

**UCLA CHEST PAIN  
AND  
ACS PATIENT MANAGEMENT  
GUIDELINE**

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UCLA Medical Center  
Los Angeles, California

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## I. Introduction

Acute coronary syndromes (ACS) most often result from disruption of an atherosclerotic plaque and the subsequent cascade of pathologic processes that critically decrease coronary blood flow. The certainty of diagnosis, severity of symptoms, hemodynamic state, medical history, electrocardiogram (ECG), and biomarkers will determine the choice and timing of therapies used in individual patients. Patients with ST segment elevation acute myocardial infarction (STEMI) require rapid initiation of therapy aimed at achieving reperfusion, and cardiovascular (CV) protective medications. Patients with unstable angina (UA)/non-STEMI (NSTEMI) require comprehensive medical therapy to prevent the evolution to MI/death. Intermediate- and high-risk patients should undergo early invasive management, and low-risk patients should undergo stress testing to further risk stratify. Once stabilized, these patients require longer-term risk stratification and secondary prevention measures. Patients with chest pain that is not due to cardiac disease need the etiology to be determined, and inpatient or outpatient medical follow-up. This guideline describes principles of patient care derived from systematic analysis of scientific literature, expert opinion, the 2002 ACC/AHA ACS Clinical Practice Guideline, the 2004 ACC/AHA STEMI Guideline, and the AHCPR Clinical Practice Guideline for UA. The diagnostic and management strategies recommended are designed to be efficacious, efficient, reasonable, and as safe as possible given the current state of medical knowledge.

This management guideline assigns patients to three diagnostic and management categories:

***Chest Pain***

***UA/NSTEMI***

***STEMI***

## II. Definitions

***Chest Pain:*** Patients without evidence of acute MI (AMI) or active myocardial ischemia on ECG with chest pain that is not definite angina. These patients are defined as not having features that give them an intermediate or high likelihood of significant coronary artery disease (CAD).

***UA:*** Patients without evidence of AMI who have chest pain (or other symptoms that may represent ischemia) and are felt to have an intermediate or high likelihood of significant CAD.

***NSTEMI:*** Patients with chest pain or other symptoms suggestive of ischemia, usually with evidence of ischemia on ECG, with elevated cardiac enzymes in a pattern consistent with infarction. Patients with ischemic ECG changes that persist for more than 30 minutes (refractory UA) are included in this category.

***STEMI:*** Patients with symptoms suggestive of MI and an ECG with an ST segment elevation of 1 mm or more in two contiguous leads or left bundle branch block (LBBB).

### III. Diagnosis

Diagnosis of ACS depends on a directed clinical history, physical examination, and immediate reading of a resting 12-lead ECG. The ECG provides crucial information in the diagnosis of STEMI and NSTEMI. In patients with chest pain, assessment of the likelihood of CAD, the patient's hemodynamic stability, biomarkers, and the risk of adverse outcome will determine the choice and timing of patient management strategies.

The major factors in the initial history and physical exam that relate to the likelihood of CAD are:

- Chest pain assessment by physician (definite angina, probable angina, probably not angina, and not angina)
- Prior MI or documented CAD
- Number of risk factors (diabetes, smoking, hypercholesterolemia, hypertension, postmenopausal)
- Age

The nature, intensity, character, location, onset, and duration of chest pain should be determined from the history and documented in the medical record. *Assessment of angina should conclude with a summary statement of the patient's symptoms to one of the following four categories: definite angina, probable angina, probably not angina, not angina.* Response to nitroglycerin (NTG) should be noted. Associated symptoms should also be documented. Sharp, stabbing, or pleuritic qualities of chest pain, although making an ischemic etiology less likely, do not completely exclude an ischemic etiology. In the Multicenter Chest Pain Study, acute ischemia was diagnosed in 22% of patients presenting with sharp or stabbing pain, 13% with some pleuritic qualities, and 7% of patients with pain fully reproduced with palpation. Patients with diabetes mellitus, women, and the elderly often present with atypical symptoms, and these patients require a higher level of suspicion.

**ECG:** The ECG is crucial in the diagnosis of UA/NSTEMI and STEMI. A recording should be made and reviewed by the physician within 5 minutes of the patient with chest pain (or other symptoms suggestive of ischemia) arriving in the emergency department (ED). ST segment elevation  $\geq 1$  mm in two or more contiguous leads strongly suggests AMI. ST depression typically signifies ischemia or NSTEMI. A completely normal ECG in the ED does not exclude acute ischemic heart disease. Of patients with chest pain and an entirely normal ECG, 1%-6% will eventually prove to have an AMI and 4% or more will have UA.

- Diagnostic criteria for STEMI:
  - $\geq 1$  mm ST segment elevation in 2 or more contiguous limb or precordial leads
  - LBBB, not known to be old
- ECG findings useful for establishing the likelihood of CAD/ACS:
  - ST segment depression  $\geq 1$  mm
  - Inverted T-waves  $\geq 1$  mm in two or more contiguous leads

*Patients who have sustained symptoms in the absence of a diagnostic ECG should have the ECG repeated within 20 to 30 minutes.* Evidence of ischemia or infarction may develop within this period. Patients who present with chest pain and evidence of ischemia on ECG should have a repeat ECG when their chest pain is relieved to ensure that ECG evidence of ischemia has resolved. This allows identification of patients with resolution of symptoms but persistent silent ischemia.

### **Summary: Estimating the Likelihood of CAD:**

Symptom characteristics, the presence of CAD risk factors, and ECG findings should be combined to estimate a patient's likelihood of having CAD:

#### Likelihood of significant CAD in patients with symptoms suggesting ACS:

The estimated likelihood of significant CAD is used to classify patients into the chest pain and UA/NSTEMI diagnostic and management categories. Biomarkers (cardiac troponin and B-type natriuretic peptide [BNP]) can be used to further improve the diagnostic probabilities. Patients presenting with symptoms categorized as having a low likelihood of disease and negative initial biomarkers can be treated in the chest pain algorithm. Patients with intermediate or high likelihood of disease can be further stratified by their risk assessment.

#### **Low Likelihood:** (eg, 1%-14% likelihood)

- Chest pain, "probably not angina" in patients with one or no risk factors, but not diabetes
- T-wave flat or inverted <1 mm
- Normal ECG

#### **Intermediate Likelihood:** (eg, 15%-84% likelihood)

- "Definite angina" in patients with no risk factors for CAD
- "Probable angina" in patients with 1 or more risk factors
- "Probably not angina" in patients with diabetes or with two or three other risk factors
- Patients with extracardiac vascular disease
- ST depression .5-1 mm
- T-wave inversion of  $\geq 1$  mm

#### **High Likelihood:** (eg, 85%-99% likelihood)

- Known history of prior MI or CAD
- "Definite angina" in males  $\geq 60$  or females  $\geq 70$
- Transient hemodynamic or ECG changes during pain
- ST segment elevation or depression of  $\geq 1$  mm
- Marked symmetrical T-wave inversion in multiple leads

## **IV. Risk Assessment**

Acute chest pain carries a risk of morbidity and mortality that is largely determined by the clinical syndrome at the time of presentation.

#### **Short-term risk of death or nonfatal MI in patients with symptoms suggesting ACS:**

##### **Low risk:**

- Nonresting angina with increased frequency, severity, or duration
- Angina provoked at a lower threshold
- Recent-onset angina over last 2 weeks to 2 months
- Normal or unchanged ECG

### **Intermediate risk:**

- Rest angina now resolved
- Rest angina <20 minutes in duration, angina with dynamic T-wave changes
- New-onset angina <2 weeks at minimal exertion
- Age >65 years
- Q-waves or ST segment depression on ECG

### **High risk:**

- Ongoing rest pain >20 minutes
- Angina with pulmonary edema, S3, or rales. Angina with new or worsening mitral regurgitation (MR)
- Rest angina with dynamic ST segment changes  $\geq 1$  mm
- Angina with hypotension

Patients with intermediate or high likelihood of disease presenting in the low-risk category and in the absence of elevated biomarkers may be treated in the chest pain algorithm. Patients with intermediate or high risk or with elevated biomarkers should be treated in the UA/NSTEMI algorithm.

This risk of death or a recurrent cardiac event following an episode of acute coronary insufficiency is time dependent: the risk is highest at the time of presentation and falls rapidly over time. Patients with ACS have a risk of cardiac death of 5% at the time of presentation when untreated. This risk then declines markedly over time. By 6 months after presentation, patients with ACS have a risk that is indistinguishable from patients with chronic stable angina (.2% risk of cardiac death per month).

### **TIMI Risk Score**

A 7-point risk score for ACS patients was developed and validated to predict the risk of death, (re)infarction, or recurrent severe ischemia requiring revascularization. The score is defined as the simple sum of the following prognostic variables:

1. Age  $\geq 65$  years
2. More than 3 coronary risk factors
3. Prior angiographic coronary obstruction
4. ST segment deviation
5. More than 2 angina events within 24 hours
6. Use of ASA (aspirin) within 7 days
7. Elevated cardiac markers

### **Overall risk assessment in patients with ACS**

The most important factors related to short-term and long-term survival in patients with ACS are:

1. Cardiac troponin I (TnI) and BNP
2. Left ventricular function (LVEF)
3. Extent of CAD
4. Age
5. Comorbid conditions
6. Unmodified coronary risk factors

Cardiac troponin and BNP are strong independent risk predictors of early and late events and mortality. Left ventricular function is also a strong predictor of subsequent cardiac death in patients with ACS. BNP adds independent prognostication to the LVEF. The extent of CAD defines both the likelihood of an acute event and the likelihood of ischemic myocardium at a distance and/or lack of collateral supply. Advanced age is an independent risk factor relating to lower functional reserve. Important comorbid conditions include renal failure, chronic obstructive lung disease, cerebral vascular disease, and malignancy. Unmodified risk factors such as ongoing smoking or untreated hypercholesterolemia leave patients at a substantially higher risk of mortality.

## V. Initial Evaluation and Treatment

The intensity and urgency of care must be appropriately matched with the severity of the presenting symptoms. Rapidly identifying patients with a STEMI is an urgent initial objective, as time to reperfusion therapy is an important determinate of outcome. For all patients, antithrombotic and antiischemic therapy should be instituted promptly in the ED as soon as the working diagnosis of ACS is established.

The initial evaluation consists of the directed history, a focused physical examination, an ECG, and laboratory testing for biomarkers (cardiac troponin and BNP). Patients can be stratified into the 3 diagnostic categories: STEMI, UA/NSTEMI, and chest pain.

### A. STEMI

Patients with ongoing chest pain or symptoms having components typical of myocardial ischemia or infarction of  $\leq 12$  hours of duration, in conjunction with a diagnostic ECG ( $\geq 1$  mm ST segment elevation in two or more contiguous limb or precordial leads or LBBB not known to be old), meet diagnostic criteria for STEMI; the Coronary Lysis on Time (CLOT) team should be activated immediately for primary percutaneous coronary intervention (PCI) (page CCU fellow on call). Patients with resolution of chest pain but ST segment elevation on ECG and those with resolution of ST segment elevation should still be considered for direct catheterization. The fundamental goal in these patients is the rapid initiation of therapy aimed at complete reperfusion.

A 12-lead ECG should be performed and shown to an experienced emergency physician within 5 minutes of ED arrival for all patients with chest discomfort or any other symptom that may indicate STEMI.

Patients with cardiogenic shock, sustained ventricular arrhythmia, complete heart block, pulmonary edema, or loss of consciousness should also be suspected of having a STEMI, and 12-lead ECG should be promptly assessed for ST segment elevation on ECG.

The treatment of STEMI is detailed in the UCLA STEMI Guideline. Initial management is briefly summarized.

1. Activate the CLOT team by paging CCU fellow on call.
2. All patients should receive regular ASA (325 mg) as soon as possible unless a definite contraindication is present (evidence of ongoing life-threatening hemorrhage or a clear history of severe hypersensitivity to ASA). Have patient chew the ASA. All patients should receive clopidogrel (600-mg dose) in combination with ASA unless contraindicated, and unless it is suspected that they have acute pericarditis, aortic dissection, or will need to undergo emergent coronary artery bypass grafting (CABG)/other surgery. If ASA allergic, use clopidogrel (600-mg loading dose) alone.

3. Patients in whom acute pericarditis or aortic dissection is not suspected, and who have no evidence of major or life-threatening hemorrhage, and no significant predisposition to hemorrhage, should be given an intravenous bolus of heparin or subcutaneous low-molecular weight heparin.
4. Patients without contraindications should be treated with intravenous followed by oral beta-blockers (exclude patients with cardiogenic shock, hypotension, symptomatic bradycardia, 2nd- or 3rd-degree heart block or decompensated heart failure [HF] prior to treatment).
5. Patients with ongoing chest pain or HF despite sublingual (SL) NTG, and beta-blockers, with SBP >90 mm Hg, should be started on an intravenous NTG drip.
6. The rapid initiation of therapy aimed at reperfusion (direct catheterization or thrombolytic therapy) should not be delayed. Direct catheterization is the preferred treatment strategy.

Echocardiography can be very helpful in patients for whom the initial diagnosis is unclear, and to distinguish between pericarditis, pulmonary embolization (PE), or infarction. In patients suspected of having a thoracic aortic dissection, transthoracic echocardiography followed by transesophageal echocardiography or chest CT scanning are the preferred diagnostic strategies, as this represents a surgical emergency. In patients with clear evidence of ischemia or infarction and in whom alternative diagnoses are unlikely, initiation of therapy aimed at reperfusion should not be delayed to obtain echocardiography.

The goal is to perform primary PCI within 90 minutes of patient arrival in STEMI patients. This requires rapid diagnosis and emergent notification of the CCU fellow on call to activate the CLOT team.

## **B. UA/NSTEMI**

Patients with intermediate or high likelihood of disease with intermediate- or high-risk features should be treated in the UA/NSTEMI algorithm. The severity of ACS symptoms, ECG evidence of ischemia, and initial cardiac enzymes will dictate the initial intensity of therapy.

### ***General care***

**Monitoring:** Patients should remain on continuous ECG monitoring for ischemia and arrhythmia detection

**Oxygen:** Patients with obvious cyanosis, respiratory distress, or high-risk features should receive supplemental oxygen. A finger pulse oximeter check should be used to confirm adequate oxygenation. If pulse oximeter saturation is <92% or if abnormalities in ventilation (ie, exchange of carbon dioxide) are suspected, full assessment, including arterial blood gas determination, should be considered prior to initiating oxygen. Routine use of oxygen in all patients is not indicated

**Activity:** Patients should be placed on bed rest during the initial phase of medical management

**Diet:** Patients should remain NPO, except for medications, until clinical stability is demonstrated and the necessity/timing of cardiac catheterization is determined

Patients with medically refractory chest pain associated with ischemic ECG changes that persist for >30 minutes (refractory UA/NSTEMI) should be included in this category and treated expeditiously using the direct catheterization strategy.

### Laboratory Testing

- ECG initially, with ongoing or recurrent symptoms, with relief of chest pain, and 6 hours after admission
- CBC with platelets
- PT, INR, PTT
- Serum electrolytes, creatinine (Cr), glucose
- Lipid panel on admission (nonfasting) unless patient has had a recent determination
- Hemoglobin A<sub>1c</sub> (screen for diabetes or assess control in diagnosed diabetics)
- TnI q6 hours x 2 and CK-MB should be measured q8 hours x 3 (omit 2nd/3rd CK-MB if 6-hour TnI is negative)
- BNP
- High-sensitivity C-reactive protein (hs-CRP) (optional)

### Cardiac Enzymes

Cardiac TnI is specific for cardiac tissue and is detected in the serum only if myocardial injury has occurred. A radioimmunoassay for cardiac TnI is now available; this test has improved sensitivity and specificity over CK-MB in the diagnosis and exclusion of myocardial injury. The TnI assay allows early identification and stratification of patients with chest pain suggestive of ischemia, allows identification of patients that present 48 hours to 6 days after infarction, and identifies patients with false positive elevations in CK-MB (such as in rhabdomyolysis).

Because TnI increases to a first peak value 40 times the detection limit versus CK-MB, only 6-9 times, there are not the borderline cases where, although the CK-MB has started to rise early, it has not yet exceeded the upper limit of normal (hence the need for the 3rd [16 hour] CK-MB measurement). By 6 hours after symptom onset using TnI, there is a 98% detection of patients who are ultimately shown to have an MI. In addition, the troponin assay is a powerful, independent mortality risk marker in patients who present with AMI.

The prognostic value of TnI in ACS has also been shown with the troponin assay, appearing to be a more sensitive indicator of myocardial cell injury than CK-MB. In the TIMI III study of 1,404 patients with ACS, the mortality rate was significantly higher in the patients with TnI >.5 ng/ml (3.7%) than in the patients with levels <.5 ng/ml (1%)  $P<.001$ . There were significant increases in mortality with increasing levels of cardiac TnI (troponin <.5 ng/ml, mortality 1%; .5-1.0 ng/ml, 1.7%; 1-5 ng/ml, 3.6%; >5 ng/ml, 6.8%). The troponin assay thus detects small amounts of myocardial injury (microinfarcts) missed by CK-MB and predicts which patients will otherwise have adverse outcomes despite ruling out for infarction by CK-MB (allowing the physician to identify which patients will benefit from intensified medical therapy and early invasive management).

There are other causes of myocardial injury besides coronary plaque rupture. Since the troponin assay is ultra-sensitive, troponin elevation may be seen in decompensated HF, myocarditis, hypoperfusion (syncope, prolonged tachycardias), and other types of myocardial injury. All troponin elevations are not MIs. Patient clinical presentation, ECG, and other findings need to be carefully considered.

BNP and hs-CRP have also been shown to provide independent prognostic information in ACS patients. A total of 450 patients in OPUS-TIMI 16 had assessment of troponin, BNP, and hs-CRP biomarkers, obtained at the time of enrollment. In a multivariable model that included each biomarker—an elevated TnI (hazard ratio [HR] 1.8,  $P=.038$ ), CRP (HR 1.5,  $P=.045$ ), and BNP (HR 2.1,  $P=.001$ )—each was an independent predictor of the composite endpoint of death, MI, or HF. This approach was validated in 1,635 patients from TACTICS-TIMI 18. In a multivariable model containing all 3 biomarkers, an elevated TnI (odds ratio [OR] 2.1,  $P=.001$ ), CRP (OR 1.5,  $P=.025$ ), and BNP (OR 1.6,  $P=.019$ )—each was an independent predictor of the composite endpoint of death, MI, or HF through 6 months. Categorizing patients on the basis of the number of elevated biomarkers at presentation, 31% had elevations in none of the biomarkers, 44% had an elevation in one, 20% had elevations in two, and 5% had elevations in all three. A statistically significant association was observed between the number of elevated biomarkers and mortality at 30 days ( $P<.0001$ ), with a doubling in mortality risk for each additional biomarker that was elevated.

Patients without elevation of either the TnI or BNP biomarker  $<100$  pg/ml on initial presentation, and without an ECG diagnostic for infarction, may be considered lower risk and appropriate for the chest pain service. Patients with BNP results between 100–400 pg/ml may also be appropriate for this service in the absence of clinical symptoms of acutely decompensated HF or PE.

### **Initial Pharmacologic Treatment**

- 1. Antiplatelet Therapy:** The combination of antiplatelet therapy with clopidogrel and ASA is recommended in all patients without contraindications (except patients receiving thrombolytics). All patients should receive regular ASA 325 mg as soon as possible unless a definite contraindication is present (evidence of ongoing life-threatening hemorrhage or a clear history of severe hypersensitivity to ASA). The initial ASA should be chewed and given even if the patient reports daily use. ASA should be continued daily (81–162 mg) thereafter, unless CAD is excluded and primary prevention is not indicated or a contraindication to ASA develops. All patients should receive clopidogrel—600 mg first dose, followed by 75 mg daily in combination with ASA. Clopidogrel should be held in patients thought likely to require emergent CABG or other surgery. Patients unable to take ASA because of a history of true hypersensitivity or recent significant ASA-induced gastrointestinal (GI) bleeding may be started on clopidogrel—600 mg first dose, followed by 75 mg daily alone. It takes up to 3 days for the maximal antiplatelet effect if a loading dose is not used. *Meta-analysis of the four largest randomized, placebo-controlled studies suggests that ASA reduces the risk of MI by 48% and the risk of death by 51% in UA. The CURE trial demonstrated that major CV events (CV death, nonfatal MI, and stroke) are reduced an additional 20% with clopidogrel plus ASA compared with ASA alone in ACS patients. More recent data support a 600-mg loading dose for more rapid onset of antiplatelet effect.*
- 2. Intravenous Heparin or Low-Molecular Weight Heparin** should be started as soon as a diagnosis of intermediate- or high-risk UA, NSTEMI, or STEMI is made. In low-risk patients, the risk–benefit ratio for heparin therapy should be considered. The initial dose of unfractionated heparin is 71 units/kg by IV bolus followed by a constant infusion of 14 units/kg/hr maintaining the activated partial thromboplastin time at 1.8 to 2.5 control (see Heparin Protocol). Alternately, enoxaparin in a dose of 1 mg/kg q12h SQ may be given. Heparin should be continued for 48–72 hours or until revascularization is performed. Heme-positive stool, without overt GI bleeding, is not a contraindication to heparin. Patients are at increased risk for recurrent ischemia in the first 24 hours that heparin is discontinued. *Five randomized studies demonstrate that heparin reduces the risk of developing MI in patients with UA. ASA, clopidogrel, and heparin's benefit in combination is suggested from the available studies and is strongly recommended as initial therapy. In the ESSENCE Trial, enoxaparin was more effective than unfractionated heparin in preventing coronary events in patients with UA and non-Q-wave MI. In A to Z and SYNERGY, there was no difference in outcome.*

3. **Beta-Blockers** should be started in all patients, in the absence of contraindications. The intravenous form should be used to initiate therapy in high-risk patients, but the oral form can be used in intermediate- and low-risk patients. Assess patient to ensure no shock or decompensated HF before administration. In the presence of precautions such as existing pulmonary disease, LV dysfunction (LVD), and bradycardia, initial selection should favor a lower dose. A history of mild or moderate chronic obstructive pulmonary disease (COPD) or asthma should prompt a trial of a short-acting agent at a reduced dose rather than complete avoidance of beta-blocker therapy. Contraindications are cardiogenic shock, hypotension, symptomatic bradycardia, 2nd- or 3rd-degree heart block without a pacemaker, until these conditions resolve. Diabetes and peripheral vascular disease are not contraindications. The target resting heart rate for beta-blockade is 50-60 beats per minute. IV metoprolol is given in 5-mg increments by slow (over 1-2 minutes) IV administration repeated every 5 minutes for a total initial dose of 15 mg followed in 1 to 2 hours by 25-50 mg by mouth every 6 hours. For patients with preserved LV function, use metoprolol or atenolol. For patients with LVD with or without HF symptoms, carvedilol is preferred. Starting doses: metoprolol 50 mg BID, carvedilol 6.25 mg BID. Titrate to target dose as tolerated (or dose below target that is best tolerated). Target doses: metoprolol 100 mg BID, carvedilol 25 mg BID. *Beta-blockers reduce the risk of progression to AMI, reduce HF, arrhythmias, and improve survival in patients with ACS.*
4. **Glycoprotein IIb/IIIa Receptor Antagonists** are indicated in patients undergoing PCI for ACS, in addition to therapy with ASA, clopidogrel, and heparin. Abciximab has been shown to reduce the risk of MI or death in patients undergoing coronary interventions, and meta-analysis/individual clinical trials demonstrated a 20% risk reduction with the small molecule platelet receptor antagonists eptifibatid and tirofiban in patients undergoing coronary intervention. Benefit is seen predominately in troponin-positive patients undergoing PCI. In patients not undergoing PCI, these agents have failed to lower the risk of clinical events. Thus, glycoprotein (GP) IIb/IIIa use is, in general, not recommended. These agents are usually started in the catheterization laboratory, but may be started in troponin-positive ACS patients in whom PCI is planned. See UCLA GP IIb/IIIa Receptor Antagonist Guideline for further details.
5. **ACE Inhibitors** are indicated in all patients with ACS, in the absence of contraindications. These agents have potent vascular and cardiac protective effects. Patients with AMI have improved early survival and less HF when treated with ACE inhibitors (ACEIs). Treatment should start within 12-24 hours, and benefit is seen within 48 hours. ACEI treatment is not recommended in the first 12 hours of AMI, to avoid early hypotension. Contraindications include history of angioedema, cardiogenic shock, hypotension, hyperkalemia, and pregnancy. Renal insufficiency in the setting of AMI is a double indication for ACEIs. The benefit of ACEIs is independent of BP or ventricular function status. Start at low dose and titrate up to clinical trial target doses. Angiotensin receptor antagonists should be used only in ACEI-intolerant patients.
6. **Statins** are indicated in all patients with ACS, irrespective of baseline LDL cholesterol. These agents have potent vascular and cardiac protective effects. Statins reduce vascular inflammation and stabilize the vulnerable atherosclerotic plaque, thereby markedly reducing the risk of vascular events. These benefits are seen in patients with cholesterol and LDL levels in the low, normal, and high range, so it is not necessary to await lipid level results prior to initiation. Clinical trials have shown mortality reduction in patients with baseline LDL levels of  $\geq 70$  mg/dL. Initiation of statin therapy in patients with ACS results in a reduction in MI, UA, stroke, need for revascularization, hospitalization, and all-cause mortality compared with patients treated with diet alone. This is true regardless of whether the patient has undergone CABG, PTCA, or is being treated medically. *These benefits are seen early, such that patients should be started on therapy within the first 24 hours of hospitalization.* Early benefits (within 8-16 weeks) can be seen in patients presenting with ACS

when started on immediate high-dose statin treatment as shown in MIRACL. PROVE-IT demonstrated greater benefits of initiating high-dose potent statin therapy as compared with a moderate-dose, less-potent statin, irrespective of baseline LDL. Use potent statin agents at a high dose (ie, atorvastatin 80 mg daily). Adherence is markedly improved with in-hospital initiation.

7. **Aldosterone Antagonists** are indicated in patients with AMI and LVEF  $\leq 40$  and who have signs or symptoms of HF, in the absence of contraindications. These agents attenuate remodeling and have been demonstrated to benefit patients with AMI with LVD with HF symptoms. Patients should be clinically stabilized prior to initiation of the aldosterone antagonist. This therapy is only indicated in patients with systolic dysfunction (LVEF  $\leq 40$ ), not all ACS patients. Start at a low dose and monitor potassium levels and renal function very closely (48 hours, 1 week, and 4 weeks). Hyperkalemia is an absolute contraindication. Use extreme caution if Cr  $>2.5$  mg/dL in men and  $>2$  mg/dL in women. Consider starting spironolactone at 6.25 mg PO daily with a target dose of no more than 25 mg daily. Eplerenone dosing is 25 mg daily (starting dose) with a target dose of 50 mg daily. *The EPHEBUS trial demonstrated a 15% reduction in mortality with the selective aldosterone antagonist eplerenone in AMI patients with LVEF  $<40\%$  with HF signs or symptoms.*
8. **NTG** should be administered sublingually to patients with chest pain promptly at the time of presentation and every five minutes. Patients whose symptoms are not fully relieved with three SL NTG tablets and initiation of beta-blocker therapy should be started on IV NTG. Patients with recurrent chest pain and at high risk for UA should also be started if their BP permits. With recurrent or ongoing chest pain, readminister SL NTG and increase IV NTG drip. Hypotension with IV NTG may require fluid administration after assessment of the patient's volume status. Patients without ongoing or refractory symptoms may receive topical or oral nitrates. Patients on IV NTG should be switched to oral or topical nitrate therapy once they have been symptom free for 24 hours. Nitrates do not routinely need to be continued beyond 48-72 hours in patients who do not have symptomatic angina. *There are no randomized studies of nitrates in UA and the use of this agent is extrapolated. Nitrate use beyond 24 hours after MI has not been shown to prolong survival or prevent recurrent coronary events.*
9. **Morphine Sulfate** can be considered for patients whose symptoms are not relieved with NTG and beta-blockers unless contraindicated by hypotension, respiratory insufficiency, or intolerance. Morphine sulfate has potent analgesic and anxiolytic effects, as well as hemodynamic effects that are potentially beneficial in UA. Morphine may mask ischemic symptoms and may not be appropriate in situations in which recurrent symptoms will alter the choice and timing of therapy.
10. **Calcium Channel Blockers** should, in general, be avoided in patients with ACS. Patients with UA that is accompanied by atrial fibrillation with rapid ventricular response who have not responded or have contraindications to beta-blockers may benefit from the short-term administration of a calcium channel blocker. *Randomized prospective studies have demonstrated an increased risk of MI or death with calcium channel blockers in patients with UA.*
11. **Thrombolytic Therapy** is not indicated in patients who do not have evidence of acute ST segment elevation or LBBB on their 12-lead ECG. *A meta-analysis of the 8 available trials show no improvement in outcome with thrombolytic therapy in patients with UA/NSTEMI.*
12. **Intra-aortic Balloon Counterpulsation (IABP)** is indicated in ACS patients who have symptoms refractory to aggressive medical management or hemodynamic instability as a bridge to stabilize the patient while being evaluated for or undergoing revascularization. IABP is contraindicated in patients with moderate or severe aortic regurgitation.

## Management Strategies

There are two alternative treatment strategies for patients with UA/NSTEMI. They are termed early invasive and early conservative. In the early invasive strategy, cardiac catheterization is performed routinely in all hospitalized patients without contraindications. In the early conservative strategy, cardiac catheterization is performed only for persistent or recurrent chest pain, HF or depressed LV function, malignant ventricular arrhythmia, or physiologic stress testing indicating high risk.

### Early invasive management

ACS patients with prior MI, PTCA, or CABG, history of HF or LVD, or persistent or recurrent chest pain/ischemia should undergo cardiac catheterization/early invasive management as the initial diagnostic and treatment strategy.

Early invasive management has been shown to be superior to conservative management in patients with intermediate- or high-risk features (TIMI risk score 3 or higher) who are potential candidates for revascularization. Early invasive management was particularly beneficial in patients with elevated troponin. In contrast, patients without elevated troponins could be equally well managed with either an invasive or conservative strategy. High-risk patients with elevated troponins should undergo cardiac catheterization in the first few hours of their hospital stay, allowing for early risk stratification and early application of definitive revascularization. Low- to intermediate-risk patients, who are hemodynamically stable and chest pain free with borderline troponins, may have catheterization performed in the first 12-24 hours of hospitalization. Cardiac catheterization can be performed safely early in the setting of acute ischemia and infarction. There is no need to delay catheterization while waiting to see if the patient rules in or rules out for MI. This strategy improves efficiency in management.

An early invasive strategy in patients with UA/NSTEMI who have any of the following high-risk indicators, in the absence of contraindications to revascularization, is highly recommended:

1. Recurrent angina/ischemia at rest with low-level activities despite intensive antiischemic therapy
2. Elevated cardiac TnI or troponin T
3. New or presumably new ST segment depression
4. Recurrent angina/ischemia with HF symptoms, and S3 gallop, pulmonary edema, worsening rales, or new or worsening mitral regurgitation
5. LVEF  $\leq$ .40
6. Hemodynamic instability
7. Sustained ventricular tachycardia
8. PCI within 6 months or prior CABG

*In the TIMI IIIB study, 1,473 patients with UA were randomized to the alternative strategies. At 45 days, 15.5% of the early invasive patients had cardiac events versus 17.7% of the early conservative patients. The conservatively managed patients had a significantly increased incidence of recurrent ischemia and rehospitalization. In FRISC II and TACTICS-TIMI 18, the early invasive strategy was associated with a lower rate of MI and death, with significant benefit in intermediate- and high-risk patients. In ISAR-COOL, PCI in the first 2-3 hours of hospitalization was associated with better outcomes than a more delayed PCI strategy (3-5 days) was used.*

An alternative strategy for low- and selected intermediate-risk patients is to perform physiologic stress testing and to catheterize only those patients with a high-risk stress test result. Troponin-positive patients derive the greatest benefit with the invasive strategy. However, there are other potential etiologies for troponin elevations such as HF, stroke, or PE. Thus, elevated troponin in isolation does not determine the need for catheterization, but must be put in the proper clinical context.

Patients without elevation of either the TnI or BNP (<100 pg/mL) biomarker on initial presentation and without an ECG diagnostic for infarction or ischemia, may be considered lower risk and appropriate for the chest pain service (see algorithm). Patients with BNP results between 100 and 400 pg/mL may also be appropriate for this service in the absence of clinical symptoms of acutely decompensated HF or PE.

Patients that present with symptoms without a diagnostic ECG and that are TnI assay and BNP negative initially, and troponin negative at 6 hours (and are chest pain free, without dynamic ischemia on ECG), may be considered good candidates for discharge with stress testing performed on an outpatient basis. Alternatively, early inpatient stress testing may be utilized. While patients with negative troponins/BNP/ECGs are at low risk for early events, they may still have significant CAD and long-term risk or other significant conditions. Further evaluation with stress testing to risk stratify patients is indicated. Patients who are TnI positive (in the appropriate clinical setting of ACS) may be better served to have early catheterization.

### Diagnostic Algorithms

#### Patient with chest pain suspicious for UA or AMI

ECG	diagnostic for STEMI	direct cath
	nondiagnostic	TnI/BNP (sent from ED STAT)
TnI	positive	early invasive management
	negative	UA/NSTEMI management
BNP	positive (>400 pg/mL)	ACS/HF/PE differential dx (high risk)
	positive (100-400 pg/mL)	ACS/HF/PE differential dx (intermediate risk)
	negative (<100 pg/mL)	UA/NSTEMI management

#### Patient admitted for UA/rule out MI who remains clinically stable for 6 hours

ECG	evolving infarction	direct cath
	nondiagnostic	TnI (sent 6 hours from admit)
TnI	positive	early invasive management
	negative	early inpatient stress testing or discharge for outpatient stress test within 72 hours

**Echocardiography** (2D) can be helpful in the stratification of patients with ongoing or recurrent symptoms in whom diagnostic ECG changes for ischemia or infarction are absent. Normal left ventricular function and the absence of wall motion abnormalities on echocardiography during chest pain, while not excluding an ischemic etiology for the symptoms, identifies patients at low short-term risk for a major cardiac event.

## ***Revascularization***

The findings at cardiac catheterization can serve to guide the choice of therapy: revascularization versus medical management. The extent of CAD angiographically along with the extent of LVD can identify patients who benefit from revascularization with CABG. In patients with less extensive disease and intermediate-grade lesions of questionable physiologic significance, stress testing should be employed to help guide the choice of therapy.

Patients found at catheterization to have significant left main disease ( $\geq 50\%$ ) or significant ( $\geq 70\%$ ) three-vessel disease with depressed LV function ( $EF < .50$ ) should be considered for early/immediate CABG. If the patient has received clopidogrel, surgery should be delayed for 5 days, unless the benefits of early revascularization are believed to outweigh the increased bleeding risk.

Patients with two-vessel disease, which includes a proximal severe stenosis ( $>90\%$ ) of the left anterior descending (LAD) vessel, and depressed LV function should also be considered for early CABG surgery.

Patients with significant CAD should be considered for prompt revascularization (PCI or CABG) if they have any of the following: failure to stabilize with medical treatment; recurrent angina/ischemia at rest or with low-level activities; and/or ischemia accompanied by HF symptoms, and S3 gallop, new or worsened MR, or marked ECG changes. Patients with elevated troponins in the ACS setting benefit from PCI.

Acute revascularization is indicated for patients with refractory pain ( $>1$  hour on aggressive medical therapy) who are found at catheterization to have an acutely occluded major coronary vessel or severe subtotal occlusion of a culprit vessel. Patients requiring emergent CABG should undergo surgery irrespective of having received clopidogrel. Patients requiring nonurgent CABG should have surgery delayed for 5 days off clopidogrel.

In patients with significant CAD not included in the above recommendations, performing PCI and/or stenting on the culprit lesion at the time of initial presentation of ACS has been shown to be superior. Alternately, aggressive medical therapy without revascularization can be utilized as the initial strategy if a culprit lesion is not clear.

## ***C. Chest Pain***

Patients with chest pain or symptoms that possibly represent ischemia who are judged in the initial evaluation phase to have a low likelihood of disease or to be at low risk for adverse outcomes and without elevation in initial TnI and BNP can be safely evaluated further on the Chest Pain Service. These patients may be admitted for an initial observation period and in the absence of recurrent symptoms undergo early physiologic stress testing or be discharged for outpatient stress testing. Alternately, in select cases these patients may be discharged directly for outpatient stress testing.

### ***Chest Pain Inpatient or Observational Care***

Patients who are judged at initial evaluation to have a low risk for adverse outcomes who are admitted to the hospital for observation or in whom after an initial observation period are reassessed to be at low risk should undergo expeditious diagnostic assessment. These patients should receive ASA as part of their initial therapy. Use of clopidogrel and heparin should be determined on an individual basis.

Patients who remain chest pain free, have no ischemic changes on their ECG, have two negative troponins 6 hours apart, and who demonstrate no hemodynamic or arrhythmic instability are candidates for outpatient stress testing. The patients may be discharged home on ASA with prn SL NTG and scheduled for outpatient stress testing within 72 hours. Treatments to reduce the patient's long-term CV risk should also be provided, as indicated.

### Initial Therapy:

**ASA:** All patients without contraindications should be started on ASA (consider clopidogrel)

**NTG SL:** Prescription and instructions on the prn use should be given

**Appointment** for stress testing within 72 hours

These patients should have a follow-up appointment within 72 hours. Exercise or pharmacologic stress testing should be an integral part of the outpatient evaluation of low-risk patients with chest pain. Testing should be done within 72 hours of presentation. Patients should have explicit written instructions as to the importance of the follow-up evaluation and to re-present immediately if chest pain recurs. Care should be taken to help to ensure that stress testing takes place **within 72 hours** and that patients are not lost to follow-up.

Patients with established CAD who are already on medical therapy and are felt to be appropriate candidates for outpatient management should have their medical regimen reviewed and dosages increased as appropriate and as tolerated.

As an alternative, early inpatient stress testing may be performed. The safety of performing stress testing 6 to 12 hours after admission has been demonstrated in a number of clinical studies. The chances of a clinically significant event being precipitated with stress testing has been shown to be very low in this setting. Early stress testing may also allow for earlier identification of the patient who is having an electrocardiographically silent ischemia at a time when they may still benefit from acute revascularization.

To expedite the patient's work-up and improve efficiency, the patient's management should be planned for in advance, communicated to the nurse, and discussed in detail with the patient and family members, and any potential delays anticipated. Stress testing can be tentatively scheduled on an inpatient basis to occur 7 hours after the patient is admitted or, alternately, on an outpatient basis to occur within 72 hours. The cardiac catheterization laboratory should be informed that a potential diagnostic catheterization may be required when the results of stress testing are available. Patients should be kept NPO, except for medications, 4-6 hours prior to stress testing so that diagnostic catheterization can be performed the same day as the stress test is obtained, if an invasive evaluation is indicated. Discharge needs and follow-up should be addressed early so that patients with negative or low-risk results can be discharged home expeditiously.

Patients with **high-risk results** on physiologic stress testing should be referred for cardiac catheterization. Patients with CAD but low- or intermediate-risk results on physiologic stress testing may be started on anti-anginal medical therapy, being referred for catheterization only if their symptoms are refractory to maximal medical therapy or medical therapy is not well tolerated.

## VI. Noninvasive Testing

Physiologic stress testing has prognostic value in chest pain and UA to predict death and MI. Exercise or pharmacologic stress testing should generally be an integral part of the inpatient or outpatient evaluation of low-risk patients with chest pain or UA. Choice of initial stress testing modality should be based on an evaluation of the patient's resting ECG, his or her physical ability to perform exercise, and the imaging modality that is the most readily available. Choice among the different imaging modalities that can be used with exercise or pharmacologic stress testing can be based on cost and accessibility of results since expertise in echocardiography and nuclear imaging is available at UCLA.

The approach to stress testing for evaluation of ischemia in patients presenting to the EMC with chest pain at UCLA has been to combine an imaging modality with stress testing in all patients. Patients with resting ST segment depression, Q-waves, LV hypertrophy, LBBB, or intraventricular conduction delay (IVCD), pre-excitation or who are receiving digoxin should be tested using an imaging modality. Exercise treadmill testing (ETT) alone maybe considered in patients who are males, with a entirely normal ECG, who are not taking digoxin, and who have a low pretest probability of ischemia. In these patients it is unclear if an imaging modality adds importantly to a standard treadmill test for initial testing. Repeat testing combined with an imaging modality should be performed in patients with a nonischemic ETT but at a low workload (<6 METs) since these patients have an intermediate risk that can be further stratified.

Patients unable to exercise due to physical limitations (eg, arthritis, amputation, severe peripheral vascular disease, severe COPD, general debility) should undergo pharmacologic stress testing in combination with an imaging modality.

Provocation of ischemia at a low workload (eg, <5 to 6 METs) signifies a high-risk patient who would generally merit referral to cardiac catheterization. Patients without ischemia with an adequate degree of stress (>6 METs) have a good prognosis and can be managed medically. Patients with only a low workload but no evident ischemia or those who develop ischemia at a high workload, represent an intermediate-risk group for whom several alternative strategies can be proposed.

<u>Exercise Test Result</u>	<u>Annual Cardiac Mortality</u>	<u>Management</u>
Low risk	<1%	Medical
Intermediate risk	2-3%	Either
High risk	>4%	Medical + Catheterization

A stress test result of intermediate risk combined with evidence of LVD should prompt referral to cardiac catheterization. An attempt to estimate a patient’s risk based on the clinical presentation, risk factors, and stress testing results provides more clinically useful information than a simple normal/abnormal reading of the stress test.

## VII. Hospital and Postdischarge Care

### *Patients With Coronary Atherosclerosis*

Patients with established coronary artery, cerebral vascular, and peripheral atherosclerosis are at high risk for vascular events and cardiac death regardless of identifiable risk factors and regardless of whether they have undergone revascularization. Combination CV protective therapy targeting the underlying atherosclerotic disease process can markedly improve clinical outcome in patients with atherosclerosis, whereas failure to employ these therapies increases patient mortality. Compliance and treatment utilization can be enhanced by employing secondary prevention measures prior to hospital discharge. Patients should not be discharged from the hospital (including chest pain, UA, AMI, cardiac catheterization, angioplasty, coronary bypass, ischemic HF hospitalizations, and diabetes hospitalization for any reason) without initiation of definitive atherosclerosis treatment, unless contraindications exist and are documented.

In patients with coronary, cerebral, or peripheral atherosclerosis and/or diabetes:

<b>Prior to hospital discharge</b>	Send admission (nonfasting) CV lipid panel and baseline liver function tests (LFTs) Prescribe antiplatelet Rx, statin, ACEI, beta-blocker, exercise, omega-3 fatty acid, and dietary Rx Document smoking status and advice to stop smoking
<b>Six-week follow-up visit</b>	Obtain fasting CV lipid panel and LFTs in 6 weeks Adjust statin dose or add combination therapy to achieve LDL cholesterol <70 mg/dL Recheck in 6 months, review medications on each subsequent visit Reinforce adherence to the atherosclerosis treatment regimen

A nonfasting lipid panel obtained in the first 6-12 hours after the onset of AMI has been shown to be relatively accurate. Subsequently, the acute phase reaction, which can begin at 12-24 hours and can take up to 6 weeks to reverse, can lower LDL levels by 25-50%. Lipid panels obtained 12 hours or more after an acute event or after CABG should be interpreted caution, recognizing the true baseline LDL is likely to be much higher requiring a higher statin dose to achieve LDL <70 mg/dL. If a lipid panel has not been obtained on admission or in the first few hours of hospitalization, empiric statin initiation and dosing is recommended.

### ***Comprehensive Risk Reduction for Outpatients With Atherosclerosis or Diabetes***

There are four classes of medications that have been proven to reduce CV events and mortality in patients with coronary, other vascular disease, and diabetes. It is recommended that patients with coronary, other vascular disease, and/or diabetes be treated with all four medications, unless contraindications exist or treatment is not tolerated. Individualization of therapy depending on other medical issues and risk of side effects may be appropriate in certain circumstances. If a patient is not treated with one or more of these medications, it is recommended that the reason be documented in the medical record. The benefits of combination medical therapy with regards to the reduction in the risk of MI, stroke, rehospitalization, need for revascularization, and death continue long term. Since patients with clinically evident atherosclerosis remain at life-long risk, life-long treatment with each agent is recommended, so long as it well tolerated.

### ***Evidence-Based, Mortality-Reducing Therapy for Patients With Atherosclerosis or Diabetes:***

<b>ASA and/or clopidogrel</b>	All patients with atherosclerosis or diabetes, life-long therapy*
<b>Beta-blocker</b>	All patients with atherosclerosis or diabetes, life-long therapy*
<b>ACEI</b>	All patients with atherosclerosis or diabetes, life-long therapy*
<b>Statin</b>	All patients with atherosclerosis or diabetes, life-long therapy*
<b>Omega-3 fatty acid</b>	All patients with atherosclerosis or diabetes, life-long therapy*

\*Unless contraindicated, not tolerated, or reason for not using documented in the medical record.

**Aldosterone antagonists:** Patients who are post-MI and LVEF  $\leq$ .40, with signs or symptoms or HF or diabetes, have reduced mortality risk with aldosterone antagonists (unless contraindicated).

In addition to treatment with the above medications, the following treatment goals should be achieved and maintained, with careful documentation in the medical record:

LDL <70 mg/dL	Once achieved, document with biannual or annual lipid panel (Secondary goal HDL >40 mg/dL, triglycerides [TGs] <150 mg/dL)
BP <140/90 mmHg	Document on each follow-up visit, with additional monitoring as indicated
BP <130/80 mmHg	If diabetes or renal failure (if diabetes and renal insufficiency BP <125/75)
No smoking	Current status with regards to smoking should be documented in all current/former smokers. Recommendation for smoking cessation and nicotine replacement/bupropion (Zyban®)/behavior modification attempts should be documented
HbA <sub>1c</sub> <7%	Diabetes management, tight control in diabetics
30-60 min, daily	Physical activity
BMI 21-25 kg/m <sup>2</sup>	Achieve weight goal via Mediterranean or therapeutic lifestyle change (TLC) diet

### **Medical Regimen for Patients With Atherosclerosis**

**ASA and/or Clopidogrel:** Antiplatelet therapy reduces the risk of vascular events in patients with atherosclerosis. Patients should continue on ASA, 81 mg to 162 mg per day indefinitely after discharge. Contraindications include true ASA allergy with nasal polyposis and active bleeding. Patients with ACS should be treated with combined ASA and clopidogrel (75 mg daily) for 12 months or indefinitely. Patients that have contraindications or intolerance to ASA should be treated with clopidogrel 75 mg daily. Patients with a recurrent event despite ASA should be considered for ASA plus clopidogrel treatment. *In patients with CAD, ASA lowers the risk of MI, UA, need for revascularization, and death. Pooling data from the four largest trials suggest a 48% reduction in the risk of MI and a 51% reduction in the risk of death. This benefit continues beyond ten years. CURE demonstrated the additional benefit of 3 to 12 months of clopidogrel in combination with ASA in ACS patients.*

**Statins and Other Lipid-Lowering Agents:** Statins have potent vascular and cardiac protective effects. Statins are indicated in all patients with atherosclerosis or diabetes. Statins reduce vascular inflammation and stabilize the vulnerable atherosclerotic plaque, thereby markedly reducing the risk of vascular events. These benefits are seen in patients with cholesterol and LDL levels in the low, normal, and high range. Clinical trials have shown mortality reduction in patients with baseline LDL levels of 70 mg/dL and above. Initiation of statin therapy in patients with documented atherosclerosis results in a reduction in MI, UA, stroke, need for revascularization, hospitalization, and all-cause mortality compared with patients treated with diet alone. This is true regardless of whether the patient has undergone CABG, PTCA, or is being treated medically.

These benefits are seen early, such that patients should be started on therapy prior to hospital discharge. Early benefits (within 8-16 weeks) can be seen in patients presenting with ACS when started on immediate, high-dose potent statin treatment (eg, atorvastatin 80 mg/d) as shown in MIRACL and PROVE-IT.

The starting dose of statin should be a dose estimated to achieve an LDL of at least <70 mg/dL based on the baseline lipid panel or empiric dosing based on clinical trials. In patients in whom the baseline LDL is known, the use of the UCLA LDL Treatment to Goal Guide is recommended. In ACS patients, high-dose potent statin treatment, regardless of baseline LDL, is recommended. In non-ACS patients in whom the baseline LDL is

pending or not known, empiric doses may be used. Patients who fail to achieve target lipid levels (LDL <70 mg/dL) at 6 weeks after initiation of therapy should have their dose increased or an additional agent (ezetimibe, niacin, or cholesterol-binding resin) added. The combination of a statin and ezetimibe may also be used as first-line therapy to achieve LDL goal, with the exception of patients with ACS in whom high-dose, potent statin therapy is preferred.

The target lipid levels in patients with atherosclerotic vascular disease (AVD) or diabetes are LDL cholesterol <70 mg/dL; HDL cholesterol >40 mg/dL; and TG <150 mg/dL. The ideal LDL in all patients is likely LDL <70 mg/dL (ongoing trials are evaluating this further). The benefits of statins are seen in men and women, older and younger patients, diabetics, and nondiabetics. Contraindications include pregnancy or serious underlying liver disease. Obtain baseline LFTs. LDL must be treated to goal first, but if HDL remains <40 mg/dL or TG remain >150 mg/dL, specific HDL-raising and/or TG-lowering interventions such as niacin, fibrates, or high-dose fish oil capsules should be considered (weighing potential benefits with the potential risk of additional side effects and drug interactions).

*Patients with atherosclerosis and/or diabetes will live longer when treated with a HMG CoA reductase inhibitor. In the 4S trial there was a 34% risk reduction in major cardiac events, a 42% risk reduction in CV mortality, and a 30% reduction in all-cause mortality associated with statin treatment. The LIPID trial demonstrated that even patients with “low or normal” levels of total cholesterol and LDL cholesterol (LDL 70-170 mg/dL) have mortality reduction with statin treatment. The HPS trial demonstrated that patients with LDL <100 mg/dL at baseline derive similar risk reduction to those with higher LDLs. Patients should be educated that these medications are for the treatment of atherosclerosis, not because the patient has “failed” dietary treatment, and that use of these medications lowers the risk of recurrent events, need for revascularization, hospitalizations, stroke, and mortality.*

**ACEIs:** These agents have potent vascular and cardiac protective effects. These agents are indicated in all patients with atherosclerosis. Patients with coronary, peripheral, cerebral vascular disease, and diabetes have reduced risk of MI, stroke, HF, and death when treated with an ACEI. This is true even if the BP and EF are normal. All post-CABG, post-PTCA, post-UA, post-MI, stable CAD, PVD, CVD, and diabetic patients should receive an ACEI, unless a specific contraindication is documented. Patients with AMI have improved early survival and less HF when treated with ACEIs. All MI patients without contraindications should be started on ACEIs within 12-24 hours and treated long term. Patients with LVD should be started and maintained on an ACEI indefinitely. Renal insufficiency in the setting of CAD or diabetes is not a contraindication, but rather a double indication for ACEIs. The benefit of ACEIs is independent of BP status. Use target doses. Contraindications include history of angioedema, cardiogenic shock, hyperkalemia, and pregnancy. Angiotensin receptor antagonists should be used in ACEI-intolerant patients.

*The HOPE and EUROPA trials demonstrated that in patients with CAD, CVD, PVD, or diabetes the use of an ACEI was associated with a reduction in CV events, CV mortality, and all-cause mortality. The PEACE trial was underpowered. This benefit was seen in patients without hypertension and with normal LVEF. Long-term treatment with ACEI is thus indicated in any patient with atherosclerosis.*

**Beta-Blockers:** These agents should be considered in all patients with atherosclerosis since they reduce the risk of MI and make it more likely that a patient will survive an infarction. These agents should be considered first-line agents for the symptomatic control of angina. In addition, these agents prolong survival in patients with previous MI as well as reduce the risk of UA in patients with CAD. These agents also attenuate the remodeling process post-MI and reduce the risk of developing HF. In a patient with CAD and hypertension,

beta-blockers are an excellent first-line agent. The duration of benefit with therapy extends indefinitely. Use target doses as clinically tolerated. In patients with LVEF  $\leq$ 40 with or without HF symptoms, carvedilol is preferred. Contraindications include symptomatic bradycardia, 2nd-/3rd-degree AV block without pacemaker, cardiogenic shock, acutely decompensated HF, severe asthma or COPD, and diabetes with recurrent life-threatening hypoglycemic episodes. Please note that diabetes, peripheral vascular disease, mild/moderate asthma or COPD, asymptomatic bradycardia, and HF are not contraindications and should not preclude the use of beta-blockers.

**Omega-3 Fatty Acids:** Omega-3 fatty acids have been demonstrated to have a variety of CV protective effects. Fish oil supplementation has been demonstrated in clinical trials to reduce the risk of CV events by 10 to 20%. This benefit was additive to CV protective medications. It is recommended that all patients with atherosclerosis or diabetes be treated with omega-3 fatty acid supplementation, with therapy beginning in the hospital. Patients may be treated with fish oil capsules containing 800 to 1,000 mg of omega-3 fatty acids (eicosapentaenoic acid, [EPA] and docosahexaenoic acid, [DHA]) PO daily. Alternative supplements include flax seed oil or canola oil.

**Aldosterone Antagonists:** These agents are indicated in patients with AMI and LVEF  $\leq$ 40 and who have signs or symptoms of HF or diabetes, in the absence of contraindications. These agents attenuate remodeling and have been demonstrated to benefit patients with AMI with LVD with HF symptoms. Patients should be clinically stabilized prior to initiation of the aldosterone antagonist. This therapy is only indicated in patients with systolic dysfunction (LVEF  $\leq$ 40), not all ACS patients. Start low dose and need to closely monitor potassium levels and renal function. Hyperkalemia is an absolute contraindication. Use extreme caution if Cr  $>$ 2.5 mg/dL in men or  $>$ 2 mg/dL in women. Starting either spironolactone at 6.25 mg PO daily with target dose of no more than 25 mg daily or eplerenone 25 mg daily starting dose with target dose of 50 mg daily. *The EPHESUS trial demonstrated a 15% reduction in mortality with the selective aldosterone antagonist eplerenone in AMI patients with LVEF  $<$ 40% with HF signs or symptoms.*

**Nitrates:** These agents should be considered second-line agents after beta-blockers for the symptomatic control of angina. There are no long-term data that nitrates improve prognosis in patients with CAD so that their use is dictated solely for symptom relief. Patients who are not having symptomatic angina do not need to be routinely discharged on long-acting nitrates. When long-acting nitrates are indicated, a daily nitrate-free interval is necessary to decrease tolerance. Patient should be discharged with prn SL NTG as well as instructions as to its use.

**Calcium Channel Blockers:** These agents decrease chest pain but do not decrease the risk of a cardiac event or improve outcome, independent of BP control. In patients with angina there is an increased risk of coronary events with calcium channel blockers as compared with angina control with beta-blockers. In patients with CAD and hypertension, these agents should be reserved for patients who are intolerant of or fail to have their BP controlled with beta-blockers, ACEIs, angiotensin receptor blockers (ARBs), diuretics, and their combination.

**Antiarrhythmic Agents:** Type I antiarrhythmic agents markedly increase the risk of sudden death in patients with CAD. This is because all type I antiarrhythmic agents markedly lower the fibrillation threshold of ischemic myocardium. Even when used to maintain sinus rhythm for atrial fibrillation or when guided by EPS or Holter monitoring, these agents increase the risk of overall mortality for CAD patients. These agents should be avoided in all patients with CAD except those with implantable cardioverter defibrillators

(ICDs) or in whom the risk benefit ratio has been carefully considered. Amiodarone should be considered the only safe antiarrhythmic agent in patients with CAD. Compared with placebo, amiodarone was neutral with respect to sudden death and mortality in post-MI trials.

**Exercise:** Patients should receive specific instructions for a minimum of 5x per week aerobic exercise program. Exercise increases HDL, reduces the risk of MI, and improves survival in patients with CAD. Either a home-based program or supervised cardiac rehabilitation can be recommended. After AMI or CABG, a supervised cardiac rehabilitation program is recommended. Exercise is an essential component of the management of patients with CAD and is highly effective in preventing subsequent cardiac events. Patients should be offered referral to a cardiac rehabilitation program in their area. In addition to a specific exercise prescription, patients require instructions on activities that are permissible and those that should be avoided (eg, heavy lifting).

**Smoking Cessation:** Particular attention should be paid to smoking cessation counseling. Patients who continue to smoke after presenting with UA have 5.4 times the risk of death from all causes compared with patients who stop smoking. Patients should be offered intensive smoking cessation intervention during hospitalization. This should include both physician and nurse counseling focusing on relapse prevention. Patients should receive a relapse prevention manual and be given written information about the outpatient behavioral modification programs available and the option of nicotine replacement therapy and/or bupropion (Zyban). The recommendation for smoking cessation should be clearly documented in the medical record.

**Diet:** Although standard dietary intervention alone has not been shown to be beneficial, other dietary interventions such as the Mediterranean diet may provide benefit. Patients and family members, if available, should receive counseling on the National Cholesterol Education Program TLC diet or Mediterranean diet and recommended body weight (BMI) during the hospitalization. Information on the outpatient dietary modification programs available should be provided. Supplementation with omega-3 fatty acids has lowered the risk of recurrent MI. Discourage use of very low-fat diets.

**Patient Education:** The patient and his or her family member or advocate should be instructed regarding the use of medications and monitoring of symptoms. The purpose, dose, and major side effects of each medication prescribed should be explained. Written medication sheets and a medication schedule should be provided to each patient. The warning signs of a heart attack should be discussed with each patient and their immediate plan of action reviewed, including calling 911. A patient education sheet should be provided. Patients should be instructed to contact their primary care physician or cardiologist if they have a nonacute change in symptom pattern and discuss whether changes in the management plan are warranted. *Patient delays in seeking medical attention are a major contributor to diminished benefit with reperfusion therapy. Detailed patient education has been demonstrated to reduce the time to treatment in AMI.*

**Follow-Up:** Continuation of the therapies targeting the underlying atherosclerotic disease process markedly improves clinical outcome in patients with atherosclerosis. The continued use of the beneficial therapies prescribed should be strongly reinforced during patient follow-up. The medications the patient is taking should be reviewed on each visit. If one or more of the survival-enhancing medications is not prescribed, the specific contraindication or intolerance should be clearly documented in the medical record.

After initial statin treatment, a fasting lipid panel should be obtained at 6 weeks to evaluate whether target lipid levels have been achieved and guide cholesterol-lowering medication dosing adjustments. Obtain LFTs at 6 weeks and with any dose escalation. CPK need only be checked if muscular symptoms arise. Document LDL <70 mg/dL on biannual or annual basis. Document BP and diabetes control. The need for daily aerobic exercise should be reinforced and the patient's progress monitored. Stress testing does not appear to be indicated in the routine follow-up of patients with CAD and should, in general, be performed for specific reasons such as a change in symptoms or in following patients with silent ischemia.

#### **Document:**

Current medications (if ASA, beta-blocker, ACEI, or statin not currently prescribed, document contraindication, intolerance, or alternative medication utilized)

- LDL, HDL, and TG (within last 1 year)
- Current BP
- Weight and height (BMI)
- If history of HF, LVEF
- If diabetes, HbA<sub>1c</sub> within last 1 year, annual ophthalmology retinal exam, foot exam and care
- If history of smoking, current status and advice to quit smoking
- Use of pneumococcal vaccination if HF, CAD, diabetes, pneumonia, age >65
- Annual influenza vaccination

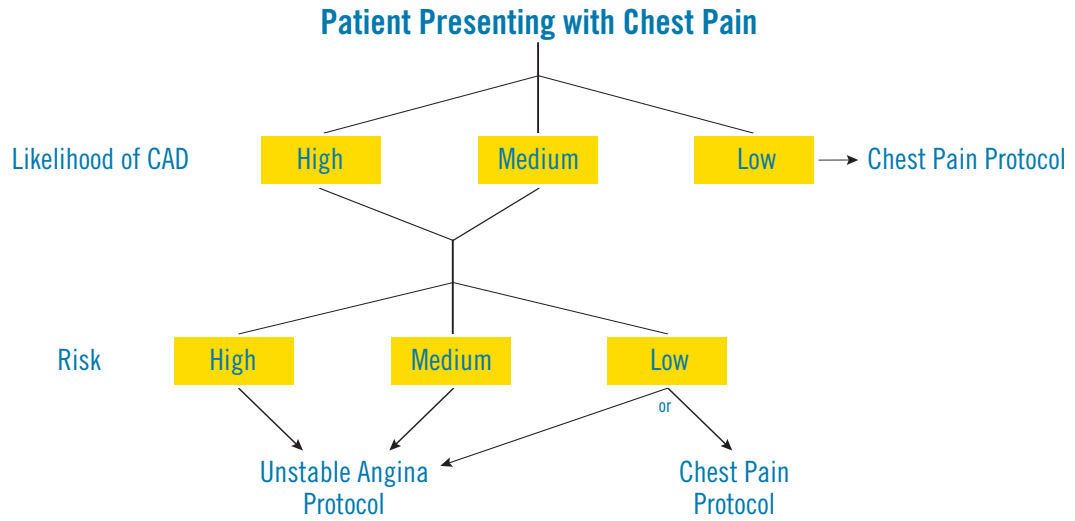
#### ***Patients without CAD***

Patients with peripheral vascular disease, cerebral vascular disease, and diabetes should be treated with the secondary prevention measures as above. Patients who, on the basis of their complete evaluation and physiologic stress testing are felt not to have clinically evident CAD, other vascular disease, or diabetes, should be advised regarding effective primary prevention measures. Therapy that appears to prolong survival in individuals without overt CAD includes ASA, smoking cessation, and exercise. Male patients over the age of 40 and females over the age of 50 with one or more additional CV risk factors without contraindications should be started on ASA at a dose of 81 mg to 162 mg daily. CV events can be reduced with control of BP using beta-blockers, ACEIs, or diuretics in patients with hypertension. Cholesterol-lowering medications can reduce the risk of MI, but no reduction in overall mortality has been demonstrated in individuals without overt CAD, PVD, CVD, or diabetes. Therapy should be reserved for patients with hypercholesterolemia in the setting of additional risk factors. Patients and their families and advocates should understand the most likely diagnosis at the conclusion of their evaluation. All patients should be counseled on risk factor modification. Patients should be advised as to the warning signs of a heart attack and to seek medical attention if suggestive symptoms occur.

#### ***Medical Record***

The patient's medical record at the time of hospital discharge should summarize cardiac events, results of diagnostic testing, current symptoms, and the discharge medical regimen. The major instructions, post-discharge follow-up plan, follow-up physician, and the patient's understanding and plan for adherence to the recommendations should be documented in the medical record. The comprehensive care plan for secondary prevention should be summarized. The primary care physician that will be providing follow-up care should be contacted and the treatment plan discussed.

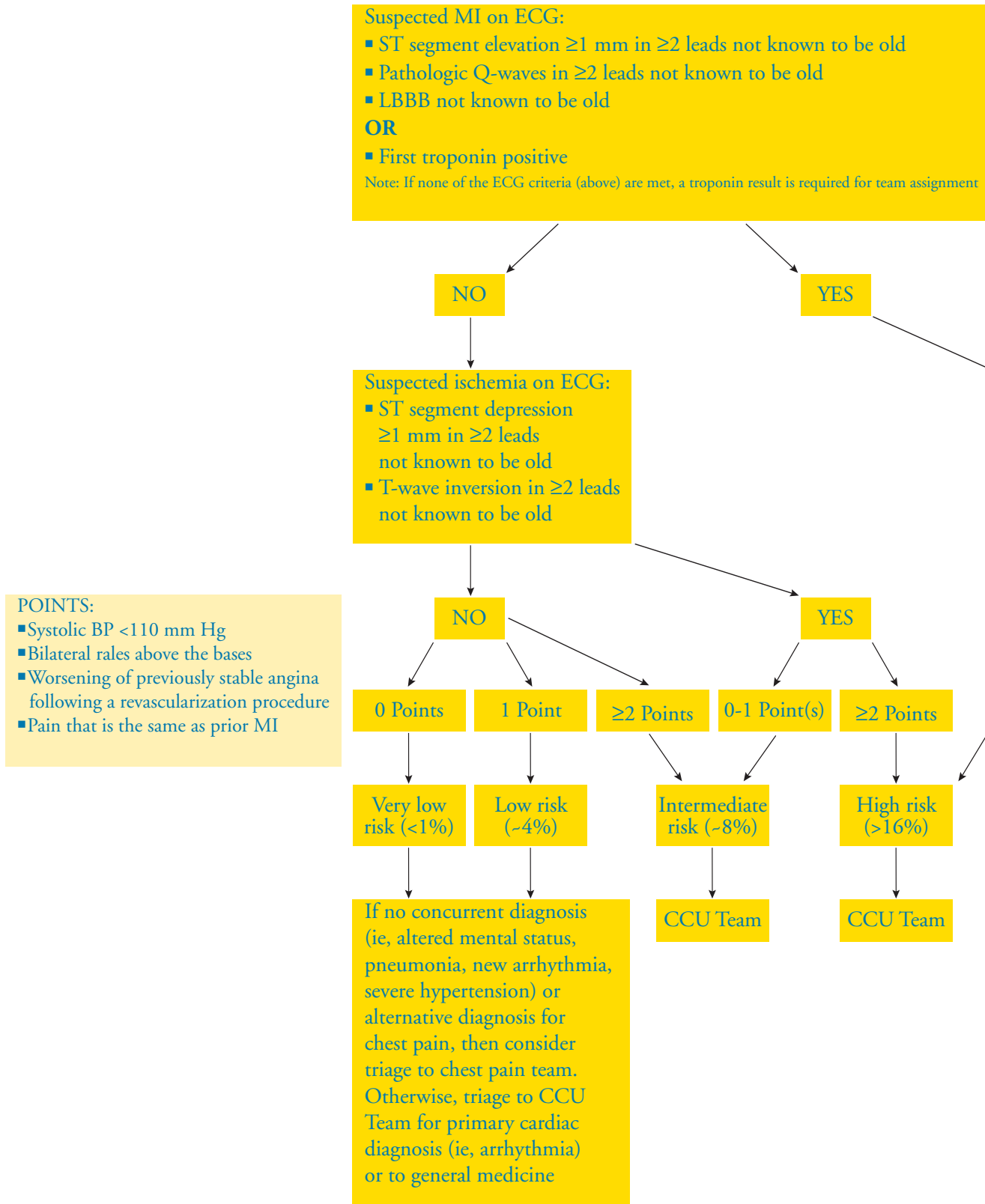
**Patient Stratification**



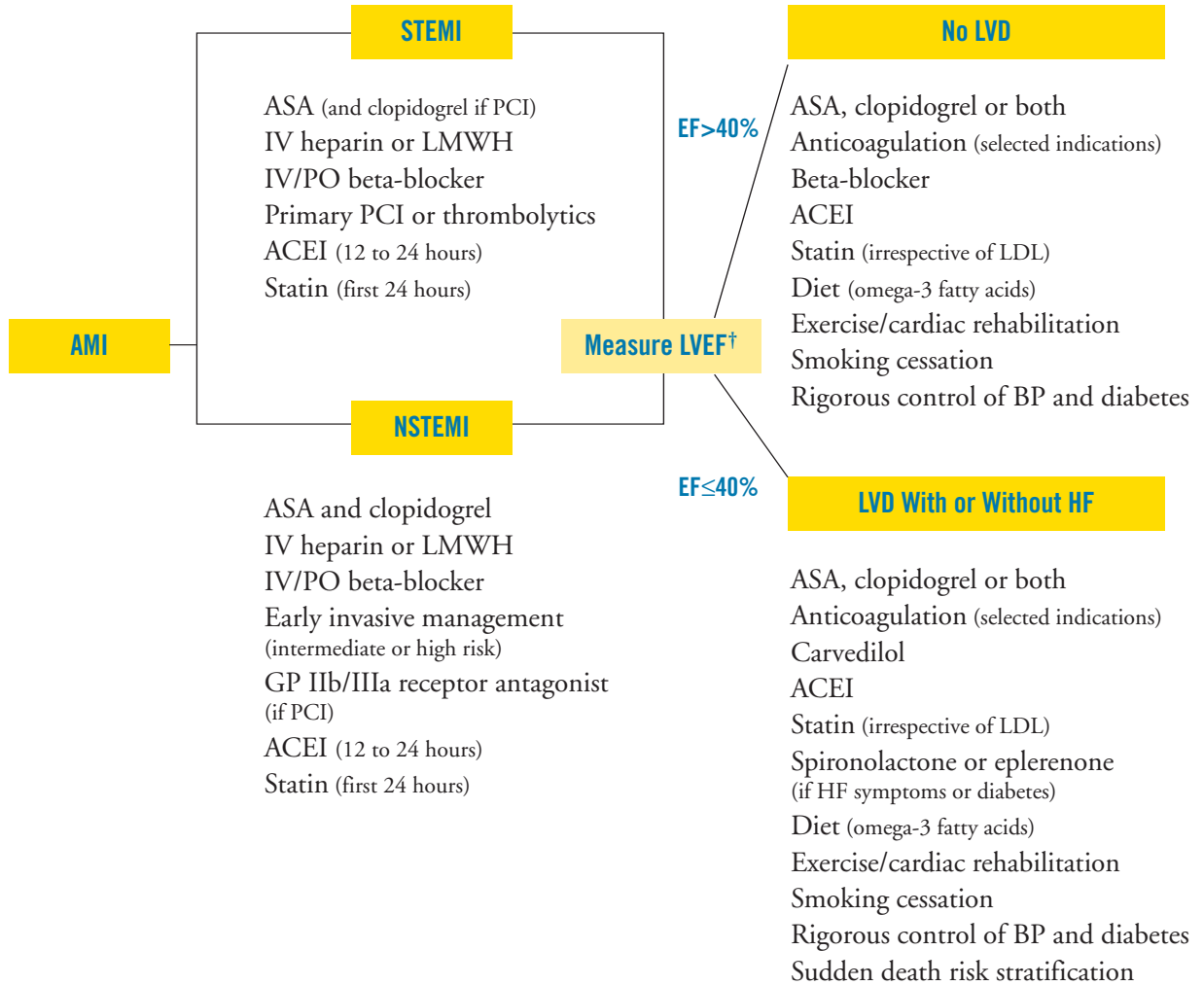
**Treatment Stratification**

	Low Likelihood	Medium Likelihood	High Likelihood
Low Risk	ASA Outpt/(Inpt) Stress Test	ASA/Clopidogrel/(Heparin) Outpt/Inpt Stress Test/Cath	ASA/Clopidogrel/(Heparin) Outpt/Inpt Cath/(Stress Test)
Medium Risk	ASA/Clopidogrel Outpt/(Inpt) Stress Test/Cath	ASA/Clopidogrel/Heparin Inpt Cath	ASA/Clopidogrel/Heparin Inpt Cath
High Risk	ASA/Clopidogrel/(Heparin) Outpt/(Inpt) Stress Test/Cath	ASA/Clopidogrel/(Heparin) Inpt Cath	ASA/Clopidogrel/Heparin/ GP IIb/IIIa receptor antagonists Inpt Cath

## Chest Pain Service Triage Algorithm



**Treatment Algorithm for AMI With or Without LVD\***



\*All patients without contraindications or intolerance.

†Include ischemic risk stratification, if not previously catheterized (ie, stress testing).

Clinical Guidelines Committee, UCLA Division of Cardiology

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