NSTEMI who have no serious comorbidity and who have coronary lesions amenable to PCI and who have any of the high-risk features listed in *Table 3.*

2. Coronary artery bypass graft (CABG) is recommended for UA/NSTEMI patients with significant left main coronary artery disease (CAD; greater than 50% stenosis). *(Level of Evidence: A)*

3. CABG is recommended for UA/NSTEMI patients with 3-vessel CAD; the survival benefit is greater in patients with abnormal LV function (LVEF less than 0.50). *(Level of Evidence: A)*

4. CABG is recommended for UA/NSTEMI patients with 2-vessel CAD with significant proximal left anterior descending CAD and either abnormal LV function (LVEF less than 0.50) or ischemia on noninvasive testing. *(Level of Evidence: A)*

5. CABG is recommended for UA/NSTEMI patients in whom percutaneous revascularization is not optimal or possible and who have ongoing ischemia not responsive to maximal nonsurgical therapy. *(Level of Evidence: B)*

6. CABG (or PCI) is recommended for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing. *(Level of Evidence: B)*

7. CABG (or PCI) is recommended for UA/NSTEMI patients with multivessel coronary disease with suitable coronary anatomy, normal LV function, and without diabetes mellitus. *(Level of Evidence: A)*

8. An intravenous platelet GP IIb/IIIa inhibitor is generally recommended in UA/NSTEMI patients undergoing PCI. *(Level of Evidence: A)*

See Figures 2, 3, and 4.

Class IIa

1. PCI is reasonable for focal saphenous vein graft lesions or multiple stenoses in UA/NSTEMI patients who are undergoing medical therapy and who are poor candidates for reoperative surgery. *(Level of Evidence: C)*

2. PCI or CABG is reasonable for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a moderate area of viable myocardium and ischemia on noninvasive testing. *(Level of Evidence: B)*

3. PCI or CABG can be beneficial compared with medical therapy for patients with 1-vessel disease

with significant proximal left anterior descending CAD. *(Level of Evidence: B)*

4. Use of PCI is reasonable in patients with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG or require emergent intervention at angiography for hemodynamic instability. *(Level of Evidence: B)*

5. It is reasonable to perform CABG with the internal mammary artery for patients with multivessel disease and treated diabetes mellitus. *(Level of Evidence: B)*

6. Repeat CABG is reasonable for UA/NSTEMI patients with multiple saphenous vein graft stenoses, especially when there is significant stenosis of a graft that supplies the left anterior descending coronary artery. *(Level of Evidence: C)*

7. CABG (or PCI) with stenting is reasonable for patients with multivessel disease and symptomatic myocardial ischemia. *(Level of Evidence: B)*

Class III

1. CABG or PCI is not recommended for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD with no current symptoms or symptoms that are unlikely due to myocardial ischemia and who have no ischemia on noninvasive testing. *(Level of Evidence: C)*

2. In the absence of high-risk features associated with UA/NSTEMI, PCI is not recommended for patients with UA/NSTEMI who have single-vessel or multivessel CAD and no trial of medical therapy, or who have 1 or more of the following:

a. Only a small area of myocardium at risk. *(Level of Evidence: C)*

b. All lesions or the culprit lesion to be dilated with morphology that conveys a low likelihood of success. *(Level of Evidence: C)*

c. A high risk of procedure-related morbidity or mortality. *(Level of Evidence: C)*

d. Insignificant disease (less than 50% coronary stenosis). *(Level of Evidence: C)*

e. Significant left main CAD and candidacy for CABG. *(Level of Evidence: B)*

IV. 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 CAD.

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 for Post-Discharge Therapy

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)*

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 min 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 min 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-min 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. Long-Term Medical Therapy and Secondary Prevention

i. Antiplatelet Therapy

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 (but with gastroprotective agents such as proton-pump inhibitors). *(Level of Evidence: A)*

3. The combination of clopidogrel (75 mg daily) and ASA (75 to 162 mg daily) should be continued for at least 1 month and ideally up to 1 year after UA/NSTEMI treated medically or with bare-metal stents for at least 12 months after treatment with drug eluting stents. *(Level of Evidence: B)*

ii. 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)*

iii. 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 (ejection fraction less than 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 greater than 30 mL per min) or hyperkalemia (potassium should be less than or equal to 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)*

iv. NTG

Class I

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

v. 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.*

vi. Warfarin Therapy

Class I

Use of warfarin in conjunction with ASA and/or clopidogrel is associated with an increased risk of bleeding and should be monitored closely. *(Level of Evidence: A)*

Class IIb

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)

continued next page

may be reasonable for patients at high CAD risk and low bleeding risk who do not require or are intolerant of clopidogrel. *(Level of Evidence: B)*

vii. Lipid Management

Class I

1. The following lipid recommendations are beneficial:

a. Lipid management should include assessment of a fasting lipid profile for all patients, within 24 h of hospitalization. *(Level of Evidence: C)*

b. Hydroxymethyl glutaryl-coenzyme A reductase inhibitors (statins), in the absence of contra-indications, regardless of baseline LDL-C and diet modification, should be given to post-UA/NSTEMI patients, including postrevascularization patients. *(Level of Evidence: A)*

c. For patients with elevated LDL-C (greater than or equal to 100 mg per dL), cholesterol-lowering therapy should be initiated or intensified to achieve an LDL-C of less than 100 mg per dL *(Level of Evidence: A).*

2. Treatment of triglycerides and non–HDL-C is useful, including the following:

a. If triglycerides are 200 to 499 mg per dL, non–HDL-C* 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-C be treated to goal after triglyceride-lowering therapy. Achievement of a non–HDL-C* less than 130 mg per dL (i.e., 30 mg per dL greater than LDL-C target) if possible is recommended. *(Level of Evidence: C)*

Class IIa The following lipid management strategies can be beneficial:

a. Further reduction of LDL-C 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-C to less than 70 mg per dL. *(Level of Evidence: B)*

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

† Patients with very high triglycerides should not consume alcohol. The use of bile acid sequestrants is relatively contraindicated when triglycerides are greater than 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.

viii. Blood Pressure Control

Class I

Blood pressure control to less than 140/90 mm Hg (or less than 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 greater than or equal to 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).*

ix. Diabetes Mellitus

Class I

Diabetes management should include lifestyle and pharmacotherapy measures to achieve a near-normal hemoglobin A_{1c} 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)*

x. Smoking Cessation

Class I 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)*

xi. Weight Management

Class Ia 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 m^2 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)*

xii. 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 min 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)*

xiii Patient Education

Class I Beyond the detailed instructions for daily exercise, patients should be given specific instruction on activities (eg, 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)*

xiv. Influenza

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

xv. Depression

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

xvi. 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)*