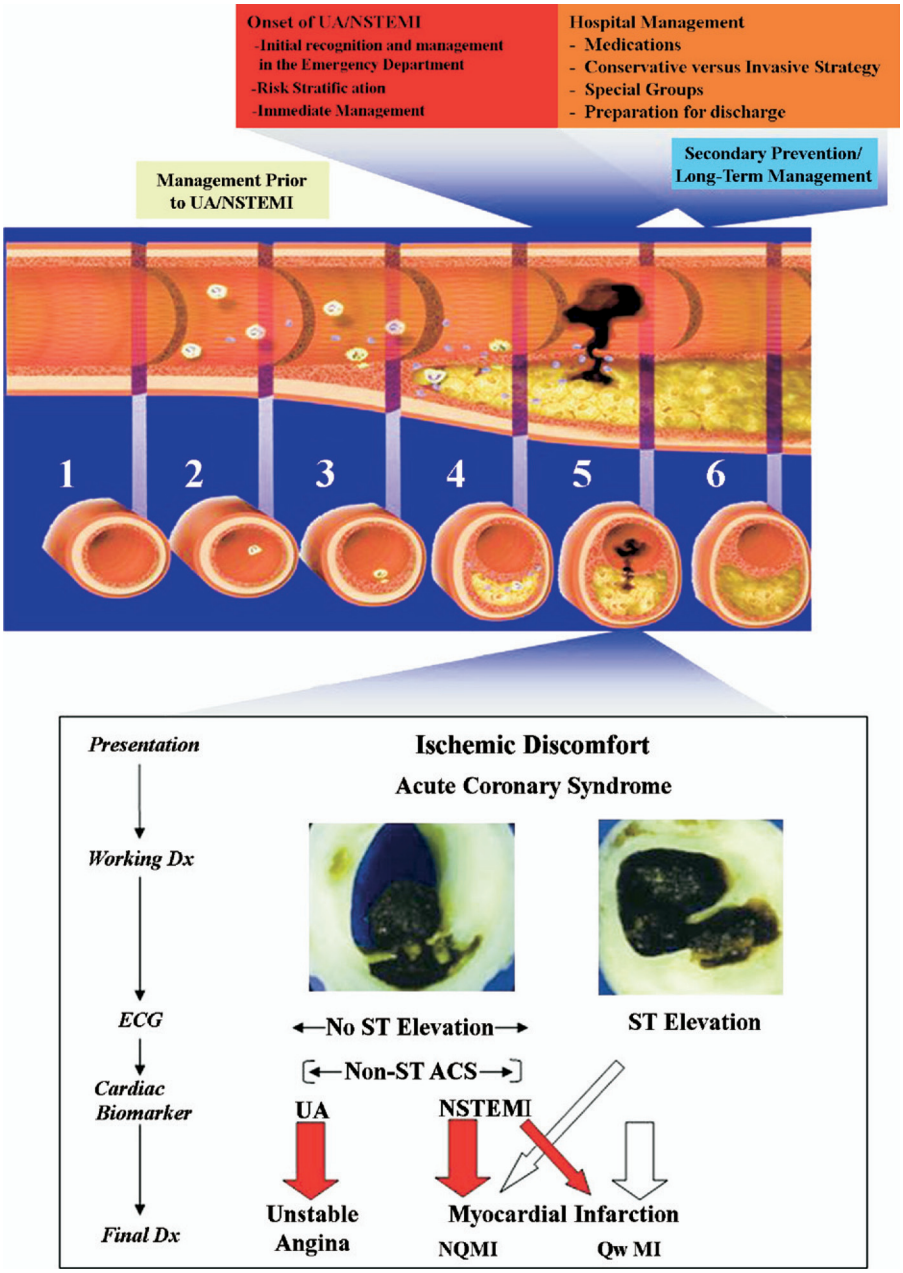

Figure 1. Acute Coronary Syndromes. The top half of the figure illustrates the chronology of the interface between the patient and the clinician through the progression of plaque formation, onset, and complications of UA/NSTEMI, along with relevant management considerations at each stage. The longitudinal section of an artery depicts the "timeline" of atherogenesis from (1) a normal artery to (2) lesion initiation and accumulation of extracellular lipid in the intima, to (3) the evolution to the fibrofatty stage, to (4) lesion progression with procoagulant expression and weakening of the fibrous cap. An acute coronary syndrome (ACS) develops when the vulnerable or high-risk plaque undergoes disruption of the fibrous cap (5); disruption of the plaque is the stimulus for thrombogenesis. Thrombus resorption may be followed by collagen accumulation and smooth muscle cell growth (6). After disruption of a vulnerable or high-risk plaque, patients experience ischemic discomfort that results from a reduction of flow through the affected epicardial coronary artery. The flow reduction may be caused by a completely occlusive thrombus (bottom half, right side) or subtotally occlusive thrombus (bottom half, left side). Patients with ischemic discomfort may present with or without ST-segment elevation on the ECG. Among patients with ST-segment elevation, most (thick white arrow in bottom panel) ultimately develop a Q-wave MI (QwMI), although a few (thin white arrow) develop a non–Q-wave MI (NQMI). Patients who present without ST-segment elevation are suffering from either unstable angina (UA) or a non–ST-segment elevation MI (NSTEMI) (thick red arrows), a distinction that is ultimately made on the basis of the presence or absence of a serum cardiac marker such as CK-MB or a cardiac troponin detected in the blood. Most patients presenting with NSTEMI ultimately develop a NQMI on the ECG; a few may develop a QwMI. The spectrum of clinical presentations ranging from UA through NSTEMI and STEMI is referred to as the acute coronary syndromes. This UA/NSTEMI guideline, as diagrammed in the upper panel, includes sections on initial management before UA/NSTEMI, at the onset of UA/NSTEMI, and during the hospital phase. Secondary prevention and plans for long-term management begin early during the hospital phase of treatment. ∗Positive serum cardiac marker. Modified with permission from Libby P. Current concepts of the pathogenesis of the acute coronary syndromes. Circulation 2001;104:365;(7) © 2001 Lippincott, Williams & Wilkins; The Lancet, 358, Hamm CW, Bertrand M, Braunwald E. Acute coronary syndrome without ST elevation: implementation of new guidelines, 1533–8. Copyright 2001, with permission from Elsevier[8]; and Davies MJ. The pathophysiology of acute coronary syndromes. Heart 2000;83:361–6.[9] © 2000 Lippincott, Williams & Wilkins. CK-MB = MB fraction of creatine kinase; Dx = diagnosis; ECG = electrocardiogram.

Table 4. Three Principal Presentations of UA

Class	Presentation
Rest angina*	Angina occurring at rest and prolonged, usually greater than 20 min
New-onset angina	New-onset angina of at least CCS class III severity
Increasing angina	Previously diagnosed angina that has become distinctly more frequent, longer in duration, or lower in threshold (i.e., increased by 1 or more CCS class to at least CCS class III severity)

*Patients with non-ST-elevated myocardial infarction usually present with angina at rest. Adapted with permission from Braunwald E. Unstable angina: a classification. Circulation 1989;80:410–4.[14]

CCS = Canadian Cardiovascular Society classification; UA = unstable angina.

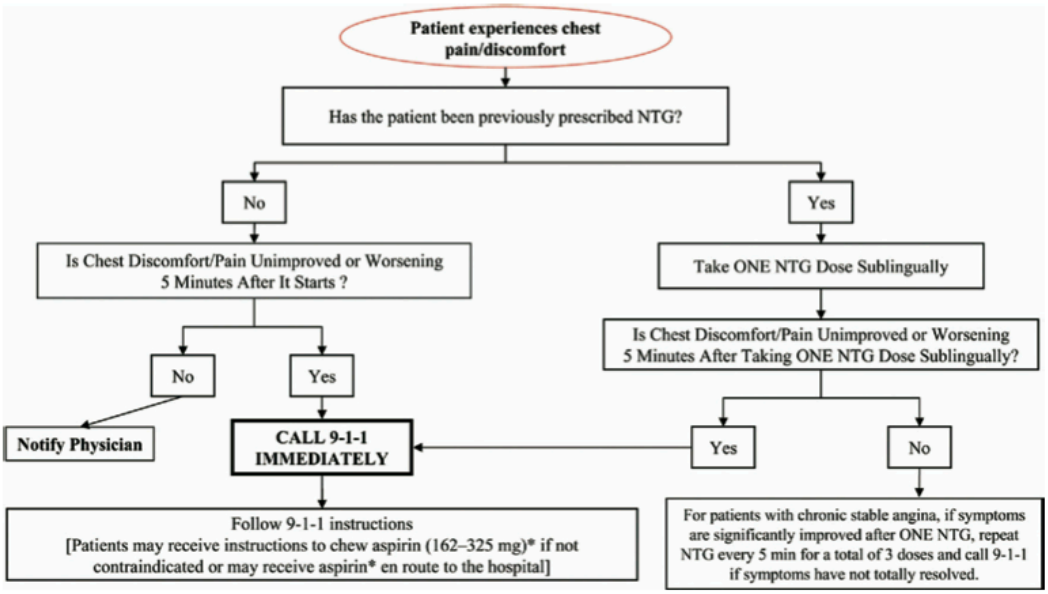

Figure 3. Patient (Advance) Instructions for NTG Use and EMS Contact in the Setting of Non–Trauma-Related Chest Discomfort/Pain. If patients experience chest discomfort/pain and have been previously prescribed NTG and have it available (right side of algorithm), it is recommended that they be instructed (in advance) to take 1 dose of NTG immediately in response to symptoms. If chest discomfort/pain is unimproved or worsening 5 min after taking 1 NTG sublingually, it is recommended that the patient call 9-1-1 immediately to access EMS. In patients with chronic stable angina, if the symptoms are significantly improved after taking 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 totally resolved. If patients are not previously prescribed NTG (left side of algorithm), it is recommended that they call 9-1-1 if chest discomfort/pain is unimproved or worsening 5 min after it starts. If the symptoms subside within 5 min of when they began, patients should notify their physician of the episode. (For those patients with new-onset chest discomfort who have not been prescribed NTG, it is appropriate to discourage them from seeking someone elses NTG [e.g., from a neighbor, friend, or relative].)
*Although some trials have used enteric-coated aspirin for initial dosing, more rapid buccal absorption occurs with non–enteric-coated formulations. EMS = emergency medical services; NTG = nitroglycerin.

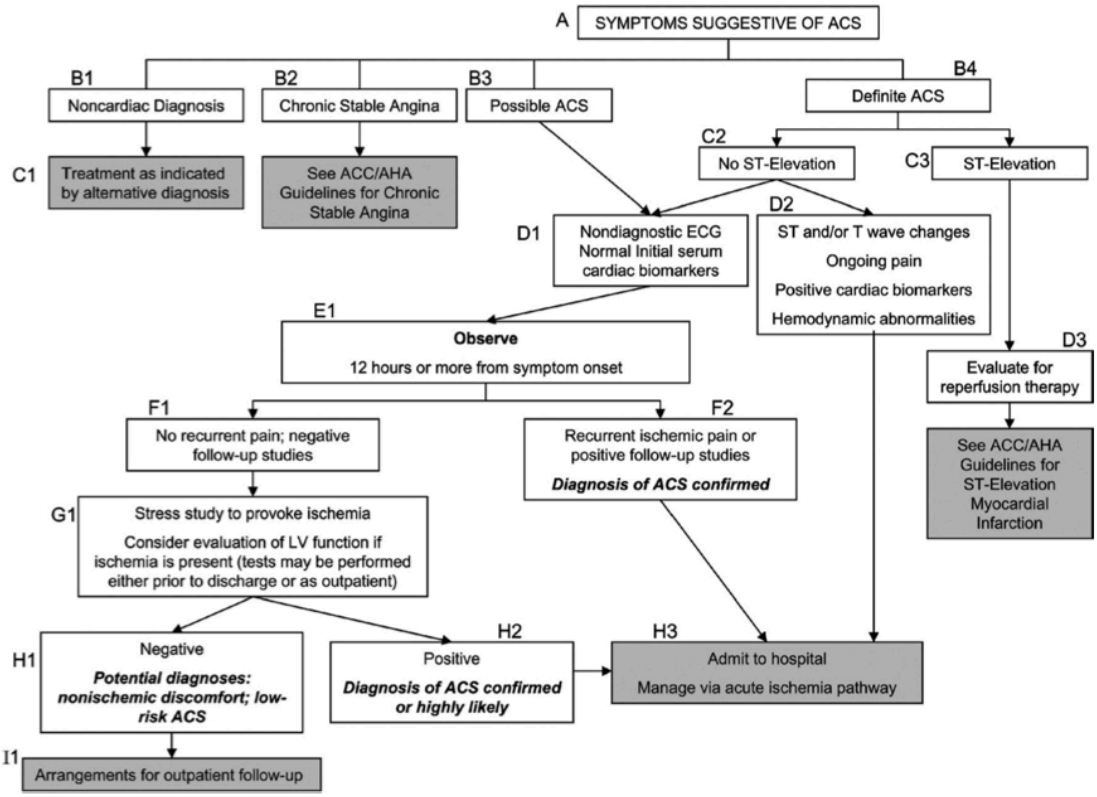

Figure 2. Algorithm for Evaluation and Management of Patients Suspected of Having ACS. To facilitate interpretation of this algorithm and a more detailed discussion in the text, each box is assigned a letter code that reflects its level in the algorithm and a number that is allocated from left to right across the diagram on a given level. ACC/AHA = American College of Cardiology/American Heart Association; ACS = acute coronary syndrome; ECG = electrocardiogram; LV = left ventricular.

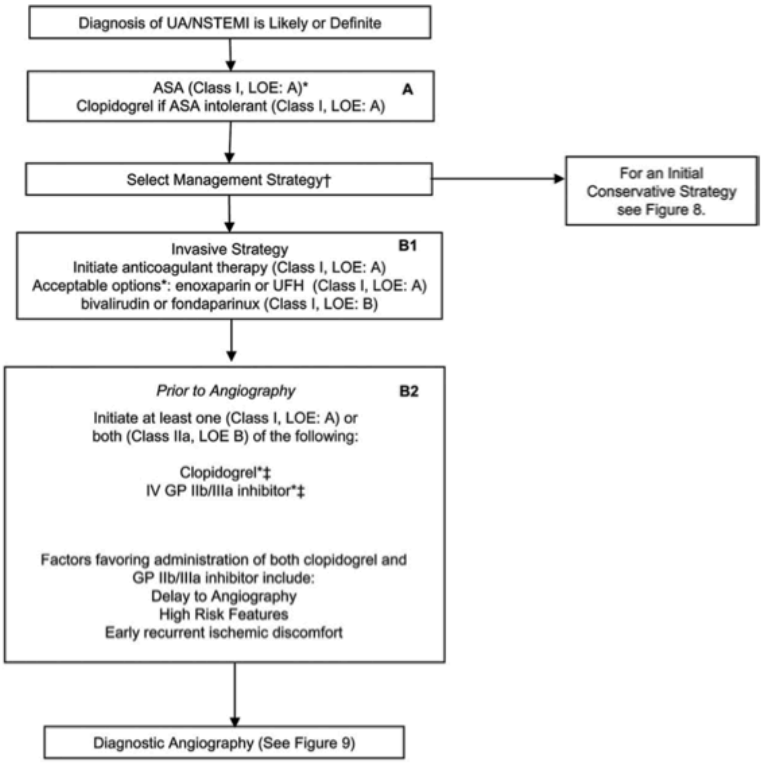

Figure 7. Algorithm for Patients With UA/NSTEMI Managed by an Initial Invasive Strategy. When multiple drugs are listed, they are in alphabetical order and not in order of preference (e.g., Boxes B1 and B2). ∗See dosing Table 13. †See Table 11 for selection of management strategy. ‡Evidence exists that 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, Level of Evidence B for clopidogrel administration) and bivalirudin is selected as the anticoagulant (Class IIa, Level of Evidence B). ASA = aspirin; GP = glycoprotein; IV = intravenous; LOE = level of evidence; UA/NSTEMI = unstable angina/non–ST-elevation myocardial infarction; UFH = unfractionated heparin.

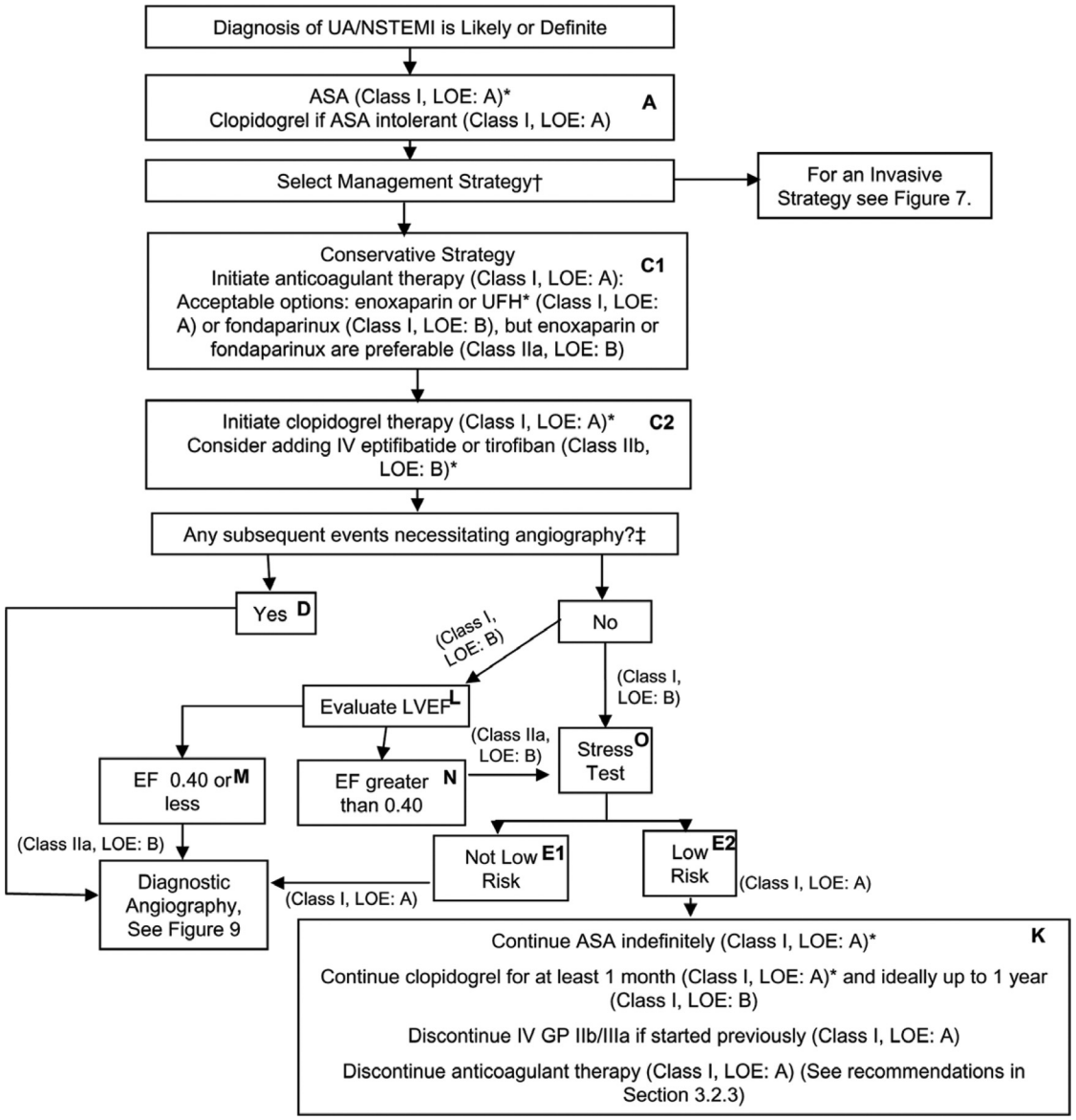

Figure 8. Algorithm for Patients With UA/NSTEMI Managed by an Initial Conservative Strategy. When multiple drugs are listed, they are in alphabetical order and not in order of preference (e.g., Boxes C, C1, and C2). ∗See dosing Table 13. †See Table 11 for selection of management strategy. ‡Recurrent 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.

4. **For UA/NSTEMI patients in whom an initial invasive strategy is selected, antiplatelet therapy in addition to aspirin should be initiated before diagnostic angiography (upstream) with either clopidogrel (loading dose followed by daily maintenance dose)∗ or an intravenous GP IIb/IIIa inhibitor. (*Level of Evidence: A*) Abciximab as the choice for upstream GP IIb/IIIa therapy is indicated only if there is no appreciable delay to angiography and PCI is likely to be performed; otherwise, IV eptifibatide or tirofiban is the preferred choice of GP IIb/IIIa inhibitor. (*Level of Evidence: B*)**
5. **For UA/NSTEMI patients in whom an initial conservative (i.e., noninvasive) strategy is selected (see Section 3.3), clopidogrel (loading dose followed by daily maintenance dose)∗ should be added to ASA and anticoagulant therapy as soon as possible after admission and administered for at least 1 month *(Level of Evidence: A)* and ideally up to 1 year. *(Level of Evidence: B)* (Fig. 8; Box C2)**
6. **For UA/NSTEMI patients in whom an initial conservative strategy is selected, if recurrent symptoms/ische-**

∗Some uncertainty exists about optimum dosing. Randomized trials establishing its efficacy and providing data on bleeding risks used a loading dose of 300 mg orally followed by a daily oral maintenance dose of 75 mg. Higher oral loading doses such as 600 or 900 mg of clopidogrel may more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive efficacy and the safety of higher oral loading doses have not been rigorously established.

Table 5. Grading of Angina Pectoris According to CCS Classification

Class	Description of Stage
I	"Ordinary physical activity does not cause ... angina," such as walking or climbing stairs. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.
II	"Slight limitation of ordinary activity." Angina occurs on walking or climbing stairs rapidly; walking uphill; walking or stair climbing after meals; in cold, in wind, or under emotional stress; or only during the few hours after awakening. Angina occurs on walking more than 2 blocks on the level and climbing more than 1 flight of ordinary stairs at a normal pace and under normal conditions.
III	"Marked limitations of ordinary physical activity." Angina occurs on walking 1 to 2 blocks on the level and climbing 1 flight of stairs under normal conditions and at a normal pace.
IV	"Inability to carry on any physical activity without discomfort—anginal symptoms may be present at rest."

Adapted with permission from Campeau L. Grading of angina pectoris (letter). Circulation 1976;54:522-3.[15]

CCS = Canadian Cardiovascular Society.

Table 6. Likelihood That Signs and Symptoms Represent an ACS Secondary to CAD

Feature	High Likelihood Any of the following:	Intermediate Likelihood *Absence of high-likelihood features and presence of any of the following:*	Low Likelihood *Absence of high- or intermediate-likelihood features but may have:*
History	Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina Known history of CAD, including MI	Chest or left arm pain or discomfort as chief symptom Age greater than 70 years Male sex Diabetes mellitus	Probable ischemic symptoms in absence of any of the intermediate likelihood characteristics Recent cocaine use
Examination	Transient MR murmur, hypotension, diaphoresis, pulmonary edema, or rales	Extracardiac vascular disease	Chest discomfort reproduced by palpation
ECG	New, or presumably new, transient ST-segment deviation (1 mm or greater) or T-wave inversion in multiple precordial leads	Fixed Q waves ST depression 0.5 to 1 mm or T-wave inversion greater than 1 mm	T-wave flattening or inversion less than 1 mm in leads with dominant R waves Normal ECG
Cardiac markers	Elevated cardiac TnI, TnT, or CK-MB	Normal	Normal

Modified with permission from Braunwald E, Mark DB, Jones RH, et al. Unstable angina: diagnosis and management. Rockville, MD: Agency for Health Care Policy and Research and the National Heart, Lung, and Blood Institute, U.S. Public Health Service, U.S. Department of Health and Human Service, 1994. AHCPR publication no. 94-0602.[124]

ACS = acute coronary syndrome; CAD = coronary artery disease; CK-MB = MB fraction of creatine kinase; ECG = electrocardiogram; MI = myocardial infarction; MR = mitral regurgitation; TnI = troponin I; TnT = troponin T.

Table 7. 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:*	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:*
History	Accelerating tempo of ischemic symptoms in preceding 48 h	Prior MI, peripheral or cerebrovascular disease, or CABG; prior aspirin use	
Character of pain	Prolonged ongoing (greater than 20 min) rest pain	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 (see Table 6)	Increased angina frequency, severity, or durationAngina provoked at a lower threshold New onset angina with onset 2 weeks to 2 months prior to presentation
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	Age greater than 70 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	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
Cardiac markers	Elevated cardiac TnT, TnI, or CK-MB (e.g., TnT or TnI greater than 0.1 ng per ml)	Slightly elevated cardiac TnT, TnI, or CK-MB (e.g., TnT greater than 0.01 but less than 0.1 ng per ml)	Normal

*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.[124]

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/nonâ€"ST-elevation myocardial infarction.

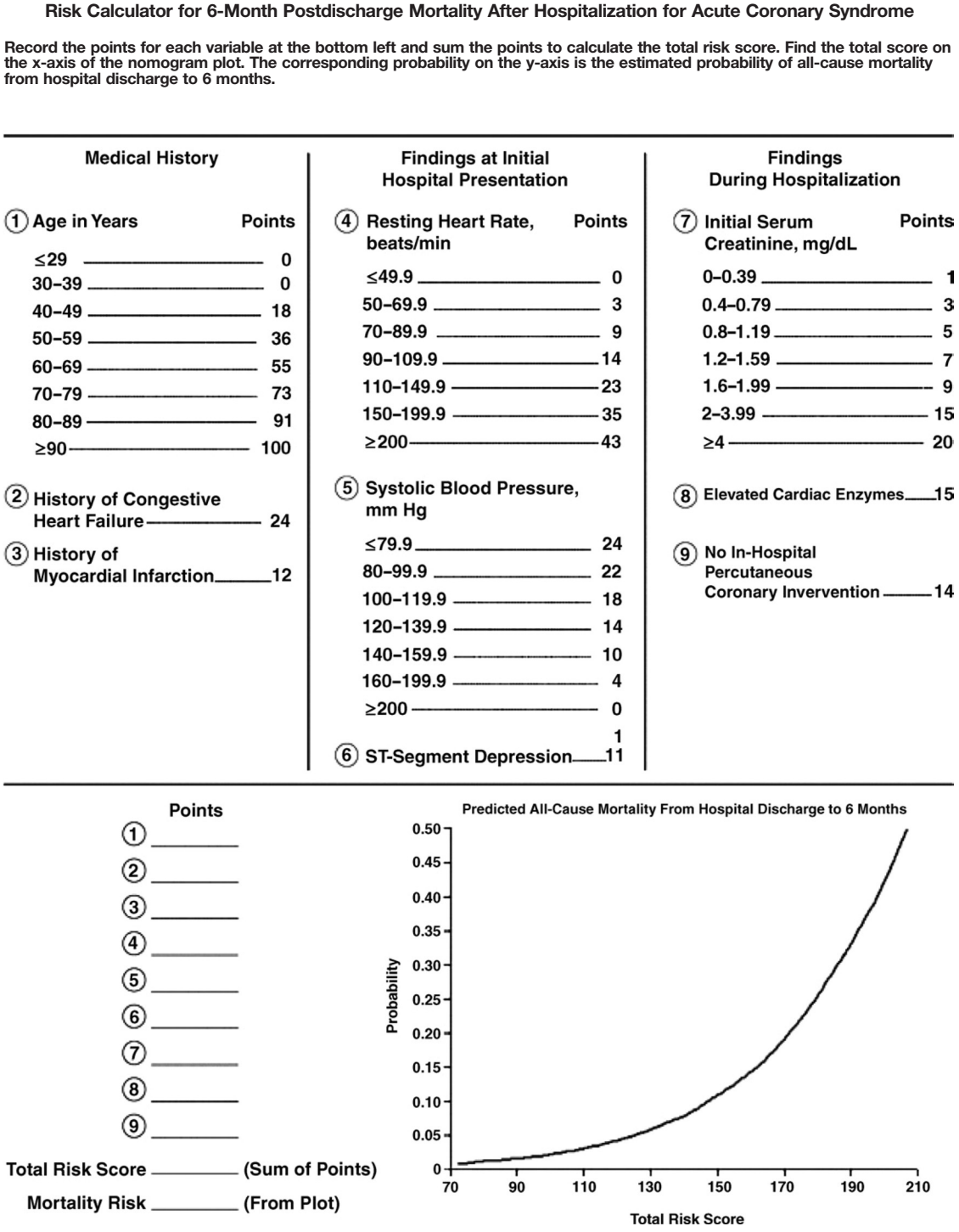

Figure 4. GRACE Prediction Score Card and Nomogram for All-Cause Mortality From Discharge to 6 Months. Reprinted with permission from Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. JAMA 2004;291:2727–33.[168] Copyright © 2004 American Medical Association.

ACS, especially in younger patients (age less than 40 years) and others with few risk factors for CAD. Urine toxicology should be considered when substance abuse is suspected as a cause of or contributor to ACS.

2.2.6. Estimation of Early Risk at Presentation

A number of risk assessment tools have been developed to assist in assessing risk of death and ischemic events in patients with UA/NSTEMI, thereby providing a basis for therapeutic decision making (Table 8; Fig. 4).[158,168,169] It should be recognized that the predictive ability of these commonly used risk assessment scores for nonfatal CHD risk is only moderate.

Antman et al. developed the TIMI risk score,[159] a simple tool composed of 7 (1-point) risk indicators rated on presen-

Table 10. Biochemical Cardiac Markers for the Evaluation and Management of Patients With Suspected ACS But Without ST-Segment Elevation on 12-Lead ECG

Marker	Advantages	Disadvantages	Point-of-Care Test Available?	Comment	Clinical Recommendation
Cardiac troponins	1. Powerful tool for risk stratification 2. Greater sensitivity and specificity than CK-MB 3. Detection of recent MI up to 2 weeks after onset 4. Useful for selection of therapy 5. Detection of reperfusion	1. Low sensitivity in very early phase of MI (less than 6 h after symptom onset) and requires repeat measurement at 8 to 12 h, if negative 2. Limited ability to detect late minor reinfarction	Yes	Data on diagnostic performance and potential therapeutic implications increasingly available from clinical trials	Useful as a single test to efficiently diagnose NSTEMI (including minor myocardial damage), with serial measurements. Clinicians should familiarize themselves with diagnostic "cutoffs" used in their local hospital laboratory
CK-MB	1. Rapid, cost-efficient, accurate assays 2. Ability to detect early reinfarction	1. Loss of specificity in setting of skeletal muscle disease or injury, including surgery 2. Low sensitivity during very early MI (less than 6 h after symptom onset) or later after symptom onset (more than 36 h) and for minor myocardial damage (detectable with troponins)	Yes	Familiar to majority of clinicians	Prior standard and still acceptable diagnostic test in most clinical circumstances
Myoglobin	1. High sensitivity 2. Useful in early detection of MI 3. Detection of reperfusion 4. Most useful in ruling out MI	1. Very low specificity in setting of skeletal muscle injury or disease 2. Rapid return to normal range limits sensitivity for later presentations	Yes	More convenient early marker than CK-MB isoforms because of greater availability of assays for myoglobin; rapid-release kinetics make myoglobin useful for noninvasive monitoring of reperfusion in patients with established MI	

ACS = acute coronary syndrome; CK-MB = MB fraction of creatine kinase; ECG = electrocardiogram; h = hours; MI = myocardial infarction; NSTEMI = non-ST-elevation MI.

published reports, physicians should work with their clinical laboratories to ensure use of and familiarity with contemporary test technology, with appropriate, accurate ranges of normal and diagnostic cutoffs, specific to the assay used.

2.2.9. Other Markers and Multimarker Approaches

Besides markers of myocardial necrosis, markers of pathophysiological mechanisms implicated in ACS are under investigation and could become useful to determine pathophysiology, individualize treatment, and evaluate therapeutic effects. In considering the clinical application of new biomarkers, it is important to determine that they provide incremental value over existing biomarkers. A multimarker approach to risk stratification of UA/NSTEMI (e.g., simultaneous assessment of cTnI, C-reactive protein [CRP], and BNP) has been advocated as a potential advance over single biomarker assessment.[262,263] Further evaluation of a multimarker approach will be of interest.

2.2.9.1. Ischemia

Other new biochemical markers for the detection of myocardial necrosis are either less useful or have been less well studied than those mentioned above. An example is ischemia-modified albumin found soon after transient coronary occlusion and preceding any significant elevations in myoglobin, CK-MB, or cTnI. This modified albumin depends on a reduced capacity of human albumin to bind exogenous cobalt during ischemia.[264,265] Choline is released upon the cleavage of phospholipids and could also serve as a marker of ischemia. Growth-differentiation factor-15 (GDF-15), a member of the transforming growth factor-β cytokine superfamily that is induced after ischemia-and-reperfusion injury,

Table 11. 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.

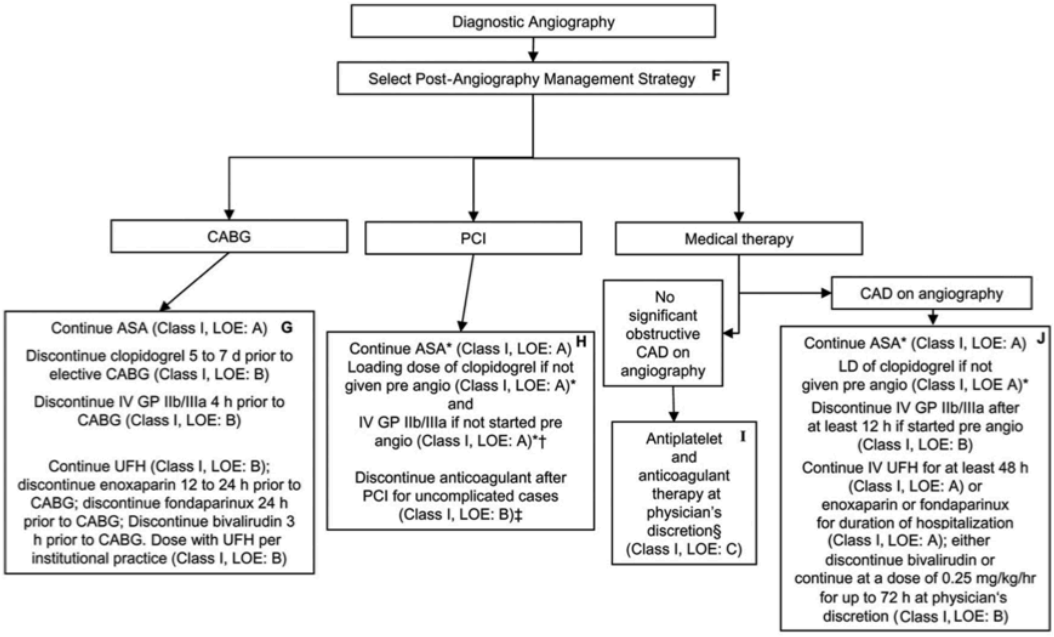

Figure 9. Management After Diagnostic Angiography in Patients With UA/NSTEMI. ∗See dosing Table 13. †Evidence exists that GP IIb/IIIa inhibitors may not be necessary if the patient received a preloading dose of at least 300 mg of clopidogrel at least 6 h earlier (Class I, Level of Evidence B for clopidogrel administration) and bivalirudin is selected as the anticoagulant (Class IIa, Level of Evidence B). ‡Additional bolus of UFH is recommended if fondaparinux is selected as the anticoagulant (see dosing Table 13). §For patients in whom the clinician believes coronary atherosclerosis is present, albeit without any significant, flow-limiting stenoses, 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.

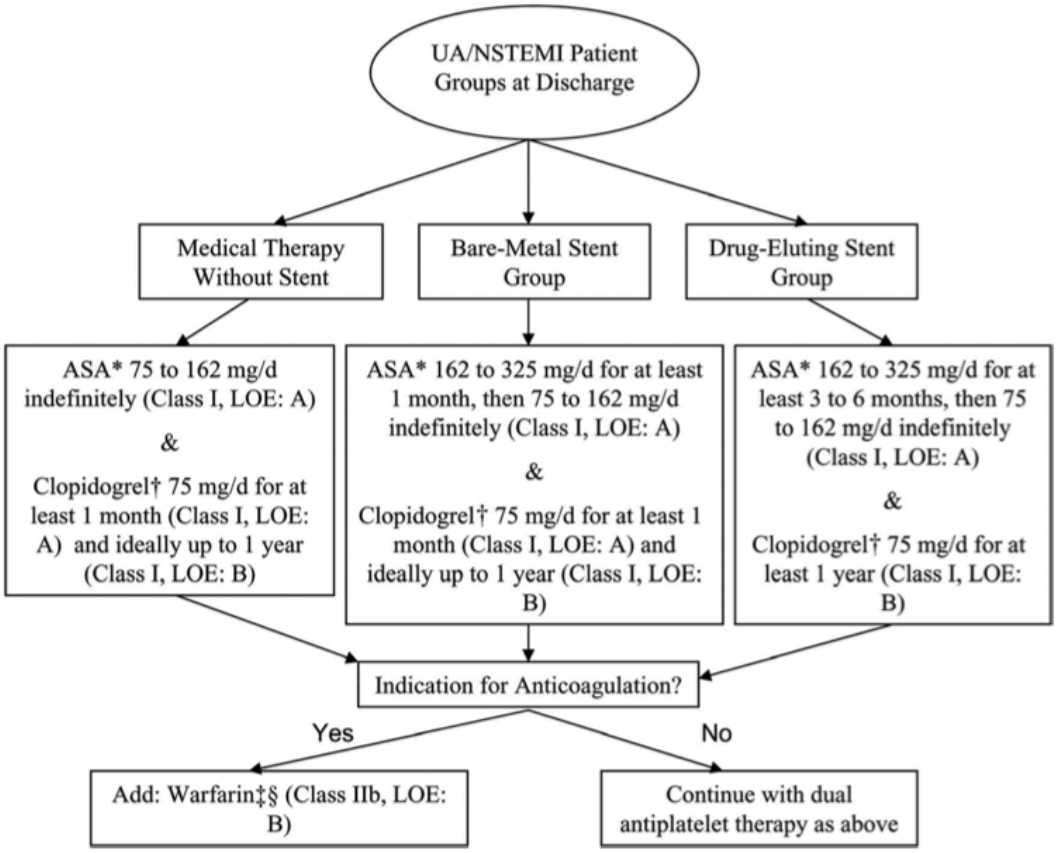

Figure 11. Long-Term Antitcoagulant Therapy at Hospital Discharge After UA/NSTEMI. ∗For aspirin (ASA) allergic patients, use clopidogrel alone (indefinitely), or try aspirin desensitization. †For clopidogrel allergic patients, use ticlopidine, 250 mg by mouth twice daily. ‡Continue ASA indefinitely and 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-elevated myocardial infarction.

Table 19. Noninvasive Risk Stratification

High risk (greater than 3% annual mortality rate)
Severe resting LV dysfunction (LVEF less than 0.35)
High-risk treadmill score (score −11 or less)
Severe exercise LV dysfunction (exercise LVEF less than 0.35)
Stress-induced large perfusion defect (particularly if anterior)
Stress-induced multiple perfusion defects of moderate size
Large, fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)
Stress-induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)
Echocardiographic wall-motion abnormality (involving more than 2 segments) developing at low dose of dobutamine (10 mcg per kg per min or less) or at a low heart rate (less than 120 beats per min)
Stress echocardiographic evidence of extensive ischemia
Intermediate risk (1% to 3% annual mortality rate)
Mild/moderate resting LV dysfunction (LVEF = 0.35 to 0.49)
Intermediate-risk treadmill score (−11 to 5)
Stress-induced moderate perfusion defect without LV dilation or increased lung intake (thallium-201)
Limited stress echocardiographic ischemia with a wall-motion abnormality only at higher doses of dobutamine involving less than or equal to 2 segments
Low risk (less than 1% annual mortality rate)
Low-risk treadmill score (score 5 or greater)
Normal or small myocardial perfusion defect at rest or with stress *
Normal stress echocardiographic wall motion or no change of limited resting wall-motion abnormalities during stress*

*Although the published data are limited, patients with these findings will probably not be at low risk in the presence of either a high-risk treadmill score or severe resting LV dysfunction (LVEF less than 0.35). Reproduced from Table 23 in Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for the Management of Patients With Chronic Stable Angina). 2002. Available at: www.acc.org/qualityandscience/clinical/statements.htm[4]

LV = left ventricular; LVEF = left ventricular ejection fraction.

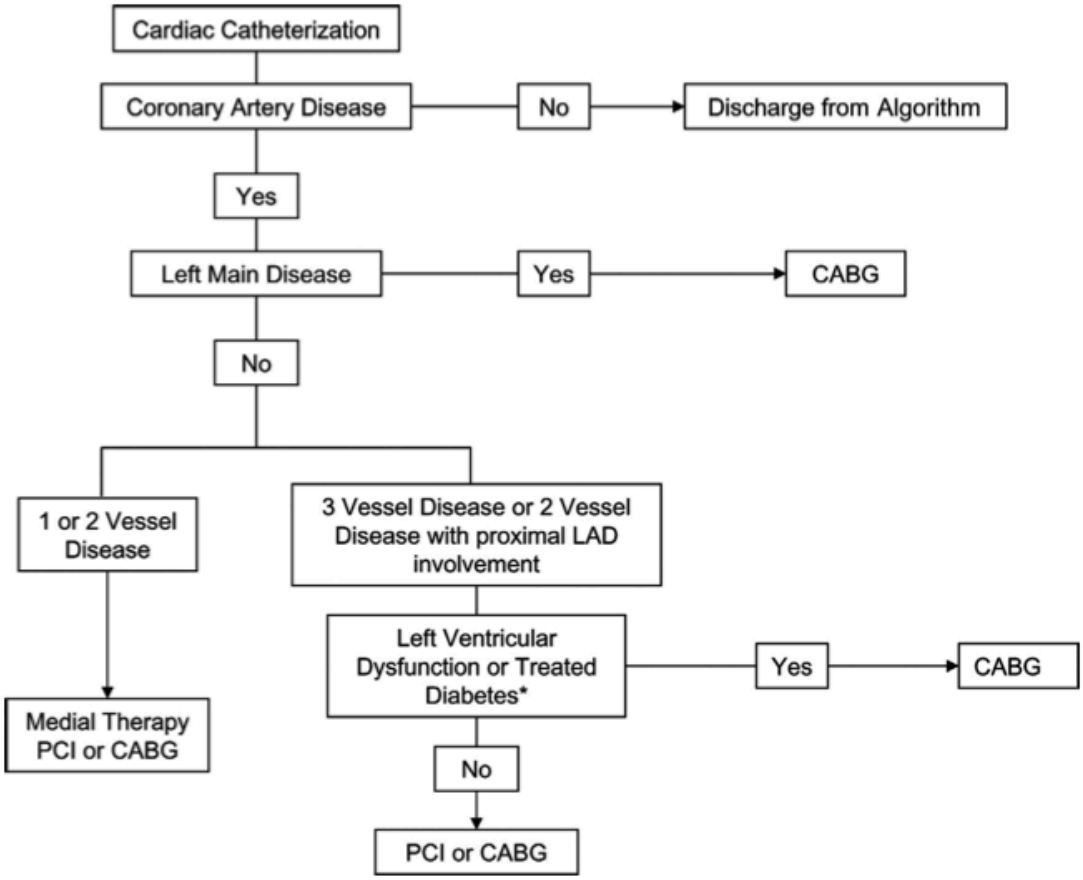

Figure 20. Revascularization Strategy in UA/NSTEMI. ∗There is conflicting information about these patients. Most consider CABG to be preferable to PCI. CABG = coronary artery bypass graft; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention UA/NSTEMI = unstable angina/non–ST-elevation myocardial infarction.

Table 22. Medications Used for Stabilized UA/NSTEMI Patients

Anti-Ischemic and Antithrombotic/Antiplatelet Agents	Drug Action	Class/Level of Evidence
Aspirin	Antiplatelet	I/A
Clopidogrel* or ticlopidine	Antiplatelet when aspirin is contraindicated	I/A
Beta blockers	Anti-ischemic	I/B
ACEI	EF less than 0.40 or HF EF greater than 0.40	I/A IIa/A
Nitrates	Antianginal	I/C for ischemic symptoms
Calcium channel blockers (short-acting dihydropyridine antagonists should be avoided)	Antianginal	I for ischemic symptoms; when beta blockers are not successful (B) or contraindicated, or cause unacceptable side effects (C)
Dipyridamole	Antiplatelet	III/A
Agents for Secondary Prevention and Other Indications	**Risk Factor**	**Class/Level of Evidence**
HMG-CoA reductase inhibitors	LDL cholesterol greater than 70 mg per dL	Ia
Fibrates	HDL cholesterol less than 40 mg per dL	IIa/B
Niacin	HDL cholesterol less than 40 mg per dL	IIa/B
Niacin or fibrate	Triglycerides 200 mg per dL	IIa/B
Antidepressant	Treatment of depression	IIb/B
Treatment of hypertension	Blood pressure greater than 140/90 mm Hg or greater than 130/80 mm Hg if kidney disease or diabetes present	I/A
Hormone therapy (initiation)†	Postmenopausal state	III/A
Treatment of diabetes	HbA_{1C} greater than 7%	I/B
Hormone therapy (continuation)†	Postmenopausal state	III/B
COX-2 inhibitor or NSAID	Chronic pain	IIa/C, IIb/C or III/C
Vitamins C, E, beta-carotene; folic acid, B6, B12	Antioxidant effect; homocysteine lowering	III/A

*Preferred to ticlopidine.

†For risk reduction of coronary artery disease.

ACEI = angiotensin-converting enzyme inhibitor; CHF = congestive heart failure; COX-2 = cyclooxygenase 2; EF = ejection fraction; HDL = high-density lipoprotein; HMG-CoA = hydroxymethyl glutaryl coenzyme A; INR = international normalized ratio; LDL = low-density lipoprotein; NSAID = nonsteroidal anti-inflammatory drug; NSTEMI = non–ST-segment elevation myocardial infarction; UA = unstable angina.